LOMA LINDA UNIVERSITY

School of Medicine

Center for Health Disparities and Molecular Medicine

19th Annual Health Disparities Research Symposium

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

PROGRAM, BIOS, AND ABSTRACTS

Wednesday, August 7, 2019
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

19th Annual Health Disparities Research Symposium

Wednesday, August 7, 2019
12:00 pm - 7:30 pm, Wong Kerlee International Conference Center

Agenda

12:00 – 1:30 pm **Scientific Presentation by Mark A. Lawson, PhD**

"Metabolic Sensing in the Pituitary Gonadotrope"

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 – 7:30 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 **Eileen Brantley, PhD**
Associate Professor
Department of Basic Sciences
School of Medicine

Remarks **Richard Hart, MD, DrPH**
President, Loma Linda University Health
Professor, School of Public Health
School of Medicine

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

Remarks

Tamara L. Thomas, MD
Dean, School of Medicine
Executive VP, Chief Medical Officer
Loma Linda University Health

Remarks

Penelope Duerksen-Hughes, PhD
Associate Dean for Basic Sciences Faculty and 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

Mark A. Lawson, PhD

Professor of OB/GYN and Reproductive Sciences
Director of UC President's Postdoctoral Fellowship Program
School of Medicine, UC San Diego

"Forging a New Path: Choosing and Pursuing a Career in STEM"

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 J. Watts, PhD
Associate Professor of Microbiology
Department of Basic Sciences
Director, SURF
School of Medicine

Final Remarks and Acknowledgements

Marino De Leon, PhD

Keynote Speaker Biography

Mark A. Lawson, PhD

Professor of OB/GYN and Reproductive Sciences
Director of UC President's Postdoctoral Fellowship Program
School of Medicine, UC San Diego

Dr. Mark Lawson is a Professor of OB/GYN and Reproductive Sciences in the School of Medicine, UC San Diego, and Director of the UC President's Postdoctoral Fellowship Program. A molecular biologist by training, Dr. Lawson has spent time in both private industry and in academia. His NIH-funded research has focused on the regulation of reproductive hormone synthesis and infertility. Much of his work is in hormone signaling and regulation of protein synthesis. During his time on the UC faculty, he has developed novel career development programs targeting undergraduates through early- career faculty, and he has championed diversity issues both within his professional field and in the broad academic community. A former PPFP and Ford fellow, Professor Lawson has worked for many years to successfully engage and promote students from diverse backgrounds into professional and academic careers. In his role as Director, he has overseen the expansion of the UC President's Postdoctoral Fellowship program and increased hiring of fellows into tenure-track positions in the UC system.

LOMA LINDA UNIVERSITY SCHOOL OF MEDICINE
CENTER FOR HEALTH DISPARITIES AND MOLECULAR MEDICINE
19TH 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 2019 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.

2019 Faculty Research Mentors

Eileen Brantley, PhD
John Buchholz, PhD
Carlos Casiano, PhD
Daisy De Leon, PhD
Marino De Leon, PhD
Penelope Duerksen-Hughes, PhD
Johnny Figueroa, PhD
David Hessinger, PhD
Mary Kearns-Jonker, PhD
Salma Khan, MD, PhD
Wolff Kirsch, MD
William Langridge, PhD
Eugenia Mata-Greenwood, PhD, PharmD
Subburaman Mohan, PhD
Susanne Montgomery, PhD
Ying Nie, MD, PhD
Kimberly Payne, PhD
William Pearce, PhD
Christopher Perry, PhD
Jeffery Rosenfeld, MD, PhD
Julia Unternaehrer-Hamm, PhD
Nathan Wall, PhD
Charles Wang, MD, PhD
Kylie Watts, PhD
Seth Wiafe, PhD
Christopher Wilson, PhD
Sean Wilson, 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.

2019 Student Research Fellows

ABC – Apprenticeship Bridge to College

Rafael Alvarez
Yaw Appiah-Boateng
Marco Baeza
Lester Cedeno
Jazmine B. Chism
Wendy Chow
Gabriel Diaz
Clarissa "Nini" Do
Tarannum Yumi Munir
Oasis Perez
Michelle Quarshie
Anthony Saldana
Kallista Tantiga
Jennifer Tran
Yoshelyn Vera

UTP – Undergraduate Training Program

Cristina A. Araújo Rosario
De'Andre Brown
Cecilia De Leon
Marleni Pagan-Ramos
Krystal R. Santiago
Emmanuel Solis
Neihyarie K. Vélez Villarrubia
Roland Williams
Shandelle Williams
Eric Xiao

MTP – Medical Training Program

Keelie Denson
Christian Irizarry Cruz
Joanneth Padro Serrano
Reuben Plasencia
Raul Rios Orsini

IMSD – PhD/MD-PhD Graduate Fellows

Victor Camberos
Tatianna Clark
Alfonso Durán
Jerry Flores
Jenniffer Licero Campbell
Karina Mayagoitia
Perla Ontiveros Angel
Greisha L. Ortiz Hernández
Foluwasomi Oyefeso
Hiel Rutanhira
Evelyn S. Sanchez-Hernandez
Nicholas Sanchez
Paul Vallejos
Julio D. Vega-Torres
Jonathan Wooten

Behavioral Health & Public Health

Raveena Chara
Nipher Malika
Simone Montgomery
Oyinkansola Ogundimu

SURF – Summer Undergraduate Research Program

Vola-Masoandro Andrianarijoana
Taylor Bothwell
Meredith Brown
Kenneth Choi
Jared Cellini
Emi Eastman
Priya Ramesh
Seung Shin
Abbie Underhill
Samuel Vander Dussen
Yucheng Yang

Guest Participants

Ryan Black
Sarah Doublet
Isaac Mitchell
Andy Paz Aldana
Kari Roberts
Chase Stephen Sugiono

Institutional Affiliations of Student Research Fellows

High Schools

Diamond Bar High School
Grand Terrace High School
Hemet High School
John F. Kennedy Middle College High School
Middle College High School
Martin Luther King High School
Ramona High School
Rancho Cucamonga High School
Redlands High School
Riverside STEM Academy
Vista del Lago High School

Universities

AdventHealth University
Andrews University
Antillean Adventist University
Azusa Pacific University
Biola University
California Baptist University
California State University, San Bernardino
California State University, San Marcos
Gettysburg College
Loma Linda University
Medical College of Georgia at Augusta University
Mercer University
Montemorelos Adventist University
Oakwood University
Pacific Union College
Ponce Health Sciences University
San Juan Bautista School of Medicine
Universidad de Puerto Rico, Mayagüez
Universidad de Puerto Rico, Rio Piedras
University of California, San Diego
University of California, San Francisco
University of Maryland
University of Redlands
University of Southern California
Walla Walla University
Whittier College

LOMA LINDA UNIVERSITY SCHOOL OF MEDICINE

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

2019 RESEARCH MENTORS

BRANTLEY, Eileen, PhD (1999), Meharry Medical College
Associate Professor, Basic Sciences, Division of Pharmacology
LLU School of Medicine
Email: ebrantley@llu.edu

BUCHHOLZ, John, PhD (1989), Loma Linda University
Professor, Basic Sciences, Division of Pharmacology
Vice Chair, Pharmacology
LLU School of Medicine
Email: jbuchholz@llu.edu

CASIANO, Carlos, PhD (1992), University of California, Davis
Professor, Department of Microbiology and Molecular Genetics, Biochemistry, and Medicine
Associate Director, Center for Health Disparities and Molecular Medicine
LLU School of Medicine
Email: ccasiano@llu.edu

DE LEÓN, Daisy, PhD (1987), University of California, Davis
Professor, Basic Sciences, Division of Physiology and Pharmacology
Assistant to the Dean for Diversity
LLU School of Medicine
Email: ddeleon@llu.edu

DE LEÓN, Marino, PhD (1987), University of California, Davis
Professor, Basic Sciences, Division of Physiology, Pharmacology, Pathology, and Human Anatomy
Director, Center for Health Disparities and Molecular Medicine
LLU School of Medicine
Email: mdeleon@llu.edu

DUERKSEN-HUGHES, Penelope, PhD (1987), Emory University
Associate Dean for Basic Science and Translational Research; Chair, Basic Sciences
Professor, Basic Sciences
Center for Health Disparities and Molecular Medicine
LLU School of Medicine
Email: pdhughes@llu.edu

FIGUEROA, Johnny, PhD (2006), University of Puerto Rico School of Medicine
Assistant Professor, Basic Sciences, Division of Physiology
Center for Health Disparities and Molecular Medicine
LLU School of Medicine
Email: jfigueroa@llu.edu

HESSINGER, David, PhD (1970), University of Miami, Miami, Florida
Professor, Basic Sciences, Division Physiology and Pharmacology and Natural Sciences
LLU School of Medicine
Email: dhessinger@llu.edu

KEARNS-JONKER, Mary, PhD (1985), McGill University, Montreal, Canada
Associate Professor, Basic Sciences, Division of Anatomy
LLU School of Medicine
Email: mkearnsjonker@llu.edu

KHAN, Salma, MD, PhD (2000), Kumamoto University School of Medicine
Assistant Research Professor, Basic Sciences, Division of Biochemistry
Center for Health Disparities and Molecular Medicine
Head & Neck Surgery
Department of Internal Medicine
LLU School of Medicine
Email: salmakhan@llu.edu

KIRSCH, Wolff, MD (1955), Washington University School of Medicine
Professor, Basic Sciences, Division of Biochemistry
Director, Neurosurgery Center for Research Training and Education
LLU School of Medicine
Email: wkirsch@llu.edu

LANGRIDGE, William, PhD (1973), University of Massachusetts, Amherst
Professor, Basic Sciences, Division of Biochemistry
Center for Health Disparities and Molecular Medicine
LLU School of Medicine
Email: blangridge@llu.edu

MATA-GREENWOOD, Eugenia, PharmD (1992), University of Costa Rica; PhD (2000), University of Illinois, Chicago
Associate Professor, Basic Sciences, Division of Pharmacology
LLU School of Medicine
Email: ematagreenwood@llu.edu

MOHAN, Subburaman, PhD (1978), Bangalore University, Bangalore, India
Professor, Medicine, Orthopedic Surgery and Biochemistry
Director, Musculoskeletal Disease Center, VA Loma Linda Healthcare System
LLU School of Medicine
Email: subburaman.mohan@va.gov

MONTGOMERY, Susanne, PhD (1987), University of Michigan
Associate Dean for Research
Professor, Social Work and Social Research
Head, Interdisciplinary Studies
School of Behavioral Health
Professor, Preventive Medicine, LLU School of Medicine
Professor, LLU School of Public Health
Email: smontgomery@llu.edu

NIE, Ying, MD (1984), Beijing University; PhD (1995), Indiana University
Assistant Research Professor, Neurosurgery
LLU School of Medicine
Email: YNie@llu.edu

PAYNE, Kimberly, PhD (1998), University of Oklahoma Health Sciences Center
Associate Professor, Basic Sciences, Division of Pathology, Human Anatomy, Pediatrics, and Medicine
Director, Translational Research, Basic Sciences
Center for Health Disparities and Molecular Medicine
LLU School of Medicine
Email: kpayne@llu.edu

PEARCE, William J, PhD (1979), University of Michigan
Professor, Department of Basic Sciences, Division of Physiology and Pharmacology
LLU School of Medicine
Email: wpearce@llu.edu

PERRY, Christopher, PhD, (1999) University of Liverpool, UK
Assistant Professor, Basic Sciences, Division of Biochemistry
LLU School of Medicine
Email: chperry@llu.edu

ROSENFELD, Jeffery, MD (1990), University of Maryland, Baltimore; PhD (1983), University of Connecticut;
Professor, Neurology
Associate Chairman, Dept of Neurology
Director, Neuromuscular ALS/MND Program
Medical Director, The Center for Restorative Neurology
LLU School of Medicine
Email: jrosenfeld@llu.edu

UNTERNAEHRER-HAMM, Julia, PhD (2004), Yale University
Assistant Professor, Basic Sciences, Division of Biochemistry
LLU School of Medicine
Email: junternaehrer@llu.edu

WALL, Nathan, PhD (2000), Wayne State University; MBA (2008), University of Redlands
Associate Professor, Basic Sciences, Division of Biochemistry
LLU School of Medicine
Email: nwall@llu.edu

WANG, Charles, MD (1983), Tongji Medical University, Wuhan, China; MPH (1988), Tongji Medical University, Wuhan, China; PhD (1999), University of Washington
Professor, Basic Sciences, Division of Microbiology
Director, Center for Genomics
LLU School of Medicine
Email: chwang@llu.edu

WATTS, Kylie, PhD (2001), University of Sydney
Associate Professor, Basic Sciences, Division of Microbiology
LLU School of Medicine
Email: kwatts@llu.edu

WIAFE, Seth, PhD (2017), University of Southampton, UK
Assistant Professor, Health Geographics
Director, Health Geoinformatics Sciences
LLU School of Public Health
Email: swiafe@llu.edu

WILSON, Christopher, PhD (1996), University of California, Davis
Associate Professor, Basic Sciences, Division of Physiology
LLU School of Medicine
Email: cgwilson@llu.edu

WILSON, Sean, PhD (1998), University of California, Davis
Associate Professor, Basic Sciences, Division of Pharmacology
LLU School of Medicine
Associate Professor, Pharmaceutical and Administrative Science
LLU School of Pharmacy
Email: seanwilson@llu.edu

Apprenticeship Bridge to College (ABC) High School Program

Rafael Alvarez
Yaw Appiah-Boateng
Marco Baeza
Lester Cedeno
Jazmine B. Chism
Wendy Chow
Gabriel Diaz
Clarissa "Nini" Do
Tarannum Yumi Munir
Oasis Perez
Michelle Quarshie
Anthony Saldana
Kallista Tantiga
Jennifer Tran
Yoshelyn Vera

RAFAEL ALVAREZ

ABC PARTICIPANT 2019

Last summer I was blessed with the opportunity to participate in this wonderful program at Loma Linda University. As opposed to school where we learn about facts and formulas seemingly unrelated to the real world, this experience taught me about how studying science can help improve people's lives. In addition to the life skills I learned, this program confirmed my desire to help others, especially impoverished and medically underserved populations burdened with health disparities. As a first-generation Hispanic student, learning that lack of education may be associated with poor healthcare is disheartening yet inspires me to pursue higher education. My father worked from a young age to support his family, and my mother ended her academic career due to financial necessity. Witnessing the struggles my parents have experienced taught me that access to quality education is a privilege that will set the foundation for a successful future.

This May I graduated from Ramona High School in Riverside, CA. In high school, I became Graphics Editor for our school's yearbook and volunteered at my church's Sunday Preschool while taking AP classes and dual enrollment courses at Riverside City College. I am excited to further my education across the country at the University of Pennsylvania where I hope to major in biology and continue exploring the field of scientific research.

This summer I had the honor of working in Dr. Sean Wilson's lab for a second year. I would like to thank him and everyone in his lab for their guidance throughout the summer. I would also like to give a special thanks to my family for their unconditional support and motivation.

HYPOXIA-INDUCED UPREGULATION OF HISTONES IN FETAL SHEEP PULMONARY ARTERIES

Rafael Alvarez, Eric Leslie, Breanna Rose Jones, Chiranjib Dasgupta, Remy Bosviel, Michael La Frano, John Newman, Oliver Fiehn, Lubo Zhang, Sean Wilson

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

Hypoxia due to living at high altitudes is a common stressor that can impact the development of an unborn child. This stressor puts infants at a greater risk of developing pulmonary hypertension, high altitude pulmonary edema, and cardiovascular diseases later in life. Previous evidence shows that fetal pulmonary arteries have medial wall thickening which is a hallmark of disease. This work aims to use a combination of proteomics and metabolomics analyses to provide insight into how prenatal hypoxia due to living at high altitudes causes vascular remodeling. For this study, normoxic pregnant or 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 hypoxia. After 110+ days of gestation, the high altitude sheep were transported to Loma Linda for study. Tissues from the pulmonary arteries of fetal sheep were prepared and frozen for metabolomics and proteomic analysis. Metabolomic analysis indicates there is an increase in ribitol and erythritol, two intermediates in the pentose phosphate pathway. This pathway leads to the production of ribose-5-phosphate, a compound necessary for the synthesis of nucleotides. Additionally, the proteomics data demonstrate an upregulation in three histones: Histone H2A, Histone H2B, and Histone H4. Histone proteins are associated with the regulation of gene transcription, DNA synthesis, and movement through the cell cycle. These results support earlier studies showing medial wall thickening. Further studies, however, are required to determine which cell types are becoming more proliferative and underlying mechanisms.

YAW APPIAH-BOATENG
ABC PARTICIPANT 2019

Before entering this program, I was pretty sure I wanted to become an oncologist and had not really considered being a researcher at all. However, these eight weeks have brought a newfound interest in the field of research. Not only that, but I have learned so much and received so much valuable advice, useful techniques, and helpful strategies. I am very blessed to have been a part of this program.

A senior at Riverside STEM Academy, I am involved in clubs and activities such as Pre-Med Club and Student Senate. I have been involved in some community service activities, serving as a counselor at La Sierra University's Vacation Bible School for two years, going on various homeless outreach days with my church and Pathfinder group, and helping out at Loma Linda's Black Men's Health Fair last April. Prior to that, I gave a presentation to my church raising awareness about prostate cancer. Prostate cancer is a very prominent cancer in African American men, but more so in Ghanaian men such as myself. As a result, I have found my calling in the field of prostate cancer. I believe being able to practice medicine and research prostate cancer are the best way to answer God's calling and enable me to be of service to my community and to mankind.

I'm thankful for my mentor Dr. Carlos Casiano for giving me the opportunity to participate in this program. I'm also thankful for my PhD student Greisha Ortiz-Hernández for teaching me a plethora of things inside and outside the lab. I'm very grateful for the other lab members and volunteers for giving me support and valuable lessons that made this summer experience memorable.

MULTIPLE TRANSCRIPTION FACTORS ARE UPREGULATED IN DOCETAXEL RESISTANT PROSTATE CANCER CELLS AND INTERACT WITH THE STRESS ONCOPROTEIN LEDGF/P75

Yaw Appiah-Boateng, Greisha Ortiz-Hernandez, Carlos 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 U.S. Current therapies for advanced PCa include androgen deprivation therapy and docetaxel (DTX) chemotherapy. Unfortunately, therapy resistance and disease progression lead to patient mortality. We have demonstrated that the stress oncoprotein 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. Different transcription factors, such as JPO2, Menin/MLL, c-MYC, IWS1, HAND2 and HRP2, have been linked to aggressive phenotypes in cancer and to stimulate HIV integration and latent infection through its binding with LEDGF/p75. However, these PPIs have not been explored in PCa chemoresistance. **Our hypothesis is that LEDGF/p75 interacts with several transcription factors to induce the expression of stress survival genes that contribute to PCa chemoresistance**. To evaluate this hypothesis, we assessed the expression of these proteins through Western blotting in DTX-sensitive and -resistant PCa cell lines (PC3 and DU145). Our data showed upregulation of these transcription factors and LEDGF/p75 in DTX-resistant cells compared to sensitive. Preliminary data from immunoprecipitation experiments suggest interaction between JPO2, Menin/MLL, c-MYC and LEDGF/p75 in chemoresistant PCa cells. Nuclear colocalization experiments by immunofluorescence microscopy are being optimized to further characterize the interaction between LEDGF/p75 and these proteins as 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.

MARCO BAEZA
ABC PARTICIPANT 2019

I have always enjoyed learning and challenging myself to gain more experience and knowledge. The summer of 2019 has done just that. At the Health Geoinformatics Lab, under Dr. Seth Wiafe, I have integrated my knowledge and passion for statistics with biomedical research. This summer I researched suicide rates across California. Using GIS software to map out suicide rates, I investigated correlations between different variables and suicide in order to gain insight as to what some reasons for suicide might be. A few of the variables I researched were suicide and poverty, suicide and tapestry segmentation, and suicide and suicide prevention resources.

I am currently a senior at Hemet High School where I play on the varsity tennis team, am an officer for Habitat for Humanity, and am a lead prosecutor on the Mock Trial team. Next year I seek to play singles in tennis, help build homes for the needy in my community in conjunction with Habitat for Humanity, and help lead my Mock Trial team to an appearance in the county finals and win. My dream is to attend Stanford University where I will major in neuroscience with the plan to later attend medical school and become a neurosurgeon. I am excited yet nervous to see what God has in store for my future.

I want to thank Dr. Wiafe and Lance Pompe for their patience, insight, and training they have given me this summer. I would also like to thank the ABC program and Loma Linda University for giving me this extraordinary opportunity. Finally, I would like to thank my parents, my brother, my grandparents, and my friends, specifically Jason and Chris, for their motivation and support.

GEOSPATIAL ANALYSIS OF SUICIDE MORTALITY IN CALIFORNIA: GAPS AND OPPORTUNITIES FOR INTERVENTION

Marco Baeza, Seth Wiafe
Center for Health Disparities and Molecular Medicine, Health Geoinformatics Lab,
School of Medicine, Loma Linda University, Loma Linda, CA

Over the last decade, the suicide rate in California has been consistently lower than the national average. With nearly three-quarters of California suicides occurring among adults in 2017, nearly four times more people died by suicide than by alcohol-related motor vehicle accidents. It is unclear where the most probable areas of suicide clusters occur. Identifying the geographic variation of suicide mortality and relating it to the distribution of community-resources will provide a strategy for suicide intervention. We analyzed data from 38,997 people who died from suicide and 2,404,463 deaths from 2007-2016. The test for spatial randomness to determine the location of any area of California with greater or less risk of suicide death adjusting for income, region (urban/rural), and area deprivation was estimated using Spatial Scan Statistics (SATSCAN). ArcGIS was used to interpolate discrete cluster locations and overlaid with mental health facilities and military bases. Twelve general areas were identified as locations where suicide clusters show up as high standardized mortality ratios (SMRs) [>1.11], that is statistically significant (P-values < 0.005). Nine of those clusters are in close proximity (20 miles) to military bases, all in southern California. Furthermore, analysis shows urban areas with more access to mental health hospitals such as Los Angeles, San Francisco, and Riverside tend to have lower suicide rates while rural areas such as Mojave, El Cajon, and Eureka with less access to mental health facilities have higher suicide rates. Our analysis suggests that the likelihood of dying by suicide is higher in areas around military bases. Geospatial approaches may become an important part of routine assessments of suicide mortality at the community level, especially in areas which are receiving inadequate mental healthcare.

LESTER CEDENO
ABC PARTICIPANT 2019

Currently, I am a senior and will endure one of the hardest years of high school at Middle College High School (MCHS) in San Bernardino. Throughout high school, I've attained excellent academic achievements and have gained an eagerness to further my academic journey for a better future and to positively impact my community.

I've been given the opportunity through MCHS to get a head start on my college career. I am currently on track to graduate high school with an A.A. in Biological and Physical Sciences. My educational aspirations include earning a bachelor's degree in biological or health science in only two years after enrollment. After my undergraduate education, I intend to enter a graduate program to obtain my MD and begin a career in the medical field. After completing graduate school, I aspire to become a pediatrician or, alternatively, a family physician.

Apart from academia, I involve myself in a variety of extracurriculars including, but not limited to, Key Club, Team Green, STEM Club, School Site Council, etc. not only to better myself but also my community. Through these clubs, I volunteer, teach, mentor, and learn alongside my peers. I also enjoy spending time with my friends and family– those who motivate me to keep pursuing my aspirations.

I attribute my success to those who have impacted my life, including teachers, mentors, friends, and family. I thank Dr. Erik Behringer and the graduate students who helped me throughout the program. I would like to give thanks to my friends for consistently motivating me and my parents and my sister for supporting me throughout my life. Without my support systems I would not have been able to make it through this program, let alone my life.

GENETIC EXPRESSION OF ENDOTHELIUM MITOCHONDRIAL CALCIUM ION CHANNELS AND ANTIOXIDANT ENZYMES OF THE BRAIN DURING ALZHEIMER'S DISEASE

Lester Cedeño, Phoebe Chum, John Buchholz, Erik Behringer
Center for Health Disparities and Molecular Medicine, Pharmacology,
School of Medicine, Loma Linda University, Loma Linda, CA

Currently, there are ~5.8 million Americans living with the Alzheimer's disease (AD) type of dementia. Development of AD has been associated with impaired blood flow in the cerebrovascular system. Consequently, delivery of oxygen and nutrients and clearance of toxic cellular byproducts (e.g., oxidants) throughout the brain are reduced. The presence of reactive oxygen species (ROS), e.g., superoxide, hydroxyl radicals, can alter vascular function while exacerbating neuronal stress. As a primary source, vascular ROS are produced by endothelial mitochondria via enhanced Ca^{2+} sequestration in the matrix and upregulated activity of oxidative phosphorylation enzymes. Thus, we tested the *hypothesis* that the *genetic expression of the mitochondrial Ca^{2+} uniporter and antioxidant enzymes increase and decrease, respectively, during progression of age-related AD in mouse cerebrovascular endothelium*. We used the triple mutation mouse model of AD (3xTgAD) to examine young control (YC; 1-2 mo), mild cognitive impairment (MCI; 4-5 mo), amyloid-β plaques (Aβ; 6-8 mo), and plaques + neurofibrillary tangles (Aβ+Tau; ≥12 mo); 3 male and 3 female mice/group. Quantitative polymerase chain reaction (qPCR) was used to examine genetic expression of isolated cerebral artery endothelium. Our preliminary results show the mitochondrial calcium uniporter (*Mcu*) increases >1.5-fold upon MCI and peaks at ~3-fold in females only during Aβ+Tau. Accordingly, MCU regulator 1 (*Mcur1*) progressively increased by >1.5-fold from female MCI through Aβ and Aβ+Tau. Antioxidant expression for superoxide dismutase (*Sod2*), catalase (*Cat*), and glutathione peroxidase (*Gpx1*) remains altogether inconclusive with the exception of upregulation (≥1.5-fold) for *Cat* and *Gpx1* upon female MCI. When complete, our results may reveal pharmacological and genetic targets for treatment of cerebrovascular disease and, thereby, help delay or prevent dementia.

JAZMINE B. CHISM
ABC PARTICIPANT 2019

I am a senior attending Vista del Lago High School in Moreno Valley, CA. I have always had an interest in learning how people function and how to enhance their experiences so they can live in their most optimal states. This drive initially began at an early age when I would ask my relatives about how certain diseases affecting our family functioned so that I could one day cure said diseases.

Currently, I am applying this ambitious behavior in various organizations. In my position as the Girl Up and Black Student Union presidents at my school, my goal is to help marginalized communities communicate problems about society in a safe space in order to create solutions for them. As a camp counselor at the Inland Empire Future Leaders Program, I help to encourage middle school and high school students to strive for higher education and embrace their cultural backgrounds. As a travel softball player, I apply my athletic and cognitive skills to effectively compete with the most competitive teams in the nation.

In my leisure time outside of school and athletics, I enjoy activities that allow me to unwind, such as reading, listening to music, dancing, and styling clothing. I also volunteer at various community events by performing with my Black Student Union members and assisting with afterschool programs for lower grade levels.

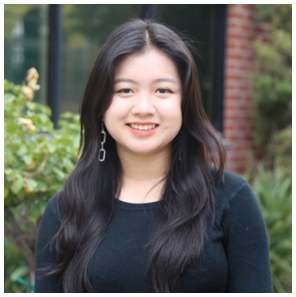
Within the ABC Program, I have been allowed to explore my curiosities about the human body regarding peritoneal cancer. Working in Dr. Nathan Wall's lab, we are discovering how to enhance the HIPEC chemotherapy procedure with curcumin, a strand of turmeric. This experience also ultimately influenced me to become a clinical researcher to further improve medicine.

CURCUMIN INCREASES CELL DEATH *IN VITRO* UNDER HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY

Jazmine Chism, Chase Sugiono, Vola Andrianarijiana, Janvierie Kabagwira, Paul Vallejos, Andrew Folkerts, Magi Senthol, Nathan Wall

Peritoneal carcinomatosis (PC) has long been deemed as a terminal disease. PC is a metastasized disease that originates from the visceral organs, such as the ovaries, digestive tract, or colon, and then migrates to the peritoneum or the abdominal cavity. When patients are diagnosed with PC, they typically have 2 years to live. However, hyperthermic intraperitoneal chemotherapy (HIPEC) has reaped positive results in regards to cancer treatment. After a patient has undergone cytoreduction of the visible tumors on the affected tissue, 42 °C chemotherapy is infused into the peritoneum to target any residual microscopic cancer cells. However, few drugs and studies evaluating HIPEC's effectiveness *in vitro* have been validated. In our lab, we are evaluating if HIPEC can be made more effective using curcumin since it has been effective in inducing apoptosis *in vitro*. In our hands, we treated the mouse colorectal carcinoma cell line (CT26) with four different doses of curcumin (0μM, 10μM, 25μM, and 50μM) and separated those cells into two different temperature groups: one heated at 42 °C and 37 °C. We then distributed those groups into subgroups by incubating them with their heat specifications for distinctive time periods (1,2, and 3 hours) and monitored their progress for 24, 48, 72 hours. Using Hoffman microscopy and Trypan Blue Exclusion assay, we assessed cell viability of the two temperature groups. Our results show the greatest effective dose and time course occurred in the cells treated at 42 °C for 3 hours. As our long-term goals include the addition of curcumin to *in vivo* human HIPEC investigations, we are now investigating if we will have the same results on human cell lines COLO205 and SNU-C1 as we recorded using the mouse cell line.

WENDY CHOW
ABC PARTICIPANT 2019



Learning didn't come easy to me. It was something that 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. As a result, this summer I have been allowed the opportunity to satisfy some of my curiosities and create a great amount more.

This September, I will be attending the University of California, Riverside. If the path I paved leads me well, I plan to obtain a Bachelor of Science in Biology with a minor in business administration and continue to Loma Linda's School of Medicine. As of now, my dream is to become a dependable primary care physician where I can contribute to the health and liveliness of my patients firsthand. My insatiable curiosity has also led me to pursue my interest in the performing arts, specifically dance and piano. The recurring enjoyment to exercise my freedom of expression through dancing in an empty room to music always whisks me away and completely immerses my soul into a different dimension each time. As a self-taught pianist, I hope to advance my musical skills with piano and other instruments.

I am exceedingly grateful to have been invited back to Dr. Eugenia Mata-Greenwood's lab in the Perinatal Department for another unforgettable summer. My respect and admiration for her only continues to grow as her zealousness leads to exceptional contributions to science. Her patience and optimism for my future success makes me want to become an even better family physician someday. Thank you, Dr. Mata-Greenwood, for making research one of the most magnificent aspects of science that I have come to love and appreciate.

ROLE OF MATERNAL OBESITY ON FETAL ENDOTHELIAL CELL-RESPONSE TO DEXAMETHASONE (STEROID) IN A SHEEP MODEL

Wendy Chow, Sara Solack, Olayemi Adeoye, Eugenia Mata-Greenwood
Center for Health Disparities and Molecular Medicine, Perinatal Biology, School of Medicine,
Loma Linda University, Loma Linda, CA

Dexamethasone (DEX) is currently used to treat newborns with respiratory distress but can cause hypertension due to the activation of the endothelial glucocorticoid receptor (GR), and its effect is worse in obese pregnancies. Our aim was to test the *in vitro* response to DEX in fetal endothelial cells obtained from obese (OB) and non-obese (CTL) pregnancies. Sheep umbilical vein endothelial cells (SUVECs) were isolated by collagenase digestion and then characterized. All SUVECs expressed the von-Willebrand factor (>94% purity). Confluent and quiescent SUVECs were treated with therapeutic doses of dexamethasone (40 nM, 200 nM, and 1000 nM) for 24 hours and analyzed for the levels of the GR protein and mRNA. As a result, there were no significant differences between non-obese and obese SUVECs in the basal or DEX-treated levels of GR mRNA or protein. SUVECs were also treated with DEX for 10 minutes to isolate cytosolic and nuclear protein fractions to study nuclear translocation. CTL SUVECs had lower basal levels of nuclear GR (0.25±0.03 vs. 0.47±0.12 non-obese versus obese nuclear/cytosolic GR) but had higher levels of nuclear GR after DEX treatment (2.04±0.5 vs. 1±0.17 non-obese versus obese nuclear/cytosolic GR). DEX did not alter the levels of the cardioprotective gene endothelial nitric oxide synthase (eNOS) in either obese or non-obese SUVECs. Finally, DEX upregulated the pro-thrombotic gene plasminogen activator inhibitor-1 (PAI1) in OB but not in CTL SUVECs. We conclude that maternal obesity does not significantly affect the total expression of GR, but it does increase the nuclear localization of GR that can explain the upregulation of PAI-1 in SUVECs collected from obese pregnancies.

GABRIEL DIAZ

ABC PARTICIPANT 2019

From a very early age, I've had a strong connection with the sciences, and to this day that connection has grown even stronger. Currently, I am a senior attending Martin Luther King High School in Riverside, CA. Throughout my high school years, I have taken many steps in furthering my knowledge in the sciences; however, the ABC program has truly given me an insight into science application and research which I haven't had before.

Both of my parents are first generation immigrants, and they both understand the importance education has on the rest of my life. They have encouraged me to reach my highest potential in my classes and extracurricular activities. After taking several AP classes, winning a national championship with my school marching band, and placing second in the category of genetics at a Science Olympiad competition, I am still seeking to push myself and to advance my education.

As I started this program, I was slightly nervous and uncertain about which project I would be participating in this summer. Health disparities cover a vast amount of illnesses, and some of these illnesses have affected several people in my life. I was notified a week before the start of the program that I would help in research pertaining to ovarian cancer. With thousands of women being diagnosed every year, I sought to contribute to research that could get humanity closer to a cure for this disease.

I would like to thank Dr. Juli Unternaehrer, Hanmin Wang, and the ABC program for accepting me into their labs and for being great mentors over the course of the summer. This summer I learned so much, and I am truly humbled and honored to have been given this opportunity.

POTENTIAL BIOMARKERS THAT CAN BE USED TO DISTINGUISH SUBTYPES OF EPITHELIAL OVARIAN CANCER

Gabriel Diaz, Hanmin Wang, Juli Unternaehrer
Center for Health Disparities and Molecular Medicine, Department of Biochemistry, School of Medicine, Loma Linda University, Loma Linda, CA

Over 22,000 women are diagnosed with ovarian cancer every year, and 90% of these are identified with epithelial ovarian cancer (EOC). In this subcategory of ovarian cancer, five different subtypes have been described: Epi-A, Epi-B, Mes, Stem-A, and Stem-B. Along with their different classifications, each subtype has different patient prognoses, growth characteristics, and proliferation rates, and, thus, it is expected that optimal treatment for each is different. Modern medicine, however, has failed to consider these differences in EOC when searching for different treatment options. Our objective in this study was to choose specific biomarkers that can be used to identify and categorize the five subtypes of EOC. To begin this process, we viewed biomarkers present for each subtype in other papers to assemble a pool of biomarkers for testing. We utilized previously-characterized cell lines as positive controls for subtypes. We developed gene expression assays by doing primer efficiency tests. From several candidate genes, we narrowed these down to ACTA2, HMGA2, SLUG, CD44, and ZEB1, specific for Mes, Stem-A, Mes, Stem-A/B, and Mes, respectively. We performed RT-qPCR to determine their expression levels in both cell lines and patient-derived cells, using ACTIN as a normalizing control. Using the list of genes, PDX cells were successfully distinguished from each other. They also showed resemblances in gene expression to cell lines whose subtypes have been previously identified. Previous studies have aimed to target the cells most responsible for the aggressiveness and recurrence of ovarian cancer. To do this targeting, the transcription factor SNAI1 (Snail) has been silenced. In the future, we intend to target Snail in these patient- derived cells to discover whether this approach is more effective in certain subtypes.

CLARISSA "NINI" DO

ABC PARTICIPANT 2019

Being the child of two immigrant parents, my parents always pushed me to excel and to live a life that they never had. As I enter my final year at Rancho Cucamonga High School, the pressing issue of college and careers is more imminent than ever. Growing up, I always knew I wanted to make a change in the world, but knowing where and how was always another story. Learning and trying new things were in my blood, and I wanted to make use of that curiosity. Throughout my high school career, I participated in Regional Occupational Programs which trained me in pharmacy, the Community Emergency Response Team (CERT), and medical assisting which ultimately became the catalyst to my love for the medical field, but it wasn't until I joined the ABC program that I truly understood the complexity of the human body and how vast medicine is.

This program pushed my limits and taught me that amazing things can come from the bleak. When concepts and experiments seemed too overwhelming, Dr. William Pearce was always welcoming and never hesitated to encourage me to be my best. It was because of this program that I truly understood the beautiful world of medicine and science and their powerful impact on the community.

After graduation, I hope to attend UCR and later on LLU for my MD/PhD so that I can pursue my ultimate goal of becoming a plastic surgeon. The winding road to my dream seems long, but the journey has only just begun.

OPTIMIZATION OF CONFOCAL COLOCALIZATION OF CONTRACTILE PROTEINS IN CEREBRAL ARTERIES

Clarissa Do, Desy Carreon, Coleen Doan, Naomi Franco, William Pearce
Center for Health Disparities and Molecular Medicine, Perinatal Biology, School of Medicine,
Loma Linda University, Loma Linda, CA

Cell biology depends on interactions among proteins that require proteins to be near one another. Colocalization of any two proteins can be determined by tagging the proteins with specific antibodies attached to wavelength-specific fluorophores, which can be imaged via confocal microscopy. However, the methods used to quantify colocalization via image analysis are highly varied and somewhat controversial. This project compares 36 different strategies of analysis. Three primary parameters were varied: **1)** minimum acceptable intensity; **2)** masking methods; and **3)** image segmentation to analyze images from P12 rat pup cerebral arteries exposed to either sham surgery (SHAM), or to unilateral carotid ligation followed by 90 minutes of 8%O_2 (ISCHEMIA). The analysis quantified contractile protein colocalization between Smooth Muscle ✔Actin with two Myosin isoforms: SM-MHC and NM-MHC. Six methods of determining minimum acceptable intensity were employed, including 3 FIXED and 3 VARIABLE, across all images. FIXED methods were applied manually, and VARIABLE methods were automated via software. Optimum statistical sensitivity was obtained by setting a FIXED minimum intensity at 10% of maximum. High precision image masking, which set all pixels to an intensity of zero except those within the Region of Interest, did not increase statistical sensitivity but reduced the false-positive rate. Analysis of segmented images revealed maximum statistical sensitivity between SHAM and ISCHEMIA groups was observed in the 20% of pixels with the highest intensity. Together, these results advocate use of a fixed low level of minimum baseline (10% of maximum), application of high precision masking, followed by segmentation to restrict analysis to 20% of pixels with highest intensity. As such, this experiment was the first comprehensive and systematic comparison of methods used to quantify confocal colocalization, particularly for vascular contractile proteins.

TARANNUM MUNIR

ABC PARTICIPANT 2019

I would have never thought I would be able to experience hands-on training in a laboratory so early on, but thanks to the ABC program, I was able to see closely the hard work and perseverance researchers commit to benefit humankind. Doing research has not only enriched me with valuable skills but given me confidence in my abilities I did not have before. I also have gained a newfound respect for biomedical research for its profound impact on remedying health disparities.

I graduated from Redlands High School and will start my undergraduate education at UC San Diego as a general biology major. Last summer I worked on a research project regarding thyroid ultrasounds at Riverside University Health System in data extraction for which I had the privilege of presenting a poster alongside my colleague Brandyn Bobb at the annual Endocrine Society Meeting in New Orleans, LA. Previous summers I volunteered a total of 200 hours with LLU's Teen Summer Program.

During my free time, I enjoy painting, singing, playing guitar and bass, and doing yoga. My favorite pastime, however, includes any time I am learning something new. I try to be my best every single day, and the ABC program has helped cultivate a confident and learned version of myself.

My time in this program was guided by Dr. William Langridge in observing whether cholera toxin B subunit fused to proinsulin (CTB-INS) upregulated the programmed death ligand (PD-L1) in dendritic cells. This research aims to find a more effective generic treatment of Type 1 Diabetes by understanding the mechanisms of immune tolerance of CTB-INS. I would like to thank both Dr. Langridge and Mary Beth Yu, whose discourse and expertise helped to challenge and teach me invaluable lessons and skills.

PROGRAMMED-DEATH LIGAND IS UPREGULATED BY HUMAN DENDRITIC CELLS TREATED WITH CTB-PROINSULIN FUSION PROTEIN

Tarannum Yumi Munir, Mary Beth Yu, William Langridge
Center for Health Disparities and Molecular Medicine, School of Medicine,
Loma Linda University, Loma Linda, CA

Type 1 Diabetes (T1D) is an autoimmune disorder prevalent in children in which insulin-producing pancreatic beta cells are destroyed by autoreactive T cells. Patients with T1D suffer from chronic hyperglycemia resulting in life-threatening complications if not managed with lifelong insulin therapy. A fusion protein composed of cholera toxin B subunit linked to proinsulin (CTB-INS) was found to suppress T1D onset in non-obese diabetic (NOD) mice. To understand the mechanism responsible for CTB-INS inhibition of T1D in patients, we examined activation of the programmed death ligand (PD-L1), which binds to its cognate receptor PD-1 on T cells. Activation of PD-1 initiates a co-inhibitory signal, inhibiting activation of T cell responses to pathogens and autoimmunity. In this study, immature dendritic cells (DCs) were differentiated from monocytes isolated from human peripheral blood. The DCs were treated with CTB-INS fusion protein at an optimum concentration of 10 ug/ml. After two days of incubation in R10 cell culture medium at 37^{o}C, the DCs were harvested and stained for surface markers for DC activation and PD-L1. Examination of the CTB-INS treated DCs by flow cytometry and western blot analysis showed that in comparison with untreated DCs, dendritic cells treated with CTB-INS synthesized increased amounts of PD-L1 on the cell surface. CTB-INS activation of DC costimulatory factor CD86 suggests CTB-INS activates receptors that can bind and stimulate T cell responses. Western blot identification of PD-L1 in homogenates of CTB-INS treated DCs suggest PD-L1 is upregulated in DCs treated with CTB-INS. Increased levels of PD-L1 synthesized in CTB-INS-treated human DCs suggest DC upregulation of this checkpoint inhibitor could play an important role in CTB-INS activation of T cell responses involved in the inhibition of type 1 diabetes.

OASIS PEREZ

ABC PARTICIPANT 2019

I was born and raised in the Inland Empire and just recently graduated from Grand Terrace High School. This fall I will be attending the University of California, Irvine, as a biology major. My interest in biology began in my high school biology class which led me to pursue a career within science. My long-term goal is to become a professor, which would allow me to combine my love for teaching and helping others while pursuing a field I am just starting to discover.

During my free time, I enjoy giving back to my community where I have been a part of many service groups throughout the years. On my high school campus, I was part of the Random Acts of Kindness Club where I orchestrated the mental health awareness division and annual wellness fair on campus. I am a member of the Girl Scouts and will receive the Gold award in September for being an advocate for mental health. I also actively participate in my city's recreational center teen advisory board.

This summer I have been lucky enough to work in Dr. Kylie Watt's lab in the Department of Microbiology where I have been studying *Pseudomonas aeruginosa* and the Aer2 chemoreceptor. Prior to this summer I had only shadowed a researcher and had no active experience in research, let alone a strong background in the field of microbiology. This experience has given me hands-on research, allowing me to learn and grow as a scientist in a way I would never have thought possible before I stepped onto a college campus.

I would like to thank my lab family for giving me the space to expand my knowledge, especially my mentor Selina Anaya who has guided me through my summer project.

HOW DO THE N-TERMINAL HAMP DOMAINS OF THE AER2 CHEMORECEPTOR FROM *PSEUDOMONAS AERUGINOSA* CONTRIBUTE TO CELLULAR LOCALIZATION?

Oasis Perez, Selina Anaya, Kylie Watts
Center for Health Disparities and Molecular Medicine, Division of Microbiology and Molecular Genetics, School of Medicine, Loma Linda University, Loma Linda, CA

Prokaryotes undergo unforeseeable changes in both their physical and chemical environments, requiring constant accommodation. Bacteria survive these changes by employing chemosensory (Che) systems that convert extracellular signals into cellular responses, allowing bacteria to sense, respond, and adapt to their surroundings. *Pseudomonas aeruginosa* is both a Gram-negative ubiquitous bacterium and an opportunistic human pathogen that can survive in different environments, utilizing 26 chemoreceptors that feed into four different chemosensory systems. The role of the fourth system, Che2, is not entirely understood. Interestingly, the Che2 system employs just one chemoreceptor, Aer2, which localizes to the cytoplasmic membrane near the cell pole by an unknown mechanism. Earlier fluorescence-based studies and recent cryoelectron tomography studies have both demonstrated this localization. Remarkably, Aer2 is a soluble receptor that lacks hydrophobic segments, yet it localizes to the cytoplasmic membrane for Che2 cluster formation and function. It is possible that Aer2 adheres to the cytoplasmic membrane via the membrane's negative electrostatic potential, or that Aer2 interacts with a membrane-embedded protein via its three N-terminal HAMP domains. To clarify the mechanism of Aer2-membrane interaction, we have generated Aer2-eGFP (enhanced green fluorescent protein) fusions containing full-length (res. 1-169) and N-terminally truncated Aer2 peptides and have begun to visualize them in *Escherichia coli* by fluorescence microscopy. In the future, these constructs will also be visualized in *P. aeruginosa*. We expect these studies will reveal the influence of the N-terminal HAMP domains on Aer2-membrane localization. We hypothesize that Aer2 peptides lacking HAMP 1 (res. 1-56) or HAMP 1-3 (res. 1-172) will not localize to the membrane, and receptors lacking their C-terminal kinase control domain (res. 386-679) will retain a wildtype localization pattern.

MICHELLE QUARSHIE
ABC PARTICIPANT 2019

Ever since childhood, I would tell friends and family about my profound interest in medicine and healthcare. Medicine and science have always stood out as a way to explore mysteries of the human body and reasons why these mysteries occur. This summer the ABC program has better shaped my understanding of research, how research contributes to the study of medicine, and made my conviction to pursue medicine even stronger.

I will be a senior at Redlands High School this fall. I have always felt music is another way of healing the mind and body. This feeling led me to play cello for five years and join my high school's vocal music program as well. I am currently president of my Computer Builders Club, the Head Spirit Task Coordinator of my Key Club division, and working on starting a March for Our Lives chapter at my high school. I have always loved serving my community and have completed over 100 hours of community service with various clubs and organizations throughout my high school career. When I am not busy with school, I enjoy playing the ukulele, songwriting, reading, and singing. In the future I would like to become a general pediatric surgeon and help children in need.

This summer I am working in Dr. David Hessinger's lab and researching the effects in the satiety response of *H. luciae* when treated with different drugs. I would like to thank Yoshelyn Vera for being a lab partner I can rely on and grow with. I would especially like to thank Dr. Hessinger for mentoring me this summer and teaching me about research and about science.

PRAZOSIN BLOCKS THE INHIBITION OF PREY-KILLING CAUSED BY THE USE OF NANA-ALANINE IN SEA ANEMONE

Michelle Quarshie, Yoshelyn Vera, David Hessinger
Center for Health Disparities and Molecular Medicine, Division of Physiology, School of Medicine, Loma Linda University, Loma Linda, CA

Cnidarians are among the simplest organisms with the simplest nervous systems. Among these cnidarians are sea anemones, specifically *Haliplanella luciae*, with robust satiety responses as they only eat until they achieve "fullness," or satiety. We hypothesize that when amino acids such as alanine come in contact with a proposed remote sensory cell in *H. luciae*, it causes the release of the adrenergic agonist known as norepinephrine (NE). NE is believed to activate adrenergic receptors on cnidocyte supporting cells and the supporting cells respond with the production of extracellular Ca^{2+} through dihydropyridine (DHP) channels. This reaction from activated N-acetylneuraminic (NANA) receptors reduces nematocyst discharge and, therefore, limits prey-killing and ingestion. We also hypothesize that prazosin reverses this effect, which returns nematocyst discharge, prey- killing, and ingestion to normal levels. To test our hypothesis, we verified that NANA-Alanine decreases prey-killing and ingestion. We also tested whether the selective adrenergic receptor blocker, Prazosin, inhibits the effect of Alanine. To do this test, similarly sized, monoclonal *H. luciae* were selected and starved for three days. These anemones were, then, incubated in different drugs such as NANA- Alanine and NANA-Alanine and Prazosin and fed a standardized number of brine shrimp to test if NANA-Alanine inhibits prey-killing and ingestion and if Prazosin blocks this effect. Our results indicate NANA-Alanine reacts with receptors in a proposed adrenergic circuit causing release of norepinephrine that increases satiety levels in sea anemone, thus inhibiting prey-killing and ingestion. The addition of Prazosin has proved to reverse this effect by blocking the release of norepinephrine into the supporting cell complex. Future research can be done to find other methods to increase satiety in anemones and decrease nematocyst discharge, prey-killing, and ingestion.

ANTHONY SALDANA
ABC PARTICIPANT 2019

As a senior from John F. Kennedy Middle College High School in Norco, CA, I was ecstatic to have the opportunity this summer to conduct research alongside experienced PhD students. Growing up, I always had an interest in the field of science and medicine although none of my family or relatives were ever as intrigued by medicine as I was. Despite having no relatives or connections to the medical field, I had a strong interest in it, and my family was supportive of my goals and aspirations. The ABC program has challenged and taught me valuable lessons to continue down the pathway to becoming a physician and has also created a new pathway and passion for research.

Prior to entering the ABC program, I had been well immersed in academia and extracurricular activities hoping that my application would stand out and get me into a program such as this one. I was ranked number five in my class, have been ASB President since I began attending my school, will graduate with over seventy college units and four Associate's degrees, have participated in the track and field team for three years, have accumulated over 200 hours of community service, and have been managing and taking part in myriads of clubs.

I would like to thank the ABC program directors Dr. Marino De Leon and Dr. Carlos Casiano for this incredible experience, thank Dr. De Leon for welcoming me into his lab, and thank Drs. Jo-Wen Liu and Alfonso Duran for guiding and patiently teaching me throughout this summer.

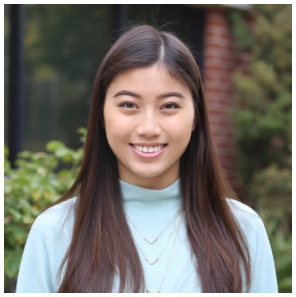
NEUROPROTECTIVE EFFECTS OF LOW DOSE DOCOSAHEXAENOIC ACID AGAINST LIPOTOXICITY-MEDIATED CELL DEATH IN IMMORTALIZED SCHWANN CELLS: IMPLICATION OF AUTOPHAGY-RELATED GENES

Anthony Saldana, Jo-Wen Liu, Manuel Montero, Marino De Leon
Center for Health Disparities and Molecular Medicine, School of Medicine,
Loma Linda University, Loma Linda, CA

Previous reports from our laboratory have shown that Docosahexaenoic acid (DHA) provides neuroprotective effect on neurons and Schwann cells against palmitic acid-induced lipotoxicity (PAM-LTx). The purpose of this study was to determine the minimum concentrations of DHA needed to protect immortalized Schwann cells (iSC). Furthermore, we examined the expression levels of autophagy-related genes, ATG5, ATG7, and ATG12, in DHA-mediated cellular protection. The iSC were plated in 6-well plates and changed to serum-free medium before PAM-LTx treatments. Next, iSC were treated with DHA (1-20μM) complexed with fatty acid-free BSA (150μM) and DHA (1-20μM) with PAM-BSA (300μM:150μM) for 24-48 hours. After treatment, cells were fixed for Crystal Violet staining to determine cell viability. Our experimental results show that DHA at 1, 2, and 5μM was not able to inhibit the loss of cell viability caused by PAM-LTx, but at 10 and 20μM, the protective effect was significant. Cell morphologies viewed under phase-contrast microscopy with Hoffman modulation indicate similar results. To further analyze autophagic mechanism during the DHA-mediated protection in iSC, total cellular RNA was extracted after treatment and cDNA synthesis was performed. Subsequently, the relative gene expression level of ATG5, ATG7, and ATG12 was determined by real-time PCR. Our preliminary results show there is a dose-dependent increase for ATG5 mRNA in DHA and PAM+DHA groups. On the other hand, ATG7 mRNA was inhibited in PAM and PAM+DHA groups. ATG12 mRNA was increased in PAM, PAM+DHA 10μM, and PAM+DHA 20μM groups. Our data indicates that as low as 10μM DHA provides significant protective effects against PAM-LTx, and ATG5 may have a potential role in DHA-mediated protection in iSC.

KALLISTA TANTIGA

ABC PARTICIPANT 2019



A senior at Diamond Bar High School, I am in the Tech Program and planning to major in biomedical engineering once in college. The ABC Program appealed to me greatly as I have only had a focus on engineering through the PLTW-pathway in my school. I realized the need for an opportunity to gain experience in the biomedical field. Some other things about me include loving to dance, playing League of Legends, baking, and creating travel vlog montages.

I am on the Diamond Bar Dance Team, where I dance for All Female hip-hop, and I, as the historian, am responsible for capturing all the memories. Through endless hours of practice and teamwork, we have managed to go undefeated in the 2018-2019 season. As a woman in the STEM field, I have always strived to represent and advance minorities in STEM. I ascended from a Secretary to the Vice-President of the Society of Women Engineers at my school. Individually, I represented my school in a PLTW competition, where my team placed fourth out of seventeen schools. Volunteering with multiple organizations, I became a Cultural-Event Assistant for the National Honor Society. As a member of Future Business Leaders of America, I have attended conferences and placed top 10 in the State Conference. I also am a member of the California Scholarship Federation and 2020 Class Committee. Throughout the year, I work as a receptionist for Yamaha Music School.

My dream is to become a biomedical engineer who opens a worldwide, networked company to provide others with biomedical engineering opportunities to make grand contributions to mankind.

I want to thank Dr. Sean Wilson for taking me in the lab and providing me with many opportunities and Sam Murray for teaching me the ropes.

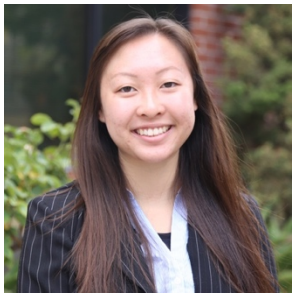
COLLAGEN CROSSLINKING AND VENTILATION OF THE FETAL SHEEP LUNG

Kallista Tantiga, Samuel Murray, Monica Romero, Steve Yellon,
Lubo Zhang, Arlin Blood, Sean Wilson
Center for Health Disparities and Molecular Medicine, Center for Perinatal Biology,
Advanced Imaging and Microscopy Core, School of Medicine,
Loma Linda University, Loma Linda, CA

Collagen is a structural protein that is one of the most common proteins found in the body. Collagen contributes to mechanical properties of tissue, and in the lung it helps provide tissue integrity, allowing for proper ventilation. Before birth, the airways are relatively collapsed, but ventilation at birth opens them. The role of changes in the structural integrity of the lung with ventilation at birth remainS poorly understood. Tissue integrity, however, is largely provided through crosslinking of the collagen fibers, which can be examined through picrosirius red staining and imaging. The focus of this work was to test the hypothesis that ventilation at birth decreases collagen crosslinking. This hypothesis was examined in tissues isolated from ventilated and unventilated lungs of fetal sheep. The lungs were sectioned at 50 microns and stained with picrosirius red. Stained sections were imaged using polarized light to visualize picrosirius bifringence due to collagen crosslinking and quantified using Image J. An unpaired T-test analysis of the data shows there is no significant difference in the picrosirius bifringence between ventilated and unventilated sheep lungs. These findings lead to the conclusion that the relationship between collagen crosslinking and ventilation is not direct. Because ventilation does not directly affect collagen crosslinking, other factors likely contribute to changes in lung structure due to ventilation. Given that the lung undergoes rapid changes in structure at birth that do not involve large-scale changes in collagen, crosslinking points to the need to examine the effects of ventilation at birth in a more wide-scale way using modern –omics approaches.

JENNIFER TRAN

ABC PARTICIPANT 2019



I recently graduated from Middle College High School as salutatorian and with two Associate's degrees in Behavioral and Social Science and Liberal Arts. As of right now, I will be attending California State University, San Bernardino, in the fall of 2019.

I would not be where I am today if it were not for service. It all began in the summer of 2011 where I volunteered at Loma Linda Rehabilitation Hospital. This program opened opportunities for those interested in exploring the medical field by associating with medically fragile and technologically dependent people of all ages. I found I am passionate about the medical field and continued to volunteer for the next six summers. I wanted to expand my horizon by exploring what other careers the medical field has that suit me by seeking different programs.

As a returning student for my second year in the ABC program, I saw how research plays a role in helping people in third world countries and nationwide get better care within their community, and I learned about the value of providing medical care to underserved populations. Income should not be a barrier when it comes to health, and everybody deserves the utmost quality of life.

I am truly grateful to work in the breast cancer research lab under Dr. Daisy De Leon and my mentors Qianwei Tan and Xousaen Helu. They showed me the essence and burning passion they have for research. I am fortunate to be in this program again, and I will hopefully continue this astonishing experience and use it towards my potential career at Loma Linda University.

VALIDATION OF PSMA AS A BIOMARKER IN TRIPLE NEGATIVE BREAST CANCER

Jennifer Tran, Qianwei Tan, Daisy De Leon, Frankis Almaguel
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. African American (AA) women have a lower incidence of breast cancer but a higher mortality rate as compared to Caucasian women (CA). Among the factors contributing to the higher mortality rate is the increased incidence of Triple Negative Breast Cancer (TNBC), the most aggressive form of BC, among AA women, and treatments currently available are limited or ineffective. Prostate Specific Membrane Antigen (PSMA) is overexpressed in prostate tumors and currently used for prostate cancer treatment. PSMA is also expressed in the blood vessels associated with the tumors, and it has also become a successful treatment for prostate cancer metastatic disease. Recent studies with PSMA-PET imaging has shown PSMA is detected in other tumors such as liver cancer and its metastatic disease. Thus, we propose that PSMA may represent a potential target in the treatment for TNBC. Our hypothesis is that PSMA is highly expressed in TNBC cells. Validation of our hypothesis will provide the foundation required to develop an animal model and assess *in vivo* whether PSMA can be used to treat TNBC. We chose four TNBC obtained from ATCC: MDA231, Hs578T (CA), MDA468, and CRL2335 (AA). We also used several BC cells that are not TNBC to compare the expression of PSMA. Cell extracts were prepared from all cells to assess the expression of PSMA by Western Blotting (WB). The protein bands of the WB were scanned and quantitated. Our results showed PMSA is expressed in all TNBC cells. The highest expression of PSMA was observed in the AA TNBC cells CRL2335. Our data warrants further analysis to validate PSMA as a biomarker and tool for imaging-based treatment and follow-up of TNBC.

YOSHELYN VERA

ABC PARTICIPANT 2019

"*Hechale ganas, mija*" was what kept me going through all academic barriers. After a certain grade level, my parents were unable to help me academically; however, they continued to support me emotionally through everything. I am now a senior at Ramona High School in Riverside, CA. I love learning and being involved in my community. I am a social member of the Riverside Youth Ambassadors and Riverside Youth Council. My career goal is to become a medical doctor in the field of neuroscience to demonstrate that my parents' efforts truly are valuable and appreciated.

This summer, I have the privilege of working in Dr. David Hessinger's lab along with my lab partner Michelle Quarshie. We are working on the overall topic of obesity by treating anemones and the effect of feeding efficiency on brine shrimp. This experience truly has allowed me to view science in a whole different perspective rather than a classroom setting. Being in the ABC program has taught me that no matter what one's background may be, here at Loma Linda we are all able to succeed and demonstrate our true abilities.

I would like to thank Dr. Hessinger for his unconditional support and patience, for giving me the opportunity to express my ideas, and for the opportunity to learn.

THE EFFECT OF PRAZOSIN IN ADRENERGIC RECEPTORS OF SEA ANEMONES

Yoshelyn Vera, Michelle Quarshie, David Hessinger
Center for Health Disparities and Molecular Medicine, Division of Physiology, School of Medicine,
Loma Linda University, Loma Linda, CA

In vertebrates, adrenergic receptors modulate biological responses. Adrenergic circuits have not been reported in cnidarians such as anemones, yet sea anemones are among the simplest animals having a nervous system. *Haliplanella luciae*, sea anemones, can relate to human beings due to their nervous system. We hypothesize that prazosin blocks the inhibition of prey-killing reversing the satiety effect in sea anemones. Satiety would be the opposite perspective of hunger which would take in consideration obesity. We tested our hypothesis using a quantitative prey-capture and feeding assay. Using a standardization technique, a number of shrimp were fed to the sea anemone being treated in the proposed solution. Considering the amount of time the sea anemones were treated in prazosin, the N-acetylneuraminic acid with amino acid, alanine (NANA-Alanine), initiated an effect on the experiment overall. Within the experiment there were four different groups of sea anemones testing different solutions including a controlled one such as artificial sea water. Understanding how *Haliplanella luciae* feeding behaviors function can demonstrate the effects of prazosin. Our results indicate that prazosin indeed does block the effect which blocks the inhibition of prey-killing. Furthermore, blocking the inhibition of prey-killing would undo the satiety effect which would make the anemone ingest more shrimp. For future directions, we would assess NANA-Glycine with the effect of prazosin instead of the NANA-Alanine to determine if it has the corresponding result.

Undergraduate Training Program (UTP)

Cristina A. Araújo Rosario
De'Andre Brown
Cecilia De Leon
Marleni Pagan-Ramos
Krystal R. Santiago
Emmanuel Solis
Neihyarie K. Velez Villarrubia
Roland Williams
Shandelle Williams
Eric Xiao

CRISTINA A. ARAÚJO ROSARIO

UTP PARTICIPANT 2019

Ever since I was very young, I have wanted to be a scientist. That is why I enrolled in the science department in Antillean Adventist University in Mayagüez, Puerto Rico, as soon as I finished high school. I just finished my third year in college and currently major in biology with a music minor. During the 2018 summer I took a class where I made a written project on prostate cancer and how less cytotoxic cures were being found in sea cucumbers. This project awoke in me a passion for cancer research. During the Christmas break 2018/2019, I volunteered in the Department of Natural and Environmental Resources (DRNA) fisheries laboratory where I continued to cultivate my love and passion for research. After I graduate, I plan to achieve a PhD in biomedical research to help contribute in the field of cancer research by discovering more selectively toxic natural compounds.

This summer I am working in Dr. Eileen Brantley's laboratory together with PhD students Jonathan Wooten and Nicole Mavingire. The lab is focused on studying signaling pathways that modulate oxidative stress and seeks to characterize cross-talk interactions between these pathways and the aryl hydrocarbon receptor signaling pathway that eventually leads to growth suppression of malignant breast cancer cells. I find this research very stimulating because we are working with plant extracts which possess fewer adverse drug reactions but are also very effective in the treatment of breast cancer compared to traditional breast cancer medications.

Being part of this program has taught me that it's most important to help others with my career, but I must also love what I do. I appreciate the opportunity Dr. Brantley has given me to work with her, her mentorship, and her students' mentorship.

PETIVERIA ALLIACEA PLANT ISOLATE DIBENZYL TRISULFIDE INDUCES APOPTOSIS IN TRIPLE NEGATIVE BREAST CANCER CELLS DERIVED FROM AFRICAN AMERICAN PATIENTS

Cristina Araújo, Jonathan Wooten, Joyce Aja, Nicole Mavingire, Eileen Brantley
Center for Health Disparities and Molecular Medicine, Department of Basic Sciences,
School of Medicine, Loma Linda University, Loma Linda, CA

One in eight women will be diagnosed with breast cancer in her lifetime in the US. African American women are nearly twice as likely to die from breast cancer than European American women though they are less likely to receive a breast cancer diagnosis. Triple negative breast cancer (TNBC), characterized by tumors that lack estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth receptor (HER2) expression, is one of the most aggressive subtypes. TNBC carries a poor prognosis in part due to a lack of clinically available targeted therapy. Previous studies indicate that dibenzyl trisulfide (DTS), derived from the *Petiveria alliacea* (Anamu) plant, exhibits potent anticancer actions in a breast cancer cell line derived from a European American patient. The purpose of our study was to evaluate the ability of DTS to inhibit proliferation and death in CRL-2335 TNBC cells derived from an African-American patient. We found DTS inhibited CRL-2335 cell migration and proliferation using the Wound Healing (scratch) and colony forming assays, respectively. Furthermore, DTS promoted apoptotic body formation and nuclear fragmentation as determined using relief contrast and fluorescence microscopy, respectively. Moreover, data from the Annexin V/PI assay revealed DTS induced early apoptosis which was partially attenuated in cells pretreated with pan-caspase inhibitor zVAD-fmk. Finally, quantitative polymerase chain reaction (qPCR) analyses revealed that DTS induced the expression of pro-apoptotic genes BAK1, LTA, and GADD45A. Our data suggest DTS effectively promotes apoptosis in TNBC cells including those derived from African American patients and represents a promising agent to treat refractory forms of cancer.

DE'ANDRE BROWN
UTP PARTICIPANT 2019

My desire for science and health was sparked relatively early in my life. My mother is an RN, and my sister, Tamara, is pursuing a medical degree. I decided in high school I wanted to become a doctor because of my passion for medicine and desire to help others. However, experience in microbiology and organic chemistry labs this past school year along with this research experience in the Undergraduate Training Program has opened my eyes to my interest in research and showed me research is another method, although indirect, of helping humanity.

I was born and raised in Queens, New York, youngest of four children and the only boy. I have many hobbies and passions, including basketball, singing, and community outreach. My parents migrated to the United States to provide me and my three sisters a chance to pursue our dreams. Growing up, I was, and still am, known for my soft spoken demeanor and mellow attitude. Currently, I attend Oakwood University in Huntsville, AL, where I am a biology major entering my junior year. I wish to attend medical school and become an orthopedic surgeon after graduation. My passion for the medical field and the sciences relates to my infatuation with the body and nature and a desire to leave a positive, tangible impact on the world.

I would like to thank Dr. Christopher Perry, Dr. Ryan Sinclair, and Kevin Nick for opening my eyes to other methods of impacting people outside of medicine through this research experience. The fact that silver and gold nanoparticles have antimicrobial properties, and microplastics polluting our environment along with these precious metals could potentially be put to good use intrigues me because of the benefit for mankind and on our environment.

ANTIMICROBIAL PROPERTIES OF SILICONE EMBEDDED WITH SILVER AGAINST *STAPHYLOCOCCUS EPIDERMIDIS* DUE TO AUGMENTATION MAMMOPLASTY

De'Andre Brown, Cassandra Drew, Brittney Springer, Ryan Sinclair, Christopher Perry
Center for Health Disparities and Molecular Medicine, School of Medicine, School of Public Health, Loma Linda University, Loma Linda, CA

Silver has emerged as an alternative antimicrobial to bacitracin, the current gold standard. The goal of this research was to determine the efficacy of coated and embedded silver against bacterial growth on silicone. Silicone is a major component of implants and tissue expanders used in breast augmentation. *Staphylococcus epidermidis*, a part of the human body's natural flora, is the most common infection because it can enter the body via a surgical incision and eventually lead to biofilm formation. We hypothesize that silver would inhibit the formation of biofilm. To test this hypothesis, Slygard 184 (Silicone) was embedded with silver sulfate (≈10 mg/10 g Slygard) or coated with silver ions using polydopamine silicone substrate or plasma-coated silicone (coated for 15 sec., 1 min., or 5 min.). Effectiveness of each coating method was determined by zone of inhibition and crystal violet biofilm assay. Dopamine-coated Slygard had greater-sized zones of inhibition (10.14mm) than the plasma-coated Slygard (average of 6.4 mm). Embedding with silver sulfate produced zones of inhibition as well with an average of 7.35 mm. Along with silver content, the experiment tested for the effect of UV light (245 nm) at different time intervals (1min., 5 min., 10 min., 15 min.) on the embedded silver sulfate silicone disc's inhibition. The UV light produced no significant statistical difference but very significant because with further research, silver in implants can be used to decrease cases of infection globally. We have begun, and hope to further pursue, using silver nanoparticles in the place of silver sulfate and silver nitrate as much less can be used due to the high surface area to volume ratio and the controlled, gradual release of ions.

CECILIA DE LEON
UTP PARTICIPANT 2019

Since I was a little girl, my dream has been to become a physician. My inspiration and motivation to follow the healthcare path has been my mom who has taught me the purpose of being a caregiver as she holistically treats her patients--body, mind, and spirit—following the healing ministry of Christ.

I am a sophomore at AdventHealth University (AHU) located in Orlando, FL. I am majoring in biomedical sciences, a career that lets me enjoy and explore the foundations of the healthcare field. For the past two years, I have been part of "SALT Outreach," an organization that has allowed me to serve the community as we feed the homeless and visit patients at different hospitals, bringing them music, prayer, and the word of God. I am a volunteer at AdventHealth for Children, where I get as much happiness as I try to bring to the patients. There we help kids feel like kids, instead of patients. At AHU I have the privilege of serving others through campus ministries as a dorm chaplain, worship member, and small group leader.

My major academic goal is to enter LLU medical school, and being part of this research program has drawn me closer to my goal. Through this experience, I have not only explored interesting fields in molecular medicine, but I have also learned lessons for a lifetime. I want to thank Dr. Penelope Duerksen-Hughes's lab for adopting me this summer. I also want to thank Dr. Jun Ling for trusting me with his project. Special thanks to my mentor Sonia Whang, who was with me every day of this journey and showed me the beauty of science in a fun and patient way.

THE ROLE OF BIOCHEMICAL MECHANISMS IN MODULATING LEVELS OF REACTIVE OXYGEN SPECIES IN PRIMARY HUMAN KERATINOCYTES

Cecilia De Leon, Sonia Whang, Meghri Katerji, Jun Ling, Penelope Duerksen-Hughes
Center for Health Disparities and Molecular Medicine, Department of Basic Sciences,
School of Medicine, Loma Linda University, Loma Linda, CA

Reactive Oxygen Species (ROS) levels can cause DNA damage and the production of oxidative stress, ultimately leading to viral integration of HR HPV into the host genome and increasing the likelihood of carcinogenesis. Our lab has collected specimens from patients who have undergone uterine prolapse and found that these cervical cells displayed varying levels of ROS. Our purpose was to better understand the molecular mechanisms underlying these differences. Multiple enzymes participate in ROS metabolism such as NOX, SOD1, SOD2, GPX, PRDX, and Catalase. We focused on Catalase and the superoxide dismutases, SOD1 and SOD2, enzymes that act as antioxidants and reduce the level of ROS in the cell. SOD1 and SOD2 control ROS levels as they dismutate the superoxide (O_2^-) radical producing H_2O_2 and O_2. Then, Catalase catalyzes the decomposition of hydrogen peroxide to oxygen and water. PDRX protects cells by preventing the metal-catalyzed oxidation of enzymes. We hypothesized that activities of such enzymes could influence the background levels of ROS. To test this hypothesis, we used western blot analysis to assess the levels of the antioxidant enzymes SOD2, Catalase, and PRDX present in the patients' primary cells where these cells expressed various levels of ROS. We grew and collected the primary keratinocytes then extracted their proteins and subjected them to gel electrophoresis. After transferring the proteins to a PVDF membrane, we probed it with anti-SOD2, anti-Catalase, and anti-PRDX antibodies. We hypothesized that patient specimens containing high levels of ROS would express lower levels of antioxidant enzymes. Our preliminary results suggest that patient specimens do express SOD2, Catalase, and PRDX. Efforts to normalize and compare these levels and to test our hypothesis are ongoing.

MARLENI PAGAN-RAMOS
UTP PARTICIPANT 2019

"Research is to see what everybody else has seen, and to think what nobody else has thought," said scientist Albert Szent-Gyorgyi. Thinking what nobody else has thought comes with some challenges, including learning from every failed experiment and with perseverance. Once I heard Dr. Carlos Casiano say that as researchers, we should not be afraid of failure; instead, we should take advantage of it. Those words inspired me. Instead of allowing frustration to deviate me from my purpose, I take advantage of the situation by learning from it and using it as fuel to work harder.

I am a senior at the University of Puerto Rico studying human approach biology. I am also a mentee of Dr. Molina-Vicenty in the Introductory Research Program of VA Caribbean Healthcare System. This summer in Dr. Casiano's lab through the Undergraduate Research Program, I have worked with Evelyn Sanchez-Hernandez, a PhD student, studying glucocorticoid signaling along with Prostate Specific Membrane Antigen (PSMA) and its effect in prostate cancer progression.

These experiences have had a wonderful impact in my life, shaping me to be the student I am today, who is always aiming for more and looking for answers to make a difference. I want to thank my mentors for their time, dedication, and much appreciated lessons.

In a world with so many difficulties, having hope can sometimes be the only thing that keeps us going. Hope is one reason I see myself as a physician and biomedical scientist in the future. My main goal in life is to make a difference and have a positive impact in society, and I can't think of a better way to accomplish my goals than providing hope through science.

PSMA IS DIFFERENTIALLY EXPRESSED IN A RACIALLY DIVERSE PROSTATE CANCER CELL PANEL

Marleni Pagán-Ramos, Evelyn Sanchez-Hernandez, Alfonso Durán, Carlos Casiano, Frankis Almaguel
Center for Health Disparities and Molecular Medicine, School of Medicine and Cancer Center,
Loma Linda University, Loma Linda, CA

Prostate cancer (PCa) is the second leading cause of cancer-related deaths among U.S. men, disproportionately affecting African American (AA) men. Androgen deprivation therapy (ADT) and chemotherapy are the standard treatments for metastatic PCa. Unfortunately, therapy resistance inevitably occurs as PCa metastasis progresses. Therefore, there is an urgent need for new options to treat PCa more effectively. The use of Prostate Specific-Membrane Antigen (PSMA) as a theranostics biomarker for PCa is attracting enormous interest. PSMA is a transmembrane protein highly expressed in metastatic PCa, particularly in lymph nodes and bone. PSMA-based radioligand therapy (RLT) is emerging as a novel theranostic strategy for metastatic PCa. Due to its promising overall survival outcomes, 177Lu-PSMA 617 is the first PSMA-RLT evaluated in phase-3 clinical trials for metastatic PCa. A racially diverse study of PCa patients treated with PSMA-RLT resulted in 82% of patients having ≥ 90% decrease in PSA levels. Therefore, PCa patients with African ancestry could benefit from this intervention. PSMA expression is enhanced in patients treated with ADT. Since ADT leads to activation of glucocorticoid receptor, we hypothesized that PSMA expression may be altered by glucocorticoid treatment, and that it may be differentially expressed in racially diverse PCa cells and tissues. In the present study, basal PSMA expression levels were assessed in a diverse panel of PCa cell lines by immunoblotting, detecting the highest expression in the AA-derived MDA-PC-2b cell line. PSMA expression measured after treatment with dexamethasone revealed a slight downregulation. Also, immunohistochemistry procedures to assess PSMA expression in PCa tissue microarrays (TMAs) were optimized. Our findings suggest that PSMA might be regulated by glucocorticoids, and may contribute to advance personalized theranostics for patients most at risk.

KRYSTAL R. SANTIAGO
UTP PARTICIPANT 2019

Someone 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, I have put a lot of effort into becoming the best student I can be. This fall I will be starting my senior year as an undergraduate at the University of Puerto Rico, Mayaguez, 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 after-school academy specialized in music and the arts. There, I learned to play the flute and I also trained my voice. I am now part of the few with a scholarship from the Coral Universitaria, a choir that represents 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.

This being my second year in the UTP, I would like to thank Dr. Salma Khan for welcoming me once again into her lab and teaching me science related to cancer. 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.

STRESS-INDUCED MICRORNA (MIRNA) SIGNATURES IN THYROID CANCER HEALTH DISPARITIES

Krystal Santiago, Ryan Davis, Erika Altamirano, Garrett Anderson, Yan Wongworawat, Mia Perez, Hanmin Wang, Juli Unternaehrer, Alfred Simental, Sourav Roy, Salma Khan
Center for Health Disparities and Molecular Medicine, School of Medicine,
Loma Linda University, Loma Linda, CA

Filipino Americans (FA) are known to have higher rates of thyroid cancer incidence and disease recurrence than European Americans (EA). FA are also known to be three times more likely to die of thyroid cancer compared to EA. Epidemiological studies in California have shown that thyroid cancer is the second most common cancer among FA women. There are no studies elucidating the reason behind these discrepancies. We decided to study the genetic and epigenetic alterations in FA versus EA with thyroid cancer. MiRNAs are linked to different types of cancers; dysregulated miRNAs can modulate tumor suppressor genes or oncogenes. No study elucidates the association of miRNAs to tumor staging or prognosis in thyroid cancer health disparities. In this study, we determined miRNA expression profiles and found significant differences in the miRNA profiles between FA and EA thyroid cancer patients. Our pilot study showed several dysregulated miRNAs from which we chose to assay dysregulated Let-7 family genes known to be associated with thyroid development. We used QIAGEN's miRNA extraction kit to obtain high-quality miRNA from paraffin-embedded thyroid tissues. We performed next-generation miRNA sequencing using FA (n=4) and EA (n=4) samples and identified the top ten significantly up- and downregulated miRNAs from the pool of differentially regulated miRNAs. We confirmed the differential expression of Let-7 family genes down-regulated in FA versus EA by qPCR assays. For our future work, we plan to analyze multiple up- and down-regulated miRNAs by qPCR, determine whether the miRNA signatures are consistent between samples from FA versus EA, and whether these can be used as diagnostic, prognostic, and predictive biomarkers for thyroid cancer.

EMMANUEL SOLIS
UTP PARTICIPANT 2019

I attend California State University, San Marcos, located in Southern California. I will be going into my fifth year pursuing dual degrees in molecular/cellular biology and biotechnology with a minor in chemistry. As a Ronald E. McNair Scholar and a Louis Stokes Alliance for Minority Participation Scholar, research has been a major contributing factor in molding my future career goals. I will be pursuing a career in medicine with a focus on improving healthcare quality and accessibility in underserved communities. Health disparities is something I am truly passionate about, and I hope to become a family physician and also a site director at a local community health clinic. This career pathway would allow me to have a major influence on improving health disparities in underserved communities.

This summer I worked with Dr. Suburraman Mohan in his research lab at the Musculoskeletal Disease Center at the Jerry L. Pettis Memorial VA Hospital. This research experience has taught me several personal and professional life lessons and values. Under the supervision of Dr. Mohan, I conducted research on the effects of traumatic brain injury on osteoblast differentiation and proliferation.

I would like to thank Dr. Mohan and his research faculty for welcoming me into the lab this summer and teaching me to become a better researcher and critical thinker. This has been such an amazing opportunity.

MILD TRAUMATIC BRAIN INJURY (TBI) IN MICE-INDUCED RELEASES OF OSTEOGENIC GROWTH FACTORS INTO SERUM: A POTENTIAL MECHANISM FOR NEUROLOGICAL HETEROTOPIC OSSIFICATION

Emmanuel Solis, Chandrasekhar Kesavan, Subburaman Mohan
Center for Health Disparities and Molecular Medicine, School of Medicine, Loma Linda University, and Musculoskeletal Disease Center, VA Loma Linda Healthcare System, Loma Linda CA

Heterotrophic ossification (HO), a disorder of an extra-skeletal bone formation in soft tissues, occurs as a common complication of trauma or in rare genetic disorders. It is now well established that patients who suffered from bone fracture combined with TBI are at significantly increased risk of HO. Although the pathophysiology of HO after TBI is poorly understood, recent findings of central nervous system control of bone mass by factors such as leptin, serotonin and neuropeptide Y suggest an important role for humoral factors from injured brain in contributing to peripheral osteogenesis at HO sites. To test the hypothesis that TBI induces release of osteogenic molecules into serum, we tested biologically active serum samples collected from mice subjected to mild TBI or control anesthesia. Eight-week-old mice were subjected to mild TBI using an established weight drop model for four consecutive days and serum collected 24 hours after the last impact. Effects of TBI and control sera on proliferation and differentiation of osteogenic cells were tested under serum-free conditions. We found TBI serum promoted cell proliferation to a greater extent (20%, $P<0.05$) than control sera in both established mouse osteoblast cell line, MC3T3-E. To determine if TBI-induced factors promoted differentiation, we measured alkaline phosphatase activity, a measure of osteoblast differentiation, after treatment with sera from mild TBI and control mice. We found sera from TBI mice increased ALP activity by 50% ($P=0.07$) compared to control sera in MC3T3. In conclusion, our *in vitro* data demonstrate TBI-induced factors in serum stimulate both proliferation and differentiation of osteoblast lineage cells, thereby providing a potential mechanism for neurological HO.

NEIHYARIE K. VELEZ VILLARRUBIA

UTP PARTICIPANT 2019

Born and raised on the beautiful island of Puerto Rico, I enjoy spending time with family and friends, playing the French horn, and participating in outdoor activities. I am currently pursuing a Bachelor of Science in Industrial Microbiology at the University of Puerto Rico, Mayagüez. Since childhood, I wondered how I could have a part in changing the world with small acts of service that bring happiness and comfort. My joy has come from these defining moments leading me to pursue a life dedicated towards serving others.

My interest in healthcare increased after participating in a medical missionary trip to Cusco, Perú. This truly eye-opening experience shaped the way I see healthcare and reconfirmed my profound desire to become a physician, researcher, and educator in the mission field. I am fascinated by the complexity of the human mind and body and how nutrition affects both. This summer has allowed me to learn more about the interplay between these factors as well as think hard, explore, and grow as a scientist and a person. Therefore, I am extremely grateful to Dr. Johnny Figueroa for the privilege of working in the Fig NeuroLab and to my mentors, IMSD graduate students Perla Ontiveros Angel and Julio Vega-Torres, for teaching me the skill set required to thrive as a researcher.

I believe this program is helping me achieve my future goal of making a personal impact on people's lives by providing whole person care to every patient as a physician. As a future provider of healthcare and following Jesus' example on earth of being a helping hand and having a compassionate heart, I want to make a difference through service, research, and innovation in order to create a more inclusive, improved and healthier tomorrow.

THERAPEUTIC POTENTIAL OF EXOGENOUS NEUREGULIN 1 FOR DIET-INDUCED HIPPOCAMPAL INFLAMMATION

Neihyarie Vélez Villarrubia, Perla Ontiveros Ángel, Julio Vega-Torres, Johnny Figueroa
Center for Health Disparities and Molecular Medicine, Department of Basic Sciences,
School of Medicine, Loma Linda University, Loma Linda, CA

Early-life exposure to detrimental environmental factors such as high-fat/high-sugar diets has been linked to the onset of cognitive and psychiatric morbidities. Consumption of obesogenic diets during adolescence causes abnormal maturation of the hippocampus, a brain structure implicated in cognition and emotional responses. However, the cellular mechanisms implicated in these structural impairments remain poorly understood. Hippocampal microglia cells are highly vulnerable to the effects of obesogenic diets and play an active role in neuroinflammation and diet-induced cognitive impairments. Recent research demonstrates that neuregulin-1 (NRG1) modulates microglial proliferation and activation and has been shown as an essential component for normal neuronal development. This study investigates the efficacy of exogenous NRG1 administration to reduce microglia-associated inflammatory responses in juvenile rats exposed to an obesogenic Western high-fat/high-sugar diet (WD). Lewis rats were randomly divided into four groups based on diet type and NRG1 administration (12-rats/group). Cytokines were measured in the hippocampus using LEGENDplex™ technology and analyzed by flow cytometry. For microglial characterization, hippocampal tissue was stained for Iba-1 using immunohistochemistry and imaged by confocal microscopy. We found the WD increased the hippocampal levels of several regulatory cytokines, including IL-1α, IL-1β, and IL-10. Interestingly, we found the WD decreased IL-6 levels in the hippocampus. Analyses showed NRG1 administration reduced the levels of the proinflammatory cytokine TNF-α. These findings confirm that the consumption of a WD activates robust inflammatory responses in the hippocampus and identify NRG1 as a potential intervention to ameliorate the detrimental effects in an otherwise vulnerable brain. These findings can lead to new interventions to improve cognitive outcomes in at-risk youth exposed to obesogenic diets.

ROLAND WILLIAMS
UTP PARTICIPANT 2019

One of the best decisions I made was when I decided I wanted to do summer research. I did not know the possible endeavors and experiences I would eventually be exposed to when I decided to apply to a research program. This summer has been very special to me because I finally was given the opportunity to have many of my scientific inquiries answered. Being exposed to the many scientific advancements I have read about made this summer a gratifying experience for me.

I currently am attending Oakwood University in Huntsville, AL. This coming fall I will be a junior and continuing my major in biology. I started my premedical journey with the aspirations of one day becoming an oncologist. While at Oakwood, I have taken many science courses that have built not only a strong foundation but a love for science.

Since I have been at Oakwood, my interest for scientific studies has multiplied exponentially. Being taught the many scientific routes to explore, a part of me grew a fitting fascination for cancer biology. I was given advice to apply to a summer research program to enrich my scientific knowledge and experience. When I was accepted, I was glad to see so many cancer research studies being done. Having so many family members and friends affected by the disease, I was happy to be participating in Dr. Kimberley Payne's research on B-Cell acute lymphoblastic leukemia (B-ALL) especially since my brother as a child had T-cell acute lymphoblastic leukemia (T-ALL).

I thank Dr. Cornelia Stoian, Mavely Baez, and the rest of Dr. Payne's lab for showing me how to become a better scientist and how the scientific community is working to treat cancer.

THE EFFECTS OF HIGH-DOSE TSLP ON B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA

Roland Williams, Hossam Alkashgari, Ineavely Baez, Cornelia Stoian, Kimberly Payne
Center for Health Disparities and Molecular Medicine, School of Medicine,
Loma Linda University, Loma Linda, CA

B-cell Acute Lymphoblastic Leukemia (B-ALL) is the most common leukemia in children and most deadly in adults. A high-risk subgroup of B-ALL is characterized by upregulation of cytokine receptor-like factor 2 (CRLF2). CRLF2 B-ALL occurs five times more often in Hispanic children with <30% survival rate. Receptors components CRLF2 and interleukin-7 receptor alpha (IL-7Ra) form a complex for the cytokine, thymic stromal lymphopoietin (TSLP), helping leukemia cells survive and proliferate. However, in high amounts, we observed TSLP has antileukemic effects, *in vivo*, in human CRLF2 B-ALL models. We hypothesize this antileukemia effect is caused by internalization of the IL-7Ra when cells are exposed to high-dose TSLP. MUTZ-5, a cell-line derived from a 26-year-old man with CRLF2 B-ALL, was cultured for one hour and twenty-four hours with and without TSLP at normal physiological levels and at increasing concentrations. We determined TSLP effects on CRFL2 signaling by culturing MUTZ-5 with different levels of TSLP. After 24 hours, TSLP was washed and rested for 2 hours. Cells were then stimulated or unstimulated by TSLP for an additional 30 minutes and assessed by phospho flow cytometry to detect STAT5 phosphorylation. Flow cytometry data showed all TSLP concentrations induced IL-7Ra internalization at one hour. At 24 hours, surface levels of IL-7Ra returned to normal or near normal levels with physiological levels of TSLP but not at higher levels. Phosphorylation assays showed cells cultured with high dose TSLP were not responsive to further stimulation with TSLP indicating CRLF2 signal inhibition. High-dose TSLP causes internalization of IL-7Ra correlating with a loss of receptor signaling. These results explain why TSLP can lead to leukemia cell survival and proliferation at low levels but exert anti-TSLP effects at high levels. These data support use of TSLP as a biologic for treating CRLF2 B-ALL.

SHANDELLE WILLIAMS
UTP PARTICIPANT 2019

Marian Wright Edelman, an American activist for children's rights, once said, "Education is for improving the lives of others and for leaving your community and world better than you found it." Serving my community has always been my desire. I started my service journey by volunteering with a medical team that travels to underserved countries providing medical, dental, and health education services. With a passion for service, I have also started an educational project where I collect school supplies and distribute them to people in underserved communities. This research program at Loma Linda University has allowed me to continue my service expedition as well as increase my knowledge of the inequalities in the healthcare field.

Born and raised on the beautiful island of Saint Lucia, I am a senior biology major at Oakwood University, Huntsville, AL. The anatomy and physiology of the human body are incredibly fascinating and inspire me to continue my search for how I can help people understand the body's systems and educate people on the benefits of a healthy lifestyle. In the future, I hope to expand my knowledge by enrolling in an MD program with a focus on primary care and continue my service journey by opening an out-patient clinic in my community.

I am incredibly thankful for this opportunity to participate in the UTP program this summer, to learn about Type 2 Diabetes on a cellular level, and to learn about health disparities. I would like to thank Dr. Marino De León for welcoming me in his lab and Dr. Alfonso Durán for challenging me intellectually and being patient.

DOCOSAHEXAENOIC ACID PROTECTS SCHWANN CELLS FROM LIPOTOXICITY BY UPREGULATING SPHINGOSINE KINASE-1: IMPLICATIONS IN PAINFUL DIABETIC NEUROPATHY

Shandelle Williams, Alfonso Durán, Jennifer Licero, Jo-Wen Liu, Marino De León
Center for Health Disparities and Molecular Medicine, School of Medicine,
Loma Linda University, Loma Linda, CA

Diabetic Neuropathy (DN), also known as distal symmetrical polyneuropathy, affects approximately 50% of individuals with type 2 diabetes; of those patients experiencing DN symptoms about half report neuropathic pain. Lipotoxicity-mediated sphingolipid metabolism dysregulation in Schwann cells (SC) is an important cellular pathway in the pathogenesis of DN. The aim of this project was to characterize how modulation of Sphingosine Kinase -1 (SphK-1) activity by DHA reverses lipotoxicity-mediated sphingolipid dysregulation in rat immortalized SC (iSC). We hypothesize that DHA will reverse lipotoxicity-mediated sphingolipid dysregulation by increasing SphK-1 activity. Characterization of SphK-1 activity was measured in both lipotoxic (palmitic acid) and lipotoxic-reversing conditions (DHA). To measure protein expression under both lipotoxic and lipotoxic-reversing conditions, western blot assays were conducted. Further, to understand the relationship between SphK-1 and autophagy, a suggested mechanism of SC protection from lipotoxicity, we measured key proteins associated with the activation of autophagy using western blot. Our results indicate that 25μM and 10μM DHA treatment at 6 hours significantly ($p<0.05$) increased SphK-1 phosphorylation compared to control (BSA). In contrast, SphK-1 was negatively modulated following 1, 3, and 6 hours of palmitic acid treatment. Additionally, western blot analysis of iSCs showed that autophagic proteins were regulated in the presence of DHA. These findings support our hypothesis that DHA can reverse toxic levels of sphingolipids and activate neurorestorative pathways that can modulate painful diabetic neuropathy.

ERIC XIAO

UTP PARTICIPANT 2019

When I was younger, I always enjoyed asking questions. Seeking those answers fulfilled my childish curiosity. But there were some questions my teachers could not answer, and there were some questions that had no definitive answer. If I wanted an answer, I would have to try to wait for research to progress or find out for myself as a researcher. This drive for answers is why I believe research and computer science are incredibly important.

I am currently a student at the University of Maryland, College Park, majoring in computer science. I believe that computer science will play a crucial role in solving modern problems, especially since many of those problems require extensive calculations. But with all the broad applications for computer science and so many unanswered questions, I am conflicted as to what specialization I want to pursue. From proving mathematical theorems to sequencing the human genome, there are many directions to choose from.

I am grateful to Dr. Charles Wang and the Center of Genomics for this opportunity to explore the field of bioinformatics. I am also grateful to the Center for Health Disparities and Molecular Medicine for their seminars and support. I hope that my time in the UTP will guide me to a successful and fulfilling career.

ALTERNATIVE SPLICING IN DOCETAXEL-RESISTANT DU-145 PROSTATE CANCER CELLS

Eric Xiao, Xin Chen, Charles Wang, Carlos Casiano
Center for Genomics, Center for Health Disparities and Molecular Medicine,
School of Medicine, Loma Linda University, Loma Linda, CA

Prostate cancer has the highest incidence rate of all cancers among men and is the second highest leading cause of cancer-related deaths among men. One of the most common forms of treatment for prostate cancer is chemotherapy which includes docetaxel (DTX). However, prostate cancer cells can develop resistance to DTX. A major mechanism responsible for DTX-resistance is the presence of "cancer stem-cells" (CSC) and different gene and isoform expressions in the CSCs. We examined differential isoforms and alternative splicing of genes using the rSeq pipeline and leafcutter pipeline between DTX-treated and non-treated Du-145 cells to identify genes and isoforms likely responsible for the development of DTX-resistant prostate cancer cells. Leafcutter was used to identify differences in exons and introns incidence between DTX-treated and control DU-145 cell groups, organized by gene and chromosome. rSeq was used to analyze isoform expression and alternative splicing events. Of 3,737 genes that showed differential expression, 145 had multiple variants with a false discovery rate of less than 5% and were likely to be alternatively spliced. Of these 145 genes, ATAD3A had the highest level of differential splicing. ATAD3A has been suggested to be associated with drug resistance in prostate cancer cells. Other genes associated with cancer cell properties, such as CEP55, were also found in the subset of 145 genes. Downregulation of CEP55 has been suggested to instigate cell apoptosis and suppress tumor growth. Of the genes identified by Gene Set Enrichment Analysis (GSEA), only WDR25 had multiple variants with a false discovery rate of less than 5% and was likely to be alternatively spliced. Several GSEA selected genes had altered relative abundances of isoforms between DTX-resistant DU-145 and control DU-145 cells.

Medical Training Program (MTP)

Keelie Denson
Christian Irizarry Cruz
Joanneth Padro Serrano
Reuben Plasencia
Raul Rios Orsini

KEELIE DENSON
MTP PARTICIPANT 2019

Motor neurons, though microscopic, have changed the trajectory of my life. As I was learning how to tie my shoes and write, my dad was losing these abilities due to the selective death of motor neurons, a disease known as Amyotrophic Lateral Sclerosis (ALS). I graduated from the University of Georgia with a degree in cellular biology several years after my dad's death, but his battle with ALS stuck with me. My ability to empathize with patients due to my personal experiences combined with my interest in science led me to pursue a medical career at the Medical College of Georgia.

My dad received care from a neurologist in Georgia who centered his clinic around aggressively fighting ALS with a positive attitude. Instead of being told he would die in three years, he was filled with hope and given the tools to live his life with purpose. The positive impact this physician had on my dad's journey with ALS, combined with my dad's perseverance and optimism, inspired me to strive to fight for patients with ALS in the same manner.

This summer I have had the opportunity to work with the neurologist who treated my father on a project deciphering the heterogeneity in ALS. I would like to thank Dr. Jeffrey Rosenfeld and the Medical Training Program for welcoming me with open arms. I am forever grateful for the knowledge I have gained, and I hope we are one step closer to ending ALS.

PHENOTYPIC HETEROGENEITY IN AMYOTROPHIC LATERAL SCLEROSIS: A POTENTIAL EXPLANATION FOR THERAPEUTIC FAILURE

Keelie Denson, Jeffery Rosenfeld
Center for Restorative Neurology, Loma Linda University, Loma Linda, CA

Current diagnostic criteria for amyotrophic lateral sclerosis (ALS) results in a heterogeneous patient population for clinical trials. The variability in patients' presentation has resulted in a large spectrum of clinical signs and symptoms that may represent distinct disease entities under the heading of ALS. This variability may explain why progress made in elucidating the etiology and pathophysiology of ALS has not been translated into effective treatments. The objective of this study was to utilize a new diagnostic scheme to stratify the disease presentation. We also identified the clinical course of the stratified groups using the ALS functional rating scale (ALSFRS-R), a highly validated measure. Retrospective chart reviews were conducted on patients with ALS presenting at Loma Linda University's ALS clinic between April 2013 and July 2019. Patients' clinical presentation was categorized on four axes, depicting the extent of upper motor neuron (UMN), lower motor neuron (LMN), bulbar (BLB), and behavioral/cognitive involvement. Heat map analysis was utilized to identify trends in phenotypic progression to determine if the pattern indicated on a patient's presentation was maintained and if there were differences in the clinical course in the various subgroups. ALSFRS-r summary score slopes were calculated for individual patients, and then average slopes for preliminary phenotypical subgroups were determined. Utilization of the four axes revealed distinct phenotypical subgroups. Of 28 patients presenting with LMN predominance, 75% remained LMN predominant, and 100% had LMN involvement one year after initial presentation. Patients with BLB predominance appeared to become more generalized after the nine-month mark when compared to one year (100% vs 45.5% remaining BLB predominant). Based on the rate of change in the ALSFRS, a distinct pattern of progression was identified for some of the subgroups. Our work demonstrates the necessity to further investigate the stratification of disease presentation in ALS.

CHRISTIAN R. IRIZARRY CRUZ

MTP PARTICIPANT 2019

You are about to witness the strength… So you just started reading my biography, and I appreciate your interest in reading it. I will start by saying I am a basketball player and hip-hop aficionado, as you notice from my opening line, and it is something that represents my personality. I consider myself an optimistic person with a positive spirit, something all my friends appreciate about me. It has been a long journey to get to this point in my short career as a student. I earned a bachelor's degree in general sciences and a master's degree in medical sciences all on the beautiful island of Puerto Rico. Now knowing this information, here is a little bit more about me in the present.

I attend Ponce Health Sciences University in Ponce, Puerto Rico, where I will be a second- year medical student. My interest in pursuing medicine stems from the passion I have for helping improve the lives of others through science. I have been mentoring pre-medical students since I started medical school. I created a group with my colleagues where we go every month to a university to mentor students about medical school and the requirements needed to get a successful admission. My goals are to provide healthcare for patients that need it the most, improve education for students, and empower everyone to improve their own lives.

I want to thank Dr. Mary Kearns-Jonker and Victor Camberos for welcoming me in their laboratory during this summer, teaching me how to work with cardiac cells, and helping me improve my knowledge in the research field. I am extremely grateful for their guidance and the skills developed that will help me in my future medical profession.

EOMESODERMIN EXPRESSION IN ISLET-1+ CARDIAC PROGENITOR CELLS

Christian Irizarry Cruz, Victor Camberos, Luz Velasco, Ana Mandujano, Leonard Bailey, Nahidh Hasaniya, Mary Kearns-Jonker
Department of Pathology and Human Anatomy and Cardiovascular and Thoracic Surgery, School of Medicine, Loma Linda University, Loma Linda, CA

Cardiovascular diseases are the leading cause of death in the United States. Various types of stem cell therapies are currently being evaluated as potential therapeutic options. Our laboratory is studying early stage cardiac progenitor cells (CPCs) that express Islet-1+, a transcription factor required for cardiac development. The objective of the current study was to determine whether or not Eomesodermin (EOMES), a transcription factor expressed transiently at the mesendoderm stage of development, is expressed in Islet-1+ CPCs and to determine whether neonatal and adult Islet-1+ CPCs express comparable levels of this early-stage transcription factor. Recent studies have shown that the Islet-1+ neonatal early–stage CPCs isolated in our lab enhance cardiac repair in sheep post-infarction. We hypothesize that expression of the transcription factor EOMES will be identified at higher levels in neonatal CPCs when compared to adults. In order to test this hypothesis, we purified RNA from Islet-1+ CPCs clones and prepared cDNA for PCR. Transcripts encoding EOMES were expressed at high levels in subpopulations of both neonatal and adult CPCs along with other early-stage markers. Gel electrophoresis confirmed the correct size of the amplified EOMES transcript. In addition to PCR analysis, flow cytometry verified EOMES expression in neonatal CPCs. Further experiments are needed to validate EOMES expression in adult CPCs via flow cytometry. Characterization of the transcriptome of neonatal and adult CPCs is needed in order to identify age- dependent differences in CPCs subpopulations that may influence the efficacy of these cells as therapeutic agents for human cardiovascular disease patients.

JOANNETH M. PADRÓ SERRANO

MTP PARTICIPANT 2019

Throughout my life, a mosaic of experiences has inspired me to choose medicine as my future career. My dedication to medical biology and the human body has guided me to pursue medicine. The opportunities I've had to volunteer in clinics and hospitals have allowed me to relate, listen, and empathize with others. In August, I will begin my second year as a medical student at the San Juan Bautista School of Medicine, located in Caguas, Puerto Rico. Currently, I am exploring various specialties, and as a future physician I aspire to work in a residency that fits my interest, passions, and capabilities.

Though rewarding, there was something missing in my vocation. My love for discovery and inquisitiveness persisted, leading me to realize that research would be an essential part of my formation as a future physician. These experiences and desires have brought me to participate in the Medical Training Program.

This summer I worked in Dr. Wolff Kirsch's lab, mentored by Nicholas Sanchez. Our research is mostly focused on establishing how copper accumulation within axons is related to Alzheimer's disease and investigating the effect of APOE4 allele on synaptic pruning and copper deposition. This program gave me an unforgettable opportunity to work with a relevant problem, awakening an immense curiosity of learning about Alzheimer's disease, and giving me the opportunity to challenge myself with new techniques and disciplines. My mentor and colleagues have been very helpful in guiding me through the program, making this experience one I will cherish for the rest of my life.

Alongside my love for science, research, and service to others, I enjoy photography which provides an outlet to view the world through a new perspective.

COPPER DEPOSIT COMPARISONS BETWEEN ALZHEIMER'S DISEASE SEVERITY IN VARIOUS BRAIN REGIONS

Joanneth Padró Serrano, Nicholas Sanchez, Wolff Kirsch
Neurosurgery Center for Research, Training and Education, Department of Biochemistry, School of Medicine, Loma Linda University, Loma Linda, CA

"Oxidative stress," particularly instigated by dysregulated transition metal metabolism in the brain, plays an important role in the pathogenesis of Alzheimer's disease (AD). Cycling copper (Cu) between monovalent [Cu(I)] and divalent [Cu(II)] states makes the element potentially neurotoxic by promoting reactive oxygen species production. Preliminary studies show 1) Cu deposits in neuronal axons, 2) decreased Cu in synaptosomal fractions, and 3) reduced Cu transport proteins as emerging diagnostic indicators in AD brains. These findings were not as apparent in patients diagnosed with AD with Cerebral Amyloid Angiopathy (CAA). **We hypothesize a greater amount of copper deposits will be observed in AD-only brain samples when compared with control or AD with CAA.** The newly developed fluorescent probe (CRISP-17), highly specific to monovalent copper, was used to visualize axonal copper in post-mortem human brain tissue. Samples used were taken from patients exhibiting a diagnosis of 1) AD, 2) AD with mild CAA, 3) AD with severe CAA, or 4) no dementia (control). Sections were taken from the frontal, temporal, and occipital lobes cut to 8 µm. Two-photon microscopy was used to acquire images in 457-536 nm and 611-750 nm wavelengths. Images were processed in ImageJ. The fluorescence ratio increased as AD diagnosis progressed with AD/CAA severe brain samples having highest readings compared with non-diagnosed samples. AD-only brain comparisons were inconsistent between brain regions, with a reduction found in the temporal lobe and increased in the occipital lobe. Frontal lobe readings varied depending on the area sampled. Findings in the temporal brain (the region most affected by AD) sections were consistent with the hypothesis. These findings are imperative for narrowing our focus in the future of this project.

REUBEN RAPHAEL PLASENCIA

MTP PARTICIPANT 2019

My interest in health disparities arises from my family history. I am a Chicago-native, born and raised by Hispanic parents (first generation immigrants to this country) from Peru. They, like any other immigrant, had to overcome the adversities of living and forming a family in a new country. One of those adversities was health (breast cancer in my mother and myocardial infarction in my father), and this is where my interest in health disparities arises.

I completed my undergraduate coursework at Southern Adventist University in 2013. Currently, I attend Montemorelos University School of Medicine in the country of Mexico. My career plans are to complete my medical school training for a medical diploma in January and go on to specialize in a primary care-oriented residency program in the United States such as internal medicine. Following residency I plan on pursuing a fellowship in lifestyle medicine. My long-term goal is to be practicing medicine as a primary care physician to a medically underserved Hispanic-majority patient-base in the United States using lifestyle medicine as my main emphasis in prevention and treatment for many of the chronic, non-communicable diseases prevalent today in underserved communities.

I want to thank Dr. Daisy De Leon's lab for welcoming me this summer and for their patience and teachings. This has been an opportunity where I have been able to develop skills as a researcher and will carry this mindset on as a clinician to better serve the underserved.

RESVERATROL SENSITIZES TRASTUZUMAB-RESISTANT BREAST CANCER CELL LINES

Reuben Plasencia, Xousaen Helu, Qianwei Tan, Daisy De Leon
Center for Health Disparities and Molecular Medicine, Breast Cancer Laboratory,
School of Medicine, Loma Linda University, Loma Linda, CA

Breast Cancer (BC) is the most frequent and deadly cancer among women. Twenty to thirty percent of all diagnosed breast cancer cases overexpress Human Epidermal Growth Factor Receptor 2 (HER2). HER2 is a tyrosine kinase receptor that plays a role in the development and aggressiveness of breast cancer. The most effective treatment for this type of BC is a monoclonal antibody that targets HER2, known as trastuzumab. Although trastuzumab is one of the most effective treatments, 30% of patients with HER2-overexpressing tumors do not benefit from it. Therefore, understanding the mechanisms of trastuzumab resistance is important for the development of new therapeutic strategies for this type of BC. Our lab demonstrated cell growth of HER2 overexpressing JIMT1 BC cells was blocked when IGF2 was inhibited with resveratrol. These findings led us to hypothesize that trastuzumab-resistant cell lines were IGF2-growth dependent. To test our hypothesis, we chose the CRL-2326 and the CRL-2330 BC cells because they are trastuzumab-resistant and they produce IGF2. Initially, we sought to characterize the protein levels of IGF2, IGF1R, InsR, HER2, and HER3 in both cell lines using Western Blot analysis. Cells were plated in 96 well plates with SF media for 72 hrs. Treatment with resveratrol was initiated at time 0 to assess if resveratrol inhibited IGF2 expression and if cells responded to trastuzumab therapy. Cell viability was assessed using WST1. Our results showed CRL-2326 and CRL-2330 cell lines have increased levels of IGF2. Resveratrol treatment decreased cell viability. Trastuzumab treatment is in progress. Characterizing the protein levels shows that IGF2 was present in these resistant cell lines and that resveratrol decreases cell viability. This work shows IGF2 could be a potential biomarker for trastuzumab therapy responsiveness.

RAUL RIOS ORSINI

MTP PARTICIPANT 2019

I am a second-year medical student at San Juan Bautista School of Medicine, a community-based medical school in Caguas, Puerto Rico. More than a medical student, I am a husband, son, and brother in an amazing family. Even more so, I'm obsessed! I am obsessed with making a difference in the quality of people's lives. I have always been driven to serve and help people. In fact, it is the reason for everything I have done, am doing, and will do. It is why I am pursuing a career in medicine and why I have participated in medical missions and exposed myself to diverse environments and opportunities focusing on being of service to people, the latest being Loma Linda University's Medical Training Program.

I had the opportunity to be part of the Fig NeuroLab™ where, alongside Matine Azadian and Julio Vega-Torres, I researched the impact a Western high-saturated fat/high-sugar diet has on the immediate-early expression of a neuronal activity marker known as c-Fos in the main corticolimbic centers. It has been a blessing to work in the Fig NeuroLab™, not only because of the amazing mentors I had in Dr. Johnny Figueroa, Perla Ontiveros Angel, Matine Azadian and Julio Vega-Torres, but because of the opportunity to delve into translational research directly related to my career goals of becoming a psychiatrist centered on treating mental illness through nutraceutical interventions and therapeutic lifestyle changes.

This program has been an enriching experience where I've furthered my academic career and skills. More importantly, it has provided invaluable insight to address health disparities and, therefore, better equipped me to make that difference in the quality of people's lives.

MAPPING THE IMPACT OF SHORT-TERM EXPOSURE TO OBESOGENIC DIETS AND FOOT SHOCK STRESS ON CORTICOLIMBIC CIRCUITS

Raul Rios Orsini, Matine Azadian, Julio Vega-Torres, Johnny Figueroa
Center for Health Disparities and Molecular Medicine, Department of Basic Sciences,
School of Medicine, Loma Linda University, Loma Linda, CA

Substantial evidence documents a complex link between obesity and stress-related mental disorders, including post-traumatic stress disorder (PTSD). Surprisingly, studies examining how early-life exposure to obesity and obesogenic diets disrupt the ability of the brain to cope with stress are lacking. Given that aberrant fear responses are fundamental to PTSD pathogenesis, the objective of this study was to determine the impact of early-life exposure to an obesogenic diet and traumatic stress on the neural activity of key corticolimbic regions involved in fear-responses. We approached this research by subjecting both adolescent and adult Lewis rats to two weeks of an obesogenic refined Western-like high-fat/high-sugar diet (WD) or a refined, ingredient-matched control diet (CD) for a total of four groups (12 rats/group). We utilized the fear-potentiated startle (FPS) behavioral paradigm and c-Fos mapping immunohistochemistry to determine the impact of the WD and age on fear behaviors and circuits, respectively. We found the rats that consumed the WD during adolescence exhibited fear extinction deficits when compared to controls. Interestingly, short-term exposure to the WD did not alter FPS behaviors in the adult rats. These behavioral outcomes were associated with reduced c-Fos immunoreactivity in the medial prefrontal cortex of the adolescent rats that consumed the WD. Our findings indicate that adolescence is a sensitive period to the effects of obesogenic diets on fear-related behaviors and circuits. Having a better understanding of early brain responses to obesogenic environments may contribute to innovative preventative, curative, and disease-modifying approaches for mental health disparities.

Initiative to Maximize Student Development (IMSD)

Victor Camberos
Tatianna Clark
Alfonso Durán
Jerry Flores
Jenniffer Licero Campbell
Karina Mayagoitia
Perla Ontiveros Angel
Greisha L. Ortiz Hernández
Foluwasomi Oyefeso
Hiel Rutanhira
Evelyn S. Sanchez-Hernandez
Nicholas Sanchez
Paul Vallejos
Julio D. Vega-Torres
Jonathan Wooten

VICTOR CAMBEROS

IMSD PARTICIPANT 2019

I am a fourth-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 that we are pursuing involves investigating the effect of spaceflight and microgravity on cardiac progenitor cells and searching for ways that 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 always been fascinated by them because stem cells offer so much potential for treating diseases and 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.

EOMESODERMIN EXPRESSION IN ISLET-1+ CARDIAC PROGENITOR CELLS

Victor Camberos, Christian Irizarry Cruz, Luz Velasco, Ana Mandujano, Leonard Bailey, Nahidh Hasaniya, Mary Kearns-Jonker
Department of Pathology and Human Anatomy and Cardiovascular and Thoracic Surgery, School of Medicine, Loma Linda University, Loma Linda, CA

Cardiovascular diseases are the leading cause of death in the United States. Various types of stem cell therapies are currently being evaluated as potential therapeutic options. Our laboratory is studying early stage cardiac progenitor cells (CPCs) that express Islet-1+, a transcription factor required for cardiac development. The objective of the current study was to determine whether or not Eomesodermin (EOMES), a transcription factor expressed transiently at the mesendoderm stage of development, is expressed in Islet-1+ CPCs and to determine whether neonatal and adult Islet-1+ CPCs express comparable levels of this early-stage transcription factor. Recent studies have shown that the Islet-1+ neonatal early–stage CPCs isolated in our lab enhance cardiac repair in sheep post-infarction. We hypothesize that expression of the transcription factor EOMES will be identified at higher levels in neonatal CPCs when compared to adults. In order to test this hypothesis, we purified RNA from Islet-1+ CPCs clones and prepared cDNA for PCR. Transcripts encoding EOMES were expressed at high levels in subpopulations of both neonatal and adult CPCs along with other early-stage markers. Gel electrophoresis confirmed the correct size of the amplified EOMES transcript. In addition to PCR analysis, flow cytometry verified EOMES expression in neonatal CPCs. Further experiments are needed to validate EOMES expression in adult CPCs via flow cytometry. Characterization of the transcriptome of neonatal and adult CPCs is needed in order to identify age- dependent differences in CPCs subpopulations that may influence the efficacy of these cells as therapeutic agents for human cardiovascular disease patients.

TATIANNA CLARK
IMSD PARTICIPANT 2019

I am a first-year student in the Biomedical Sciences PhD program at Loma Linda University as well as an IMSD student. I completed my undergraduate work at San Diego State University where I studied public health and kinesiology.

Prior to my time here at Loma Linda, my research career began in a cancer disparities lab where we focused on healthcare policies and socioeconomic barriers affecting equitable access to cancer care for minorities. This work opened my eyes to the many surmountable barricades to quality health outcomes that need only the right amount of pressure to be removed. Since then, I have settled my passions on perinatal and developmental sciences where I intend to improve maternal and fetal health, giving extra attention to African Americans and other people of color known to experience disparate health outcomes. My life-long goal is to serve these communities by improving scientific knowledge, policy, and care. I believe in the concept of "a preferential option for the poor." It's what drives me in this work where "poor" can be seamlessly interchanged for all underserved.

While at Loma Linda, I have been able to conduct research in both of my areas of interest with specific focus on maternal and fetal morbidities such as preeclampsia and limb dysmorphia.

ACTIVITY OF AN *LMX1B*-ASSOCIATED CIS-REGULATORY MODULE SUGGESTS FUNCTIONS IN MULTI-ORGAN DEVELOPMENT

Tatianna Clark, Kenrick Wysong, Charmaine Pira, Kerby Oberg
Center for Health Disparities and Molecular Medicine, Pathology and Human Anatomy, School of Medicine, Loma Linda University, Loma Linda, CA

Lmx1b is a transcription factor critical for the normal development of the cerebellum, eyes, kidneys, and limbs. However, the induction and regulation of *Lmx1b* are poorly understood. We previously identified two conserved *Lmx1b*-associated regulatory modules (*Larm1/2*) that are bound by Lmx1b, autoamplify limb-specific *Lmx1b* expression, and are required for normal limb development. In addition to these limb-specific cis-regulatory modules (CRMs), another potential CRM is located 10 kb upstream of *LARM1/2*. Although ChIP-seq analysis did not demonstrate Lmx1b binding to this CRM, its proximity to *Lmx1b* and active chromatin marks suggest activity during limb development. We hypothesized that this third regulatory module (*LARM3*) was also involved in *Lmx1b* regulation. To test this hypothesis, we isolated *LARM3* from mouse genomic DNA and generated a GFP-reporter construct. This *LARM3*-reporter construct was electroporated into the presumptive limb of Hamilton-Hamburger stage 14 (HH14) chicken embryos. To determine whether *LARM3* was involved in the regulation of other Lmx1b-associated organs, we performed whole embryo electroporation (HH4). *LARM3* activity during development was digitally recorded using fluorescence microscopy up to 48 hours after transfection. We found that *LARM3* was active within limb mesoderm without dorsoventral bias. *LARM3* also had punctate activity in intermediate mesoderm consistent with mesonephric (kidney) development. These data suggest that *LARM3* may function to regulate *Lmx1b* expression in multiple Lmx1b-associated organs. Further studies are warranted to confirm these findings and evaluate possible cerebellar and eye *LARM3* activity.

ALFONSO DURÁN
IMSD PARTICIPANT 2019

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, improving a community's health is almost impossible, especially when dealing with chronic diseases such as obesity and diabetes.

Thus, I elected to put residency on hold and pursue a PhD in physiology. My current research involves metabolomics studies of Latinos with chronic diseases to identify critical bio-markers and elucidate major metabolic pathways involved in the pathophysiology contributing to health disparities. Metabolomics can inform 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.

METABOLOMICS UNCOVERS KEY NEURORESTORATIVE PATHWAYS AFTER DIETARY OMEGA-3 POLYUNSATURATED FATTY-ACID SUPPLEMENTATION IN PARTICIPANTS WITH TYPE 2 DIABETES

Alfonso Durán, Justin Câmara, 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 the metabolomic impact of dietary omega-3 polyunsaturated fatty acid (PUFA) supplementation on neurorestorative pathways associated with anti-nociception in participants with type 2 diabetes (T2DM). Forty volunteers with T2DM, with and without neuropathic pain symptoms, enrolled in the "En Balance-Plus" program. The program provided weekly nutrition-diabetes education and daily supplementation with 1,000mg of docosahexaenoic acid and 200mg of eicosapentaenoic acid over three months. The study assessed plasma samples from all participants at baseline and three months. Metabolon® performed the untargeted semiquantitative metabolomic analysis. A bioinformatics approach was performed to elucidate if important neurorestorative metabolomic features and pathways were associated with supplementation. A total of 659 compounds of known identity were classified using an untargeted metabolomics approach. Matched pairs t-test was used, $p<0.05$, to identify biochemicals differing significantly between experimental groups. An estimate of the false discovery rate (q-value) was calculated to take into account multiple comparisons in this study. One hundred twenty-four compounds significantly changed from baseline; specifically, 74 increased while 49 biochemicals decreased in relative abundance. Random Forest (RF) classification of samples collected at baseline and three months was 91 % accurate. Further, taking several bioinformatic approaches, key features contributing to group separation were enriched with compounds of glycolipids, glucose, cysteine, methionine, and glutathione metabolism. Metabolic profiling was conducted to observe how dietary omega-3 PUFAs affected the metabolic phenotype of participants with T2DM. High-level analysis of data by RF and p-value sorting pointed to changes in omega-3 PUFA metabolism, glycerolipid metabolism, cysteine, methionine, glutathione metabolism, and fatty acid homeostasis. These findings support using omega-3 supplementation as part of a balanced diet may improve neuronal metabolic profiles of individuals with T2DM.

JERRY FLORES
IMSD PARTICIPANT 2019

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 pathophysiologyies. Through this program, I met Dr. John 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 3 first and 27 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, which is 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 Zhang
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.

JENNIFFER LICERO CAMPBELL

IMSD PARTICIPANT 2019

Jenniffer Licero, a name which some have correlated with the feelings bubbly and happy, is a courageous, humble, hardworking, devoted, focused and happy 29-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 if 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. I am excited for what the future holds and cannot wait to continue growing professionally and also contribute to the greater body of thinkers who want to learn more about the world and make it a better place.

EFFECTS OF FABP4 INHIBITION ON FUNCTIONAL AND AUTONOMIC RECOVERY IN RATS FOLLOWING SPINAL CORD INJURY

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

Fatty Acid Binding Protein 4 (FABP4) is a modulator of inflammation that promotes a pro-inflammatory environment not conducive to cell survival. Upregulation of this protein in cancer and chronic inflammatory diseases such as diabetes and metabolic syndrome is becoming increasingly important in the etiology of these conditions. Nevertheless, its presence and function in the context of spinal cord injury (SCI) has not been reported. The pathology of traumatic spinal cord injury (SCI) results from an initial mechanical insult followed by secondary, inflammatory, processes. The secondary phase of injury is characterized by a marked deregulation in lipid metabolism leading to an inflammatory response known to cause axonal dieback, neuronal and oligodendrocytic death, and expansion of the injury. Lipid binding proteins, like fatty acid binding protein 4 (FABP4), are known to guide macrophage differentiation, particularly in the presence of pro-inflammatory lipids. The present study (1) examines the spatial-temporal expression and functional context of FABP4 following SCI in injured spinal cord epicenters and (2) studies the effects of FABP4 inhibition on locomotor and bladder recovery in rats. We are the first to report the significant upregulation of FABP4 protein and mRNA and the effects of its inhibition on autonomic and functional recovery in the injured rat spinal cord. Our data indicates that intrathecal administration of the FABP4 inhibitor BMS309403 promotes autonomic bladder recovery and significantly improves locomotor function in treated rats when compared to vehicle controls. Furthermore, we found that inhibition of FABP4 promotes axonal regeneration in treated rats as demonstrated by GAP43 staining. We propose that FABP4 is an attractive candidate for modulating inflammatory responses in the injured spinal cord.

KARINA MAYAGOITIA
IMSD PARTICIPANT 2019

I am a native Southern Californian, raised in an Adventist household in the beautiful city of Yucaipa by two wonderful parents. I graduated from Yucaipa High School in 2010. I was ranked in the top ten percent of my class and graduated with honors. After high school, I attended Crafton Hills College for two years and completed my general education classes. I then transferred to Pacific Union College and graduated in 2015 with a BS in Chemistry with biochemistry emphasis. Pacific Union College is nestled in the beautiful Napa Valley mountains surrounded by beautiful and vibrant colored vineyards. In the summer of 2015, I was accepted into the IMSD PhD program at Loma Linda University. I have completed my fourth year in the PhD program and look forward to starting my fifth year.

I'm extremely privileged to be working in an Alzheimer's disease research laboratory under the leadership of Dr. Salvador Soriano. The lab studies the role amyloid plays in an adaptive response against cholesterol dysregulation and how the outcome of the response can lead to progression of Alzheimer's disease.

In my free time, I enjoy being outdoors exploring nature and exercising. I have always had the curiosity of learning a martial art so I am learning Muay Thai. Exercise is my way of taking a break from the science world and getting reenergized to work even harder in the lab.

I have a passion for research, and my hope is to one day have my own lab studying neurodegenerative diseases. I know that with God on my side, great things are yet to come as I begin my career as a scientist.

CHOLESTEROL METABOLITE 27-HYDROXYCHOLESTEROL AND ITS EFFECTS ON INFLAMMATION AND MEMORY

Karina Mayagoitia, Sam Shin, Isaac Mitchell, Ryan Black, Salvador Soriano
Center for Health Disparities and Molecular Medicine, Division of Human Anatomy, School of Medicine, Loma Linda University, Loma Linda, CA

Late-onset Alzheimer's disease (AD) affects 5.8 million Americans with costs estimated at $290 billion for 2019 and is projected to increase to unmanageable numbers if a treatment is not found. The etiology of AD is unknown, but genome-wide association studies have identified numerous risk factors in genes related to cholesterol and inflammation in AD patients. These findings have led our lab to investigate the connection between cholesterol dysregulation and inflammation, and we believe the cholesterol metabolite 27-hydroxycholesterol (27-OHC) could be the link between them. 27-OHC is of interest because it is elevated in AD brains, it causes memory loss in mice, it increases expression of inflammatory markers in vitro and induces neuronal death. To elucidate the mechanism by which 27-OHC induces neurodegeneration we will use a hypercholesterolemia mouse model known to increase 27-OHC levels and induce memory loss. Wildtype mice will be given a control diet or a high cholesterol diet (HC) for five weeks followed by behavioral testing including open field to assess anxiety, novel object recognition to assess long-term memory, and Y-maze to assess hippocampal dependent spatial memory. We hypothesize mice on the HC diet will have impaired memory and increased inflammation in the brain compared to control mice. Here we will present evidence that mice on the HC diet had impaired spatial memory and decreased anxiety compared to control mice. Future studies are needed to confirm that 27-OHC levels were increased by the HC diet and that inflammation in the brain was affected. Confirmation of a neurodegenerative and inflammatory role of 27-OHC could provide a potential therapeutic target for AD.

PERLA ONTIVEROS ANGEL

IMSD PARTICIPANT 2019

I am a first-year student in the Neuroscience, Systems Biology and Bioengineering PhD program and part of the IMSD initiative at Loma Linda University School of Medicine. I was born in Mexico to a small family, and for as long as I can remember, I have always been extremely curious, resilient, and a problem solver. Little did I know, I was a mini scientist all along! I also love connecting with people. From an early age, along with pursuing my education, I have always had a part- or full-time job, volunteered at my SDA church, and served on several mission trips. These experiences made me appreciate humanity as a whole and be especially compassionate towards minorities and underserved communities.

I am now pursuing my doctorate in neuroscience because of many people who invested and believed in the power of supporting girls towards STEM education and leadership roles. Being the first person from my family to attend college, I was blessed to find mentors that gave me answers, encouraged critical thinking, and motivated me to pursue higher education and to bring representation to the health disparities conversation. Thus, I am very grateful that now I get to study the effects of psychosocial stress and environmental factors like diet-induced obesity in adolescents exposed to chronic stress in childhood and early adolescence.

With the invaluable help and mentorship of Dr. Marino De Leon and his team and doing research in Dr. Johnny Figueroa's lab, I am looking forward to continuing to explore the impact of stress at a molecular level and join in bringing awareness of the importance of equality in physical, emotional and spiritual health. I believe by doing so we are contributing to the mandate of making man whole as Jesus would do.

SHORT-TERM OBESOGENIC DIET CONSUMPTION INDUCES RESISTANCE TO EXOGENOUS GROWTH FACTOR NEUREGULIN-1

Perla Ontiveros Ángel, Neiyharie Vélez Villarubia, Julio Vega-Torres, Johnny Figueroa
Center for Health Disparities and Molecular Medicine, Department of Basic Sciences,
School of Medicine, Loma Linda University, Loma Linda, CA

Childhood obesity is a significant public health challenge with a broad impact on metabolic and mental health. Obese children are particularly at risk of cognitive impairments and exhibit symptoms of anxiety and stress-related mental disorders. However, the mechanisms underlying these environmentally driven vulnerabilities are poorly understood. Substantial evidence demonstrates that obesogenic diets rich in saturated fats and simple sugars can cause cognitive impairments in humans and rodents, even before obesity signs manifest. These findings support the notion that the dietary macronutrient profile may be as crucial for cognitive health as is obesity status or total energy intake. More importantly, this idea provides a context in which early metabolic adaptations to an obesogenic diet could be examined without the confounding comorbid conditions implicated in obesity. Neuregulin-1 (NRG1) is a growth factor with emerging roles in the regulation of metabolic homeostasis. This study investigated the effects of a short-term obesogenic Western high-fat/high-sugar diet (WD) on NRG1-mediated metabolic actions. Juvenile Lewis rats were divided into four groups based on diet type and NRG1 administration (12 rats/group). Enzyme-Linked Immunoassays (ELISAs) data revealed no significant changes in insulin, triglycerides, corticosterone, and NRG-1 levels. Interestingly, exposure to Western Diet had an effect in Glucose, Leptin and Fibroblast growth factor 21 (FGF21) levels, confirming that NRG1 is a major secretagogue of FGF-21 even in a pre-obese state and suggesting disruptions in NRG1 signaling may contribute to the vulnerabilities observed in childhood obesity. We anticipate this study will inform a new path to needed biomarkers and interventions for improving cognitive health in children exposed to obesogenic diets.

GREISHA L. ORTIZ HERNÁNDEZ

IMSD STUDENT 2019

Growing up on the beautiful island of Puerto Rico, I discovered that my biggest passion, other than cooking and the outdoors, is the sciences. 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 degree in biology from Universidad Metropolitana (UMET) in Puerto Rico, I was ready to apply for graduate school at Loma Linda University. When doing so, however, my family and I received heartbreaking news. My grandfather, who 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 enjoyed greatly the last days of my Guelo. This process taught me to enjoy every path in my life and be grateful for it. Spring 2015, I reapplied to 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 Casiano's prostate cancer research laboratory. For my research work, I'm studying the contribution of protein-protein interactions to LEDGF/p75-mediated upregulation of stress oncoproteins to tumor aggressiveness and chemoresistance. Three months ago, I transitioned from being a PhD student to being a PhD candidate after successfully defending my doctoral proposal. My plans for the summer are to finish the required experiments for the first aim of my proposal and have enough data to start the process of writing my first author paper.

MULTIPLE TRANSCRIPTION FACTORS ARE UPREGULATED IN DOCETAXEL RESISTANT PROSTATE CANCER CELLS AND INTERACT WITH THE STRESS ONCOPROTEIN LEDGF/P75

Greisha Ortiz-Hernandez, Yaw Appiah-Boateng, Carlos 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 U.S. Current therapies for advanced PCa include androgen deprivation therapy and docetaxel (DTX) chemotherapy. Unfortunately, therapy resistance and disease progression lead to patient mortality. We have demonstrated that the stress oncoprotein 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. Different transcription factors, such as JPO2, Menin/MLL, c-MYC, IWS1, HAND2 and HRP2, have been linked to aggressive phenotypes in cancer and to stimulate HIV integration and latent infection through its binding with LEDGF/p75. However, these PPIs have not been explored in PCa chemoresistance. **Our hypothesis is that LEDGF/p75 interacts with several transcription factors to induce the expression of stress survival genes that contribute to PCa chemoresistance**. To evaluate this hypothesis, we assessed the expression of these proteins through Western blotting in DTX-sensitive and -resistant PCa cell lines (PC3 and DU145). Our data showed upregulation of these transcription factors and LEDGF/p75 in DTX-resistant cells compared to sensitive. Preliminary data from immunoprecipitation experiments suggest interaction between JPO2, Menin/MLL, c-MYC and LEDGF/p75 in chemoresistant PCa cells. Nuclear colocalization experiments by immunofluorescence microscopy are being optimized to further characterize the interaction between LEDGF/p75 and these proteins as 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.

FOLUWASOMI OYEFESO
IMSD PARTICIPANT 2019

My love of science was born from tragedy. The day after Christmas, 2004, I lost my young cousin to leukemia. The progression of the disease was slow but its impact significant. I began to study different diseases to understand them in hopes of treating terminal/chronic illnesses. My desperation developed into an intrigue and passion for scientific discovery. Through this difficult experience I learned the importance of advancing medical technology with a specific focus on individualized treatment. Thus, I pursued a bioengineering degree at Walla Walla University in part because of my Adventist upbringing. I became immersed in topics on science and engineering and soon began to ask my science professors how I could become involved in research. While keeping up with my academics, leadership positions, and sports, I also worked on engineering a neural tissue scaffold using 3D printing and electrospinning techniques under the instruction of Dr. Janice McKenzie. From this experience I learned the qualities that make a good researcher: passion, patience, and honesty.

In 2015, I found great purpose in another goal: engaging youth from my hometown in STEM education. I became a S.T.E.A.M. coordinator at the Santa Monica Boys & Girls Club to help provide opportunities and mentorship unavailable to me growing up. My future plan is developing S.T.E.A.M. programs for inner-city youth, disadvantaged socially or financially. God is leading me to achieve that goal, and I am now at Loma Linda University to complete a PhD in Bioengineering. I am grateful to the Pecaut lab for their mentorship as I investigate in the fields of neuroscience and regenerative medicine.

CEREBRAL ORGANOIDS: DEVELOPING A MODEL TO ASSESS MORPHOLOGICAL CHANGES IN THE MICROENVIRONMENT OF THE BRAIN FOLLOWING EXPOSURE TO IONIZING RADIATION

Foluwasomi Oyefeso, Nathan Wall, Michael Pecaut
Division of Biomedical Engineering Sciences, School of Medicine,
Loma Linda University, Loma Linda, CA

Exposure to ionizing radiation can elicit serious consequences such as organ dysfunction and increased risk of cancer. Exposure of central nervous system (CNS) tissues to radiation increases risks for progressive neurodegeneration and, consequently, long-term cognitive deficits. Epidemiological studies involving survivors of Chernobyl and research involving animal models indicate low doses of ionizing radiation can cause neuroinflammation and tissue damage, leading to disruptions in signaling and cognitive dysfunction. Clearly, it is critical that we understand physiological processes involved in neurodegeneration initiated by radiation-induced damage. Commonly used 2-D cell culture systems cannot model the 3-D structure, complexity, and connectivity inherent to the human brain that is necessary to understand the extent of radiation-induced damage. Fortunately, 3-D "cerebral organoid" culture models have emerged as a system to identify novel pathways and targets with roles in CNS development, damage, and disease, modeling aspects of neurodevelopmental disorders with remarkable accuracy. The objective of this study is to use organoids to identify cellular and biomolecular mechanisms contributing to neurodegeneration in response to radiation exposure. **Central hypothesis: Exposure of iPSC-based cerebral organoids to ionizing radiation will lead to specific and dose-dependent changes in neurogenesis, cell signaling, and neuroinflammation.** The proposed work will evaluate organoids as a physiologically relevant model to assess radiation-induced damage. We will culture cerebral organoids from human-induced pluripotent stem cells and address the central hypothesis through three specific aims: 1) Characterize changes to neural progenitor populations following exposure; 2) Evaluate radiation dose-dependent modulation to neurite formation; 3) Determine the extent of microglial migration and alterations to cytokine levels. These results will substantiate use of cerebral organoids as an effective translational model to evaluate neurodegenerative risk to the central nervous system due to physiological stressors.

HIEL RUTANHIRA
IMSD PARTICIPANT 2019

I am a fifth-year PhD student in Dr. Hansel Fletcher's lab at Loma Linda University in the Department of Microbiology and Molecular Genetics and a member of the IMSD program. Our lab's research focuses on periodontal disease and microbes, *Porphyromonas gingivalis* and *Filifactor alocis,* which potentiate disease progression. My interest in microbiology began in college at Southern Adventist University (SAU). There I was able to do research which led me down this career path. However, for high school I attended Mount Vernon Academy in Ohio, and that is where Mrs. C, my science teacher, made me fall in love with biology. This love for biology helped me decide to major in biology with a biomedical emphasis. I was born in Zimbabwe, Africa, and my parents brought us to the United States in 1999 for a better education, which facilitated my educational growth in the science field.

During my time at SAU, I was inducted into the Tri-Beta Biological National Honor Society which piqued my interests in other areas of biology besides medicine. I had always had a dream of attending Loma Linda University to pursue a medical degree but was drawn to medical research in my senior year at SAU. Upon acceptance into Loma Linda, I began working for Dr. Fletcher where I was partnered with Dr. Yuetan Dou, who has been the driving force 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 to be published next year.

Outside of the laboratory my interests include sports, music, weight lifting, and spending time with family.

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

Hiel Rutanhira, Yuetan Dou, Hansel Fletcher
Division of Microbiology and Molecular Genetics, School of Medicine, Loma Linda University, Loma Linda, CA

Porphyromonas gingivalis, a Gram-negative anaerobic bacterium, is considered a keystone pathogen associated with periodontal disease. In the inflammatory microenvironment of the periodontal pocket, the survival of *P. gingivalis* requires mechanism(s) to overcome oxidative stress in addition to other environmental stress conditions. Extracytoplasmic function (ECF) sigma (σ) factors are known to play a role in adaptation to environmental stress conditions. The role of several of the ECF σ factors in *P. gingivalis* was evaluated. Using DNA microarray analysis, ECF σ factor PG0162, in an overexpression strain, upregulated the *PG1662-PG1663-PG1664-PG1665* gene cluster annotated as an ABC Transporter in addition to ECF σ factor PG1660 previously shown to play a role in the oxidative stress resistance of *P. gingivalis*. Reverse transcriptase PCR was used to confirm the *PG1662-PG1665* gene cluster as a transcriptional unit with *PG1662* annotated as a hypothetical gene of unknown function. Allelic exchange mutagenesis using the *ermF* antibiotic cassette was used to replace the *PG1662-PG1665* operon. In comparison to the parent strain, FLL500 (*ΔPG1662-PG1665*) showed a 40-50% decrease in gingipain activity in addition to increased sensitivity to H_2O_2. PG1663, annotated as ABC transporter ATP binding protein in this ABC transporter operon, shows about 40% sequence homology to the YecC ATP binding protein described in *Escherichia coli* as being involved with cystine transport. Cysteine metabolism has been shown to play a role in oxidative stress resistance in bacteria. Collectively, the data suggest 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.*

EVELYN S. SANCHEZ-HERNANDEZ

IMSD PARTICIPANT 2019

I graduated from California State University, Northridge (CSUN) in May, 2017, with a Bachelor of Science in Cell and Molecular Biology. 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. Additionally, 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 scientists seek in their laboratories. I want to contribute to increasing our understanding of complex diseases such as cancer.

I recently completed my second year as a PhD student here at Loma Linda University in the division of Cancer, Development and Regenerative Biology (CDRB). I am in Dr. Carlos Casiano's laboratory, and my project focuses on studying the role of glucocorticoid receptor (GR) signaling in prostate cancer (PCa) and how it may contribute to chemotherapy resistance. African American (AA) men are disproportionately affected by PCa since they have a higher incidence and mortality than European American (EA) men. My project involves the study of how GR signaling is enhanced and how it may contribute to the aggressive phenotype observed in AA patients with PCa. I love conducting biomedical research, and my goal is to play a role in elucidating the mechanisms by which GR signaling may contribute to chemoresistance in PCa and its potential contribution to health disparities in PCa.

PSMA IS DIFFERENTIALLY EXPRESSED IN A RACIALLY DIVERSE PROSTATE CANCER CELL PANEL

Evelyn Sanchez-Hernandez, Marleni Pagán-Ramos, Alfonso Durán, Carlos Casiano, Frankis Almaguel
Center for Health Disparities and Molecular Medicine, School of Medicine and Cancer Center,
Loma Linda University, Loma Linda, CA

Prostate cancer (PCa) is the second leading cause of cancer-related deaths among U.S. men, disproportionately affecting African American (AA) men. Androgen deprivation therapy (ADT) and chemotherapy are the standard treatments for metastatic PCa. Unfortunately, therapy resistance inevitably occurs as PCa metastasis progresses. Therefore, there is an urgent need for new options to treat PCa more effectively. The use of Prostate Specific-Membrane Antigen (PSMA) as a theranostics biomarker for PCa is attracting enormous interest. PSMA is a transmembrane protein highly expressed in metastatic PCa, particularly in lymph nodes and bone. PSMA-based radioligand therapy (RLT) is emerging as a novel theranostic strategy for metastatic PCa. Due to its promising overall survival outcomes, 177Lu-PSMA 617 is the first PSMA-RLT evaluated in phase-3 clinical trials for metastatic PCa. A racially diverse study of PCa patients treated with PSMA-RLT resulted in 82% of patients having ≥ 90% decrease in PSA levels. Therefore, PCa patients with African ancestry could benefit from this intervention. PSMA expression is enhanced in patients treated with ADT. Since ADT leads to activation of glucocorticoid receptor, we hypothesized that PSMA expression may be altered by glucocorticoid treatment, and that it may be differentially expressed in racially diverse PCa cells and tissues. In the present study, basal PSMA expression levels were assessed in a diverse panel of PCa cell lines by immunoblotting, detecting the highest expression in the AA-derived MDA-PC-2b cell line. PSMA expression measured after treatment with dexamethasone revealed a slight downregulation. Also, immunohistochemistry procedures to assess PSMA expression in PCa tissue microarrays (TMAs) were optimized. Our findings suggest that PSMA might be regulated by glucocorticoids, and may contribute to advance personalized theranostics for patients most at risk.

NICHOLAS SANCHEZ
IMSD PARTICIPANT 2019

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 multiple disciplines. My efforts have been focused on the pathogenesis of neurodegenerative diseases, specifically on copper dysregulation and its role in the onset of dementia, which 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. 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 by those who provide support and to be in an institution that allows me to thrive.

COPPER DEPOSIT COMPARISONS BETWEEN ALZHEIMER'S DISEASE SEVERITY IN VARIOUS BRAIN REGIONS

Nicholas Sanchez, Joanneth Padró Serrano, Wolff Kirsch
Neurosurgery Center for Research, Training and Education, Department of Biochemistry, School of Medicine, Loma Linda University, Loma Linda, CA

"Oxidative stress," particularly instigated by dysregulated transition metal metabolism in the brain, plays an important role in the pathogenesis of Alzheimer's disease (AD). Cycling copper (Cu) between monovalent [Cu(I)] and divalent [Cu(II)] states makes the element potentially neurotoxic by promoting reactive oxygen species production. Preliminary studies show 1) Cu deposits in neuronal axons, 2) decreased Cu in synaptosomal fractions, and 3) reduced Cu transport proteins as emerging diagnostic indicators in AD brains. These findings were not as apparent in patients diagnosed with AD with Cerebral Amyloid Angiopathy (CAA). **We hypothesize a greater amount of copper deposits will be observed in AD-only brain samples when compared with control or AD with CAA.** The newly developed fluorescent probe (CRISP-17), highly specific to monovalent copper, was used to visualize axonal copper in post-mortem human brain tissue. Samples used were taken from patients exhibiting a diagnosis of 1) AD, 2) AD with mild CAA, 3) AD with severe CAA, or 4) no dementia (control). Sections were taken from the frontal, temporal, and occipital lobes cut to 8 µm. Two-photon microscopy was used to acquire images in 457-536 nm and 611-750 nm wavelengths. Images were processed in ImageJ. The fluorescence ratio increased as AD diagnosis progressed with AD/CAA severe brain samples having highest readings compared with non-diagnosed samples. AD-only brain comparisons were inconsistent between brain regions, with a reduction found in the temporal lobe and increased in the occipital lobe. Frontal lobe readings varied depending on the area sampled. Findings in the temporal brain (the region most affected by AD) sections were consistent with the hypothesis. These findings are imperative for narrowing our focus in the future of this project.

PAUL VALLEJOS

IMSD PARTICIPANT 2019

I received my Bachelor of Science in Biochemistry from Arizona State University. During my time at Arizona State, I worked in a pharmaceutical engineering research laboratory. After graduation, I started working in the pharmaceutical industry as a clinical research analyst. With my time in the pharmaceutical industry, I was exposed to the process of drug development and the FDA approval process. Although I learned a lot while working in the pharmaceutical industry, I realized my passion for learning was not satisfied, and I decided to apply for an advanced degree.

I have recently completed my first year in Loma Linda University's Cancer, Developmental, and Regenerative Biology PhD program. I am currently working in Dr. Nathan Wall's cancer laboratory in the Center for Health Disparities and Molecular Medicine, where my research is focused on the metastatic manifestation of colorectal cancer, Peritoneal Carcinomatosis. My research will specifically focus on analyzing the varying expression levels of microRNAs present within exosomes, extracellular vesicles, isolated from liquid biopsies.

I would like to personally thank my mentor Dr. Wall and laboratory partner Janviere Kabagwira for all their help and guidance throughout my first year in the program. Additionally, I would like to thank the IMSD program and the Center for Health Disparities and Molecular Medicine for their support.

PERITONEAL CARCINOMATOSIS: THE NEED FOR LIQUID BIOPSY BIOMARKERS

Paul Vallejos, Mei Li Kwong, Vola-Masoandro Andrianarijaona, Janviere Kabagwira, Chase Sugiono, Tiantian Liu, Charles Wang, Maheswari Senthil, Nathan Wall
Center for Health Disparities and Molecular Medicine, Division of Biochemistry, School of Medicine, Loma Linda University, Loma Linda, CA

Peritoneal Carcinomatosis (PC) is a metastatic manifestation of several gastrointestinal cancers, including colorectal. Due to the difficulty in early diagnosis, patients with colorectal PC have a median survival of five months. Therefore, there is a need to identify biomarkers for early detection and prognosis of the disease. Liquid biopsies which utilize plasma exosomes are ideal targets for biomarker development. The objective of this study is to identify unique plasma molecular targets which will aide in the early detection of PC compared to other metastatic forms, such as visceral metastasis (VM). Exosomes were isolated using ExoQuick®, and then Next-Generation Sequencing (NGS) analysis was performed on nine patient plasma exosome samples. VM of the liver (n=4) and PC (n=5). NGS allowed for analysis of microRNA (miRNA) expression, which found 1,386 potential biomarkers. Differential expression analysis (Deseq2) resulted in 390 upregulated miRNAs and 20 downregulated miRNAs; PC compared to VM ($p < 0.05$). Pathway and genetic target analysis (SpidermiR and Ingenuity Pathway Analysis) were conducted and from the 410 miRNAs, there were 140,270 possible genetic targets. Using this information, we were able to analyze their relationships with the hallmarks of cancer. By analyzing the top 30 miRNAs, it was found that 18 were involved in metastasis and 12 were involved in proliferation. These results show promising potential biomarkers for the early diagnosis and prognosis of colorectal PC.

JULIO D. VEGA-TORRES
IMSD PARTICIPANT 2019

I am currently a PhD candidate in the Department of Physiology with a specific focus on neuroscience. My main interest is to understand the implications that nutrition has on fear, dopamine, neuregulin, and brain circuitry. More importantly, my long-term goal is to improve the guidelines regarding the quality of psychological disorders management in at-risk populations, especially the adolescent community.

I am blessed to be part of FigNeuro Lab Inc., Dr. Johnny Figueroa's laboratory. The lab has been privileged with the contribution of many summer students throughout the years. This summer we have a hard-working UTP student, Neihyarie Villez Villarrubia, with great interest in research. Additionally, we have the privilege of having Raul Rios Orsini as part of the MTP program. His hard-working attitude, enthusiasm, and excellent work ethic motivate me to continue mentoring the future generation of scientists.

Apart from working in the lab, I love spending time with my wife and friends, playing the saxophone, playing tennis, 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).

DISRUPTED HIPPOCAMPAL MATURATION AND NEUREGULIN-ERBB4 SIGNALING IN RATS EXPOSED TO A SHORT-TERM HIGH-FAT/HIGH-SUGAR DIET CHALLENGE

Julio Vega-Torres, Perla Ontiveros-Angel, Amandine Jullienne, Elizabeth Haddad,
Angela Avitua, Byron Ford, Andre Obenaus, and Johnny Figueroa
Center for Health Disparities and Molecular Medicine, School of Medicine,
Loma Linda University, Loma Linda, CA

Substantial evidence indicates that obesogenic diets rich in saturated fats and simple sugars can cause cognitive impairments in humans and rodents, even in the absence of obesity. However, the mechanisms underlying these impairments are poorly understood. Neuregulin-1 (NRG1) and its ErbB4 receptor play critical roles in hippocampal neurogenesis and optimal cognitive function. This study investigates the effects of a short-term high-fat/high-sugar Western diet (WD) on hippocampal maturation and NRG1-ErbB4 signaling. Lewis rats were randomly divided into four groups (12 rats/group): 1) control diet (CD) + vehicle injections; 2) CD + NRG1 injections; 3) WD + vehicle injections; 4) WD + NRG1 injections. We performed behavioral tests (fear-potentiated startle, prepulse inhibition, elevated plus maze, and Y-maze) and neuroimaging (magnetic resonance imaging). The left hippocampus was harvested to determine NRG1-ErbB4 protein levels and signaling. We found that rats that consumed the WD exhibited reduced hippocampal volumes (8% reduction relative to CD rats) and exhibited deficits in cued fear conditioning. Interestingly, while NRG1 administration modulated hippocampal volume and behaviors in CD rats, it had no effect in WD rats. Western blot analyses demonstrated a significant reduction of ErbB4 protein levels in WD + vehicle (45.2%) relative to CD + vehicle rats. These data indicate that a short-term dietary challenge with an obesogenic diet disrupts NRG1 activities in the hippocampus. Together, this study suggests that aberrant NRG1-ErbB4 signaling may contribute to abnormal hippocampal structural and cognitive vulnerabilities in individuals that consume obesogenic diets.

JONATHAN WOOTEN
IMSD PARTICIPANT 2019

I am an alumnus of Oakwood University in Huntsville, AL, where I majored in chemistry. At this institution 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 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 for achieving this goal, having recently completed my fourth 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, Associate Professor in the Division of Pharmacology, on a fascinating research project which focuses primarily on determining the potential anticancer actions of plant-derived 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.

PETIVERIA ALLIACEA **PLANT ISOLATE DIBENZYL TRISULFIDE INDUCES APOPTOSIS IN TRIPLE NEGATICE BREAST CANCER CELLS DERIVED FROM AFRICAN AMERICAN PATIENTS**

Jonathan Wooten, Cristina Araújo, Joyce Aja, Nicole Mavingire, Eileen Brantley
Center for Health Disparities and Molecular Medicine, Department of Basic Sciences,
School of Medicine, Loma Linda University, Loma Linda, CA

One in eight women will be diagnosed with breast cancer in her lifetime in the US. African American women are nearly twice as likely to die from breast cancer than European American women though they are less likely to receive a breast cancer diagnosis. Triple negative breast cancer (TNBC), characterized by tumors that lack estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth receptor (HER2) expression, is one of the most aggressive subtypes. TNBC carries a poor prognosis in part due to a lack of clinically available targeted therapy. Previous studies indicate that dibenzyl trisulfide (DTS), derived from the *Petiveria alliacea* (Anamu) plant, exhibits potent anticancer actions in a breast cancer cell line derived from a European American patient. The purpose of our study was to evaluate the ability of DTS to inhibit proliferation and death in CRL-2335 TNBC cells derived from an African-American patient. We found DTS inhibited CRL-2335 cell migration and proliferation using the Wound Healing (scratch) and colony forming assays, respectively. Furthermore, DTS promoted apoptotic body formation and nuclear fragmentation as determined using relief contrast and fluorescence microscopy, respectively. Moreover, data from the Annexin V/PI assay revealed DTS induced early apoptosis which was partially attenuated in cells pretreated with pan-caspase inhibitor zVAD-fmk. Finally, quantitative polymerase chain reaction (qPCR) analyses revealed that DTS induced the expression of pro-apoptotic genes BAK1, LTA, and GADD45A. Our data suggest DTS effectively promotes apoptosis in TNBC cells including those derived from African American patients and represents a promising agent to treat refractory forms of cancer.

School of Behavioral Health & School of Public Health

Raveena Chara
Nipher Malika
Simone Montgomery
Oyinkansola Ogundimu

RAVEENA CHARA

BEHAVIORAL HEALTH PARTICIPANT 2019

The bridge between health and psychology has always intrigued me. Early in life I learned physical wounds often receive attention and usually heal whereas psychological wounds often do not. This disparity piqued my interest in studying human behavior, and I soon discovered my passion in the field of psychology. I was fortunate enough to pursue my passion and obtain a degree in psychology from California State University, San Bernardino. While in college, I 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. These experiences have 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 underserved communities. 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 not only in my community but other communities as well 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 had 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.

WEIGHT IS NOT MY PROBLEM: SOCIOCULTURAL INFLUENCES ON OBESITY IN IMMIGRANT HISPANIC WOMEN

Raveena Chara, Maud Célestin, Carmen Soret, Susanne Montgomery
Behavioral Health Institute, Loma Linda University, Loma Linda, CA

Preventing and reducing obesity, diabetes and other weight-related medical conditions is a growing priority in the US. Hispanics, one of the fastest growing sub-groups, have among the highest prevalence of obesity, are least likely to enroll in weight reduction programs, complete them, and successfully lose weight though reasons why remain elusive. Obesity is a complex biophysical phenomenon shaped by many factors, including a person's social environment and health. Culture permeates many aspects of one's life including how a person views weight and behaviors associated with eating and physical activity. Indeed, values and norms about what is culturally acceptable "body weight" vary from culture to culture. Our study used qualitative methods to examine sociocultural influences on weight in a sample of local immigrant Hispanic men and women. Nine semi-structured key informant interviews and 3 focus groups were conducted in Spanish and English, coded, and analyzed using Grounded Theory methods. Participants were asked questions about perceived influences on weight gain/loss, community perceptions of obesity, religious and cultural influences on weight, and support systems for losing weight. Of the five themes that emerged, two were structural: the influence of immigration to the US, the lack of easily accessible and affordable produce; and three were socio-cultural: the lack of family and community support for weight loss due to the central nature of food in social life, cultural views about weight and beauty, and eating as coping. For weight loss to become successful for immigrant Latinos, weight loss programs should address both structural as well as sociocultural factors. Weight loss and lifestyle programs need to find practical and culturally informed ways to help Latino immigrants to lose weight as they have a unique set of challenges to implement lifestyle changes.

NIPHER MALIKA

BEHAVIORAL HEALTH PARTICIPANT 2019

I am a PhD student studying Social Policy and Social Research 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 barriers to prostate cancer screening for black men. Prostate cancer is the second leading cause of cancer-related death among black men, and reducing this high incidence and mortality rate is of interest to me. Therefore, identifying the best way to break these barriers and intervene is of great importance to public health.

Aside from research, I volunteer at Youth Hope, a nonprofit helping homeless, runaway, and at-risk youth in Redlands and the Inland Empire. My role at Youth Hope is to help 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.

CHRONIC ABSENTEEISM: WHAT CAUSES LOW-INCOME MINORITY STUDENTS TO MISS SCHOOL?

Nipher Malika, Berenice Medina, Hector Murrieta, Juan Carlos Belliard, Susanne Montgomery
The Institute for Community Partnerships and Behavioral Health Institute
Loma Linda University, Loma Linda, CA

Chronic absenteeism is a national problem with over 7 million students (k-12 grade) missing school. Minority and low-income students are more likely to miss school affecting their academic standards, graduation rates, long-term health, and economic stability. Although minority and low-income populations are more vulnerable to chronic absenteeism, there has been little research identifying the social determinants that predispose students to chronic absenteeism. Therefore, the aim of this study was to identify the social determinants that affect school absenteeism in low-income minority populations. A cross-sectional study with students (N=24,439) attending grades 5-12, was conducted in a low-income (89.3% + free lunch eligible) minority school district in southern California. Specifically, we explored the role of physical health, mental health, neighborhood safety, and family risk behaviors has on absenteeism. Descriptive and regression analyses were conducted with SAS 9.4. In this minority group of students, being younger, in lower grades, Hispanic, low-income, having poor physical health (asthma, diabetes, and obesity) and high family risk factors (adults who use illegal drugs, are gang members, have trouble with police, sell/deal drugs, and approve of students being in gangs) were associated with chronic absenteeism, revealing that health conditions and family dynamics play a big role in a student's educational chances for success. Breaking the cycle of absenteeism among low-income minority students calls for a comprehensive approach that tackles the barriers involved. Some of our results were unexpected and helped contextualize who and why especially young students miss school. More importantly, our results identify the social determinants that act as barriers to school success and overall health and well-being among minority students.

SIMONE MONTGOMERY

PUBLIC HEALTH PARTICIPANT 2019

I am a fourth-year MD/MPH dual degree candidate at Keck School of Medicine of USC. I was awarded the Dean's Research Year scholarship to complete a year of research in the emerging field of Skin of Color dermatology. In 2014, I received a Bachelor of Arts in Psychology from Northwestern University while working with low income youth of various backgrounds during the school year and doing health disparities research in the summers. This summer, I am working as a research assistant in Dr. Susanne Montgomery's summer research group at Loma Linda University and as a research fellow to Dr. Nada Elbuluk of the Department of Dermatology at USC.

My passion for health disparities and rebuilding broken relationships between medical professionals and marginalized populations led me to pursue a dual degree program in medicine and Public Health. Though I had a few experiences my first two years of medical school that sparked my interest in dermatology, it was during my third-year rotations I found my passion and decided to pursue a career in the field. I intend on specializing in Skin of Color to address health disparities within the field of dermatology to ensure access to culturally-appropriate, quality dermatological care for all. My current research with Dr. Elbuluk is focused on vitiligo, a condition disparately affecting minority patients.

I am currently a mentor to numerous pre-medical, minority students on the USC and UCLA undergraduate campuses and a track mentor to a group of 35 third-year medical students to help guide them to success on the wards. While I have achieved numerous academic and extracurricular successes, my most rewarding experiences remain mentoring the next generation of minority students from elementary to those applying to medical school.

SHOULD PEOPLE OF COLOR USE SUNSCREEN? A REVIEW OF THE LITERATURE

Simone Montgomery, Susanne Montgomery
Keck School of Medicine, University of Southern California; Behavioral Health Institute,
Loma Linda University, Loma Linda, CA

Skin cancer is the most common malignancy in the United States, but its incidence remains relatively low in minority communities. However, once cancer occurs, it is usually more aggressive and has poorer outcomes, often because patients believe they are not at risk and thus present at a later stage. Given this significantly lower lifetime risk of skin cancer in minority patients, recent community concern in the grey (popular) literature has centered on reassessing the risk-benefit of sunscreen use for persons who already have "built-in" melanin protection due to their darker skin. Moreover, few people of color participated in the clinical studies informing current guidelines. Relevant peer-reviewed studies were identified searching PubMed and Google Scholar; abstracts were screened for relevancy, then studies were selected for inclusion to compare the positive and adverse effects of sunscreen use. While daily use of sunscreen has been widely established to significantly reduce incidence of squamous cell carcinoma and melanoma, data has emerged linking the active ingredients in most chemical sunscreens to endocrine and reproductive disruption. Furthermore, a recent study showed maximal use of common sunscreens resulted in plasma concentrations of the active ingredients that exceeded the FDA-established threshold. Given the limited peer-reviewed literature on this issue, until further evidence supports community concerns about the safety of sunscreen, it is my conclusion to continue to follow the current American Academy of Dermatology recommendations to use daily sunscreen rather than rely on the photo-protective effect of melanin to prevent skin cancer in brown and black patients.

OYINKANSOLA OGUNDIMU

BEHAVIORAL HEALTH PARTICIPANT 2019

In my brief practice of medicine after earning my medical degree from the prestigious College of Medicine of the University of Lagos in Nigeria, I have come to realize the importance of research in the medical field. I wanted to gain more research experience to complement my clinical experience which is why I joined the team researching African immigrant health rates, knowledge, and perceptions of prostate cancer.

During the data gathering process of the research, I came to understand certain factors that may increase the rates of prostate cancer in African men. This knowledge has helped broaden my perspective as a physician, and I am able to see the cause of a disease in a person or group of people may be multi-factorial, and the clinician may need to understand this complexity to better improve the health of the person or community.

I am currently a student at the Loma Linda University School of Public Health working on obtaining my certificate in Health and Wellness Coaching, and I also plan to earn an MPH in Health Education and Wellness Coaching. I hope to start my medical residency training with the June/July 2020 set of interns.

I want to thank Drs. Susanne Montgomery and Nipher Malika for welcoming me whole-heartedly into the team, helping me to achieve my goal of becoming more proficient in research, and, ultimately, helping me become a better physician.

AFRICAN IMMIGRANT HEALTH: KNOWLEDGE AND PERCEPTIONS OF PROSTATE CANCER

Oyinkansola Ogundimu, Nipher Malika, Carlos Casiano, Lisa Roberts, Susanne Montgomery
Behavioral Health Institute, Loma Linda University, Loma Linda, CA

Prostate cancer is the second leading cause of cancer-related death in men in the US. Although prostate cancer affects men regardless of racial and ethnic group, a disproportionate burden is experienced by Black men who are 2.2 times more likely to die of prostate cancer compared to White men. Men from Africa experience similarly high rates of prostate cancer, and while many immigrate to the US, little is known about their rates as US data for all Blacks are reported in aggregate. Indeed, in the prostate cancer literature in the US, Blacks have mostly been treated as a homogenous group, including African Americans, Caribbeans, European Blacks, and African immigrants, though little research has explored how prostate cancer-related attitudes, knowledge, and behaviors may be different in these populations. This study aimed to understand knowledge and perceptions of African immigrant men towards prostate cancer and screening. A qualitative descriptive methodology was used that included triangulation and semi-structured key informant interviews with men (n= 7) and women (n=2) residing in different parts of the country. Tape-recorded interviews were transcribed and analyzed using the constant comparative method by 2-2 independent researchers. After inductive coding and generation of themes independently, readers came to consensus regarding six identified themes: the role of African culture in the perception of prostate cancer, limited knowledge about the disease, perception associated with prostate cancer, the role of stressors, screening embarrassment, and fear of impotency. This study's results will help health practitioners and researchers better understand the knowledge, perceptions, and behaviors of African immigrant men about prostate cancer which will influence their likelihood of seeking prostate cancer screening, a critical behavior to manage their elevated risk and to reduce the disparities in prostate cancer seen among Black men.

Summer Undergraduate Research Program (SURF)

Vola-Masoandro Andrianarijoana
Taylor Bothwell
Meredith Brown
Kenneth Choi
Jared Cellini
Emi Eastman
Priya Ramesh
Seung Shin
Abbie Underhill
Samuel Vander Dussen
Yucheng Yang

VOLA-MASOANDRO ANDRIANARIJAONA

SURF PARTICIPANT 2019

As a first-generation immigrant, living in the United States has highlighted the beneficial contribution healthcare has for the lives of human beings. It has also provided me with the opportunity to immerse myself in an academic environment in which I have become fascinated by the meticulous knowledge and creative innovations produced by scientists. I adore science and the essential information it has provided for effective healthcare. It is clear to me that research is crucial to our understanding of human disease in order to discover and improve treatments.

This school year, I will be completing my BS in Chemistry at Pacific Union College, a Christian liberal arts college located in Northern California. Given this background in chemistry, working with Paul Vallejos and Janviere Kabagwira in Dr. Nathan Wall's laboratory has been a novel and fascinating experience. Each day has been unique, and I have learned profoundly from my mentors in this field of biomedical research. Throughout this summer, I have realized the immense amount of planning and adaptation research requires to produce relevant experimental data efficiently. I appreciate the hard work, time, and dedication scientists put into research, and I would be honored to take part in these ambitious endeavors as I plan on going to graduate school and obtaining a PhD to pursue research.

I genuinely appreciate the privilege and opportunity I have been given to perform research in Dr. Wall's laboratory. I am thankful for the time and guidance Janviere Kabagwira, Paul Vallejos, and Dr. Wall have given in helping me learn in this new and exciting research environment. All have been mentors from which I have learned immensely regarding research and its powerful application to the wellbeing of human life.

A POSSIBLE CORRELATIVE ROLE FOR EXOSOMAL MICRORNA LET-7 IN COLORECTAL CANCER METASTASIS

Vola-Masoandro Andrianarijaona, Paul Vallejos, Janviere Kabagwira, Mei Li Kwong, Maheswari Senthil, Nathan Wall
Center for Health Disparities and Molecular Medicine, Division of Biochemistry, School of Medicine, Loma Linda University, Loma Linda, CA

Colorectal cancer (CRC) is the third most common cancer worldwide with the majority of patients dying from their disease. CRC can metastasize to various sites, including the visceral organs and the peritoneum, which significantly reduces survival rate. Biomarkers specific to CRC metastatic sites are needed for earlier diagnosis and better prognosis. Potential biomarkers include microRNAs (miRNAs), which play a major role in regulating gene expression. These miRNAs can be extracted from tumor derived exosomes, which are extracellular vesicles ranging 30-150nm. Next-generation sequencing (NGS) can then be used to identify specific miRNAs, like the dominant miRNA let-7 family. The miRNA let-7 family regulates cell proliferation and differentiation and is considered a tumor suppressor. Given that cancer mutates the proliferative signaling of a cell, we hypothesized that metastatic CRC cell lines would have a change in the expression of miRNA let-7 compared to that of a normal colon cell line. To test this hypothesis, we compared exosomes, taken from the serum of patients diagnosed with peritoneal carcinomatosis (PC) or lung metastasis, using proteomics (data not shown) and NGS. NGS provided information on 410 miRNAs of which 390 were upregulated and 20 downregulated in PC compared to lung metastasis. Of these miRNAs, all eight let-7 isotypes were found upregulated with significance. In order to determine the significance of the finding, CRC cell lines representing PC, lung metastases, ascites metastases, and normal colon were grown and evaluated for the let-7 family. It is our long-term goal to be able to use these vesicles and their contents for diagnosis, prognosis, and determining treatment efficacy for CRC.

TAYLOR BOTHWELL
SURF PARTICIPANT 2019

I am an avid reader and first realized the fascinating world of biomedical research existed while reading Richard Preston's *The Hot Zone* and *The Demon in the Freezer* in middle school. Ever since then, I have been captivated by the idea of being on the front lines of scientific discovery and innovation.

This coming fall I will be entering my junior year at Pacific Union College (PUC), after taking the past year off to serve as a student missionary in Pohnpei, a small island in the Pacific Ocean. During my time in Pohnpei, I taught mathematics and science to high school students, coached the girls' basketball team, and served as the junior class and student association sponsor. The two degrees I am pursuing are Biomathematics and Global Development Studies; I hope they will give me not only a technical understanding of the world around me but also an empathetic one. Being involved in the spiritual life at PUC has been of continued importance to me. I spent more than a year running a student-led church service, and this next school year, I will be the student chaplain. As for my plans beyond college, I picture myself always being on a journey of discovery, whether that be discoveries about science, God, myself, or other cultures. I aspire to never stop asking questions. Currently, my plans include the pursuit of a PhD in biomedical science.

I would like to extend my gratitude to Dr. Juli Unternaehrer and everyone in her lab, most especially Tise Suzuki, for making this summer program a time of intense excitement and learning.

SNAIL KNOCKDOWN IN OVARIAN CANCER CELLS USING MESOPOROUS SILICA NANOPARTICLES

Taylor Bothwell, Tise Suzuki, Hanmin Wang , Ruining Wang, Jeffrey Zink, Juli Unternaehrer
Department of Basic Sciences, Division of Biochemistry, School of Medicine, Loma Linda University, Loma Linda, CA; Department of Chemistry and Biochemistry, University of California, Los Angeles, CA

SNAI1 (Snail) is a transcription factor that has been strongly implicated in triggering the epithelial-to-mesenchymal transition in cells. This transition is responsible for increasing a cell's ability to migrate and invade, leading to the formation of metastases by cancer cells. Mesoporous silica nanoparticles (MSNs) have a positively-charged coating that is hydrophobic, allowing them to be attracted to and taken up by cells. The goal of this study was to knock down Snail in OVCAR8, an ovarian cancer cell line, using MSNs as a delivery vehicle. OVCAR8 was selected because it contains high levels of Snail and has high chemoresistance. Small interfering RNA (siRNA) that targets Snail was attached to the MSNs and placed in culture with OVCAR8 cells. Different cell counts, amounts of MSN, and types of siRNA were tested to find the most effective means of knocking down Snail. Snail knockdown was assessed using RT-qPCR. The results showed that a count of 3200 cells/mm^2 and MSN amount of 0.0004 uL/cell returned the highest level of Snail knockdown. There was no significant difference between three different siRNAs. With the achievement of a consistent Snail knockdown using MSNs, in the future the model can be tested to see if there is a change in the stemness, chemoresistance, or tumorigenicity of the cells. If the Snail knockdown demonstrates a strong alteration in any of these capabilities, it has the potential to be a target for ovarian cancer treatment.

MEREDITH BROWN
SURF PARTICIPANT 2019

Throughout my education and research, I have come to understand the paradox, "The more you learn, the less you know." I am fascinated by the profound detail of nature that has yet to be uncovered. This curiosity has led me from central Pennsylvania to Loma Linda University where I have had the opportunity to continue exploring science at the Center for Genomics. My project investigates the genome editing efficiency of stem cells, ultimately to improve their differentiation process to cardiomyocytes. Because of the SURF program, I not only learned a great deal, but I gained a deeper appreciation of the human complexities yet to be understood.

I am currently a junior at Gettysburg College where I am majoring in biochemistry and molecular biology. Outside of academics, I love playing basketball and painting. I also enjoy working as an EMT, a position that has sparked my passion for furthering medical treatments and helping patients.

My long-term goal is to attend an MD/PhD program. Currently, I am interested in exploring applications of precision medicine to the treatment and prevention of disease. In my future career, I hope to serve as a physician while also advancing the field of biomedical research.

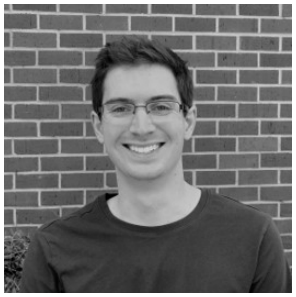
I would like to thank Dr. Charles Wang for welcoming me to his lab and for his guidance and support. I am also thankful for Dr. Xiao-Bing Zhang, Dr. Wanqiu Chen, and Hannah Choi for their continuous teaching and collaboration throughout the summer.

HISTONE DEACETYLASE INHIBITORS IMPROVE EDITING EFFICIENCY OF HUMAN iPSCs FOR CARDIOMYOCYTE REPORTER LINE

Meredith Brown, Hannah Choi, Wanqiu Chen, Xiao-Bing Zhang, Charles Wang
Center for Genomics, Department of Basic Sciences, Loma Linda University, Loma Linda, CA

Direct differentiation of human-induced pluripotent stem cells (iPSCs) to cardiomyocytes offers a promising future for cardiac regeneration. Development of cardiac reporter lines will allow us to screen for potential cardiac reprogramming factors and to purify desired cell populations. We aim to generate a reporter line via a CRISPR/Cas9-mediated knockin at cardiac-specific loci, *MYH6* and *GATA4*. However, precise knockin efficiency of iPSCs is a notorious challenge. By applying histone deacetylase inhibitors (HDACi) to transfected iPSCs, we attempt to increase accessibility of editing factors to regions of innately closed chromatin. We first tested knockin of GFP in K562 leukemia cells, which are more readily programmable, and then knockin of a 6 base-pair tag in human iPSCs. Additionally, we compared the knockin efficiencies of Cas9 enzymes with and without an EP300 histone acetyltransferase protein. After electroporation of CRISPR/Cas9 plasmids and BCL-XL (an anti-apoptotic factor), cells were separately treated with the following HDACi: sodium butyrate (NaB), valproic acid (VPA), suberoylanilide hydroxamic acid (SAHA), and trichostatin A (TSA). After 3-4 days of culture, knockin efficiency was quantified in K562 cells by flow cytometry of GFP and in iPSCs by PCR of the targeted locus followed by Sanger sequencing and Interference of CRISPR Edits (ICE) analysis. HDACi improved knockin rates in both K562 cells and iPSCs. Closed chromatin in iPSCs had notably improved knockin rates with the addition of HDACi, particularly SAHA. However, open chromatin in iPSCs exhibited varied knockin efficiencies and needs further testing. In both cell types, Cas9/EP300 complexes did not improve editing efficiency. Future directions include using ATAC-seq to understand how HDACi affect epigenomic reprogramming, i.e., chromatin accessibility. Our work offers an improvement in generating iPSC-derived cardiomyocytes and has applications to drug screening and disease modeling.

JARED CELLINI
SURF PARTICIPANT 2019



I can ask a million questions and still not have asked enough. My inquisitive mind forces me to ponder everything I come across and examine it until I have accounted for every last detail. When I visited Loma Linda University in the past, I always wondered what it would be like to attend this university. SURF is the first step to figuring out that question, and I have been blessed to have this opportunity.

My major at the University of Redlands is biochemistry and molecular biology with a major emphasis in chemistry. I am a part of chemistry research, I tutor chemistry individually and for the whole department, and I live and breathe chemistry. I decided to step out of my comfort zone and apply for the research opportunities at LLU. By the grace of God I was given this opportunity, and I am thankful for everyone's faith in me even though my faith in myself can falter. Now, I am able to apply a new perspective to an already difficult subject.

The atmosphere at LLU is vastly different from the extremely liberal and, at times, anti-Christian feeling at the liberal arts university I attend. This new atmosphere is refreshing and beyond what I could imagine. From this experience I hope to learn if the MD/PhD route is aligned with God's plan or not.

I would like to thank Dr. Erik Behringer and Charles Hewitt for allowing me to take part in their research, explaining the complexities of physiology, being patient with me, and dealing with my shenanigans.

NOREPINEPHRINE LEVELS IN THE MOUSE BRAIN WITH ALZHEIMER'S DISEASE

Jared Cellini, Charles Hewitt, John Buchholz, Erik Behringer
Department of Basic Sciences, Division of Pharmacology, School of Medicine,
Loma Linda University, Loma Linda, CA

Alzheimer's disease (AD) is a neurodegenerative disease and the sixth leading cause of death in the United States. The development of AD has been associated with decreased delivery of oxygen and nutrients throughout the brain due to impaired cerebral blood vessel function. Resistance vessels undergo balanced coordination of vasodilation and vasoconstriction to ensure optimal blood flow throughout the brain as needed for cognitive function. The catecholamine norepinephrine (NE) is central to control of cerebral vasomotor tone via stimulation of smooth muscle adrenergic receptors. Thus, we are testing the hypothesis that *norepinephrine levels may decrease with the progression of age-related AD*. Our approach includes measurement of NE levels throughout the brain of the triple mutation mouse model of AD (3xTgAD) in parallel with cognitively healthy C57BL/6 and mitochondrial catalase overexpressing (mCAT) mice. First, dissected and homogenized regions (e.g., cortex, hippocampus) are centrifuged to separate supernatant containing catecholamines. Based on the dissociation constant of NE, the solid phase extraction technique is applied at pH 8.6 (protonated to neutral charge) to sequester catecholamines using alumina. Next, catecholamines are disassociated from alumina using perchloric acid (neutral charge to protonated). Finally, for NE quantitation, a High Performance Liquid Chromatography apparatus (C-18 reverse phase column, electrochemical detector) is used at a flow rate of 0.5 ml/min [water-acetonitrile-$NaH_2PO_4 \bullet H_2O$ (89%-10%-1%) mobile phase]. Our preliminary data suggest that 3xTgAD mice (mild cognitive impairment & amyloid-β) contain lower levels of NE in the cortex and hippocampus regions vs. C57BL/6 and mCAT mice. Thus far, NE levels are similar among groups in the remaining portion of the brain including the locus coeruleus (source of NE). When complete, this approach may illuminate NE homeostasis and function in the brain during development of AD.

KENNETH CHOI

SURF PARTICIPANT 2019

I was born and raised in Southern California as a second generation Korean-American. I attended San Gabriel Academy and graduated from Andrews University in 2016 with a degree in integrated science secondary education. I spent a year teaching math and science at an international high school in South Korea during the 2016-17 school year. After returning to the States, I took several courses to complete the pre-med coursework. I hope to start Loma Linda University's MD/PhD program in the fall of 2020 because I am currently at Andrews University studying in a master's program in divinity.

Part of my research this summer consisted of performing feeding assays on sea anemones to elucidate the pathway associated with nematocyst discharge on sea anemone tentacles. My previous research experience involved using GIS to map and analyze prairie dog sightings under the mentorship of Dr. Tom Goodwin at Andrews University for my Honors thesis.

In my free time, I enjoy playing volleyball, basketball, piano, and making YouTube videos.

BK CHANNELS ONLY OCCUR IN ANIMALS WITH NERVOUS SYSTEMS

Kenneth Choi, Matthew Kimble, Caitlyn Pang, David A. Hessinger
Division of Physiology and Pharmacology, Loma Linda University, CA

Cnidarians, including sea anemones, hydra, and corals, have the simplest nervous, muscular, and digestive systems. Anemones serve as model organisms to study conserved feeding behaviors. During feeding, they deploy eversible, venomous nematocysts from tentacle cnidocytes to capture, kill, and ingest prey. Anemones possess three types of cnidocyte/supporting cell complexes (Type A, B, and C CSCCs), each with distinct arrays of sensory receptors and complementary roles. Types A, B, and C kill brine shrimp prey in a ratio of 1:2:4, respectively, in the anemone, *Haliplanella luciae*. Although potassium ion channels are ubiquitous among all organisms, Ca^{2+}-activated, big-conductance potassium (BK) channels seem restricted to animals, especially the Bilateria (i.e., protostomes and deuterostomes). We recently discovered that some non-bilaterians encode BK channel-like transcripts, but this observation has not been confirmed functionally. We **hypothesized** that functional BK channels associate with CSCCs and are involved in prey killing. In *H. luciae,* we found that 10^{-6}-10^{-7} M paxilline, a selective BK channel blocker, inhibits about 10% of prey killing, corresponding to prey killing from vibration-sensitive Type A CSCCs. Higher paxilline levels inhibit killing by approximately 55%, possibly corresponding to Type A+B killing. We conclude that fully functional BK channels occur only in animals possessing nervous systems, including non-bilaterians.

EMI EASTMAN

SURF PARTICIPANT 2019

No one goes through life without the help of others—whether it is from family, friends, or complete strangers— so I want to make sure that my profession helps people the same way that so many have helped me. Almost everyone that I know has been directly or indirectly affected by cancer. It is one of the most detrimental illnesses, and most treatments are almost as agonizing as the cancer itself. The pain of cancer treatment is why it is my main goal to improve the way we treat cancer, and medical physics research allows me to do that.

I graduated from Whittier College in May of 2019, where I received a bachelor's degree in physics. Through my research this summer, I was able to explore a method to reduce the range uncertainty in particle therapy. Improving the safety and accuracy of this technique could potentially eliminate one of the main factors limiting the use of particle therapy on tumors near vital structures. I hope to spend my career making novel radiation therapy treatments more accessible to the people who need them. Next fall, I will take the next step toward that goal by pursuing a graduate degree in medical physics.

I would like to thank Dr. Reinhard Schulte for the opportunity to work in his exceptional lab. His guidance, patience, and enthusiasm made for an incredible learning experience. I would also like to thank Dr. Kylie Watts for her efforts in making this program possible.

A METHOD TO REDUCE RANGE UNCERTAINTY IN PROTON THERAPY

Emi Eastman, Lennart Volz, Charles-Antoine Collins-Fekete, Reinhard Schulte
Department of Basic Sciences, Division of Biomedical Engineering Sciences,
School of Medicine, Loma Linda University, Loma Linda, CA

One of the benefits of proton therapy is the ability to concentrate dose in a tumor while reducing the dose delivered to healthy tissue. However, the use of proton therapy is limited by the range uncertainty associated with it. The goal of this work was to reduce the component of the range uncertainty resulting from the non-patient-specific conversion of Hounsfield units (HU) to relative stopping power (RSP) in the planning CT. The standard method (stoichiometric calibration) converts HU to RSP based on atomic compositions of average human tissue published by the ICRU and CT scanner-specific measurements of tissue-equivalent plastics. In order to improve this method, we suggest to add patient proton radiograph (pRad) projections and use an optimization algorithm to correctly assign RSP values to HU values. To test this method, the TOPAS Monte Carlo code was used to simulate the transport of 230 MeV protons through a digital pelvic model. One anterior-posterior pRad projection of the phantom was simulated. A pRad is a 2-D map of water equivalent thickness (WET) values in the direction of the projection. In addition, a digitally reconstructed pRad (DRpR) was also generated from the x-ray CT scan. An optimized calibration curve was then created based on the best fit between the DRpR and the simulated pRad. The optimized calibration curve was compared to the standard calibration curve obtained from the TOPAS program. The results of the comparison indicate that the patient-specific calibration curve reduces errors in RSP values. We conclude that this approach can improve the HU to RSP conversion and would enhance the accuracy of proton therapy treatments.

PRIYA RAMESH
SURF PARTICIPANT 2019

"Question everything. Learn something. Answer nothing" by Euripedes is one of my favorite quotes. I love science because every discovery leads to more questions. Science helps me understand myself and the world around me.

In 2017, I traveled from India to the United States to pursue a bachelor's degree in neuroscience at Mercer University in Georgia. I also enjoyed volunteering at Be The Light organization. Be The Light organization encourages education in impoverished children. I want to pursue a career in medicine and research so that I can explore the human body and the world around me.

This summer I am working in Dr. Kylie Watts's lab with my research mentor Erwin Stuffle. We are currently working to understand the Aer2 receptor in *Vibrio vulnificus.* This summer experience has helped me learn new things and challenge myself. I want to thank Dr. Watts for providing me this great opportunity.

CHARACTERIZING HEME AND OXYGEN BINDING TO THE PAS DOMAINS OF *VIBRIO VULNIFICUS* AER2

Priya Ramesh, Erwin Stuffle, Kylie Watts
Division of Microbiology and Molecular Genetics, School of Medicine,
Loma Linda University, Loma Linda, CA

Vibrio vulnificus is an opportunistic pathogen that causes the majority of seafood-associated deaths in the USA. This bacterium uses chemoreceptors like Aer2 to sense and respond to stimuli. Aer2 receptors sense O_2 by binding it to their PAS-heme domains. *V. vulnificus* Aer2 (*Vv*Aer2) is unique compared to previously studied Aer2 receptors (i.e., in *Vibrio cholerae* and *Pseudomonas aeruginosa*) in that it has three PAS-heme domains versus two such domains in *V. cholerae* Aer2 (*Vc*Aer2) and one in *P. aeruginosa* Aer2 (*Pa*Aer2). The PAS domains of *Vc*Aer2 and *Pa*Aer2 coordinate heme via a His residue on their Eη helix and stabilize O_2 binding via a Tyr residue on their Gβ strand and/or a Trp residue on their Iβ strand. To determine whether *Vv*Aer2 uses similar mechanisms to stabilize heme and O_2 binding, and to ascertain the roles of each of the three PAS domains, we replaced PAS Eη His residues with Ala, Gβ Tyr residues with Leu and Iβ Trp residues with Leu. The behavior of the full-length receptors was then analyzed in *Escherichia coli* after switching cells from N_2 to O_2 (wild-type *Vv*Aer2 elicits a signal-off response in N_2 and a signal-on response in O_2). Aer2 signal-on responses cause *E. coli* to tumble. In *E. coli*, the *Vv*Aer2-PAS1 His and Trp replacements, and the PAS2 His replacement, did not alter *Vv*Aer2 function. In contrast, the PAS2 Trp replacement resulted in a signal-on biased receptor (10% of cells tumbled in N_2), and the PAS3 Trp replacement resulted in a signal-on receptor (cells tumbled in both N_2 and O_2). These data will now be compared with the results of heme- and O_2-binding assays so that the roles of the individual PAS domains can be determined.

SEUNG SHIN
SURF PARTICIPANT 2019

I currently attend Biola University in La Mirada, CA, where I will be a third-year student this upcoming fall. At Biola, I am working on my BS in Human Biology as well as three minors in chemistry, business administration, and theological studies. I have been blessed to have received several honor recognitions at Biola by being on the Dean's list these past four consecutive semesters. In the future I hope to enroll in an MD/PhD program to pursue clinical research while simultaneously practicing medicine in a pediatric setting. In my free time I volunteer at the UCI Medical Center in Orange and serve at my local church in both children's ministry and the worship team. I love to watch the NBA, especially my favorite team from my hometown, the Phoenix Suns. I also love to shoot and edit short films whenever I have the opportunity to pick up a project.

This summer I had the honor of working in the perinatal lab under the guidance of both Dr. Mike Kirby and Dr. Steven Yellon. Our research specifically focused on inflammation- induced cervical remodeling and some of the precursor mechanisms that lead to preterm birth. My specific project in this lab was to study the role of Progesterone Receptor B in cervical remodeling and subsequent preterm birth. The most interesting part about this project to me has been seeing how pivotal inflammatory responses are in leading to complications associated with preterm delivery. My biggest takeaway from this summer experience has been seeing how research is a collaborative effort.

I am immensely grateful for the mentorship of both Drs. Kirby and Yellon along with the laboratory technicians and fellow students for guiding me along this process.

UNDERSTANDING THE SYSTEMIC INFLAMMATORY DRIVE OF CERVIX RIPENING AND PRETERM BIRTH

Seung Shin, Jennifer Ebling, Michael Kirby, Steven Yellon
Longo Center for Perinatal Biology, School of Medicine, Loma Linda University, Loma Linda, CA

A well-established model for preterm birth is to induce inflammation by injecting the endotoxin lipopolysaccharide (LPS) into the uterus of mice (PMID25747535). However, this model is no longer thought to reflect ascending infection associated with chorioamnionitis in women. Rather, preterm birth may be a consequence of systemic actions of LPS associated with cervix remodeling. The effects that systemic LPS has on characteristics of cervix ripening are unknown and represent a major gap in understanding the inflammation-induced preterm birth process. Thus, the objective of the present study was to test the hypothesis that LPS induces signs of cervix ripening in advance of preterm birth. Pregnant BALB/c mice received an intraperitoneal injection of LPS (60 µg/0.1ml i.p.; O55:B5 Sigma) on day 15 of pregnancy which was empirically determined to induce preterm birth within 24 h. Controls received saline (0.1ml, i.p.) and remained pregnant until term. The prepartum cervixes were collected 6 h after treatment (n=5 ea). Cervix sections were immunohistologically stained to assess resident F4/80 macrophages (brown) and density of cell nuclei (methyl green counterstained) as before (PMID2723375). Results indicate that the cervix of LPS-treated mice had an increased density of macrophages, but no significant difference in cell nuclei counts compared to the saline-treated controls. Thus, within 6 h, recruitment of macrophages was associated with premature ripening while no change in cell nuclei density may indicate a lack of specific inflammation related to edema or expansion of the extracellular matrix. Conceivably, the increase in macrophages could drive proinflammatory activities that advance cervical ripening. Understanding inflammation related to immigration of macrophages in the prepartum cervix may lead to the development of diagnostic biomarkers to assess risk or interventions that forestall preterm birth.

ABBIE UNDERHILL

SURF PARTICIPANT 2019

When tasked to compose this biography, I must admit to a certain level of writer's block. What could I include about myself that would be intriguing, and what about my research would be compelling? So, I have decided to start with the basics. I am the proud middle child of a family of five who has grown up in Southeastern Washington with a firm belief in my own invincibility. Pain is not a deterrent but simply the body informing the brain that something is not quite right, that something needs to be fixed. It is this mentality, this idea that the source of pain can be repaired, that has led me to where I am today with the intent to be a part of the healing process of others.

Currently enrolled at Walla Walla University, I will be entering my senior year in the bioengineering program this fall. My studies in engineering have taught me to embrace an analytical mindset geared towards problem solving while my focus in biology has solidified my desire to be involved in the medical field. I can think of no better way to integrate an engineering mindset with medicine than to engage in biomedical research. Being accepted to the SURF program has actualized my desire to be a part of a group of people seeking to improve the human condition as I have had the privilege of working in Dr. Kerby Oberg's lab on projects involving limb development.

I would like to thank Dr. Oberg, Charmaine Pira, and Kate Ball, along with the rest of the amazing people working in the lab, for challenging me and providing me with invaluable advice and mentoring over the course of the SURF program.

THE HAND2 BINDING SITE IN THE ZPA REGULATORY SEQUENCE IS NOT ESSENTIAL FOR REGULATION OF LIMB-SPECIFIC SHH

Abbie Underhill, Kathryn Ball, Charmaine Pira, Kerby Oberg
Department of Pathology and Human Anatomy, Loma Linda University, Loma Linda, CA

Polydactyly, a congenital limb condition characterized by extra digits on the hand or foot, manifests in about 1 in 700 people. Digit number and pattern are established by a cluster of cells in the distal posterior limb mesoderm called the zone of polarizing activity (ZPA). These cells secrete Sonic Hedgehog (Shh), a protein essential for normal limb patterning. The ZPA regulatory sequence (ZRS), a conserved enhancer 1Mb upstream of *Shh*, precisely regulates the temporal and spatial pattern of *Shh* expression. Oligozeugodactyly chickens have a ZRS deletion and are thus *SHH*-deficient; they lack posterior zeugopod bones (ulna and fibula) and digits except digit 1. Hand2 is a transcription factor restricted to the posterior limb mesoderm that is essential for *Shh* expression. Hand2 loss of function results in a loss of *Shh* expression and a *Shh*-deficient phenotype. Within the ZRS sequence there is a conserved Hand2 binding site. We hypothesized that Hand2 activates the ZRS through the binding site, and mutation of this site will eliminate ZRS activity. To test this hypothesis *in vivo*, we used a *ZRS*-GFP reporter and mutated the Hand2 binding motif using site-directed mutagenesis. Constructs were transfected into Hamilton-Hamburger stage 14 chicken presumptive forelimbs via electroporation. Fluorescence imaging of the limbs showed GFP activity in both native and mutant *Hand2* constructs. These results suggest this binding site in the ZRS is not essential for Hand2 regulation of *Shh*, and an alternative mechanism such as an indirect or co-factor mediated process is in play.

SAMUEL VANDER DUSSEN

SURF PARTICIPANT 2019

I have found that experiences and learning are some of the greatest privileges and responsibilities in the world. I was blessed by God to have received this opportunity in the SURF program to learn and perform research at Loma Linda University. I hope I brought a new perspective to the research in Dr. Chris Wilson's lab.

I am a recent graduate from Azusa Pacific University with a Bachelor of Science in Engineering with an emphasis in systems engineering and a minor in mathematics. I just returned from a mission trip where we turned waste plastics into valuable oil and diesel in Ukraine as a part of Operation Mobilization and their plastic pyrolysis project. This is one of many experiences I have had in different fields of science and engineering. SURF additionally exposed me to new areas of research and science. I will take the knowledge and techniques I learned here and continue to expand on them and apply them to my future endeavors.

I will begin work at Raytheon Technologies as soon as the program is over as an electrical engineer in their Space and Airborne Systems Department. In the future I hope to head towards research in biomedical engineering or a surrounding field, keeping the possibility of a PhD or MD open. I am just going to see where God leads me.

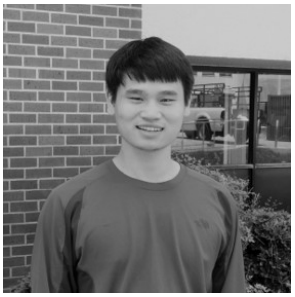
I want to thank Dr. Wilson for choosing me to be a part of his lab. It was the perfect fit for me. I also want to thank Lorraine Siebold for letting me help her with her research project and be a part of something I believe is a significant issue in medicine. I was challenged, grew, and learned so much about myself, science, and my career.

SYNTHETIC CORTICOTROPIN ALTERS MICROGLIAL MORPHOLOGY AND IMPROVES BEHAVIORAL OUTCOMES FOLLOWING TRAUMATIC BRAIN INJURY

Samuel Vander Dussen, Lorraine Siebold, Camille Krueger, Christopher Wilson
Department of Perinatal Biology, School of Medicine, Loma Linda University, Loma Linda, CA

Traumatic Brain Injury (TBI) is a major cause of morbidity and mortality with greater rates in military personnel and athletes. TBI can result in prolonged brain inflammation, neuronal cell damage and death, and blood brain barrier breakdown. TBI produces a varied response including microglia activation, cytokine expression, and behavioral deficits. Melanocortin receptor (MCR) agonists such as adrenocorticotropic hormone (ACTH) alleviate inflammation and are candidates for therapeutic treatment of TBI. We hypothesized that a synthetic ACTH, Cosyntropin, would be neuroprotective and reduce microglia activation following TBI in adult C-57BL/6 mice. To test this hypothesis, we used the controlled cortical impact model of experimental TBI. Microglia activation was evaluated by morphological data that was acquired using immunohistochemistry with IBA-1 staining and quantified using FracLac for ImageJ. We compared sham (treated and untreated) and TBI-injured (treated and untreated) animals using Two-Way ANOVA. Density (p-value = 0.014), mean radius, and maximum span across the convex hull had a significant difference between groups. We then used hierarchical cluster analysis to group the samples from the subjects. The clustering shows that the treated TBI group is closer to the sham groups than the TBI without treatment group**.** Therefore, we can conclude that Cosyntropin alleviated the severity of injury-induced microglia activation. We used novel object recognition, Morris water maze, and open field to evaluate behavioral outcomes. Behavioral data from the TBI-treated group exhibited a trend towards improved memory performance compared to untreated TBI mice. This finding further supported our hypothesis of Cosyntropin being an effective therapeutic treatment for TBI. In future studies we plan on adding more endpoints to our data analysis to give our hypothesis robust support and greater clinical relevance.

YUCHENG YANG
SURF PARTICIPANT 2019



I am from China and have stayed in the United States for six years. I am a second-year mechanical engineering student from Walla Walla University (WWU) and working with my SURF mentor, Dr. Reinhard Schulte, and Dr. Vladimir Bashkirov at Loma Linda University. We are currently working on a 2D Ion Detector that has a wide range of applications, including early-stage cancer detection. Dr. Venkatraman Pitchaikannu, a colleague of Dr. Schulte in India, has verified the detector's ability to detect malignant lung and breast cancers. At this stage, we wish to make the detector more compact and portable for future applications in the clinical environment.

Before the SURF program, I was working with Dr. Qin Ma, an engineering professor at WWU, on whether or not the pedicle screw thread shape will affect the stress concentration when the pedicle screw is under lateral bending. I was selected as the finalist and will present my work at the American Society of Mechanical Engineers Pressure Vessel Piping Conference's student paper competition.

During my downtime, I am interested in public philosophy and psychology and trying to understand what drives the general public's decision making. In the future, I want to become a researcher in the area of engineering applications and invent engineering products based on basic science principles.

My sincere appreciation goes to Dr. Schulte for giving me this incredible opportunity to learn basic scientific knowledge beyond an undergraduate education. I also want to give my thanks to Dr. Bashkirov, who invented the original detector, for being extremely willing to patiently answer all my questions about the detector. Such a rigorous learning process teaches me how to prepare myself for future projects that may be unfamiliar to me.

DETAILED DESIGN OF A PCB-BASED ION DETECTOR FOR APPLICATIONS IN CANCER RESEARCH

Yucheng Yang, Vladimir Bashkirov, Jeremy Rood, Reinhard Schulte
Department of Basic Sciences, School of Medicine, Loma Linda University, Loma Linda, CA

The modern clinical environment is demanding a low-cost, compact, and user-friendly device for cancer research and diagnosis. These needs initiated study of a printed circuit board (PCB) based-ion detector (PCB-ID). A recent publication has shown that a PCB-ID can distinguish between malignant and non-malignant tissues based on the volatile organic compounds (VOCs) released by these tissues; it may even discriminate different stages of malignancy. The purpose of this project was to design and build a prototype PCB-ID in order to validate the published results and perform further research. The working environment of the detector was a closed low-pressure chamber (1-10 Torr) which allows a small tissue sample to release VOCs into the chamber within a few seconds. A corona discharge was used to ionize the VOCs surrounding the tip of a needle that is connected to a voltage source. A drift electric field, which is produced by applying a positive voltage to a copper mesh and a negative voltage to the copper-clad PCB, transported the ionized VOCs toward the PCB. The PCB contains a regular grid of 576 1-mm-diameter holes. Inside the holes, a strong electric field will cause VOC-ion-induced impact ionizations which ultimately lead to an electric avalanche registered by a digital storage oscilloscope. Different types of VOCs were expected to induce signal characteristics which allow distinguishing normal and malignant tissues. The outcome of this project was a detailed design that encompasses all the required components of a functioning detector. This prototype establishes the foundation for future studies in this cancer research field at Loma Linda University. However, the device requires more detailed characterization and optimization before it can become a fully functional detector for applications in cancer research and diagnosis.

Guest Participants

Ryan Black
Sarah Doublet
Isaac Mitchell
Andy Paz-Aldana
Kari Roberts
Chase Stephen Sugiono

RYAN BLACK
GUEST PARTICIPANT 2019

I discovered the beauty and complexity of science my sophomore year of high school and was immediately intrigued with the prospect of using this knowledge to help those in need. My various mission trips to Haiti and Costa Rica grew that passion as I perceived how the many areas of science could each have a powerful and lasting impact on the community. Back in the States, I began volunteering at Riverside Community Hospital and Cornerstone Community Clinic where, through the incredible interactions with patients and healthcare teams, I found the future as an MD was where I was being called to go.

On top of my passion for medicine, I also love to teach and interact with other students. I have been given a great opportunity to teach a few of the basic science labs at Cal Baptist and have absolutely loved the experience. I hope to incorporate this love of teaching into my practice and eventually hope to enter into academia and further this enjoyment at a university. My teaching experience has also created a desire to understand how basic research is done, and connections through my professor, Dr. Alexandra Shin, led me to Dr. Salvador Soriano's research on the basic molecular mechanisms behind the impact of APP and tau on neurodegeneration.

I want to thank Dr. Shin for the great opportunity to do research at Loma Linda. I want to thank Dr. Soriano for allowing me to do research in his lab and for taking the time to teach me the "why" behind all the science. I also want to thank Dr. Soriano's PhD student Karina Mayagoitia for the immense help she has been during this entire summer.

CHOLESTEROL METABOLITE 27-HYDROXYCHOLESTEROL AND ITS EFFECTS ON MONOCYTE CHEMOATTRACTANT PROTEIN AS A POTENTIAL LINK BETWEEN CHOLESTEROL DYSREGULATION AND NEURONAL INFLAMMATION

Ryan Black, Isaac Mitchell, Karina Mayagoitia, Salvador Soriano
Center for Health Disparities and Molecular Medicine, Department of Human Anatomy,
School of Medicine, Loma Linda University, Loma Linda, CA

Late-onset Alzheimer's disease (AD) affects 5.8 million Americans with costs estimated at $290 billion for 2019 and projected to increase to unmanageable numbers if a treatment is not found. The etiology of AD is unknown, but genome-wide association studies have identified numerous risk factors in genes related to cholesterol and inflammation in AD patients. These findings have led our lab to investigate the connection between cholesterol dysregulation and inflammation, and we believe 27-hydroxycholesterol (27-OHC) could be the link because it is elevated in AD brains, causes memory loss in mice, and increases expression of inflammatory markers *in vitro*. Another molecule of interest, cytokine monocyte chemoattractant protein (MCP-1), has been shown to be upregulated by 27-OHC. In addition, MCP-1 has been shown to play a role in initial signaling and activation of microglia prior to neurodegeneration, and its concentration is increased in CSF of AD patients. This information has led us to believe MCP-1 could be an early factor responding to 27-OHC and thereby initiating neurodegeneration. To elucidate the mechanism by which 27-OHC induces MCP-1 and the downstream effects of MCP-1, we plan to treat a neuroblastoma cell line (SH-SY5Y) with varying 27-OHC concentrations then measure MCP-1 levels via an ELISA assay to determine its fluctuations. Neuronal death will also be determined using fluorescent detection of activated caspases 3&7. Here we present evidence that 27-OHC upregulated MCP-1 and recombinant MCP-1 did not induce neuronal death in a monoculture. Future studies will measure MCP-1 levels in response to MCP-1 receptor inhibitors and assess neuronal health. Determination of which pathways MCP-1 works through may lead to a therapeutic approach for inhibiting neuroinflammation onset.

SARAH B. DOUBLET
GUEST PARTICIPANT 2019

Currently, I am a senior at California State University, San Bernardino, where I major in biology and minor in chemistry. My interests in medicine peaked throughout my childhood experiences with my own medical conditions. Being born with a congenital heart defect and having reparative open-heart surgery at Loma Linda Children's Hospital was a defining moment in my life. From there, my interests in sciences grew as I have always been fascinated by science and ways biological processes connect and relate to each other in the function of the human body.

Working in Dr. Kimberly Payne's lab as an intern through a grant from the California Institute of Regenerative Medicine, I am researching B-cell acute lymphoblastic leukemia and the ability for TSLP as a potential therapeutic. I spend time working with animal models, running flow cytometry, doing tissue culture work, and processing patient samples. I work primarily with Jaqueline Coats on *in vivo* bioluminescence experimentation and statistical analysis.

When not in lab, I enjoy spending time volunteering with children's ministry and volunteering in the Emergency Room at Loma Linda Medical Center. I also enjoy going to Disneyland and Huntington Beach with my family and friends. In the future, I plan to attend medical school, hopefully at Loma Linda University, and go on to specialize in pediatric medicine and pursue research.

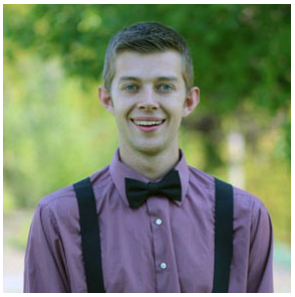
This opportunity has been an amazing experience that has opened my eyes to the world of research and how it defines the practice of medicine. I would like to thank Dr. Payne for welcoming me into her lab and the other members of the Payne Lab for their help.

TSLP AS A POSSIBLE THERAPEUTIC STIMULATING ANTI-LEUKEMIA EFFECTS IN B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA

Sarah Doublet, Jaqueline Coats, Kimberly Payne
Center for Health Disparities and Molecular Medicine, Department of Anatomy, School of Medicine, Loma Linda University, Loma Linda CA

Acute lymphoblastic leukemia (ALL) is the most common cancer in children and adolescents, killing more pediatric patients every year than any other malignancy and is more prevalent in Hispanic children. This type of leukemia has a particularly high percentage subtype called CRLF2 B-cell precursor and is characterized by the overexpression of the cytokine receptor CRLF2. CRLF2 forms a functional complex with thymic stromal lympho-protein (TSLP) and IL-7 capable of stimulating cell proliferation. TSLP plays several key roles in normal hematopoietic cell development and function. High levels of the cytokine TSLP have the possibility to have anti-leukemia effects and expand the production of normal B cells with no reduction in other immune cells. We created CRLF2 B-ALL Xenografts using a cell line of MUTZ-5-transduced cells to express +luciferase in order to monitor tumor burden and chimerism with luciferin. Leukemia progression was tracked in mice using IVIS and monitored weekly using the IVIS Lumina III. The mice were then treated with recombinant h-TSLP daily and hs-TSLP, produced by injected human bone marrow stroma cell line, hs27 cells weekly. Percent chimerism seen in the mice during IVIS correlates with chimerism found once bone marrow was harvested from euthanized mice and analyzed using flow cytometry, looking at the presence of CRLF2 and IL-7. Mice injected with MUTZ-5-transduced cells showed a reduction in chimerism when treated with r-TSLP and hs-TSLP. Reduction in leukemia cells seen *in vivo* is important because this finding demonstrates the ability for TSLP to be used as a therapeutic drug for cases of B-ALL. From this finding we can investigate what effects high dosages of TSLP have on downstream pathways and cell function.

ISAAC MITCHELL
GUEST PARTICIPANT 2019



This last year I developed a keen interest in neuroscience. I caught a glimpse of the elegance and intricacy of the human nervous system while taking a course in neuroscience, taught by Dr. Brad Cole, as a part of my medical school curriculum. In the human nervous system, reality is transformed into perception, interactions with the physical world into sensation, the depolarization of membrane potentials and release of neurotransmitters into thought, and thought into action. There is no other organ system so intertwined with personality, identity, and the human experience.

Unfortunately, given the cruciality of the nervous system, disruptions of its proper functioning can be equally profound and devastating. I have witnessed firsthand the effects of traumatic brain injury, Alzheimer's disease, and multiple sclerosis. In light of the gravity of neurological conditions and the many unanswered questions which remain in neuroscience, I sought to perform research in the realm of neurodegenerative diseases this last summer. I had the wonderful experience of working under Dr. Salvador Soriano, to whom I give great thanks, in pursuit of a better understanding of the neuroinflammation associated with Alzheimer's disease. I also owe many thanks to doctoral student Karina Mayagoitia for her abundant help and guidance throughout my research project.

MECHANISMS OF NEUROINFLAMMATION IN ALZHEIMER'S DISEASE

Isaac Mitchell, Ryan Black, Karina Mayagoitia, Salvador Soriano
Center for Health Disparities and Molecular Medicine, Department of Human Anatomy,
School of Medicine, Loma Linda University, Loma Linda, CA

Late-onset Alzheimer's disease (AD) afflicts 5.8 million individuals in the United States, and this statistic is expected to nearly triple by 2050. Unfortunately, there is neither a cure nor an effective treatment for AD. Chronic neuroinflammation is a major driving force in AD progression, yet the underlying mechanisms involved remain unknown. In pursuit of characterizing AD-related neuroinflammation, we investigated neuronal responses to chemokine IP-10 (CXCL10), an AD-associated marker of inflammation. IP-10 was recently shown to be an early marker of neuroinflammation in Neimann-Pick Type C (NPC) disease, which is an established model of cholesterol dysregulation-induced inflammatory neurodegeneration that causes AD-like pathology in the brain. It is accepted that astrocytes produce IP-10, for which neurons have receptors, yet the role of IP-10 in the CNS remains largely unknown. To quantify neuronal responses to administered IP-10, we measured neuronal apoptosis through the presence of cleaved caspases 3 and 7 and neuroinflammation via MCP-1 production. MCP-1 is an AD-associated cytokine which has also been implicated in cholesterol dysregulation. Additionally, plasma MCP-1 levels have been positively correlated with severity of AD and rapidity of AD cognitive decline. I hypothesize that IP-10 mediates both apoptosis and MCP-1 production, which could aid in our understanding of AD-related neuroinflammation. Given the role of IP-10 in cholesterol dysregulation, confirmation of my hypothesis could also suggest a point of interaction between cholesterol metabolism dysregulation and chronic neuroinflammation in AD. Here I provide evidence which suggests that IP-10 does indeed mediate MCP-1 production and neuronal apoptosis.

ANDY PAZ-ALDANA
GUEST PARTICIPANT 2019

I am a recent California State University, San Bernardino graduate, with a Bachelor of Science in Biology. Currently, I am working as a California Institute for Regenerative Medicine intern at Dr. Kimberly Payne's laboratory studying the therapeutic effects of the cytokine TSLP. I have always had a strong desire to help people in need and have the opportunity to be more involved in academia.

Before becoming a CIRM scholar, I was involved in undergraduate research at CSUSB studying a novel phylum discovered in the United States Great Basin. I was also involved in student organizations such as The American Medical Student Association, where I served as President for two years, and the Community Outreach Program, where I served as the Outreach and Communications Chair. I also had the opportunity to be a part of the sponsorship committee for the Medical and Pre-Health Student Society that hosts an annual conference at CSUSB.

In the future I would like to continue doing research by earning an MD/PhD with a focus on infectious diseases. I hope to be able to gain prominent expertise in my desired field to not only benefit other scientists but people within health disparities. The experience and knowledge I have gained as an intern in Dr. Payne's lab are invaluable and will help me in pursuit of my endeavors.

EFFECTS OF THE NOVEL BIOLOGIC TSLP ON CRLF2 B-CELL TYPE ACUTE LYMPHOBLASTIC LEUKEMIA: DETERMINING EXPRESSION OF SOCS PROTEINS, 1L7R AND CRLF2

Andy Paz-Aldana, Cornelia Stoian, Kimberly Payne
Center for Health Disparities and Molecular Medicine, Department of Anatomy,
School of Medicine, Loma Linda University, Loma Linda, CA

CRLF2 B-cell type Acute Lymphoblastic Leukemia (CRLF2 B-ALL) is a type of blood cancer most commonly found in children and adolescents. It is caused by the overexpression of Cytokine Receptor-Like Factor 2 (CRLF2). CRLF2, together with the interleukin-7 receptor alpha chain (IL7R), forms a cytokine receptor complex. Stimulation of this receptor complex by normal levels of TSLP causes survival and proliferation of leukemia cells. Recently we found that high levels of TSLP can act as a novel biologic, selectively inhibiting the signaling pathway that produces CRLF2 B-ALL while sparing normal blood cells. We hypothesize that Suppressors of Cytokine Signaling (SOCS) genes are upregulated in response to TSLP in leukemia cells, and at high doses of TSLP the expression of SOCS genes will increase. Further, high expression of SOCS genes is anticipated to lead to the shutdown of CRLF2 signaling in leukemia cells but not in normal B cell progenitors. We do not expect that high-dose TSLP exerts its effects by reducing IL7R and CRLF2 gene expression. Preliminary flow cytometry analysis results have revealed that SOCS protein expression is increased in MUTZ-5 cells treated for 24 hours with high-dose TSLP. These results support our hypothesis that high-dose TSLP will increase SOCS gene expression. Further analyses through RT-PCR and flow cytometry of patient samples and MUTZ-5 cells treated with TSLP will provide additional verification. Comparing protein and gene expression will provide insights on whether changes in protein levels are due to changes in gene expression and/or protein stability or degradation. The overall main focus of this study is understanding the cellular mechanisms that allow TSLP to target malignant B-cell progenitors.

KARI ROBERTS
GUEST PARTICIPANT 2019

I am a medical student about to enter into my second year at Loma Linda University School of Medicine. Last year I graduated from Point Loma Nazarene University in San Diego, CA, with a bachelor's in biochemistry. I have been so blessed to be able to continue my education studying medicine at Loma Linda. My first year in medical school came with many ups and downs, but it ultimately left me yearning for more knowledge. I am eager to learn more about the human body, and part of that learning comes from the research lab.

My experiences at Loma Linda thus far have been preparing me for my future aspirations. I hope to become a pediatric otolaryngologist 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. If it is in God's plan for my life, I long to be an ENT who can provide that comfort to others.

It has been a great privilege to work in Dr. Salma Khan's lab and gain insight to a different side of medicine. I have shadowed many doctors in clinic and seen what goes on during the face to face appointments with patients. It has been another experience entirely to catch a glimpse of the benchwork that goes into the treatments that physicians prescribe in clinic. Our work this summer has the potential to contribute to early diagnosis in thyroid cancer patients, which would help endocrinologists and ENT physicians offer more accurate prognoses and treatment to their patients. I'd like to thank Dr. Khan and the rest of my team for helping me learn, grow, and challenge myself this summer.

ANALYSIS OF DIFFERENTIAL ENIGMA GENE EXPRESSION IN THYROID CANCER VS BENIGN NODULES

Kari Roberts, Sang Hee Choi, Ethan Frank, David Foulad, Saeid Mirshahidi, Mia Perez,
Alfred Simental, Anthony Firek, Salma Khan
Center for Health Disparities and Molecular Medicine, School of Medicine,
Loma Linda University, Loma Linda, CA

Thyroid cancer incidence is rising worldwide. Although fine-needle aspiration biopsy (FNAB) is an accurate modality for evaluating thyroid nodules, up to 25% of FNABs still yield indeterminate results. An increasing number of thyroidectomies are due to indeterminate nodules by FNAB alone. Therefore, there is a need for a more accurate and time-efficient diagnostic approach for analyzing indeterminate thyroid nodules. Recently, the osteogenic protein Enigma has been associated with different cancer types, including thyroid cancer progression and calcification through its interaction with bone morphogenic protein-1 (BMP-1) and tyrosine kinases linked to mitogenic signaling pathways. Our published data on Enigma protein analysis with immunohistochemistry showed promising results in discriminating between malignant versus benign thyroid nodules and showed correlation with thyroid cancer staging. In this study, we investigated Enigma at a gene expression level by RT-qPCR, a quantitative and more time-efficient method that requires smaller samples (FNA) than immunohistochemistry. We analyzed Enigma mRNA expression levels to determine if Enigma-qPCR could be used as a diagnostic tool to improve the accuracy of FNAB in both malignant and benign thyroid tissues. We extracted mRNA/DNA/proteins from fresh malignant and benign thyroid nodules using a QIAGEN DNA/RNA/Protein Kit and ran isolated pure mRNA through Enigma-qPCR. The results showed the Enigma-mRNA expression level was 3-fold higher in malignant as compared to benign thyroid tissues. This finding supports our previous Enigma immunohistochemistry data and shows a relative quantitative difference in Enigma-mRNA expression level between malignant and benign thyroid nodules. We conclude Enigma-RT-qPCR can be used effectively in FNAB samples derived from thyroid nodules. This method could potentially enhance the diagnostic accuracy of indeterminate nodules and decrease diagnostic thyroidectomies.

CHASE STEPHEN SUGIONO

GUEST PARTICIPANT 2019

Even in my earliest memories, I have always sought to understand the underlying mechanisms and functions that drive the world around me. Diagnosed as a diabetic at age 5, I sought to learn more about how the body supports life and why some diseases are easily remedied and others remain terminal. This summer, I was given a chance to experience what scientists go through in order to make advancements in treatment, knowledge, and understanding through my volunteering in Dr. Nathan Wall's cancer lab. Here, I gained further insight into the depth of knowledge and breadth of experience necessary for commitment to helping those diagnosed with cancer. I cannot express the gratitude I have for being able to aid research that will help further the understanding of cancer.

I graduated from the University of California, San Diego, in June of 2019 with a bachelor's of science degree in general biology. Previously, I had been a part of Campus Ministries at LLA and wanted to continue helping others. Initially, I entered the Jacob's School of Engineering for a degree in Bioengineering. Realizing I wanted a closer connection to those I endeavor to help, and more tactile strategic work, I changed my direction towards biology with an intention to pursue dentistry. By gaining this brief experience in research, I am hopeful I can continue to explore new ideas in my future profession of dentistry. Dr. Wall's lab, full of faith, commitment, and selflessness, has only kindled my passion to help others.

I would like to thank Dr. Wall and Dr. John Buchholz for making this opportunity possible. Thank you.

SENSITIZATION OF PANC-1 PANCREATIC CANCER CELLS TO GEMCITABINE VIA SURVIVIN SPLICE VARIANT 2β KNOCKDOWN

Chase Sugiono, Janviere Kabagwira, Paul Vallejos, Jazmine Chism,
Vola-Masoandro Andrianarijaona, Nathan Wall
Center for Health Disparities and Molecular Medicine, Department of Basic Sciences,
Division of Biochemistry, School of Medicine, Loma Linda University, Loma Linda, CA

Survivin plays a significant role in the inhibition of apoptosis in cancer cells that results in their ability to resist chemotherapy. The upregulation of survivin has been associated with many cancers including cancers of the prostate, breast, colon, and pancreas. There are six *survivin* splice variants (SVs), which consist of *Wild Type (WT), Δex3, 2α, 2β, 3α,* and *3β*. Our goal was to assess the effects of *survivin* splice variant *2β* on chemoresistance within pancreatic cancer cells. In order to test our hypothesis, we used the pancreatic cancer cell line PANC-1, which displays an overexpression of all SVs, to test the effect of *2β* knockdown on chemoresistance. PANC-1 cells were treated with antisense 2′-Deoxy, 2′-Fluoroarabino Nucleic Acid (FANA) Oligonucleotides (ASO) and Gemcitabine for 48 hours to knockdown *survivin 2β*, testing this effect on Gemcitabine chemoresistance. Following knockdown of *survivin 2β*, the treated samples along with control (vehicle only) samples were harvested, and their viability assessed using Hoffman microscopy and trypan blue. Total RNA was isolated followed by reverse transcription to synthesize complementary DNA (cDNA) which we used for RT-qPCR employing SVs specific primers. Our results show that the FANA designed to target *survivin 2β* was not specific as off-target SV's also exhibited enhanced reduction. The knockdown using *survivin 2β* FANAs did, however, appear to sensitize PANC-1 cells to Gemcitabine, and the knockdown of all SVs did not present a comparable effect. We will therefore design a vector-based siRNA capable of targeting *survivin 2β* in order to obtain more specific and reliable results.

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