LOMA LINDA UNIVERSITY
School of Medicine
Center for Health Disparities & Molecular Medicine

17th Annual Health Disparities Research Symposium

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

PROGRAM, BIOS, & ABSTRACTS

Wednesday, August 2, 2017
12:00 pm – 7:30 pm
Wong Kerlee International Conference Center
Loma Linda University School of Medicine
Loma Linda, California

LOMA LINDA UNIVERSITY

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Center for Health Disparities &
Molecular Medicine

LOMA LINDA UNIVERSITY SCHOOL OF MEDICINE

17th Annual Health Disparities Research Symposium

Wednesday, August 2, 2017
12:00 pm-7:30 pm, Wong Kerlee International Conference Center

Agenda

LLU-NIH IMSD Alumni Scientific Panel

Moderator: Daisy D. De Leon, PhD – Loma Linda University

12:00 – 1:30 pm

Gabriel Linares, PhD – University of Southern California
Stem cells: An emerging platform for cell therapy and drug discovery in neurodegenerative diseases

Frankis Almaguel, MD/PhD – Loma Linda University
Improving outcomes by Imaging Molecules

Dequina Nicholas, PhD – Boston University
Lipid metabolism supports Th17 cytokine production in type 2 diabetes inflammation

Poster Session

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

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

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

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

Evening Program

5:30 pm – 8:00 pm

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

Invocation — **Susan A. Gardner, PhD**
Professor of English
Department of English
Walla Walla University

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

Remarks

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

Remarks

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

Remarks

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

Introduction of Keynote Speaker

Marino De Leon, PhD
Director, CHDMM

Keynote Speech

Frank Bayliss, PhD

Professor of Biology
Director, Student Enrichment Opportunities Office
San Francisco State University, College of Science and Engineering
UCSF Adjunct Professor of Biochemistry and Biophysics

"Scientific Apprenticeships: Mentoring by Individuals and Programs"

Acknowledgement of Students

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

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

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

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

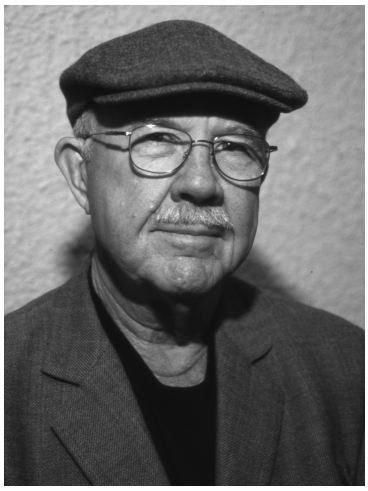
Final Remarks and Acknowledgements

Marino De Leon, PhD

Keynote Speaker Biography

Frank Bayliss, PhD

Professor of Biology
Director, Student Enrichment Opportunities Office
San Francisco State University, College of Science and Engineering
UCSF Adjunct Professor of Biochemistry and Biophysics



Frank Bayliss graduated with a BS in Zoology in 1965 from Long Beach State University, completed a PhD in Microbiology at the University of California, Davis, in 1971, and has been on the biology department faculty at San Francisco State University since 1975. Dr. Bayliss has focused on developing opportunities for underrepresented (URM) students since 1992 and has served as Program Director (PD) for a number of federally funded grant programs. He has been the PD of the NIH Minority Access to Research Careers (MARC), the Research Initiative for Scientific Enhancement (MBRS-RISE), Post-baccalaureate Research Education Program (PREP), the Bridge to the Baccalaureate, and MS/PhD Bridge to the Doctorate programs. He was also the PD for the Beckman Scholars program and is currently the PD for the Genentech Foundations Dissertations Scholars program. In addition, he has been PD for the USDEd GAANN, Department of Defense DOD Scholars, and an NSF REU program. Since 2000, his research focus has been on determining the efficacy of interventions in URM training. He was a co-participant on a joint NIH R0-1 grant with California State University, Los Angeles, and New Mexico State University for the "Research and Evaluation of Students Using Long-Term Studies." Dr. Bayliss has served on a number of review panels—NIH MARC/RISE, NIH BUILD, and NCI Comprehensive Cancer—as well as NSF review panels including the PAESMEM reviews. He has served as the Director of the Student Enrichment Opportunities office within the College of Science and Engineering at SFSU since 1996. Dr. Bayliss received the Presidential Award for Excellence in Science, Mathematics and Engineering Mentoring (PAESMEM) in 2008.

LOMA LINDA UNIVERSITY SCHOOL OF MEDICINE
CENTER FOR HEALTH DISPARITIES AND MOLECULAR MEDICINE
17TH 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 2017 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.

2017 Faculty Research Mentors

Abigail Benitez, PhD
Carlos Casiano, PhD
Daisy De Leon, PhD
Marino De Leon, PhD
Penelope Duerksen-Hughes, PhD
Johnny Figueroa, PhD
Hansel Fletcher, PhD
David Hessinger, PhD
Salma Kahn, PhD
Wolff Kirsch, MD
William Langridge, PhD
Saied Mirshahidi, PhD
Subburaman Mohan, PhD
Susanne Montgomery, PhD
Ying Nie, MD, PhD
Kerby Oberg, MD
Kimberly Payne, PhD
William Pearce, PhD
Christopher Perry, PhD
Ryan Sinclair, PhD
Julia Unternaehrer-Hamm, PhD
Nathan Wall, PhD
Charles Wang, MD, 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
Nathan Wall, PhD, Project Director
Bertha Escobar-Poni, MD, Program Coordinator
Matt Riggs, PhD, Evaluator, Professor of Psychology, California State University, San Bernardino

CHDMM Administrative Staff

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

School of Medicine Office of Diversity

Venice Brown – 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.

2017 Student Research Fellows

ABC – Apprenticeship Bridge to College

Heide Buri
Haydee Gallegos
Esmeralda Garcia-Orozco
Lien Hardister
Varsha Hunter
Andy Nguyen
Cassandra Orozco
Omar Panse
Mark Parent
Selorm Quarshie
Joshua Ramirez
Salvador Ramos
Girisch Senthil
Desiree Torres
Natalia Zamora Zeledon

UTP – Undergraduate Training Program

Ravon Baynard
Christine Castanon
Yamiko Chanza
Kirlann Danclar
Brea Fleming
Brandon McNichol
Antoinette Moore
Brandon Ng
Ashley Vasquez
Cristian Vera-Torres
Jasmine Walsh
Chidinma Wilson

MTP – Medical Training Program

Yadier Brito-Cuas
Kristoff Foster
Emil Harty
Jean-Paul Inesta-Rivera
Amanda Ortiz Vicil

IMSD – PhD/MD-PhD Graduate Fellows

Ivana Alicea Polanco
Leanne Woods-Burnham
Katherine Concepcion
Alfonso Duran
Christina Cajigas-Du Ross
Jenniffer Licero Campbell
Richard Lindsey
Shannalee Martinez
Karina Mayagoitia
Greisha Ortiz Hernández
Hiel Rutanhira
Nicholas Sanchez
Julio Vega-Torres
Jonathan Wooten

Behavioral Health & Public Health

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Simran Brar
Guljinder Chera
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Carmen Soret
Krystle Wiley

SURF – Summer Undergraduate Research Program

Adam Bennani
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Mindy Lombere
Vanessa Lopez
Simone Moore
Alice Nam
Phoebe Nye
Karndeep Rai-Bahatti
Jessica Reyes
Erwin Stuffle
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Jonathan Thomas
Natalie Wolske

Guest Participants

Marvin Amen
Anna Kwon
Chelsea Lee
Raechel Ospahl
Kari Roberts

Institutional Affiliations of Research Fellows

High Schools

Arroyo Valley High School
Beaumont High School
Bloomington High School
Diamond Bar High School
Citrus Hill High School
Eleanor Roosevelt High School
Etiwanda High School
Martin Luther King Jr. High School
Middle College High School
Redlands High School
Riverside Poly High School
San Jacinto High School
Vista del Lago High School
Wester Center Academy

Universities

Adventist University of Health Sciences
Brandeis University
California State University, Maritime Academy
California State University, San Bernardino
Loma Linda University
Occidental College
Oakwood University
Point Loma Nazarene University
Rensselaer Polytechnic Institute
Rollins University
San Juan Bautista School of Medicine
University of California, Los Angeles
University of California, Riverside
University of California, San Diego
University of Southern California
Walla Walla University

LOMA LINDA UNIVERSITY

School of Medicine

Center for Health Disparities & Molecular Medicine

LOMA LINDA UNIVERSITY SCHOOL OF MEDICINE

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

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Apprenticeship Bridge to College (ABC) High School Program

Heidi Buri
Haydee Gallegos
Esmeralda Garcia-Orozco
Lien Hardister
Varsha Hunter
Andy Nguyen
Cassandra Orozco
Omkar Panse
Mark Parent
Selorm Quarshie
Joshua Ramirez
Salvador Ramos
Girish Senthil
Desiree Torres
Natalia Zamora Zeledon

HEIDI BURI

ABC PARTICIPANT 2017

From my earliest memory, I have always had a passion for science, specifically biology. This passion has had an influence on every aspect of my life. This coming school year I will enter my junior year at Western Center Academy located in Hemet, CA. Throughout high school, my interest in biology began to flourish, and due to this fascination, during college I plan to major in bioengineering.

I have always thought the body and mind coincide with each other, which has influenced me to play tennis for a majority of my life. Beginning my freshman year, I have played varsity doubles. During the most recent tennis season, I advanced to CIF Team and CIF Individuals and also was given most valuable player.

Aside from tennis, I also play the piano. Through playing the piano, I am able to share my gift in an assisted living home. Volunteering has allowed me to share my gift in a positive way, and I enjoy seeing the smiles I bring to everyone in the home that listens. Many times ladies dance as I play, and some just come to visit.

I am thankful for the ABC program because of the opportunities it has provided me. Currently, I am working in Dr. Daisy De Leon's breast cancer research lab with Xousaen Helu. I am very thankful for my mentor's guidance in every aspect of the research and also thankful to my family for their love and support.

INHIBITION OF HER2 AND IGF-II IN JIMT1 BREAST CANCER CELLS INHIBITS CELL PROLIFERATION

Heidi Buri , Xousaen Helu, Daisy De León

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

Worldwide, breast cancer is the most common cancer among women. Among 20% of breast cancer cases, Human Epidermal Growth Factor Receptor 2 (HER2) is overexpressed. HER2, a membrane tyrosine kinase receptor, drives tumor development by providing potent proliferative and anti-apoptotic signals. Due to the overexpression of HER2, targeting the receptor has served as an effective breast cancer treatment. Trastuzumab (TRA), a recombinant monoclonal antibody, inhibits HER2 by binding to the HER2 receptors. Attachment of TRA to the many HER2 receptors in breast cancer cells causes decreased or inhibited tumor growth. Although TRA is an effective cancer treatment, 30% of the patients that overexpress HER2 are resistant to Trastuzumab and do not respond to treatment. Our breast cancer lab previously demonstrated HER2+ cell resistant to Trastuzumab had higher levels of IGF2 compared to HER2+ cells that responded to TRA. Thus, we proposed IGF-II as a key factor in response to TRA by HER2+ breast cancer. To determine if IGF-II is required to promote resistance to TRA treatment, we chose the JIMT1 breast cancer cell line that is HER2+ and naturally resistant to TRA. We also selected Chromeceptin to treat these cells since IGF-II expression can be inhibited by Chromeceptin (CHR). This study's aim was to test the hypothesis that cell viability and proliferation of TRA-resistant HER2+JIMT1 cells will decrease in response to combined treatment of TRA and CHR. JIMT1 cells were treated with DMSO, TRA, CHR, and combined TRA and CHR. After 20 hours, cell viability was measured by adding WST-1, a reagent measuring cell viability and proliferation through the convergence of WST-1 to a dye through mitochondrial activity. Our results showed a significant decrease in cell viability of both JIMT1 cells treated with CHR and the TRA-CHR combined treatment. These results suggest IGF-II is an effective target in reducing resistance to TRA treatment and effectively improving survival of women with HER2+ breast cancer.

HAYDEE GALLEGOS

ABC PARTICIPANT 2017

To a vast majority of the student population, education means wasting seven hours of a day, sitting around in a classroom, and being surrounded by other students with unenlightened mindsets who are completely unmotivated and could care less about the fact they are fortunate to have the privilege of learning and expanding their knowledge as well as awareness of the world. To me, education is my admission ticket that will open a gateway of opportunities to receive a quality, academic experience, help me pursue my career of choice, and aid me in avoiding a limited lifestyle resulting from educational deprivation.

Since a young age, I recognized the fact that my family and I are financially unstable. I understood the importance of an education and its endless blessings. I remember my father holding me by the hand, gazing into my eyes, and telling me, "Everything, I couldn't do in this world, you have the potential and ability to accomplish. Use your power and knowledge to transform this world." A veil was thus lifted. I was exposed to a world suffering from health disparities, and I knew my purpose was to serve those in desperate need of assistance. The opportunity to participate in the ABC program was the shining beacon I have been in search of.

I would like to thank Dr. Johnny Figueroa, Ivana Alicea-Polanco, and Julio Vega-Torres for welcoming me into their lab where I was awarded the chance to gain a hands-on experience to explore the complexity and nature of the brain and understand how the comorbidity of psychological trauma and obesity is a grave risk factor for psychiatric disorders. This learning experience was an exceptional milestone in my path towards a career in neuroscience.

JUVENILE OBESITY LEADS TO ABNORMAL MATURATION OF NEURAL SUBSTRATES UNDERPINNING FEAR AND ANXIETY

Haydee Gallegos, Ivana Alicea-Polanco, Julio David Vega-Torres, Johnny Figueroa

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

Obesity is a major risk factor for mental and neurodevelopmental disorders. We showed that consumption of an obesogenic high-fat diet (HFD) during adolescence results in stress-induced anxiety-like behaviors in rats. These behavioral findings were associated with marked impairments in the development of the brain prefrontal cortex (PFC), which plays a major role in anxiety and stress disorders. The aim of this study was to examine the cellular basis of these alterations in the developing PFC. Adolescent male Lewis rats (postnatal day 28; n = 51) were fed for eight weeks with either the experimental HFD diet (41.4% kcal from fat) or the control diet (16.5 % kcal from fat). Fear-potentiated startle (FPS) responses were assessed to determine the effects of the HFD on conditioned fear. Diffusion-tensor imaging (DTI) was used to determine the fractional anisotropy (FA) as a measure of white matter structural integrity of the fiber tracts connecting the fear neurocircuitry. We used the Nissl staining technique to measure the effects of a HFD on the PFC cellular morphology, patterns, and density in rats. The rats that consumed the WD exhibited associative-learning deficits as evidenced by blunted FPS responses. These behavioral effects were associated with a robust disruption in the medial prefrontal cortex (mPFC) structural integrity (increased FA) and higher corticosterone levels. Nissl staining revealed smaller cell bodies and decreased cell numbers in the PFC prelimbic and infralimbic regions of rats that consumed the HFD when compared to controls. These results provide evidence that consuming an obesogenic diet during adolescence can have a major impact in the development of brain regions implicated with stress-related psychiatric disorders. The implications of this research are significant by identifying potential cognitive and neuroimaging markers of risk for stress-related psychopathology in the growing obese population.

ESMERALDA GARCIA-OROZCO

ABC PARTICIPANT 2017

"Make us proud" revolves in my thoughts daily, the only thing I can think about. My parents relinquished everything for me, leaving behind their lives to give me an opportunity to dream big. Their constant support and love elevates my ambition, causing me to think I could potentially become a successful oncologist, regardless of the stereotypes trailing my race.

Raised in San Bernardino, the infamous city known for its poverty and crime, I had my eyes opened to health disparities. Most people in my community cannot afford to see a doctor; they lack resources available to those offered in other places. My parents face the same dilemma of having deplorable health as well as being underserved.

I attend Arroyo Valley High School where most of the student body does not aspire to become more than what our stereotypes set, which motivates me to inspire and lead young Hispanics into STEM careers, creating change and diversity in race and gender, disrupting barriers. I would like to ultimately open a non-profit hospital, assisting everyone, no matter their economic status. Presently I volunteer at the Dignity Health Hospital, an organization that serves minorities offering care to all. My goal is to give back to my community as it has shaped me to be the woman I am today.

This summer I was welcomed into Dr. Kimberly Payne's lab with Dr. Cornelia Stoian, Inneavely Baez, and Jacqueline Coats, all of whom had much patience assisting me with my experiments. With their guidance I was able to gain knowledge about the B-cell and leukemia. This interesting and amazing experience in a lab consisting only of intelligent women reinforced my love of research. The complexity of the body is truly spectacular; there is certainly not another field like science.

THE IMPACT OF TSLP CYTOKINE ON THE EXPRESSION OF CIS AND SOCS1 IN B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA (B-ALL)

Esmeralda Garcia-Orozco, Hannah Choi, Cornelia Stoian,
Hossam Alkashgari, Kimberly Payne

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

Acute Lymphoblastic Leukemia (ALL) constitutes 25% of childhood cancers, making it the most common childhood malignancy. Eighty-five percent of ALL cases arise from the B-cell lineage (B-ALL). B-cells that are unable to mature, are still developing at a rapid rate and not dying can potentially become leukemic. Hispanic and Latino children are especially susceptible as they are five times more likely to develop a particular type of high-risk B-ALL in comparison to other racial groups. This high-risk form of B-ALL, called CRLF2 B-ALL is characterized by mutations that lead to overexpression of CRLF2 and does not respond well to chemotherapy. CRLF2 is part of the Type I cytokine receptor family, and is a receptor for the cytokine, TSLP. Binding of TSLP to CRLF2 and the IL-7 co-receptor activates the JAK/STAT5 signaling pathways. Activation of the JAK/STAT5 pathway promotes survival and proliferation of cells. Cytokine signaling can upregulate expression of the SOCS (Suppressor of Cytokine Signaling) family of proteins, which in turn shut down the cytokine signals through various mechanisms. Our early studies suggest that TSLP has anti-leukemia effects, and we hypothesize that these effects are caused by TSLP-induced upregulation of SOCS genes that shut down CRLF2 signals. SOCS1 and CIS are two of the SOCs family regulatory proteins. We used the CRLF2 B-ALL cell lines MUTZ-5 and CALL-4 to determine whether TSLP induces SOCS1 and CIS upregulation over time. Flow cytometry was used to quantify the level of SOCS protein expression. Our data show that SOCS1 is upregulated as early as day 1, and this upregulation is maintained after 3 days in culture. Preliminary data suggest that CIS may also be upregulated by TSLP. These data provide a mechanism by which TSLP can exert therapeutic effects in CRLF2 B-ALL.

LIEN HARDISTER

ABC PARTICIPANT 2017

In June, I graduated from Eleanor Roosevelt High School with "honors with distinction." During high school I was a part of many extracurricular activities and sports on campus. I have been captain of the girls' golf team for the past two years, a member of Roosevelt's cheer team, and a competitive dancer in the genres of Jazz and Hip-Hop for about 10 years. Besides sports, I was a part of various service clubs including California Scholarship Federation, Black Student Union, Youth Service America, and Red Cross. Outside of school, I'm a very creative person who enjoys painting, dancing, and writing poetry in my free time. I will be continuing my education at UC San Diego in the fall, majoring in biochemistry and cell biology with a minor in art.

I am a returning ABC student. The program has already had a significant influence on my view of my own capabilities and my future career. Most importantly, this experience has reaffirmed my decision to major in biochemistry, and it has given me greater self-confidence in my ability to accomplish my goals. In the future, I plan to become a physician or a primary investigator of a biomedical research lab at a university. I hope to make a lasting impact by providing health services and working in underserved communities to help minimize health disparities.

My mentors are Dr. Sean Wilson and Sam Murray in a pharmacology lab that specializes in pulmonary vascular disease research. I want to thank Sam Murray for his limitless patience and Dr. Sean Wilson for his relentless encouragement throughout this process which has allowed me to test and challenge myself.

A23187 INDUCED RELAXATION OF ADULT SHEEP PULMONARY ARTERIES

Lien Hardister, Varsha Hunter, Raechel Opsahl, Monica Romero, Sam Murray, Lubo Zhang, Sean Wilson

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

Stimulation of the endothelium elicits calcium responses that lead to vascular relaxation. Our studies indicate that maturation and long term hypoxia modify relaxation due to bradykinin stimulation of the endothelium and the relationship calcium has to the relaxation response. To begin addressing this question we tested the hypothesis that A23187 would increase cytosolic calcium in endothelial cells and would cause relaxation of pulmonary arteries. To test this hypothesis, we measured the endothelial cytosolic Ca2+ and contractility responses of pulmonary arteries from normoxic sheep and the ability of the ionophore A23187 to cause relaxation. Following sheep sacrifice, the lungs were harvested and the 5^{th} generation pulmonary arteries dissected. Wire myography and calcium imaging were performed on these arterial segments. Contractility was induced with 10 micromolar serotonin and then arteries were exposed to 1 micromolar A23187 to elicit endothelial dependent relaxation. Our data indicate that A23187 elicits calcium responses in endothelial cells and causes arterial relaxation.

VARSHA HUNTER

ABC PARTICIPANT 2017

My mother always held onto this fantasy of me becoming a doctor in the future. I always told her: "We'll see." This conversation occurred from way back in my pre-school days to the absolute present. To this very moment, I am still "seeing" things. I see how through such a prolonged amount of time, my goals haven't changed, yet uncertainty still remains as I have a lot left yet to see. This feeling exists as my motivation to pursue the ABC program. In order to "see" what truly the scientific and medical field is made up of, I chose to participate in the program in order to direct me onto the right path in the future.
Do I truly want to be a doctor? Or does another career path inspire me more?

I've always believed in the practice of getting a taste of everything before coming to a final decision (which makes this decision all the more important because it identifies my true life-long career passion). As an upcoming senior at Etiwanda High School in Rancho Cucamonga, I've been able to participate in clubs such as Red Cross and Black Student Union. Music and art are other activities I explore. Through painting and playing the upright bass, I come in touch with my creative side. Despite my creative passions, science and medicine have found ways to capture my attention. Forensics, psychology, astronomy, and, of course, research are fields I wish to continue to explore before I determine my career path.

Overall, this ABC program is one of my pathfinding endeavors. By participating in Dr. Sean Wilson's lab, I've come to learn and "see" so much. I want to thank Dr. Wilson for providing me with this experience that truly opened my eyes.

PULMONARY ARTERIES FROM FETAL SHEEP ARE UNRESPONSIVE TO STIMULATION OF THE ENDOTHELIUM WITH A23187

Varsha Hunter, Lien Hardister, Raechel Osphal, Monica Romero, Sam Murray, Lubo Zhang, Sean Wilson

Center for Health Disparities and Molecular Medicine, Lawrence D. Longo Center for Perinatal Biology, Advanced Imaging and Microscopy Core, School of Medicine, Loma Linda University, Loma Linda, CA

The transition at birth is marked by a large increase in pulmonary vascular blood flow and vessel relaxation is an important part of this process. Previously we showed that pulmonary arteries of fetal sheep were largely unresponsive to vasodilators including acetylcholine and bradykinin. Because the arteries were unresponsive to endogenous agonists, we wanted to test the hypothesis that endothelial vasodilatory pathways are uncoupled from elevations in cytosolic Ca2+. In order to test this hypothesis, we directly increased cytosolic Ca2+ in the endothelium with the calcium ionophore A23187, which was expected to cause dilation. These experiments were performed on fetal sheep extracted from pregnant ewes raised at 700 m. From these fetuses, arteries were harvested from their lung tissue. Endothelial cells were imaged to determine the extent to which A23187 caused calcium responses. Vessel reactivity was measured using wire myography, and contractility was induced using serotonin. Relaxation of the serotonin-contracted arteries was then induced by treating with A23187 or DMSO. Our results show that A23187 caused calcium responses but did not reduce arterial tension. This finding leads us to conclude that fetal arteries calcium responses are uncoupled from vascular relaxation. Thus, our hypothesis was supported by the experiments that followed.

ANDY NGUYEN

ABC PARTICIPANT 2017

Ever since I could remember, I've always pushed myself to my limits and embraced challenges. In May, I graduated as Salutatorian of my class at Middle College High School. At the age of seventeen, two days after my high school graduation, I graduated from San Bernardino Valley College with my Associate of Arts degree in Biological and Physical Sciences. I've dedicated over 1,500 hours of my time providing free tutoring to community college students and low-income elementary school students. At the end of my high school career, I was shocked to discover I was awarded full ride scholarships to three schools: UC Berkeley, UC Los Angeles, and UC San Diego. After an entire month of contemplating, I am proud and happy to say that I will be studying biochemistry at UCLA next fall!

Now that I am a high school graduate, I am often asked, "What are your career goals?" Typically, my answer to that question is "I don't know yet." However, I know I want to pursue a career that will allow me to make positive contributions/impacts in my community. Education and family are extremely important for me. My ultimate goal in life is to repay my parents for everything that they have sacrificed for me.

I am beyond blessed to be participating in the ABC program again for a second summer. Dr. Oberg, who graciously took me into his lab once again, has taught me so much. Being in his lab has inspired me to want to work even harder to accomplish my goals.

THE ROLE OF LMX1B-ASSOCIATED CIS-REGULATORY MODULES IN LMX1B REGULATION AND NAIL-PATELLA SYNDROME

Andy Nguyen, Endika Haro, Charmaine Pira, Kerby Oberg

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

Lmx1b is a homeodomain transcription factor expressed in dorsal limb mesoderm responsible for dorsalization. Mice lacking Lmx1b exhibit ventral-ventral limbs while ventral overexpression generates dorsal-dorsal limbs. In humans, haploinsufficiency of LMX1B causes Nail Patella Syndrome (NPS), a disorder with incomplete dorsalization characterized by poorly developed nails and kneecaps (patellas). We have identified 2 conserved Lmx1b-bound *cis*-regulatory modules approximately 60 kb upstream from the Lmx1b coding sequence. Gene array data indicate that Lmx1b upregulates its own expression over 5 fold. Interestingly, NPS patients without coding sequence mutations have recently been reported, and one has a rare collection of single nucleotide polymorphisms (SNPs) within LARM2. We hypothesized that mutation of these Lmx1b-associated regulatory modules (LARM1/2) could reduce Lmx1b levels and cause NPS. To document activity, we isolated LARM1/2 from human genomic DNA. We placed the isolated fragments upstream of a basal thymidine kinase promoter linked to a GFP reporter. We then electroporated the constructs into the presumptive limb of chick embryos and recorded activity 48 hours later. We also performed site directed mutagenesis on the LARM2 reporter construct to generate a SNP variant that matched the patient with NPS and evaluated activity using the chick limb bioassay described above. Both human LARM1 and LARM2 were active in the dorsal mesoderm of the embryonic chick limb. Remarkably, the SNP mutations greatly diminished LARM2 activity. These data demonstrate that human LARM1/2 likely function to upregulate Lmx1b and further suggest that disruption of activity can cause NPS.

CASSANDRA OROZCO

ABC PARTICIPANT 2017

Science in all its ways is beautiful, complex, and astonishing. It is a field that keeps expanding with endless discoveries. Having the privilege to participate in this year's ABC Program, I am amazed by how much I was able to learn. From the diverse seminar topics, individual lab experiences, and the atmosphere of community, I have fallen deeper in love with the subject of science. My curiosity in asking questions has shaped me to keep pursuing knowledge and undertake any challenges that may occur.

This upcoming year I will be a senior graduating from Citrus Hill High School in Mead Valley. I am involved in various activities such as ASB, mock trial, the Youth Advisory Counsel for the city of Riverside, and volunteer weekly at my church, The Rock Church and World Outreach Center. On Sundays I rotate from being a teacher of four-year-olds to teaching second through fourth grade. I stay active in my community and love working with children. For the future I would like to pursue majoring in science in hopes of becoming a doctor specializing in neonatal care.

This summer I had the opportunity to be placed in Dr. Charles Wang's genomics lab. His lab closely focuses on next generation sequencing related to the human genome project. The work done in his lab is truly fascinating and microscopic; his research revolves around the very basic subject that is in all forms of life, DNA. I believe the work produced in his lab has extensive potential to change the future, and I am honored to have been mentored by him. I would like to thank Dr. Wang and his team—Diana Ho, Dr. Zheng Chen, and Dr. Xin Chen—for being welcoming and helping me through my learning process.

MICROBIOME IDENTIFICATION OF SOIL AND DOORKNOB DNA THROUGH 16S RIBOSOMAL RNA DEEP SEQUENCING

Cassandra Orozco, Zheng Chen, Charles Wang

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

Microbiomes are microorganisms in collective communities that contain genomes residing in environmental places. The microorganisms form interactive, distinct communities in surrounding environmental niches on or inside our bodies. Each of those microorganisms has its own genomes which can be used to identify the host microorganisms. The focus of this work is to identify and to test the feasibility of isolating microbial genomic DNA from small soil and doorknob swab samples and to test the quantity and quality of these DNA using 16s rRNA gene sequencing which allows us to identify the host microorganism and study the diversity of the microbial community by comparing the DNA samples. Genomic DNA was isolated using Dulbecco's Phosphate Buffer Saline (DPBS) to re-suspend the sample. DNA was isolated from soil and doorknob samples using Qiagen DNA Blood Mini Kit. The microbial 16s rRNA genes were amplified from genomic DNA using Polymerase Chain Reaction (PCR) and primers targeting the 16s RNA gene. The PCR product was cleaned up with magnetic beads and quantitated with Qubit 3.0 fluorimeter. Our results concluded with 1.4 ng/µl of doorknob DNA and 3.78 ng/µl of soil DNA. From our results we discovered that the lowest amount of DNA we were able to use to get results can be as low as 1 nanogram. Our work focused on isolating the doorknob and soil DNA to review the quality of DNA in small samples.

OMKAR PANSE

ABC PARTICIPANT 2017

"Success is not a random act. It arises out of a predictable and powerful set of circumstances and opportunities." Those words expressed by author Malcolm Gladwell have taken on a whole new meaning to me after my time in the ABC program this summer. The work I engaged in fits Gladwell's description perfectly: predictable yet powerful. To the outside eye, the research work I did over the summer may seem extremely tedious and calculated. However, my experience in the ABC program caused me to have a newfound appreciation for the research process. Extreme precautions are taken to make sure that the results turn out useful, and the implications of some of the research conducted is extremely powerful.

I am currently a senior at Martin Luther King High School, and I've been involved with various extracurricular activities that have further solidified my life goals of becoming involved in the medical field. For one, I've worked together with the Mayor of Riverside through the Riverside Youth Council to try to institute city-wide programs aimed at addressing youth obesity and health disparities in underserved communities. I've also volunteered at the Hemet Hospital for 3 years and served as president of the UNICEF club and captain of the Varsity Tennis Team at my school. My experiences outside of school as well as in the ABC program have directed me on a path towards a career in medicine.

I would like to thank Jenniffer Licero and Dr. Marino De Leon for their incredible patience and guidance in ensuring that I had a complete grasp of all of the information and techniques necessary for my research to succeed. Taking part in the ABC program has truly been a blessing.

mRNA EXPRESSION OF FABP4, PPARγ, PRO-IL-1β, UCP2, IκBα, TNFα, NFκB1, AND p65 IN RATS POST SPINAL CORD INJURY

Omkar Panse, Brandon McNichol, Jenniffer Licero, Marino De Leon

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

Over 300,000 people in the United States currently suffer from spinal cord injury, and over 17,000 people are added to that total every year. Research shows pro-inflammatory immune responses to central nervous system (CNS) injury result in loss of locomotor and sensory function. Studies investigating the role of pro-inflammatory macrophages and reactive glial cells show they are major contributors to axonal dieback. Classical differentiation of macrophages results in an M1 phenotype involved in coordinating glial scar deposition whereas M2 differentiation is known to mediate an anti-inflammatory response resulting in axonal regeneration. Pro-inflammatory lipids, released because of injury, are phagocytized by peripheral macrophages and bind to fatty acid binding protein 4 (FABP4), a protein known to coordinate M1 macrophage differentiation. Notably, the role of FABP4 in SCI has not been elucidated. We seek to investigate FABP4's involvement in macrophage differentiation and transcription. mRNA samples were extracted from sham (control) and injury epicenters collected at 7 and 28 days post-injury. mRNA expression of Pro-Interleukin 1 beta (IL-1β), transcription factor p65 (RelA), mitochondrial uncoupling protein 2 (UCP2), fatty acid-binding protein 4 (FABP4), inhibitor of NF-κB (IκBα), peroxisome proliferator-activated receptor (PPARγ), nuclear factor kappa beta 1 (NFκB1), and tumor necrosis factor alpha (TNFα) were measured using real time RT-PCR and normalized with glyceraldehyde 3-phosphate dehydrogenase (GAPDH) and control. We hypothesize that upregulation of pro-inflammatory genes within macrophages is associated with increased levels of FABP4 mRNA in injury. Our results show that SCI results in significant gene upregulation of FABP4 and TNF-α as well as notable upregulation in Pro- IL-1β, IκBα, NfκB1, and UCP2 at 7 days post injury. Conversely, PPARγ mRNA levels were not significantly different from sham at either time point. While the data indicates a possible association between FABP4 and pro-inflammatory gene expression, further investigations are needed to confirm FABP4's role in macrophage function post SCI.

MARK PARENT

ABC PARTICIPANT 2017

When I was younger, I learned a valuable life lesson that I can do anything I set my mind to. The outspoken Kanye West once said, "Our work is never over." Though I may not succeed the first time, I know the key to success is to not lose hope and confidence in myself, be resilient, and work more intelligently the next time around. My long-term goal is to have a career in sports medicine, and I know my goal of helping others to heal and recover faster will take a lot of research, learning, and dedication.

I am seventeen years old and was born and raised in southern California. I will be entering my senior year at Diamond Bar High School and am looking forward to graduating as Valedictorian. I play Varsity Water Polo for DBHS and also participate on a club water polo team. Outside of sports, I am involved in several clubs on campus, including being the vice president of the Black Student Union and the treasurer of the Brahma Tech Academy. Brahma Tech is a four-year STEM program with an emphasis on the relevance and application of science, technology, engineering, and mathematics in the workplace today.

I am currently working in the Department of Microbiology and Molecular Genetics under Dr. Hansel Fletcher. Our research focuses on periodontal disease and the aspects that promote the development of the disease. I would like to thank the ABC program, Dr. Hansel Fletcher, and his lab, especially Hiel Rutanhira and Dr. Yuetan Dou, for this wonderful opportunity and the patience they have had with me over the past weeks.

CONSTRUCTION AND CHARACTERIZATION OF PG1439 MUTANT IN *PORPHYROMONAS GINGIVALIS*

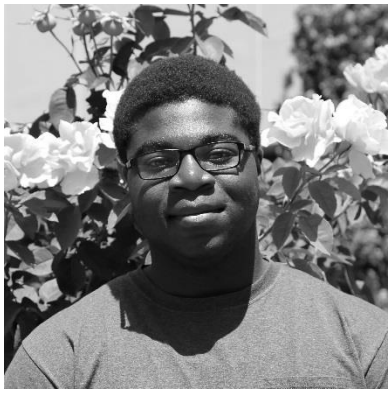
Mark Parent, Hiel Rutanhira, Yuetan Dou, Hansel Fletcher

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

Periodontal disease is known to affect about 50% of the adult population and is characterized by bone resorption and loss of the supporting structures of the teeth. *Porphyromonas gingivalis*, a gram-negative anaerobic bacterium, is strongly associated with the progression of this disease along with other organisms of the "red complex." In order to influence the disease phenotypes, *P. gingivalis* must adapt to the oxidative environment of the periodontal pocket. Due to the need for environmental stress response, various genes are upregulated to aid in survival. A recent study in our lab gave supporting evidence to *PG1439* gene being upregulated about 4-fold when *P. gingivalis* was exposed to 0.25mM of H_20_2. Taken together, this evidence suggests that this gene may be involved in oxidative stress response. The *PG1439* gene is 2076 base pairs in length and codes for a hypothetical protein that has 691 amino acids. According to NCBI blast results, *PG1439* protein has no known conserved domains. To determine the functional role of *PG1439* in oxidative stress response, a mutant with a defect in this gene was created by means of overlap-extension PCR, using the *ermF* cassette for colony selection. The *PG1439* defective mutant was characterized in comparison to the W83 wild type. The growth curve under oxidative stress conditions (H_20_2, 0.25mM) showed no significant differences in comparison to the wild type. However, a major virulence factor of *P. gingivalis* called gingipains, cysteine proteases (Rgp and Kgp), Rgp activity in the *PG1439* mutant, was decreased by 20% in contrast to W83. Furthermore, hemagglutination activity was also reduced in relation to the wild type. Preliminary data suggest further characterization of *PG1439* mutant must be conducted to determine the functional role of this gene in *P. gingivalis*.

SELORM QUARSHIE

ABC PARTICIPANT 2017



I am an incoming senior at Redlands High School. Throughout my life I was always excited to learn about the complex mysteries associated with mathematics and science because, unlike other fields of interest, world problems brought forth to be answered by mathematics and science evolve with humankind. Whether its disease or the necessity to find new energy sources, mathematics and science, just like people, always adapt.

In my high school I rank in the top 5% of my class and am involved in various programs. I have participated in my high school's instrumental music program as a brass player for the past six years. I am involved in my school's Academic Decathlon program that represents my school in county and state competitions. I also compete in Destination Imagination, a STEM-based competition. Within Academic Decathlon I have won awards in science, essay, and interview while also winning regional, state and global recognition in Destination Imagination.

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

Within the ABC program I am researching satiety in *Haliplanella Luciae,* a species of sea anemone, with colleagues Alice Nam and Desiree Torres, under Dr. David Hessinger. The research's focus on the nervous system and cell response to stimuli resonates with me personally because in the future I would like to major in neuroscience with the aspiration to be either a neurologist or a neurosurgeon.

TRP CHANNELS TRIGGER NEMATOCYST DISCHARGE IN SEA ANEMONES

Selorm Quarshie, Desiree Torres, Alice Nam, David Hessinger

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

While humans can consume food in excess, sea anemones cease ingesting prey when they achieve "fullness" due to a robust satiety response. Because overeating is the major cause of human obesity, studying anemone satiety may illuminate conserved satiety pathways applicable to human health. Among animals, sea anemones possess the simplest nervous systems. They also employ stinging nematocysts to capture and kill prey. Nematocysts are eversible organelles produced by cnidocytes, yet little is known about the mechanism of nematocyst discharge. Because the contact-sensitive mechanoreceptors (CSMs) that initiate nematocyst discharge are likely targets of satiety regulation, the goal of this study is to characterize the CSMs. Since TRP channels can be mechanically gated, we predicted that blocking TRP channels would inhibit triggering of nematocyst discharge. Same-sized, starved, monoclonal anemones (*Haliplanella luciae*) were selected and incubated in different concentrations of non-selective TRP channel blockers, lanthanum [$La(NO_3)_3$], or gadolinium ($GdCl_3$). They were then fed a standardized number of brine shrimp larvae to test if blocking TRP channels decreased prey killing. Both rare earth salts potently inhibited prey killing in a dose-dependent manner consistent with TRP channel blocking. Menthol, a selective TRPM8 channel activator, unexpectedly blocked killing and ingestion in a manner consistent with action on TRPM8 channels while also rendering anemones unresponsive to touch stimuli. Our findings indicate that blocking TRP channels, in general, inhibits nematocyst discharge. The role of TRPM8 channels, along with aminoglycoside-sensitive TRPC1 channels from previous studies, suggests more than one type of TRP channel may be involved. Future studies with additional, selective TRP blockers may identify specific TRP channels as CSMs in triggering nematocyst discharge and their possible role in feeding and satiety.

JOSHUA RAMIREZ

ABC PARTICIPANT 2017

Outside of school I actively volunteered and founded a tutoring center for children K-3 from low-income and abused families in San Bernardino, CA. At our center, I find engaging ways to help them learn common core subjects in math and science while helping them conquer their fear around them.

Aside from academics, I am a competitive classical pianist. I am grateful to have participated and won competitions through the Music Teachers National Association. When I am not in competitions or exploring Chopin's thrilling cadenzas, I love playing the piano and volunteer at Loma Linda Children's and Adult hospitals. It is the most remarkable event in the world to see how my passion for music can be used to bring healing to cancer patients and their loved ones in the hospitals. I see these life experiences preparing me to one day combine a healing environment with medicine.

My career goal is to become a surgeon and volunteer my services to less fortunate children domestically and in third world countries. Thus, academically I have been attending Mt. San Jacinto College since the age of 13 and have graduated with four associates' degrees. This fall, I will be attending UCLA as a neuroscience major in the honors program.

I would like to thank those who made this summer an unforgettable experience as well as extend a special appreciation to Dr. Carlos Casiano for always making me think a step ahead, Christina Du Ross for patiently mentoring me, Leanne Burnham for always making long lab days full of laughter, and Greisha Ortiz for helping me know how to properly conduct lab work while salsa-ing to despacito!

RNA SEQUENCING ANALYSIS OF CHEMORESISTANT PROSTATE CANCER CELLS REVEALS POTENTIAL CANDIDATE GENES FOR THERAPEUTIC TARGETING

Joshua Ramirez, Christina Cajigas-Du Ross, Kristoff Foster, Xin Chen, Charles Wang, Carlos Casiano

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

Prostate cancer (PCa) is the most commonly diagnosed cancer in American men and the third leading cause of male cancer deaths. PCa patients undergoing treatment often develop metastasis and castration-resistant prostate cancer (mCRPC). Docetaxel (DTX) is the current standard of care for mCRPC; unfortunately, disease progression and chemoresistance occurs in DTX-treated patients and leads to high mortality. Understanding chemoresistance mechanisms is important to lessen the burden of prostate cancer mortality, particularly in African American men who develop more aggressive prostate tumors and suffer from disproportionate PCa mortality compared to other ethnic groups. Using RNA sequencing (RNAseq) to compare the transcriptomes of chemosensitive and chemoresistant mCRPC cells (PC3 and DU145)**,** we identified new candidate targets for combinatorial therapies. To validate RNAseq findings for selected candidate genes, we used in-house quantitative polymerase chain reaction (qPCR) to confirm elevated mRNA expression and immunoblotting to confirm elevated protein expression in chemoresistant mCRPC cells relative to chemosenstive cells. The increased expression of fatty acid binding protein 5 (FABP5), nestin (NES), and dipeptidyl pretidase (DPP4) revealed by RNAseq was confirmed in DTX-resistant PCa cells. In addition, Ingenuity Pathway Analysis (IPA) of RNA sequencing data identified downregulated genes associated with cellular movement and migration in the taxane-resistant PCa cells, consistent with results observed *in vitro* using wound-healing assay. Taken together, these results suggest that differences in gene expression between DTX-sensitive and DTX-resistant PCa cells may influence the migration and metastatic potential of these cells. Exploring the mechanisms involved in PCa treatment resistance will lead to the discovery of novel targets for combinatorial therapies aimed at attenuating chemoresistance.

SALVADOR RAMOS

ABC PARTICIPANT 2017

I am a rising senior from Vista Del Lago High School, and I participate in baseball, Upward Bound Math and Science, National Honor Society, and Early Academic Outreach Program. Currently, I am at the top of my class. By participating in the ABC program, I have gained better insight into the need of minority representation in the field of medicine. For me, it is important to represent my Hispanic culture in as many ways possible, which is why I also dance Ballet-Folklorico and am in M.E.Ch.A.

In the future, I am not absolutely sure of what I want to study or where I even want to go to school. I know for a fact I will pursue a medical career, but I am uncertain whether I will pursue oncology or another discipline that I might come across in the future. The school I am thinking about going to is UC Santa Barbara (or Davis) because of its location near the beach.

This summer I had the opportunity to work alongside Dr. Salma Khan as well as with my incredible lab partners Kari Roberts, Anna Kwon, and Chelsea Lee, researching thyroid cancer. I am thankful that they had the patience to help guide me through the lab because they had to teach me everything from scratch and deal with my simple mistakes. I am also thankful for the guidance of God, as well as my friend Christine, who both led me to this amazing opportunity where I learned things that most people can only dream of.

"I can do all things through Christ who strengthens me" (Philippians 4:13).

LINKING HIGH BODY MASS INDEX AND LEPTIN RECEPTOR TO THYROID CANCER HEALTH DISPARITIES

Salvador Ramos, Kari Roberts, Mia Perez, Iqbal Munir, Alfred Simental, Marino De Leon, Salma Khan

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

With regard to global health disparities, Filipino Americans (FP) are at highest risk for the development of thyroid cancer (TC). Our previous study provides evidence that loss of vitamin D binding protein (VDBP) is more frequent in Filipino American (FP) patients with TC than in their European American (EA) counterparts. Thyroid cancer (TC) has been linked to obesity, and obesity has been linked to vitamin D deficiency and high leptin. Vitamin D suppresses Leptin; low vitamin D has been shown to be associated with loss of VDBP, suggesting the possibility of interplay between obesity-linked high leptin and low VDBP-related low vitamin D (VD3) in the development of TC and health disparities in the Filipino population. Obesity increases leptin, a hormone producing visceral adipose tissue associated with cancer. Direct effects of obesity on leptin levels are compounded by the loss of VD3 because VD3 normally aids in suppressing leptin expression. Our preliminary data is the first to suggest a genetic link between obesity, VD3, leptin, and thyroid cancer carcinogenesis in the Filipino population. In this study, we have analyzed the following in both ethnicities: staging of thyroid cancer from our patient demographic data, body mass index (BMI), and leptin receptor expression by immunohistochemistry. Our data provides evidence that FPs present with higher staging than EAs. Expression of the leptin receptor protein is upregulated in thyroid cancers from FPs vs. EAs. Taken together, these data implicate the obesity-leptin pathway as a potential contributing mechanism which produces aggressive thyroid cancer leading to cancer health disparities. These studies suggest that increased leptin signaling contributes to thyroid cancer onco-genesis/progression in thyroid cancer health disparities in Filipinos.

GIRISH SENTHIL

ABC PARTICIPANT 2017

"The moment you doubt whether you can fly, you cease forever to be able to do it." This quote has guided me throughout my junior year and has also inspired me to challenge myself to take part in the ABC program. Along with taking challenging AP classes in school, I also participate as a Varsity player on the boys' tennis team, and together we have won 3 CIF championships consecutively for the past 3 years. In addition to tennis, I also participate in many clubs, including Gateway to Medicine, Ping-Pong Club, and Cultures for Youth.

This program has taught me much more than just school would have been able to. My mentor, Dr. Nathan Wall, and PhD students Amber Gonda, Janviere Kabagwira, and James McMullen have all helped and taught me how to approach a lab efficiently and effectively. Of all the techniques used in the lab, the Western blot is my favorite without a doubt. We use techniques such as Western blots in order to discover more in the research area my mentor and I are working on, which is receptor-mediated endocytosis uptake of survivin. We hope to find proteins and specific receptors that indicate the uptake of survivin, allowing us to further understand the role of surviving plays in cancer cells and regular cells.

My dreams and goals are to go to either UCLA or Stanford and to major in biochemistry. I would like to ultimately gain admittance to medical school and to do a general surgery residency. I would not have been able to do any of the work that is done in the lab without the help and support of my mentor, and I thank Dr. Wall and the PhD students for being patient and generous with their knowledge.

RECEPTOR-MEDIATED ENDOCYTOSIS OF EXTRACELLULAR SURVIVIN

Girish Senthil, Amber Gonda, Nathan Wall

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

Survivin is an inhibitor of apoptosis protein (IAP) that affects cancer cell proliferation, apoptotic activity and metastasis. Survivin has been found within the extracellular environment of a cell and has been shown to be transported within exosomes. These nanovesicles allow for Survivin to be released from their cell of origin and taken up by cells within the tumor microenvironment resulting in a modified phenotype which in cancer will increase the aggessiveness of the disease. To be taken up by the cell, we hypothesize that there is an endocytosis of Survivin, mediated by a receptor-ligand complex. To test this hypothesis, we treated four cell lines with conditioned media (CM) containing exosomes that have Survivin within them. CM are media taken from growing cancer cells and has been shown to contain exosomes as well as growth factors and cytokines needed for physiological function. After treating the cell lines with the conditioned media, a BCA was performed on the harvested cell samples in order to quantify the amount of protein concentration that is within the samples. After having an accurate protein concentration, Western blotting was performed to identify if extracellular Survivin was internalized into the cancer cell lines from the Survivin-containing exosomes incubated with them. Western blots identified the endocytosis-associated receptors; Endothelin B Receptor (ETBR) and Glucocorticoid Receptor (GR) were the most expressed among all the cell lines. In addition, Tumor Necrosis Factor Receptor (TNFR) and Low Density Lipid Receptor (LDLR) were not highly expressed within the Hela cell lines but did appear among the other cell lines. This information on which receptors are present within the cell lines allows future studies on Survivin uptake to be more efficient. Also, if a receptor is identified to be an important receptor that greatly impacts the endocytosis of extracellular Survivin, then specific drugs can be created to block or regulate that receptor's activity.

DESIREE TORRES

ABC PARTICIPANT 2017

The summer of 2017 is one that is unique compared to any other summer I've ever had. First, I've never had a job, so the ABC program is the first, but I have a feeling it's one of the best jobs I'll ever have. The experiences and exposure that working in the ABC program have given me are priceless, and I will always cherish the relationships made and the knowledge gained.

This upcoming fall I will become a senior at Etiwanda High School in Rancho Cucamonga. I plan to attend a university, hopefully one of my dreams like UCLA or Stanford, and in the moment, I plan on majoring in forensic pathology. I'm the captain of my water polo team and I really enjoy the sport. I have honors recognition at school as I have completed every year with higher than a 4.0. In my free time I like to volunteer at elder homes and hospitals. I love reading novels, listening to music, watching movies, and sleeping.

In Dr. David Hessinger's lab this summer, I have been studying the feeding habits and satiety of sea anemone for a possible discovery of a satiety inducer to prevent people from overeating. I love doing research and experimenting because exploring new and unknown territories is exciting. I have become very close this summer with my fellow ABC partner Selorm Quarshie and colleague Alice Nam, and we all work really well together, especially when it's 4:45 and all the anemone need cleaning. I appreciate and thank Dr. Hessinger for allowing the development of individuality and independence while working in this lab but also providing guidance and inspiring me with his unique personality and quirkiness.

TRP CHANNELS TRIGGER NEMATOCYST DISCHARGE IN SEA ANEMONES

Desiree Torres, Selorm Quarshie, Alice Nam, David Hessinger

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

While humans can consume food in excess, sea anemones cease ingesting prey when they achieve "fullness" due to a robust satiety response. Because overeating is the major cause of human obesity, studying anemone satiety may illuminate conserved satiety pathways applicable to human health. Among animals, sea anemones possess the simplest nervous systems. They also employ stinging nematocysts to capture and kill prey. Nematocysts are eversible organelles produced by cnidocytes, yet little is known about the mechanism of nematocyst discharge. Because the contact-sensitive mechanoreceptors (CSMs) that initiate nematocyst discharge are likely targets of satiety regulation, the goal of this study is to characterize the CSMs. Since TRP channels can be mechanically gated, we predicted that blocking TRP channels would inhibit triggering of nematocyst discharge. Same-sized, starved, monoclonal anemones (*Haliplanella luciae*) were selected and incubated in different concentrations of non-selective TRP channel blockers, lanthanum [$La(NO_3)_3$], or gadolinium ($GdCl_3$). They were then fed a standardized number of brine shrimp larvae to test if blocking TRP channels decreased prey killing. Both rare earth salts potently inhibited prey killing in a dose-dependent manner consistent with TRP channel blocking. Menthol, a selective TRPM8 channel activator, unexpectedly blocked killing and ingestion in a manner consistent with action on TRPM8 channels while also rendering anemones unresponsive to touch stimuli. Our findings indicate that blocking TRP channels, in general, inhibits nematocyst discharge. The role of TRPM8 channels, along with aminoglycoside-sensitive TRPC1 channels from previous studies, suggests more than one type of TRP channel may be involved. Future studies with additional, selective TRP blockers may identify specific TRP channels as CSMs in triggering nematocyst discharge and their possible role in feeding and satiety.

NATALIA MARIA ZAMORA ZELEDON

ABC PARTICIPANT 2017

I've always loved the human body; I love everything from the chemistry that makes a single cell function to the different taste buds in the tongue. I've also always had a passion for helping people. I have thought about what careers would allow me to pursue my passion for science and helping others, and the idea of being a research scientist popped up. This idea led me to join the ABC program, and my experiences here have truly proved to me that this is what I am meant to be.

I attend San Jacinto High School as an incoming junior, but I was born and raised in Costa Rica for eleven years until moving to the United States in December, 2011. During my last three years in Costa Rica, I was bullied, mainly because of my intelligence. That experience has shaped my personality completely, and I attribute it to allowing me to leave my beautiful, beloved country without hesitation. Either way, I will never forget my country and the sacrifice my parents, a doctor and an engineer, made for my brother's and my education. They left everything they worked hard to get for a place where they would be nothing and have nothing— all for us.

I take AP classes, college classes at MSJC, and am part of the varsity tennis team, National Honor Society, and various clubs. My goals are to attend a prestigious university, such as Stanford or Johns Hopkins, major in biochemistry or molecular biology, and later pursue a PhD. I plan to dedicate my life to finding a cure for a health disparity that forces millions of innocent people to suffer plus contribute to or create various charities around the world that help defeat hunger, poverty, and violence.

EFFECTS OF HYPOXIA ON MLCK ABUNDANCE, VASCULAR CONTRACTILITY, AND VASCULAR FUNCTION IN FETAL SHEEP

Natalia Zamora Zeledon, Chidinma Wilson, Dane Sorensen, William Pearce

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

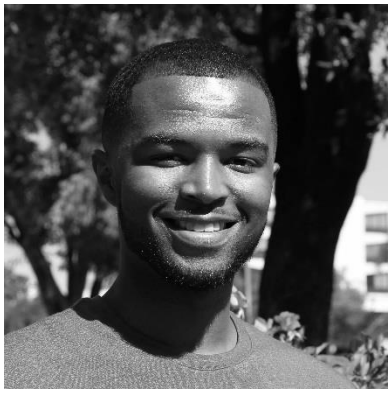
Intrauterine hypoxia, a causative factor in several conditions, can lead to prenatal and neonatal death and various cardiovascular issues possibly leading to death in adults. These problems can be caused by improper adaptation of fetal vasculature, such as reduced contractility. A main process causing contractility in vascular smooth muscle cells is phosphorylation of myosin light chain 20 (MLC-20) by the protein myosin light chain kinase (MLCK). The goal of this project was to test the hypothesis that hypoxia reduces fetal vascular contractility by increasing the degradation of MLCK via the ubiquitin-proteasomal pathway (UPP). To test this hypothesis, fetal arteries were either taken from sheep exposed to hypoxic or normoxic conditions or cultured under those conditions for 72 hours in the presence or absence of the proteasomal inhibitor Epoxomicin and then assessed for MLCK abundance through homogenization, protein assays, gel electrophoresis, Western blots, and Dot blots. We also tested the amount of MLCK mRNA with real-time PCR. Effects of changes in MLCK abundance and hypoxia on artery structure were assessed via measurements of medial thickness, and the effects on function were determined by measuring contractility. Previously published results from our lab indicated MLCK mRNA levels were not affected by hypoxia, but MLCK levels were affected, suggesting the reason for the lowered levels is a post-transcriptional issue. Our results show no difference in MLCK mRNA levels and in MLCK protein levels between fresh (non-cultured) normoxic and hypoxic samples. Samples cultured in the presence of Epoxomicin showed unchanged levels of MLCK. In addition, hypoxia increased the strength of myogenic and potassium-induced contractions in the vessels and decreased the thickness of medial layer in hypoxic samples. These results indicate MLCK protein is being transcribed and translated, and when the proteasome is inhibited, there are no changes in MLCK, suggesting there is no degradation via the UPP.

Undergraduate Training Program (UTP)

Ravon Baynard
Christine Castanon
Yamico Chanza
Kirlann Danclar
Brea Fleming
Brandon McNichol
Antoinette Moore
Brandon Ng
Ashley Vazquez
Cristian Vera-Torres
Jasmine Walsh
Chidinma Wilson

RAVON BAYNARD

UTP PARTICIPANT 2017



I am a current third year psychology student at Oakwood University in Huntsville AL. During my time at Oakwood, I have worked with Professor Rhem using computational chemistry. Outside of doing research, I am a part of a thriving drama ministry, and I serve as a resident assistant and mentor for psychology underclassmen as well. These two activities allow me to not only show others the love of Christ but introduce them to my life's motto: "Change I must or die I will." This quote inspires me to never be complacent or settle for society's norms. In fact, it pushes me to achieve all that God has for me while I am on this earth. Thus, I will achieve my degree in medicine in the future because I believe it is my specific calling to bring restoration to those who are in need.

I am truly honored to be working with Dr. Ying Nie and Dr. Esther Kim, two individuals who are dedicated to improving the lives of others. This summer I studied the amount of post-operative pain patients experience while taking Exparel after spinal surgery.

Outside of my research experience, Dr. Nie and Dr. Kim have both taken their time to give me knowledge, not only about neurosurgery, but how to provide patients with quality service. My career goal is to create a program that will provide minorities with quality mental health care, mentorship, and extracurricular activities.

THE EFFECTIVENESS OF LIPOSOMAL BUPIVACAINE INJECTION FOR POSTOPERATIVE RECOVERY AND PAIN CONTROL IN PATIENTS UNDERGOING LAMINECTOMIES

Ravon Baynard, Ying Nie, Esther Kim

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

Unfortunately, most people in the United States will experience lower back pain in their lifetime. Aggressive back pain can cause disability or other severe damage to the human body. Awareness about lower back pain has increased along with the amount of treatments. This project focuses specifically on a surgery treatment known as a laminectomy. This procedure is used for low back pain with neurodegenerative claudication or radiculopathy. The purpose of this study was to measure the effectiveness of liposomal bupivacaine once injected into patients. Patients who have liposomal bupivacaine injected during their laminectomy will experience less post-operative pain and gain motor function quicker than patients who do not. Patients who did not undergo laminectomies were excluded from this study. The effectiveness of liposomal bupivacaine was measured using the difference of preoperative and postoperative Oswestry Neck and Back Questionnaire and pain scores. The results show that the majority of patients who had laminectomies not only received liposomal bupivacaine injections but experienced improvements in motor function and less postoperative pain, thus, proving the hypothesis to be correct. While this is one study of liposomal bupivacaine, it is evidence that these injections can be used effectively outside of joint surgeries.

CHRISTINE PADILLA CASTAÑON

UTP PARTICIPANT 2017

Currently, I am beginning my second-year at UCLA to earn a degree in neuroscience, am a student in the Program for Excellence in Education and Research in the Sciences, and working toward a minor in disability studies. During my first year at UCLA, I have been able to serve on the Music Ministry Leadership Team for the University's Catholic Center and will be serving as a student leader for our parish this upcoming academic year. This year, I also completed my tenth year of training in classical ballet. With this background, I hope to create a program that teaches ballet to young students who are not financially able to enroll in a ballet school. After completing my undergraduate degree, I aspire to attend medical school and become a research physician to work with health disparities and aid patients in medically underserved areas.

After participating in the ABC Program last summer, I have been fortunate enough to return to Loma Linda and continue working in Dr. Unternaehrer's ovarian cancer research lab. Dr. Unternaehrer and my mentor, Sang Nguyen, have been beyond patient with me. There are no words to explain how grateful I am for the time they have invested in my education and future. Their constant motivation and support have allowed me to grow as a student, researcher, and overall person. This summer, my research focused on assisting to develop a combination chemotherapy treatment for relapsed ovarian cancer patients.

Psalm 121: 7-8 says, "The Lord will keep you from all harm—he will watch over your life; The Lord will watch your coming and going both now and forevermore." He has truly watched over me because without Him, I would not be where I am today.

DUAL TARGETING HOMOLOGOUS REPAIR PATHWAY AND EPITHELIAL-MESENCHYMAL TRANSITION IN HIGH GRADE SEROUS OVARIAN CANCER WITH BRCA1/2 MUTANTS

Christine Castañon, Sang Nguyen, Alyse Hill, Juli Unternaehrer

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

Ovarian cancer is the most lethal gynecological cancer and fifth leading cause of cancer deaths among women. Currently, patients are treated with cisplatin and paclitaxel, but patients often relapse months to years after the initial treatments due to cancer stem cell resistance. Targeted therapies are under development to exploit the vulnerabilities, such as DNA mutations, of individual patient tumors. One useful mutation is the BRCA1 and 2 genes. Cisplatin causes double-stranded DNA breaks, which are usually repaired by homologous recombination (HR). If a BRCA gene is mutated, HR is not available to the cell, so an alternative pathway involving Poly-ADP-Ribose-Polymerase (PARP), will repair the damaged DNA. PARP inhibition (PARPi) can be used to prevent DNA damage repair, creating synthetic lethality and resulting in apoptosis. This treatment has significantly improved survival in ovarian cancer patients. We are studying the interaction of BRCA, PARP, and the epithelial-mesenchymal transition factor SNAI1 (Snail) to determine their role in ovarian cancer stem cells and chemoresistance. Both Snail and PARP have been shown to play roles in cancer cell stemness. The lab hypothesizes that a combination therapy of Snail inhibition and PARPi will overcome mechanisms of relapse in advanced stages of ovarian cancer having BRCA1/2 mutations. Western blots were initially run to show SNAIL1 was present in cell lines examined. We used cell lines known to be mutant or not for BRCA1/2, proteins of 240 and 460kD, respectively, and confirmed this by Western blot. To test the role of these proteins in stemness, spheroid assays were initiated; these studies are ongoing. We are using flow cytometry to detect cancer stem cell marker surface expression in spheroid vs. bulk cell populations. We are using qRT-PCR to detect pluripotency and DNA damage pathway factors in these cells. We plan to treat BRCA1/2 positive and negative cells with PARPi to test synthetic lethality.

YAMIKO JESSICA CHANZA

UTP PARTICIPANT 2017

This is my third summer in a CHDMM program, and my return has reminded me of all the reasons I have strived toward a career in science. My inspiration for joining this program comes from my natural love of science and my hope to someday improve on the healthcare of my community, even if it is in a small way. Mahatma Gandhi best described why I chose to do research again this summer when he said, "The best way to find yourself is to lose yourself in the service of others."

This upcoming school year I will be attending Oakwood University in Huntsville, AL, as a sophomore where I will continue to pursue my Bachelor's degree in biomedical science. After completing my Bachelor's, I will attend graduate school and pursue a career in global health. My family originates from Malawi, Africa, and after hearing many of the stories that express the lack of appropriate medical care available, I was inspired to become a health advocate for underserved areas similar to the cities in which my parents were raised.

Outside of school, I enjoy playing instrumental music and have been playing for eleven years. I play the euphonium and the flute and am a member of Oakwood University's Dynamic Praise Choir. Alongside music, I am involved in the Oakwood University Biomedical Association and the Minority Association of Premedical Students.

I would like to thank Dr. William Langridge, Mary Beth Yu, and Timothy Torrez for welcoming me into the lab this summer and allowing me to observe, understand, make mistakes, and, most importantly, learn.

BLOCKING THE A2B ADENOSINE RECEPTOR DECREASES IL-17 SECRETION IN HUMAN WHITE BLOOD CELLS

Yamiko Chanza, Mary Beth Yu, William Langridge

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

Pro-inflammatory Th17 cells are thought to play a major role in development of the autoimmune respiratory disease asthma, especially asthma that is resistant to steroid therapy. The role of Th17 cells in asthma is to promote neutrophil inflammation, a key element in the development of airway hyper-responsiveness. The literature suggests the major connection between asthma and Th17 cells is aberrant adenosine signaling. Recent studies found that elevated levels of adenosine in the lungs of asthmatics correlate with increased inflammation. Adenosine has also been found to induce acute bronchoconstriction in asthmatics, but not in people who do not suffer from asthma suggesting the presence of a dysregulated response to adenosine in asthmatics. Further, in mice, adenosine was shown to promote differentiation of Th17 cells via activation of the adenosine receptor (A_{2B}AR) found in dendritic cells. However, this function has never been assessed in human cells. Here we report for the first time that human white blood cells (WBCs) cultured with the A_{2B}AR antagonist alloxazine demonstrate decreased production of IL-17, a pro-inflammatory cytokine specifically associated with Th17 cells. We expected exposure to the A_{2B}AR agonist BAY 60-6583 would elevate levels of IL-17. However, the A_{2B}AR agonist had no detectable effect on IL-17 production. Together, our data suggest that an antagonist for the A_{2B} adenosine receptor may reduce the severity of autoimmune hyper-responsiveness in steroid-insensitive asthma. However, further research will be needed to clarify the role of A_{2B}AR in modulation of Th17 cell stimulated asthma.

KIRLANN DANCLAR

UTP PARTICIPANT 2017

Science is a field I have always loved and knew I would avidly participate in it in the future. There was never a doubt or question about that for a very long time until I reached college. My freshmen year was a year of discovery, and I learned a lot about who I was. One of the first things I learned was that the hard science courses were not for me. I became a psychology major, and I have been in love ever since.

I attend Oakwood University and am fortunate to have become a mentee to a fantastic advisor. She saw the potential I possessed and took it upon herself to nurture and harvest that potential which explains why a psychology major is a part of the UTP program. She saw my interest in neurological disorders and decided I needed to pursue that interest. She advised me to join IMARI (Increasing Minority Admission to Research Institutions), and that is why this summer I was able to conduct research on a neurological disorder. This experience will help fulfil my dreams of attending Georgetown University attaining a PhD in Psychology with a concentration in cognitive neuroscience.

I would like to thank Dr. Charles Wang for accepting me into his lab and allowing me to learn all I could about Parkinson's disease. I would also like to thank Dr. Xin Chen, Dr. Seta Stanbouly, and Diana Ho for helping me understand what intricate details working in the lab on a specific project entails. Finally, I would like to thank God for placing these individuals in my life. I greatly appreciate them and know this incredible opportunity will take me far in my academic career.

TOP CANONICAL PATHWAYS OF PARKINSON'S DISEASE

Kirlann Danclar, Xin Chen, Seta Stanbouly, Charles Wang

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

Parkinson's disease (PD) is a chronic and progressive movement disorder (symptoms worsen over time). Diagnosing Parkinson's disease is quite difficult especially in mild cases. Physicians have to look carefully into a patient's neurological history and perform very basic examinations. These examinations, though, are only capable of identifying the clinical signs and symptoms. The only time a final confirmation can be made of whether or not a patient truly had PD is after death during an autopsy. Having acknowledged the degenerative nature of the disease, specifically the malfunction and death of neurons in the brain, scientists have furthered their research to learn that dopamine neurons found in the substantia nigra pars compacta is reported to be associated with the disease. PD patients may lose 50% to 70% of dopamine neurons by the time the disease has run its course. The aim of this study was to understand the data analysis of the prominent genes in PD. What is necessary to recognize is whether the onset can be leading in understanding the genetics of the disease. There are different subgroups for the age of onset in Parkinson's disease—younger than 50 years, 50–59 years, 60–69 years, and 70 years or older— and the phenotype of the disease is different depending on the age of onset. There have been gene mutations that can cause PD, but they represent a small number. Several of the gene mutations belong to Dopamine-DARPP32 Feedback in cAMP Signaling, Protein Kinase A Signaling, Nitric Oxide Signaling in the Cardiovascular System, Cardiac B-adrenergic Signaling, Phosphatidylethanolamine Biosynthesis II, Corticotropin Releasing Hormone Signaling, Molecular Mechanisms of Cancer and ErbBH Signaling. By learning and analyzing the behavior of these mutations scientists may be able to identify the earlier signs of Parkinson's disease which may regress and possibly prevent the onset of the disease.

BREA FLEMING

UTP PARTICIPANT 2017

In the fall I will be entering my third year as a biology undergraduate student at Oakwood University in Huntsville, AL. Attending a historically black institution gives me an opportunity to explore all my passions: faith, education, service, and black culture. I am afforded the opportunity to teach in the biology and chemistry departments as a lab instructor. My co-curricular activities include Cancer Awareness Research Association (CARA), Pre-Dental Society, and United Student Movement Senate. In my spare time, I listen to music and sing to my heart's content.

My aspiration is to obtain a DDS/PhD to become a pediatric dentist and to explore the relationship between oral health and cancer which could lead to early diagnosis, better treatment options, and outcomes in the minority population.

Walking to lab on my first day in the UTP program, I came across a wall, and on it was the scripture "Be joyful in hope, patient in trials, constant in prayer" (Romans 12:12). In these past 8 weeks, this scripture became progressively relevant to me. The experiments I performed required a great deal of focus and even more patience. This summer I was blessed to be working under Dr. Saied Mirshahidi in his bio specimen lab. Under the supervision of my mentor, Dr. Rosalia Campion, I was able to study how the YM155 treatment influences splicing of various genes in the HL60 AML (acute myeloid leukemia) cell line.

I would like to express my gratitude to Dr. Mirshahidi and Dr. Campion for training me with such kindness and patience. My life has been truly enriched from this opportunity and from the insight I now have of the dedication of those who work towards the unending pursuit of eliminating health disparities.

YM155 TREATMENT PROMOTES PRO-APOPTOTIC SPLICING OF MCL-1 IN ACUTE MYELOID LEUKEMIA

Brea Fleming, Saied Mirshahidi, Mark Reeves, Rosalia de Necochea-Campion

Department of Medicine, Basic Sciences and Biospecimen Laboratory, Loma Linda University Cancer Center, Biospecimen Laboratory, Department of Surgery, School of Medicine, Loma Linda University, Loma Linda, CA

Acute Myeloid Leukemia (AML), a cancer of the myeloid line of blood cells, develops in the bone marrow and hinders the production of normal blood cells. Current therapies for the treatment of AML are associated with high rates of relapse and poor survival outcomes for many patients. As our understanding of molecular factors involved in disease aggression grows, the search for therapeutic targets to improve treatment outcomes continues. Recently, recurrent mutations in spliceosome machinery and aberrant splicing events have been recognized as an important component of AML development. Alternative splicing, normally a highly regulated process, enables an mRNA strand to produce transcript variants that may code for different proteins with opposing functions. Dysregulation of alternative splicing mechanisms in AML is associated with changes in the apoptotic signaling network, chemoresistance, and poor patient prognosis. Conversely, anticancer drugs with the ability to increase pro-apoptotic splicing events may overcome some chemoresistance mechanisms and improve treatment efficacy. YM155 (Sepantronium Bromide), a novel therapeutic in clinical development as an anticancer drug, can induce apoptosis in AML cells and was shown to alter apoptotic gene splicing in a previous study. In this study, we examined YM155's ability to change the splicing patterns of three genes in the apoptotic signaling network: *Mcl-1*, *Bcl-x*, and *Caspase-9*. Each of these genes produces alternatively spliced transcripts with conflicting functional roles. *Mcl-1*$_S$, *Bcl-x*$_S$, and *Caspase-9a* are pro-apoptotic isoforms while *Mcl-1*$_L$, *Bcl-x*$_L$, and *Caspase-9b* are anti-apoptotic isoforms. We exposed an acute promyelocytic leukemia cell line (HL-60) to a physiologically relevant concentration of YM155 and measured changes in expression of these alternatively spliced transcripts. Our results provide insight into YM155 apoptotic mechanisms in AML and may help expand options for targeted therapeutic strategies in the future.

BRANDON McNICHOL

UTP PARTICIPANT 2017

Art and science, two sides of the same coin, a coin which serves as a representation of my life and academic work. From a young age, my parents fostered within me a love for music and biology, both of which I proudly study at Rollins College in Winter Park, FL, where I am currently pursuing a double major in biochemistry and cello performance. Although these areas of study might seem unrelated, I found connection between the two. The ordered systems of biological pathways mirror the mathematical form seen in music just as the emotional content of a composition reflects the nuance of the human body.

I am honored to participate in the UTP program at Loma Linda University. It was here my mother and father received their advanced educations. I hope to follow in their footsteps as I strive to become a medical doctor. After working with Jenniffer Licero and Dr. Marino De Leon, I have a more complete picture and deeper appreciation for how important research is in terms of tackling health disparities.

I plan to take the many valuable lessons I learned this summer and apply them to the laboratories at my present institution and my future medical school. After participating in the UTP program, now more than ever, I am inspired to pursue an MD-PhD degree and combine the power of research with the practice of medicine. In this work, I hope to further my understanding of the world of science and better appreciate the art that encapsulates it.

UPREGULATION OF FATTY ACID BINDING PROTEIN 4 IS ASSOCIATED WITH INCREASED LEVELS OF PROINFLAMMATORY PROTEINS

Brandon McNichol, Omkar Panse, Jenniffer Licero, Marino De Leon

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

Spinal cord injury (SCI) is characterized by permanent loss of motor and sensory function. The lack of neuroregeneration is attributed to scar formation and secondary damage to neural tissue due to prolonged inflammation at the site of injury. Classically activated monocytes, M_1 macrophages, inhibit neuroregeneration as they orchestrate the neuroinflammatory response. In atherosclerosis, insulin resistance, and metabolic syndrome, it is well documented that polarization of macrophages to the M_1 phenotype is mediated by the activity of Fatty Acid Binding Protein 4 (FABP4). However, the role of FABP4 in macrophage polarization in SCI is underexplored. In this study, the relationship between FABP4 and pro-inflammatory proteins NF-κB and phosphorylated P-IκBα and anti-inflammatory protein UPC2 in SCI were examined. We hypothesized that high levels of FABP4 correlate with high levels of proinflammatory proteins and low amounts of anti-inflammatory proteins in the injured rat spinal cord. In order to test our hypothesis, spinal cord epicenters of injured and sham rats at 7 and 28 post injury were collected. Protein was extracted and levels of FABP4, UPC2, P-IκBα and NF-κB were determined using gel electrophoresis and immunoblotting. Results show significant upregulation of FABP4, NfκB, p-IkBα, and UCP2 protein levels in injured animals as compared to sham. NFκB expression increased as FABP4 levels increased while p-IkBα and UCP2 decreased as FABP4 increased. Our findings suggest there may be a possible link between FABP4 upregulation and increased expression of pro-inflammatory proteins in the injured rat spinal cord. With these findings the role of FABP4 in macrophage polarization can be better understood in SCI and methods to address neuroinflammation might be developed.

ANTOINETTE CHRISTINA MOORE

UTP PARTICIPANT 2017

I was born on the beautiful island of Barbados and raised in the United States of America. Seventh-day Adventism is my faith, and my mother has always encouraged me to place my faith in God and never question His plans for me. In my spare time, I love to draw. I am under President Obama's Deferred Action for Childhood Arrivals program, which allowed me to enter school at 21 years old, an answer to prayer from God. Asthma runs in my family, which is one of the driving forces behind my current career aspirations to be a pulmonologist. Along with my plans to run a low-cost clinic with an ethnically diverse staff of medical professionals, I also plan to create a long-term mentorship connecting underrepresented medical professionals with minority children to guide them on their career pathways.

I am a junior at Oakwood University in Huntsville, AL. I was encouraged to apply to the UTP program by Dr. Marie-Claire Boutrin who received her PhD from Loma Linda University. She is not only my boss but also a caring mentor, professionally and spirituality. I would like to become more involved in pulmonary research as well as other health disparities, which is why I greatly appreciate this program.

This summer, I am working in Dr. Valery Filippov's lab. We studied peptides as potential biomarkers as a non-invasive method for monitoring renal disease as a result from surgery.

I am forever blessed and grateful to Dr. Filippov for encouraging and guiding me along with my project and putting up with my thousands of questions. This program has fueled the fire in me to pursue my personal passion and apply my knowledge to help others.

PEPTIDES AS POTENTIAL BIOMARKERS FOR URINARY TRACT INJURIES

Antoinette Moore, Valery Filippov, Guangyu Zhang, Sam Siddighi,
Penelope Duerksen-Hughes

Center for Health Disparities and Molecular Medicine, Department of Basic Sciences, Division of Biochemistry, Department of Gynecology and Obstetrics, School of Medicine, Loma Linda University, Loma Linda, CA

Although urinary tract injuries in gynecologic surgery are rare, complications can pose serious issues often associated with morbidity. Delayed diagnosis of these injuries is a major factor that increases the risk of such complications. Peptides circulating in urine are considered one of the best candidates for biomarkers of urinary tract injury and disease. The aim of this project was to estimate the number of peptides in urine samples, through the use of LC-MC chromatography, in order to evaluate the potential of using peptidomics in a search of biomarkers for urinary tract injuries. Seventeen urine samples were clinically annotated from patients who underwent gynecologic surgery. Of these seventeen samples, five samples were used for further analysis to detect peptide composition. Three separate aliquots of 12 ml for each sample were subjected to peptide purification using the solid-phase extraction method. Purified peptides were desalted using Pierce C18 tips and run on a LTQ-Orbitrap Velos mass spectrometer. Peptides were identified by a search against the human protein database. We were able to identify 79 peptides and 38 proteins in the analyzed urine samples. Our results indicated that this approach is capable of detecting a significant number of protein molecules suitable for biomarker analysis. However, additional improvements in the method used and the analysis of obtained data are needed. The results of this experiment will contribute to finding reliable and cost-effective biomarkers to minimize the risk of complications of urinary injuries, both intraoperative and postoperative.

BRANDON NG

UTP PARTICIPANT 2017

"Fail forward" sounds contradictory at first, but in practice it makes sense. These words my father has told me time and time again really struck a chord when I became more interested in exploring science. I understood this saying through the only way one could: making mistakes and learning to move forward and advance instead of dwelling on them. Laboratory research is no different.

Repeated failed experiments and the rare, sweet taste of success have challenged me immensely and taught me how to be patient and tenacious. But more than that, it is opportunities like these that God has given me to learn and to give me a chance to meet so many like-minded and driven individuals in the UTP and summer programs here at Loma Linda University for which I am so grateful.

I have just finished my first year at Rensselaer Polytechnic Institute in Troy, NY, as part of the 7-year physician-scientist accelerated medical program in conjunction with Albany Medical College. I plan to pursue a Distinction in Research for my MD and am considering pursuing a PhD as well.

This summer I had the pleasure of working in Dr. Kimberly Payne's lab under the tutelage of Dr. Cornelia Stoian on high-risk B-cell Acute Lymphoblastic Leukemia (B-ALL) and in particular the variant characterized by the overexpression of CRLF2 (CRLF2 B-ALL). Our research focused on the potential use of the SOCS family genes (specifically SOCS2 and SOCS3) to turn off receptor signaling of the cytokine TSLP which normally activates the CRLF2 pathway for cell survival and proliferation. We were also interested in seeing the regulation of SOCS gene expression due to TSLP at various time points in our experiment.

UPREGULATION OF SOCS GENE EXPRESSION: A MECHANISM FOR THE ANTI-LEUKEMIA EFFECTS OF TSLP IN HIGH-RISK CHILDHOOD LEUKEMIA

Brandon Ng, Hannah Choi, Cornelia Stoian, Kimberly Payne

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High-risk B-cell Acute Lymphoblastic Leukemia (B-ALL) is one of the most aggressive forms of childhood leukemia. One subtype of this disease is characterized by overexpression of the cytokine receptor, CRLF2. This CRLF2 B-ALL disproportionately affects Hispanic children who have almost five times the risk of developing this cancer and relapsing after treatment as compared to children of other races. The CRLF2 receptor is activated by the cytokine, TSLP. TSLP-induced activation of CRLF2 stimulates the JAK2/STAT5 pathway which promotes increased cell survival and proliferation. Thus, overexpression of CRLF2 likely contributes to leukemia by promoting survival and proliferation of cancer cells, and shutting this pathway down could be an effective way to treat this leukemia. CRLF2 signaling in normal cells is temporary because activation of CRLF2 also leads to upregulation of the Suppressor of Cytokine Signaling (SOCS) family of genes that shut down the CRLF2 signaling pathway through several different mechanisms. We hypothesize that TSLP can be used to upregulate expression of the SOCS genes (SOCS 2 and SOCS 3) and ultimately be used to shut down CRLF2 signals as a treatment for CRLF2 B-ALL. The intent of this research is to determine if TSLP upregulates expression of SOCS2 and SOCS3 and, if so, the time course for upregulation. The two CRLF2 B-ALL cell lines, MUTZ-5 and CALL-4, were treated with and without TSLP (15 ng/mL) and evaluated by flow cytometry to determine expression of SOCS2 and SOCS3 after 1, 2 and 3 days of culture. Our results showed variable results for SOCS2 expression; however we found that TSLP upregulated SOCS3 beginning at day 1 and continuing through day 3 in both MUTZ5 and CALL-4 cell lines. These data support the use of TSLP as a biologic for the treatment of CRLF2 B-ALL to reduce pediatric cancer health disparities for Hispanic children.

ASHLEY VAZQUEZ

UTP PARTICIPANT 2017

Fall 2016 I started my undergraduate education at the University of California, Riverside, as a biochemistry major, but by the end of my first year, I decided to change into cell, molecular, and developmental biology. This change was inspired by my previous research in the ABC program and my newly found passion for molecular biology.

To be a leader and successfully aid those around me has always motivated me to continue my education and reach my goal to become involved in the medical field.
My ambition to become either a pediatrician or a medical researcher revolves around my passion to further improve the health and lives of everyone and give back to my community. As I continue to learn and grow in my skills within the lab, I have also grown spiritually. As Maria Montessori once said, "The things he sees are not just remembered; they form a part of his soul."

I would like to thank Dr. Sean Wilson's lab for welcoming me back another summer and allowing me to fully experience the life of a scientist. With the guidance of both my mentors and peers, I have been able to further develop my career interest as a biomedical researcher as well as broaden my knowledge on the health impact that our research holds.

EFFECTS OF CHRONIC HYPOXIA TO BETA ADRENERGIC INDUCED VASODILATION IN FETAL AND ADULT SHEEP

Ashley Vazquez, Marvin Amen, Brandon Painter, Raveena Jalota, Quinton Blood, Lubo Zhang, Sean Wilson

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

Hypoxia, the lack of oxygenation in tissues, can be associated with high altitude living. Fetuses afflicted with such conditions are subjected to high mortality and morbidity rates. It can lead to developmental abnormalities in vasoreactivity of the pulmonary arteries that may contribute to pulmonary hypertension in fetuses and adults. While the role of beta adrenergic signaling is a major focus for treatment of asthma, far less is known about its role in pulmonary arterial function. Previous evidence illustrates that beta adrenergic signaling pathways hold promise for the treatment of pulmonary hypertension. As Ca^{2+}-activated K^{+} channels (BK_{Ca}) are important to beta adrenergic-mediated pulmonary vasorelaxation, their dysfunction may contribute to chronic hypoxia-induced pulmonary hypertension. We hypothesize that beta-AR-mediated vasodilation may be reduced following chronic hypoxia due to the loss of dependency on BK_{Ca} channels. Such channels may therefore provide a powerful therapeutic advancement in the treatment pulmonary hypertension. We isolated pulmonary arteries from adult or fetal sheep that gestated at 700 meters (normoxic) or 3,801 meters for 110+ days. Then, we performed myography to measure isometric tension in pulmonary arteries and studied their vasorelaxation due to the beta-agonist Isoproterenol (ISO) and the methylxanthine phosphodiesterase inhibitor, IBMX. Our data shows that ISO-mediated relaxation was preserved following chronic hypoxia in fetal and adult sheep; however, the effect was greater in arteries from adult hypoxic groups than fetal hypoxic ones. The addition of the BK_{Ca} channel inhibitor, tetraethylammonium (TEA), reduced the effects of ISO-mediated vasorelaxation, suggesting the BK_{Ca} channel is important to vasorelaxation in hypoxic conditions. Overall, these studies provide significant evidence that beta adrenergic pathways rely on BK_{Ca} in fetal groups more than adult hypoxic groups. The BK_{Ca} channel could be therapeutically significant, and alterations in their activity may contribute to the development of disease.

CRISTIAN VERA-TORRES

UTP PARTICIPANT 2017

"Do not withhold good from those to whom it is due, when it is in your power to act" (Proverbs 28). This principle I will continually follow, for living to serve others is a purpose that has always been embedded within me. It wasn't until my participation in the ABC program last year that I began to understand how I wanted to help bring change to the lives of others. I was exposed to the unfortunate reality that certain populations in our society are underrepresented and underserved. They are burdened with overwhelming disadvantages, a few being discrepancies in genetics, socioeconomic status, inadequate healthcare, and lack of education. These factors all partly contribute towards health disparities as certain chronic diseases are more prevalent in these populations than others. It frustrates me to see this very phenomenon apparent in my own family background as many of my relatives in the underprivileged parts of Mexico struggle with high rates of hypertension, diabetes, and neurodegenerative diseases. I hope to uphold my purpose by giving a voice and a hand to those hindered with health disparities through scientific research and medical practice.

I realize I cannot help alleviate our societal health issues without being properly prepared. Hence, I am currently studying at UC San Diego as a biochemistry major with plans of pursuing an MD/PhD in the future. I am grateful to be able to return to Dr. Marino De Leon's laboratory under the guidance of Perla Ontiveros Angel. As a first-generation college student from immigrant parents, I will not take my schooling nor this program for granted. Rather, I'll continue to find opportunities to translate my knowledge towards means of improving the wholeness of others.

THE INTERPLAY EFFECT BETWEEN REACTIVE OXYGEN SPECIES AND CELL VIABILITY IN NGFDPC12 CELLS TREATED WITH PALMITIC ACID AND DOCOSAHEXAENOIC ACID

Cristian Vera-Torres, Perla Ontiveros Ángel, Jo-Wen Liu, Marino De León

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

Reactive oxygen species (ROS) are critical for proper cellular function since they can oxidize or take electrons from other chemical substances to complete their electron shell and gain stability. However, excessive amounts of ROS in cells can lead to a stress-inducing oxidation cascade that can modify vital cell structures, such as DNA, proteins, and polyunsaturated fatty acids to become damaged and unstable. Consequently, these processes can result in cellular dysfunction and death. This phenomenon is an important component attributed to widespread conditions such as peripheral neuropathy and neurodegenerative diseases. Previous publications from our laboratory have shown palmitic acid (PA), a saturated fatty acid, induces lipotoxicity or injury caused by overloading of fats while significantly increasing ROS generation and loss of cell viability. However, detrimental effects of lipotoxicity can be suppressed by the polyunsaturated omega-3 fatty acid, docosahexaenoic acid (DHA). In this study, we investigated the association of ROS accumulation and cell viability in nerve growth factor-differentiated pheochromocytoma (NGFDPC12) cells treated with PA, DHA and PA/DHA to further understand the protective mechanism of DHA during lipotoxicity. The cellular ROS level after 16 hours of fatty acids treatment was determined by detecting the oxidation of the ROS marker, 2',7'-Dichlorofluorescin diacetate (DCFDA) via flow cytometry, and cell viability was measured by colorimetric analysis of crystal violet staining of attached cells at 40 hours after treatment. In addition to DHA, oxidized DHA, considered an ROS itself, is included in the treatment. Our results indicate that although DHA and oxidized DHA increase ROS level similarly to PA, they both yield contrary effects to PA-induced lipotoxicity by stimulating cell survival and increasing cell viability. The data suggest treatment with DHA and oxidized DHA produces ROS beneficial for cellular homeostasis, resulting in cell survival while-PA induced lipotoxicity produces ROS promoting cellular stress capable of disrupting cell functions resulting in cell death.

JASMINE WALSH

UTP PARTICIPANT 2017

During my time at Oakwood University in Huntsville, AL, I have learned that I am most passionate about making meaningful changes in my community. I am currently a junior biochemistry major with a food and nutrition minor as I enjoy both chemistry and learning more about healthy living. As a part of the healthy campus 2020 ambassadors, I work to encourage my peers to make meaningful lifestyle changes. Furthermore, I am a chemistry tutor and enjoy helping my tutees with special needs or difficulties in chemistry excel in the course.

The research that I have been doing at Loma Linda under Dr. Chris Perry and Dr. Kwon has been eye opening. I have learned so much from the lab experience as well as the lab meetings. The most exciting part about research so far is realizing just how much knowledge is yet to be discovered. Our research is literally centered on answering questions that don't have answers. Furthermore, the answerless questions I thought of while researching have inspired me to one day conduct experiments of my own. I can honestly say that I am more confident in my research abilities because of this program. I am thankful to Dr. Perry and to the program directors for allowing me to have this opportunity.

TOOTH STAIN PENETRATION SIMULATED WITH GOLD NANO-TECHNOLOGY

Jasmine Walsh, Stephanie Merlos, Elvin Walemba, Christopher Perry, So Ran Kwon, Yiming Li

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

As the demand for whiter teeth among the general population has increased, different forms of anti-staining and whitening products have increased as well. However, the mechanism of stain penetration that could propel innovations in preventative tooth staining treatments remains unknown. The objective of this study is to determine the mechanism of the stain internalization process using re-structured gold nanoparticles of varying surface chemistries (biomolecules, polar organic, and lipid). We hypothesize that the rates of staining and penetration are dependent on the chemical classification of the stain. The initial part of this study was performed by synthesizing gold nanorods with cationic and anionic surface coatings and characterizing their absorption on hydroxyapatite substrates. Cationic gold nanorods are synthesized using standard borohydride reduction with 0.1 M cetyl trimethyl ammonium bromide (CTAB) as the capping agent. To make anionic gold nanorods, CTAB is substituted with 11-mercaptoundecanoic acid (MUDA), which is covalently bonded to the nanorods to simulate polar organic stains. The gold nanorods are characterized using infrared and UV-VIS spectroscopies along with atomic force (AFM) and scanning electron microscopies (SEM). Localized plasmon absorption peaks at 550 nm and 700 nm on the UV-VIS spectrometer with an aspect ratio of approximately 3:5 on SEM confirm the synthesis of gold nanorods. AFM and SEM imaging results are optimized with three dilutions (1/10, 1/100, 1/300) of 50 mM 3-Amminopropyltrimethoxysilane (APS) fixative and gold nanorod concentrations (1/10, 1/50, 1/100). Hydroxyapatite discs immersed in CTAB and MUDA substituted gold nanorods are imaged with SEM and show a difference in surface interaction with the hydroxyapatite. Upcoming experiments will include time course penetration measurements into the enamel subsurface bovine teeth.

CHIDINMA WILSON

UTP PARTICIPANT 2017

As a young woman who has moved between three states over six times, I am no stranger to change. Throughout every residence, school, and climate adjustment, one thing remained: my passion for medicine. Through exposure to various economic and racial demographic groups, my eyes were opened to disparities in the healthcare system. Thus, my fascination with the effects of socioeconomic status on physical wellbeing blossomed. My career goal is to remedy this issue via the practice of emergency medicine and research on the sociological and biological aspects of health disparities.

I am currently a junior at Oakwood University with a double major in Spanish and biomedical sciences. The verse, "I can do all things through Christ who strengthens me" (Philippians 4:13), has been one of the driving forces that brought me through my college education thus far. By His grace, I have been able to participate in extracurricular activities such as choir and school clubs, volunteer with community outreach groups, and maintain a competitive GPA. Whenever I have down time, I love to read or travel. These two activities have a seemingly magical ability to take me on an adventure to either a fantasy world or a new, breathtaking location. This past year, I studied abroad in Argentina at Universidad Adventista del Plata. It was a life changing experience in which I not only learned Spanish but also gained an understanding of local health disparities. I am looking forward to what the Lord has in store for me, both as a researcher and as a healthcare professional.

I would like to acknowledge Dr. William Pearce for mentoring me as I conducted research in his perinatal laboratory, and Dane Sorensen for taking the time to educate me daily as I worked on this project.

EFFECT OF HYPOXIA ON MYOSIN LIGHT CHAIN KINASE ABUNDANCE IN ADULT OVINE ARTERIES

Chidinma Wilson, Natalia Zamora, Dane Sorensen, James Williams, William Pearce

Center for Health Disparities and Molecular Medicine, Perinatal Biology,
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Vascular structure and function adapt dynamically during normal physiological maturation and in response to pathophysiological stresses, such as atherosclerosis, tumorigenesis, and long term hypoxia. Recent publications from our laboratory demonstrate that long term hypoxia alters the abundance of the rate limiting enzyme for smooth muscle contraction, myosin light chain kinase (MLCK). As for all proteins, MLCK abundance is determined by the balance between its synthesis and its degradation. Whereas the ubiquitin proteasome pathway (UPP) is a major mechanism governing the degradation of many proteins, its role in regulating MLCK abundance is unknown, particularly under conditions of hypoxia. The aim of this study was to test the hypothesis that chronic hypoxia attenuates vascular contractility through increases in proteasomal degradation of MLCK protein. To explore the role of the UPP in MLCK degradation, we used gel electrophoresis to assess the impact of long-term hypoxia on MLCK abundance in fresh arteries. Next, we developed an *in vitro* organ culture hypoxic injury model to study the effects of proteasomal inhibitors (Epoxomicin) on rates of MLCK degradation. Finally, we quantified the effects of proteasomal inhibition on artery structure and function as revealed by changes in medial wall thickness, arterial stiffness, myogenic tone, and potassium-induced contractility. Although different from our previously published results, our findings indicate that MLCK abundance was increased in long term hypoxic adults. This discrepancy is most likely due to a change in homogenization technique. Additionally, we discovered that hypoxia increased both medial thickness and arterial stiffness while it negatively affected myogenic tone as well as potassium-induced contractility. Together, these results suggest that regulation of MLCK abundance is an important component of vascular adaptation to chronic hypoxia. In turn, clinical manipulation of these effects has the potential to yield improved strategies for management of diseases characterized by chronic hypoxia, such as asthma, COPD and PPHN.

Medical Training Program (MTP)

Yadier Brito-Cuas
Kristoff Foster
Emil Harty
Jean-Paul Inesta-Rivera
Amanda Ortiz Vicil

YADIER BRITO-CUAS

MTP PARTICIPANT 2017

One of the most successful German biathletes of all time, Magdalena Neuner, once said, "Do my best, so that I can not blame myself for anything." I take these words to heart, striving to be dedicated and enthusiastic about medicine and doing my best every day so that one day I can provide the best possible care for my future patients. Yet, giving our best all the time is not easy, even though this medical career requires it. I will endeavor still to do my best.

Currently, I have just completed my first year of the medical doctor program at San Juan Bautista School of Medicine in Caguas, Puerto Rico. One of the school's missions is commitment to helping the community, and this commitment resonates with me. The devotion to helping others has always been part of my life. Community service activities through my life have given me more than I was able to give to those in need. This desire to give back to the less fortunate led me to choose a career in medicine and is also the reason behind my love for research. After I complete medical school, I would like to do a rigorous internal medicine residency.

I love that research by scientists can help provide physicians with the tools to help patients. This program not only lets me learn and develop new research skills, but it exposes me to those who are underserved in this country. I want to thank Dr. Abigail Benitez for giving me the opportunity to work with her during this summer. Her teaching and mentorship will help me achieve the next level in my research skills, which I plan to use in the future to help others.

DIFFERENCES IN MEMORY B CELL HOMEOSTASIS BETWEEN AFRICAN-AMERICAN, HISPANIC, AND CAUCASIAN KIDNEY TRANSPLANT PATIENTS ON LOW DOSE THYMOGLOBULIN

Yadier Brito Cuas, Terry-Ann Milford, Jill Weissman, Pedro Baron, Lorena Salto, Kimberly Payne, Abigail Benitez, Michael De Vera

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

Antibody mediated rejection (AMR) in kidney transplant patients is difficult to detect during early stages, and a need exists for biomarkers that detect these early stages. Moreover, health disparities exist among kidney transplant patients. Studies show that African American patients have difficulty acquiring a donor kidney and also have worse clinical outcomes post-transplant that may lead to rejection. Our study aims to evaluate memory B cell subsets and B cell activating factor (BAFF) homeostasis as biomarkers to detect early stages of AMR among African-Americans, Hispanics, and Caucasians. Peripheral blood was drawn from end-stage renal disease patients pre-transplant and at post-transplant time points. Immunosuppression therapy included low dose thymoglobulin (2.3-5.4 mg/kg), tacrolimus, MMF, and prednisone. PB was stained for flow cytometry to assess memory subsets. Our results showed no significant differences in serum creatinine, GFR, and immunosuppression therapy between the 3 ethnic groups. Between time points, we noted significant decreases in MMF and prednisone administration ($p < 0.0001$) after 3 months post-transplant. Memory B cells were not significantly different between ethnic groups. Combined patient analysis showed significant differences in BAFF levels ($p < 0.0001$), decreasing between pre-transplant and 1 month and rising again at 6 months. Naïve ($p = 0.0305$), unswitched memory ($p = 0.0258$), and switched ($p = 0.0225$) memory cells showed significant alterations. Future studies will focus on health disparities differences that were not apparent perhaps due to our small sample size among African-American and Caucasian patients. B cells play a crucial role in the development of AMR, and they could potentially provide a biological rationale that will translate into how immunosuppression therapy is administered to kidney transplant patients at risk of developing AMR.

KRISTOFF FOSTER

MTP PARTICIPANT 2017

In June I ended my first year of medical school here at Loma Linda University. Before coming here, I graduated from Oakwood University in May, 2016. My undergraduate experience exposed me to service opportunities both in my school community and the Huntsville community at large. Since medical school, I've been able to stay involved in the community through programs such as CKC music, where we teach elementary school children music skills, and Student National Medical Association, an association dedicated to improving health disparities in the US.

This summer I have been working in the lab of Dr. Carlos Casiano. My project involved purifying an important prostate cancer resistant protein, LEDGF, so we can eventually understand the ability of certain small molecule inhibitors to re-sensitize chemoresistant metastatic prostate cells to chemotherapeutic drugs. I've had so much fun working with all the members of the lab. Thank you so much!

While I don't know what type of physician I'll become, I'm grateful I got to work at the Center for Health Disparities and Molecular Medicine here at Loma Linda because it reaffirmed my passion and commitment to serving underrepresented minorities and helping to eliminate health disparities. I still have a long, exciting, yet uncertain path to follow until my formal education ends. Through this educational journey a quote by Ellen White gives me comfort: "It is not the capabilities you now possess or ever will have which will give you success. It is that which the Lord can do for you. We need to have far less confidence in what man can do, and far more confidence in what God can do for every believing soul…Put your talents into the work, ask God for wisdom, and it will be given you."

PURIFYING RECOMBINANT LEDGF/P75 FOR USE IN BINDING STUDIES INVOLVING REPOSITIONED HIV-BASED SMALL MOLECULE INHIBITORS

Kristoff Foster, Christina Cajigas-Du Ross, Alfonso Duran, Leslimar Rios-Colon, Tino Sanchez, Carlos Casiano

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

Prostate cancer (PCa) is the most commonly diagnosed cancer in American men and the third leading cause of male cancer deaths. PCa patients undergoing treatment often develop metastasis and castration-resistant prostate cancer (mCRPC). Our group has shown that expression of lens epithelium-derived growth factor protein of 75 kDa (LEDGF/p75) is elevated in PCa cells and tissues. LEDGF/p75 is a stress transcription co-activator that protects PCa cells against death induced by taxane drugs such as Docetaxel (DTX). DTX is the current standard of care for patients with mCRPC; unfortunately, disease progression and chemoresistance occurs in DTX-treated patients contributing to high patient mortality. We have shown previously that targeting LEDGF/p75 with siRNA-mediated knockdown partially re-sensitized taxane resistant PCa cells to DTX treatment. Our group and others have also established a role for LEDGF/p75 in promoting increased cancer cell proliferation and clonogenicity, leading to enhanced cell survival. We seek to target LEDGF/p75 by repositioning HIV-based small molecule inhibitors (SMIs) originally designed to block its interaction with the HIV integrase. The goal is to use these inhibitors to resensitize taxane resistant PCa cells to DTX treatment. Preliminary studies with SMIs shows resensitization of our DTX-resistant PC3-DR and DU145-DR (high LEDGF/p75 expression) PCa cells to DTX treatment. To demonstrate that these SMIs bind directly to LEDGF/p75 and disrupt its function, we need recombinant protein. This study involves optimizing the procedure for purifying recombinant LEDGF/p75 from *E. coli* strains overexpressing histidine (His)-tagged LEDGF/p75 induced by IPTG. An agarose nickel bead column was used to capture His-tagged LEDGF/p75, which was subsequently eluted with imidazole. Future directions include further optimization to improve recombinant protein yield and decrease potential breakdown products of LEDGF/p75 by addition of protease inhibitors to stabilize LEDGF/p75. Purified LEDGF/p75 will then be combined *in vitro* with SMIs to determine binding using isothermal calorimetry.

EMIL HARTY

MTP PARTICIPANT 2017

Having just completed my first year at Loma Linda School of Medicine, I can truly say the human body is a work of art. It is my goal to really understand the intricacies of our body in order to meaningfully serve all people I encounter. The specialties I am currently considering include emergency medicine (or a combination of ER with internal or family medicine) or surgery (possibly, cardio-thoracic).

Besides being a medical student, I also am a musician and lay my claim to the piano and upright bass. I particularly enjoy listening to music and have recently appreciated Joe Hisaishi's work. Music has been a life-changing experience and has placed friends in my life who will change the world.

Being a part of this program gave me the opportunity to learn the varying factors that contribute to disparities in healthcare in our country. It encouraged me to think what I could do as a physician to bridge these gaps and reach out to all people. It is my goal to make a difference in underprivileged communities by collaborating with colleagues to set up clinics, create forums and discussions to tackle issues that hinder access to healthcare, to advocate for them, to educate, and, above all, to inspire them to persevere. Someday, I also hope to travel abroad and serve in this capacity. In the words of the incredible Dr. Martin Luther King Jr., "If you can't fly, then run; if you can't run, then walk; if you can't walk, then crawl, but whatever you do, you have to keep moving forward."

Lastly, I'd like to express my appreciation and thanks to Dr. Subburaman Mohan and Richard Lindsey for allowing me to participate in their research department and deepening my knowledge of cartilage and bone development.

EPIGENETIC REGULATION OF OSTEOBLASTS BY VITAMIN C

Emil Harty, Richard Lindsey, Subburaman Mohan

Musculoskeletal Disease Center, VA Loma Linda Healthcare System,
Center for Health Disparities and Molecular Medicine,
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Vitamin C (ascorbic acid, AA) plays a significant role in skeletal tissue development, and a deficiency in AA is known to cause scurvy. In genetic mouse models, disruption of genes involved in AA biosynthesis results in spontaneous fractures in early life. Vitamin C has been established as a key cofactor of prolyl hydroxylase domain-containing (PHD) proteins, enzymes involved in collagen synthesis in bone cells. Consistent with a role for PHDs in mediating AA effects in bone cells, conditional disruption of *Phd2* gene in osteoblasts using Cre/LoxP technology results in decreased trabecular bone mass. In stem cells, AA has also been shown to increase activity of Ten eleven translocation (TET) methylcytosine dioxygenases, which demethylate DNA via hydroxylation, thereby increasing gene transcription and expression. Since both PHDs and TETs are activated by AA and belong to the same family of Fe(II) and 2OG-dependent dioxygenases, we considered the possibility that AA mediates its effects epigenetically via TET- and/or PHD-dependent hydroxymethylation of DNA. To test this hypothesis, we undertook experiments to determine if TETs and PHDs are expressed in osteoblasts, localized in the nucleus, and contribute to regulation of gene transcription via changes in DNA demethylation. Evaluation of expression levels of *Phds* and *Tets* by real-time RT-PCR revealed that, while all *Tets* and *Phds* are expressed in osteoblasts, their relative expression levels vary dramatically over the course of 24-day AA-induced osteoblast differentiation. Furthermore, immunoblotting confirmed that PHDs and TETs are localized in both the nucleus and cytoplasm in osteoblasts. These results demonstrate that TETs and PHDs are present and regulated during osteoblast differentiation, and their localization in the nucleus confirms the plausibility of direct epigenetic regulation of osteoblasts by these enzymes. Future studies will investigate roles of the various TET and PHD isoforms mediating vitamin C effects on osteoblasts via epigenetic regulation to discover novel therapeutic approaches for such devastating conditions as osteoporosis.

JEAN-PAUL INESTA-RIVERA

MTP PARTICIPANT 2017

I consider myself a highly determined and energetic individual with a great interest in the medical field. I obtained both my BS and MPH from the University of Puerto Rico. Recently, I started my second year of medical school at San Juan Bautista School of Medicine and am very satisfied in having the opportunity to study in an institution that allows me to contribute my multidimensional skills, commitment, and leadership abilities in my career development.

Medicine is a field where not everything is known. We always encounter new cases, and these experiences contribute the most to our hunger for knowledge. These are the reason I feel persuaded by the research field, having to deal with all the challenges and puzzles found on a daily basis. Research experience with Dr. Wolff Kirsch, Nicholas Sanchez, and other colleagues in the laboratory have been a great contribution to the development of my career. The brain's complexity reminds us of how great science is and how many challenges are still ahead. Currently, we are studying the etiology of Alzheimer's, a disease threatening more than 5 million Americans. This number could rise as high as 16 million by 2050 if we don't find a way to prevent it.

My goal is to be a physician and clinical researcher for a hospital near a community where people trust my commitment to improving their welfare through my humanitarian virtues and cognitive abilities in medicine. As a Puerto Rican and Hispanic, I'm conscious of the numerous diseases in my community. Society should be aware how to manage and prevent these. As a future physician, I need more experience in hot topics in medicine that enhances my knowledge toward helping fight health issues affecting underserved populations.

ASSESSING COPPER LOCALIZATION TECHNIQUES: A PATH IN IDENTIFYING THE MOST ACCURATE FLUORESCENT PROBES IN NEUROPATHOLOGICAL DISEASES

Jean-Paul Iñesta-Rivera, Nicholas Sanchez, Wolff Kirsch

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

Copper dysmetabolism has been observed in numerous neurodegenerative diseases and is believed to be a common precipitating factor. Menkes disease (MK), Alzheimer's disease (AD), and Wilson's disease (WD) are related to dysfunctional copper transport, leading to pathological hallmarks in the brain and variations of cognitive decline. Not only is copper required for enzymatic reactions, but it also plays a more sophisticated role in synaptic transmission, neurite outgrowth, axonal targeting, and modulation of signaling cascade. In order to investigate copper, it has to be specifically localized via specialized fluorescent probes, some of which are more successful than others. The aim of this work was to test which probe was more effective at localizing copper for use with confocal fluorescence microscopy. Using two types of probes, CTAP-3 and TM4-157, we stained several types of brain tissue samples (mouse WD and controls, and human AD and controls) to compare the efficacy of these tools. Additionally, we stained neuroblastoma cell (SH-SY5Y) with both probes and AD brain tissue with CTAP-3 and Synaptophysin antibody. These preliminary studies demonstrate that TM4-157 is more appropriate for copper localization and are more feasible to use in future research. It is imperative to know which probe is more accurate in localizing copper within brain tissue samples, allowing us to specifically study the metal's role in relation to transporters, chaperones, and their relationship with pathophysiologic diseases.

AMANDA YADIRAH ORTIZ VICIL

MTP PARTICIPANT 2017

Born and raised in Guayama, Puerto Rico, I have always considered myself a small town girl with big aspirations. Living on a small island can cause those dreams to seem far away, but my family has always inspired me to reach for the stars, and so I did.

My grandparents have always shown me the value of helping others, and since I was little, I have been doing community service in The Lions Club in Guayama.

My elementary education was at Guamani Private School, secondary school at Colegio Ponceño in Ponce, my bachelor's degree in microbiology in Mayaguez, and I am currently studying medicine at San Juan Bautista School of Medicine in Caguas, Puerto Rico, where I just finished my first year. It has truly been an exhilarating journey to be able to study in different parts of Puerto Rico and see the well-prepared institutions the island offers. I have always been very proud of my heritage and the ability to show the world Puerto Rico has excellent institutions to prepare their students. My biggest goal has always been to take my knowledge from the island, expand it to different parts of the world, learn from the experiences outside of Puerto Rico, and incorporate them all in my life. This is when I got the opportunity to apply to the summer Medical Training Program offered by Loma Linda University.

I am currently working in Dr. Daisy De Leon's breast cancer research laboratory, a truly great opportunity to expand my studies abroad and learn from research professionals. I would like to thank the laboratory of Dr. Daisy De Leon for accepting me this summer and for all the great lessons I have learned thanks to them.

CHARACTERIZATION OF A NEWLY IDENTIFIED DIFFERENTIALLY METHYLATED REGION OF THE IGF-II GENE IN PAIRED BREAST CANCER TISSUES FROM AFRICAN AMERICAN AND CAUCASIAN PATIENTS

Amanda Ortiz Vicil, Vinodh Radhakrishnan and Daisy De León

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

Triple Negative Breast Cancer (TNBC) is characterized by the lack of Estrogen (ER-), Progesterone (PR^-) and Human epidermal growth factor receptor 2 ($HER2^-$) receptors. TNBC accounts for 15 - 20% of all breast cancers, yet it disproportionally affects African American (AA) women, who represent one third of this breast cancer group. We previously demonstrated that IGF-II levels are higher in breast cancer tissues from AA women compared to Caucasians (CA). Surprisingly, significantly higher levels of IGF-II were detected in normal tissues of AA in contrast to CA women. Methylation is an epigenetic event that regulates the expression of the IGF-II gene at the transcriptional level. Paired (normal/malignant) breast cancer tissues were obtained from the Cooperative Human Tissue Network. The frozen samples are accompanied by a set of Hematoxylin and eosin-stained slides analyzed by a pathologist to identify normal/malignant samples. To analyze the methylation of the IGF-II gene, the gDNA was isolated from these samples, and methylation analysis was performed using Methylation Sensitive (MSRE) and Methyl Dependent (MDRE) restriction enzyme digestion methods. The collected methylated and unmethylated sample fractions were quantitated using qPCR Δct comparisons between sham, methylated, and unmethylated DNA fractions. Analysis of the % methylation of the IGF-II gene revealed a new differentially methylated region named the IGF-II DV-DMR that consists of 257 bp located in the chromosome region between Exon 1 and Exon 2 of IGF-II gene (chr11:2148098–2148354) annotated using the Insilico UCSC human genome browser. Our results demonstrate IGF-II DV-DMR is hyper-methylated in normal samples and hypo-methylated in the malignant samples. Furthermore, Western blot analysis showed IGF-II levels correlated with the % methylation of the DV-DMR. Thus, we propose DV-DMR can be used as an effective epigenetic biomarker to predict aggressiveness of the TNBC patients.

Initiative to Maximize Student Development (IMSD)

Ivana Alicea-Polanco
Leanne Woods-Burnham
Katherine Concepcion
Alfonso Duran
Christina Cajigas-Du Ross
Jenniffer Licero Campbell
Richard Lindsey
Shannalee Martinez
Karina Mayagoitia
Greisha Ortiz Hernández
Hiel Rutanhira
Nicholas Sanchez
Julio Vega-Torres
Jonathan Wooten

IVANA ALICEA-POLANCO

IMSD PARTICIPANT 2017

I was born and raised in Puerto Rico where I studied and graduated from Antillean Adventist University in 2015 with a BS in Biology. I was then allowed the opportunity to come to Loma Linda University and study to obtain a PhD in Physiology. Throughout my life, I have had the privilege of serving my community through leadership and volunteering, which has made me passionate about finding ways to serve others and provide change in my community. Because it gives me an opportunity to serve and improve my community in a unique and long lasting way, that's why I love biomedical research.

I am currently a part of Dr. Johnny Figueroa's lab where I study the interplay between diet and neurobehavior and the mechanisms involved in this relationship. I feel grateful to be a part of this lab and to do research with my labmate Julio Vega and my mentor, Dr. Figueroa. They both have been influential in my development as a scientist. I am excited to share and continue to develop findings which will help our society understand the influence that nutrition has on our mental health. I'm passionate about the topic of nutrition and mental health, which is why my future career goals are to develop ways to apply the research our team is working on through public health education.

I would like to thank my wonderful labmate Julio Vega for teaching me to be more meticulous and thorough with my research as well as being kind and helpful when I need it the most. I also want to thank my mentor and PI, Dr. Johnny Figueroa, for his incredible patience and for challenging me to become the best researcher I can be.

JUVENILE OBESITY LEADS TO ABNORMAL MATURATION OF NEURAL SUBSTRATES UNDERPINNING FEAR AND ANXIETY

Ivana Alicea-Polanco, Haydee Gallegos, Julio David Vega-Torres, Johnny Figueroa

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

Obesity is a major risk factor for mental and neurodevelopmental disorders. We showed that consumption of an obesogenic high-fat diet (HFD) during adolescence results in stress-induced anxiety-like behaviors in rats. These behavioral findings were associated with marked impairments in the development of the brain prefrontal cortex (PFC), which plays a major role in anxiety and stress disorders. The aim of this study was to examine the cellular basis of these alterations in the developing PFC. Adolescent male Lewis rats (postnatal day 28; n = 51) were fed for eight weeks with either the experimental HFD diet (41.4% kcal from fat) or the control diet (16.5 % kcal from fat). Fear-potentiated startle (FPS) responses were assessed to determine the effects of the HFD on conditioned fear. Diffusion-tensor imaging (DTI) was used to determine the fractional anisotropy (FA) as a measure of white matter structural integrity of the fiber tracts connecting the fear neurocircuitry. We used the Nissl staining technique to measure the effects of a HFD on the PFC cellular morphology, patterns, and density in rats. The rats that consumed the WD exhibited associative-learning deficits as evidenced by blunted FPS responses. These behavioral effects were associated with a robust disruption in the medial prefrontal cortex (mPFC) structural integrity (increased FA) and higher corticosterone levels. Nissl staining revealed smaller cell bodies and decreased cell numbers in the PFC prelimbic and infralimbic regions of rats that consumed the HFD when compared to controls. These results provide evidence that consuming an obesogenic diet during adolescence can have a major impact in the development of brain regions implicated with stress-related psychiatric disorders. The implications of this research are significant by identifying potential cognitive and neuroimaging markers of risk for stress-related psychopathology in the growing obese population.

LEANNE WOODS-BURNHAM

IMSD PARTICIPANT 2017

I am working towards a PhD in Physiology focusing on health disparities among Black men with prostate cancer. My background has motivated me for several reasons. First of all, my father is a Black man with biochemical recurrence of prostate cancer. Secondly, I lived in an underprivileged area of Akron, OH, for most of my life and grew frustrated with the health disadvantages and lack of options I observed. As an undergraduate at the University of Akron, I explored these issues. I interned at Cleveland Clinic Minority Men's Health Clinic and personally witnessed the detrimental facets of health disparities among patients. In addition to clinical rotations, I observed surgical procedures treating prostate cancer and other urological ailments. During the same time frame, I also worked in a cancer biology lab at Lerner Research Institute of Cleveland Clinic. It was there I acquired the necessary skills to conduct biomedical research.

Since attending Loma Linda University, my research has been translational within Dr. Carlos Casiano's lab and as a volunteer with Project CHANGE—a collaborative team that organizes and conducts community health fairs for Black men while obtaining serum samples for research purposes. My project focuses on the contribution of the biological stress response, which occurs frequently in Black men, to increased prostate cancer tumor aggressiveness.

I have enjoyed my summer students' contributing their enthusiasm to my project during the previous four years, and it has brought me joy to be able to include my most exceptional mentees as co-authors on manuscripts for publication. I look forward to successfully completing this final graduate year and moving forward with plans for the future.

GLUCOCORTICOID-MEDIATED UPREGULATION OF STRESS ONCOPROTEINS ASSOCIATED WITH CHEMORESISTANCE: IMPLICATIONS FOR PROSTATE CANCER HEALTH DISPARITIES

Leanne Woods-Burnham, Christina Cajigas-Du Ross, Arthur Love, Anamika Basu, Evelyn Sanchez, Laura Stiel, Susanne Montgomery, Colwick Wilson, Sourav Roy, Carlos Casiano

Center for Health Disparities and Molecular Medicine, School of Medicine, School of Behavioral Health, Loma Linda University, Loma Linda, CA; Department of Entomology, University of California, Riverside, CA

Prostate cancer (PCa) presents the greatest U.S. cancer health disparity in terms of incidence and mortality, disproportionately affecting African American (AA) men. The mechanisms underlying increased PCa tumor aggressiveness in AA men are not fully understood; therefore, there is a need to identify contributing biological determinants. Glucocorticoids, a type of stress hormone, have been implicated as drivers of PCa progression. The underlying mechanism involves endogenous glucocorticoid (cortisol) binding to its glucocorticoid receptor (GR) and activating genes that are androgen-regulated and promote tumor aggressiveness and therapy resistance. A clinical dilemma exists as glucocorticoids, important in the palliative care of PCa patients, are now emerging as disease accelerators. Chronically elevated levels of cortisol are also documented in AA men, leading to hypersensitive glucocorticoid signaling. This study examined the effects of glucocorticoids on the expression of stress oncoproteins, LEDGF/p75 (Lens epithelial-derived growth factor of 75kd) and CLU (Clusterin), which are upregulated in PCa tumors and promote tumor aggressiveness and chemoresistance. We exposed a racially diverse panel of PCa cell lines, MDA-PCa-2b, 22Rv1, PC3, and DU145, to glucocorticoids (cortisol and dexamethasone), and observed by immunoblotting the upregulation of LEDGF/p75 and CLU, more robustly in AA cells. Inhibiting GR, either genetically using siRNA or pharmacologically with mifepristone, attenuated the glucocorticoid-induced upregulation of these stress proteins. We also observed, using ELISA, increased circulating levels of LEDGF/p75 in serum from AA PCa patients and increased levels of CLU in normal AA patients. These findings imply that activation of GR-signaling by glucocorticoids contributes to the activation of stress survival genes associated with PCa aggressiveness and chemoresistance. These results add to the emerging contribution of GR signaling in PCa, particularly in the context of PCa health disparities.

KATHERINE CONCEPCION

IMSD PARTICIPANT 2017

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

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

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

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

Katherine Concepcion, Yong Li, Lubo Zhang

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

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

CHRISTINA CAJIGAS-DU ROSS

IMSD PARTICIPANT 2017

My research experience began in the ABC program in 2004 with plant vaccines in Dr. Langridge's lab. In 2009, I graduated with a Bachelor of Arts in Biology and Sociology from Case Western Reserve University in Cleveland, OH. As an undergraduate, I researched plant molecular genetics studying how Linum insertion sequence-1 (*LIS-1*) contributes to gene alterations in flax (*Linum usitatissimum*) in stressed-induced environments. In 2011 I graduated with a Master's of Science in Biology from Case Western with a focus on plant molecular genetics.
Currently a PhD student in Dr. Carlos Casiano's prostate cancer laboratory, my research has focused on targeting multiple proteins involved in drug resistance including LEDGF/p75 and Clusterin. Understanding these pathways is important in discovering novel therapeutic targets for combinatorial therapies to kill prostate tumors and simultaneously attenuate chemoresistance, especially important among the African American population, who present with more aggressive prostate tumors and a higher mortality when compared to other ethnic groups.

After graduation, I plan to return to Ohio and work at the Cleveland Clinic Lerner Research Institute as a postdoctoral fellow. California has given me a wonderful husband (Jonathon), a perfect baby boy (Clayton), and an appreciation for cloudy days. I spend most of my free time cooking, cleaning, doing laundry, and being with my beautiful family. One day I will have more freedom to diversify my "outside-of-the-lab" activities, but for now I love being a working mom and wife, and I love science!

I am grateful to the Initiative for Maximizing Student Diversity program and the Center for Health Disparities and Molecular Medicine for the opportunities given me as a PhD student. I would also like to thank my fellow laboratory members and summer students Josh Ramirez and Kristoff Foster for their friendship, advice, help, and support.

RNA SEQUENCING ANALYSIS OF CHEMORESISTANT PROSTATE CANCER CELLS REVEALS POTENTIAL CANDIDATE GENES FOR THERAPEUTIC TARGETING

Christina Cajigas-Du Ross, Joshua Ramirez, Kristoff Foster, Xin Chen, Charles Wang, Carlos Casiano

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

Prostate cancer (PCa) is the most commonly diagnosed cancer in American men and the third leading cause of male cancer deaths. PCa patients undergoing treatment often develop metastasis and castration-resistant prostate cancer (mCRPC). Docetaxel (DTX) is the current standard of care for mCRPC; unfortunately, disease progression and chemoresistance occurs in DTX-treated patients and leads to high mortality. Understanding chemoresistance mechanisms is important to lessen the burden of prostate cancer mortality, particularly in African American men who develop more aggressive prostate tumors and suffer from disproportionate PCa mortality compared to other ethnic groups. Using RNA sequencing (RNAseq) to compare the transcriptomes of chemosensitive and chemoresistant mCRPC cells (PC3 and DU145)**,** we identified new candidate targets for combinatorial therapies. To validate RNAseq findings for selected candidate genes, we used in-house quantitative polymerase chain reaction (qPCR) to confirm elevated mRNA expression and immunoblotting to confirm elevated protein expression in chemoresistant mCRPC cells relative to chemosenstive cells. The increased expression of fatty acid binding protein 5 (FABP5), nestin (NES), and dipeptidyl pretidase (DPP4) revealed by RNAseq was confirmed in DTX-resistant PCa cells. In addition, Ingenuity Pathway Analysis (IPA) of RNA sequencing data identified downregulated genes associated with cellular movement and migration in the taxane-resistant PCa cells, consistent with results observed *in vitro* using wound-healing assay. Taken together, these results suggest that differences in gene expression between DTX-sensitive and DTX-resistant PCa cells may influence the migration and metastatic potential of these cells. Exploring the mechanisms involved in PCa treatment resistance will lead to the discovery of novel targets for combinatorial therapies aimed at attenuating chemoresistance.

ALFONSO DURAN

IMSD PARTICIPANT 2017

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

I elected to put residency on hold and pursue a PhD in physiology. My current research focus involves metabolomics studies of Latinos with chronic diseases. Using metabolomics, we can identify key bio-markers and elucidate major metabolic pathways involved in the pathophysiology contributing to health disparities. Further, in the context of health disparities, metabolomics can inform about mechanisms that underlie variation in response to interventions/treatments, thereby directing 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.

MUTANT EPIDERMAL FATTY ACID-BINDING PROTEIN R129A RETAINS ANTIOXIDANT PROTECTIVE FUNCTION AGAINST INDUCED LIPOTOXIC INJURY

Alfonso Durán, Jo-Wen Liu, Marino De Leon

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

Epidermal fatty acid-binding protein (E-FABP/FABP5/DA11) belongs to a family of intracellular 14-15 kDa lipid-binding proteins, whose functions are associated with fatty acid signaling and transport, cell growth, and protection against lipotoxic injury. For example, E-FABP protects neuronal cells from reactive oxygen species (ROS) and cell death after palmitic acid-induced lipotoxic injury (PA-LTx). The mechanism of this process remains unclear; however, an antioxidant role against ROS through covalent modification of Cys-120 residue may be important. Additionally, E-FABP can bind free fatty acids in the cytoplasm rendering them unavailable and, therefore, decreasing lipotoxic injury. This study focuses on modifying E-FABP binding pocket to understand the structure and function of E-FABP. The amino acids responsible for binding of fatty acids in E-FABP binding pocket are Arg109, Arg129, and Tyr131. Arg129 forms a salt bridge with the carboxylate group of fatty acids essential for stabilizing fatty acid binding. Our objective is to construct a mutant E-FABP recombinant protein that abolishes binding affinity to palmitic acid and examine whether it retains protection against ROS in nerve growth factor-differentiated PC12 cells (NGFDPC12). Therefore, we targeted Arg129 (CGG) residue, essential for FA binding, and mutated residue by site-directed mutagenesis to Alanine129 (GCC). The wild type E-FABP and mutant E-FABP-R129A recombinant proteins were produced in *E. coli* and purified to homogeneity. The arginine-to-alanine alteration was confirmed by peptide sequencing. Isothermal titration calorimetry demonstrated that recombinant rat E-FABP-R129A exhibits a significant reduction of binding to palmitic acid (Kd non-measurable, non-ordered binding) versus wild type E-FABP (Kd459±30 nM). Moreover, we found E-FABP-R129A also showed reduced binding to arachidonic acid and oleic acid (Kd non-measurable, non-ordered binding). Furthermore, we found NGFDPC12 cells are protected against ROS when recombinant E-FABP-R129A is delivered by BioPORTER. These findings suggest E-FABP antioxidant function is independent of fatty acid binding supporting that E-FABP can function in cellular mechanisms beyond its role as an intracellular fatty acid transporter.

JENNIFFER LICERO CAMPBELL

IMSD PARTICIPANT 2017

Jenniffer Licero, a name which some have correlated with the feelings bubbly and happy, is a courageous, humble, hardworking, devoted, focused and happy 27-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 grandparent's 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. Having recently entered my 5th year as a PhD student, I cannot wait to publish and have my work join the greater body of thinkers who want to learn more about the world and make it a better place.

UPREGULATION OF FATTY ACID BINDING PROTEIN 4 IS ASSOCIATED WITH INCREASED mRNA AND PROTEIN LEVELS OF PROINFLAMMATORY/STRESS-RESPONSE PROTEINS

Jenniffer Licero Campbell, Miguel Serrano Illán, Brandon McNichol, Omkar Panse, Johnny Figueroa, Marino De Leon

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

The pathology of traumatic spinal cord injury (SCI) results from an initial mechanical insult followed by a secondary inflammatory response. The secondary phase of injury is characterized by marked deregulation in lipid metabolism leading to M1 macrophage-mediated inflammation 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 and are ideal targets for modulating macrophage function. The present study explores potential associations between FABP4 upregulation and levels of pro- or anti-inflammatory proteins in rats post SCI. We hypothesize increased FABP4 expression correlates with upregulated levels of known pro-inflammatory/stress response proteins. The multicenter animal spinal cord injury study (MASCIS) injury model was used to generate a contusion to the T-10 spinal segment of rats. Spinal cord samples were collected and analyzed at 7 and 28 days post-injury (peaks of inflammatory response) to determine the mRNA expression of FABP4, Pro- IL-1β, IkBα, TNF-α, Nfκβ1, PPARϒ, and UCP2, through real-time RT-PCR, as well as protein expression of FABP4, p-Nfκβ p65, p-IkBα, and UCP2 using Western blot. Our results show injury to the spinal cord results in significant upregulation of FABP4 and TNF-α mRNA and notable upregulation in Pro- IL-1β, IkBα, Nfκβ1, and UCP2 mRNA at 7 days post injury. Conversely, PPARϒ mRNA levels were not significantly different from sham at either time point. Furthermore, we also show significant upregulation of FABP4, p-Nfκβ p65, p-IkBα, and UCP2 protein levels in injured animals compared to sham. These findings suggest a possible link between FABP4 upregulation and increased expression of pro-inflammatory/stress proteins in the injured rat spinal cord. As studies have indicated direct links between FABP4 expression and pro-inflammation, further investigations looking at the effects of FABP4 inhibition on these protein levels are needed to directly link FABP4 upregulation with transcription of pro-inflammatory proteins, and orchestration of M1- macrophage differentiation. These studies may elucidate viable ways that modulation of macrophage differentiation can be effectively achieved.

RICHARD LINDSEY

IMSD PARTICIPANT 2017

I am a sixth-year student in Loma Linda University's MD/PhD program, having completed two years of medical school and three years of the PhD program. In 2012, I graduated from Biola University with a degree in biochemistry, and I am a perpetual member of Biola's Torrey Honors Institute, a great books program taught in the Socratic style. I intend to use my education from both Biola and LLU to pursue a career in endocrinology research with an eye toward understanding and eliminating health disparities. Recently, my professional interests have expanded to include data science, R programming, and reproducible research methodologies. Moreover, I am interested in Christian theology and philosophy of science, and I want to contribute both to science and to the way people perceive and relate to science. In an effort "to glorify God and to enjoy him forever" (*Westminster Shorter Catechism*), I want to ensure that Man's conquest of Nature does not become Nature's conquest of Man (CS Lewis, *The Abolition of Man*). For recreation, I enjoy reading (currently Smith's *Desiring the Kingdom* and Jordan's *The Handwriting on the Wall*) and, when I'm feeling particularly ambitious, trying—failing, mostly—to learn Koine Greek.

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

EPIGENETIC REGULATION OF ARTICULAR CHONDROCYTES BY VITAMIN C

Richard Lindsey, Shaohong Cheng, Sheila Pourteymoor, Catrina Godwin, Subburaman Mohan

Musculoskeletal Disease Center, VA Loma Linda Healthcare System, Center for Health Disparities and Molecular Medicine, School of Medicine, Loma Linda University, Loma Linda, CA

Vitamin C (ascorbic acid, AA) deficiency leads to spontaneous fractures, and the AA effect on osteoblast differentiation via regulation of osterix is well established. Additionally, AA affects chondrocytes (CCs), and epidemiological studies link low AA intake with increased osteoarthritis (OA) risk. However, the mechanism of AA regulation of articular CCs remains unclear. Since chondrocyte-specific conditional knockout (cKO) of prolyl hydroxylase domain-containing protein 2 (PHD2), a known mediator of AA, leads to an OA-like phenotype due to increased differentiation of articular cartilage (AC) progenitors, we predicted that the AC phenotype of AA-deficient mice should mimic that of PHD2 cKO. Accordingly, we found AA-deficient *Gulo* mutant mice had decreased femoral and tibial AC area (21% and 15%, respectively, $P < 0.05$) and decreased (8%) femoral AC width compared to AA-replete littermates. Furthermore, *in vitro* AA treatment of articular CCs increased mRNA expression of immature CC markers and decreased a CC differentiation marker. Due to the recent finding that AA promotes demethylation of gene promoters via ten eleven translocases (TETs) in stem cells, and because PHDs, like TETs, are 2-oxoglutarate-dependent dioxygenases needing AA to function, we hypothesized AA effects on articular CCs are in part due to TET- and/or PHD-mediated conversion of 5-methylcytosine (5-mC) to 5-hydroxymethylcytosine (5-hmC) in the promoters of target genes. All TETs and PHDs are expressed in articular CCs. However, AA treatment in articular CCs increased expression of all TETs while PHD expression was largely unchanged. AA treatment of cultured articular CCs led to a 4.5-fold increase in 5-hmC content compared to untreated cells. Furthermore, inhibition of PHD2 decreased 5-hmC in the promoters of known target genes in AA-treated articular CCs. Taken together, these data suggest that AA promotes transcription of target genes in part by PHD2-mediated epigenetic demethylation of DNA in articular CCs, and this mechanism should be exploited towards development of therapies for OA.

SHANNALEE MARTINEZ

IMSD PARTICIPANT 2017

I am a seventh year MD/PhD student at Loma Linda University pursuing research in cancer and developmental biology. In particular, I am interested in understanding how stress signaling is regulated under a variety of situations including cancer and fetal development. I began my training as part of the UPWARD, now Apprenticeship Bridge to College (ABC), program at Loma Linda University as a high school student attending Loma Linda Academy. After graduation, I attended Southern Adventist University in Tennessee to study chemistry with a focus on biochemistry.

During my undergraduate studies I continued doing research at Loma Linda University as part of the Undergraduate Training Program (UTP). Upon graduating from college, I took one year to work as a research technician in Dr. Carlos Casiano's laboratory in the Center for Health Disparities and Molecular Medicine at Loma Linda University. In 2010 I was accepted to the MD/PhD program at Loma Linda University and went on to complete two years of basic sciences training in the medical program. I have since then been in the PhD program, working under the mentorship of Drs. Kimberly Payne, Lubo Zhang, and Carlos Casiano.

I have been blessed to have received such wonderful opportunities for growth as a physician, scientist, and human being. I'm thankful for the chance to do what I love, in the hope that it will bring time and meaning to the lives of others.

REGULATION OF THE GLUCOCORTICOID RECEPTOR IN THERAPY-RESISTANT PROSTATE CANCER

Shannalee Martinez, Leanne Burnham, Lubo Zhang, Carlos Casiano

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

Prostate cancer (PCa) is the third leading cause of deaths due to cancer in American men. Approximately 26,000 men will die from PCa in the United States this year, and African American men will die disproportionately from this malignancy compared to men from other ethnic/racial groups. While most men respond to therapy, drug resistance remains a major barrier to curing prostate cancer. Inhibition of androgens (hormones that promote prostate growth) via androgen deprivation therapy is a mainstay of advanced PCa treatment; however, PCa cells eventually become resistant to androgen blockade by activating glucocorticoid receptor (GR) signaling. The next tier of therapy for advanced PCa includes chemotherapy using docetaxel, a drug that blocks the division of cells and induces cell death. Recent evidence has implicated GR in the development of resistance to androgen depletion therapy as well as docetaxel. Unfortunately, the promise of targeting the GR as part of the treatment strategy for prostate cancer is hindered by the dependence of almost every cell in the body on the GR for survival. Thus, we aim to identify mechanisms underlying the induction of GR expression in PCa cells during the development of resistance to therapy. Recently, we began exploring a model in which specific microRNAs (miRNAs) may regulate GR expression during progression from AR dependence to GR dependence in advanced PCa. By stabilizing the regulatory network that suppresses GR in PCa cells, we plan to maintain cancer cells in a drug-sensitive phenotype that is more susceptible to available therapies.

KARINA MAYAGOITIA

IMSD PARTICIPANT 2017

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 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 B.S. 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 second year in the PhD program and look forward to starting my third year.

I'm extremely privileged to be working in an Alzheimer's disease research laboratory under the leadership of Dr. Salvador Soriano and Dr. Brendan Gongol. 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 jogging and kickboxing. I have always had the curiosity of learning a martial art, so I am slowly 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 also enjoy volunteering in Vacation Bible School at Calimesa Seventh-day Adventist Church.

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.

AMYLOID PRECURSOR PROTEINS AND ITS POTENTIAL ROLE IN PROTECTING NEURONS AGAINST 27-HYDROXYCHOLESTEROL IN ALZHEIMER'S DISEASE

Karina Mayagoitia, John Jeppson, Sam Shin, Brendan Gongol, 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) has no cure or effective treatment, and it affects 1 in 8 people 65 and older. For more than two decades, researchers have been led by the amyloid cascade hypothesis, which assumes that accumulation of the amyloid peptide Aβ, derived by proteolytic processing from the amyloid precursor protein (APP), is the key pathogenic trigger in AD. However, therapies focused on removing Aβ from the brain do not work, and levels of Aβ in the brain do not correlate with cognitive function. Instead, current evidence suggests that dysregulation of cholesterol homeostasis, including the accumulation of the oxysterol 27-hydroxycholesterol (27-OHC), could be the primary pathogenic trigger of AD, and that APP has a protective role against such dysregulation. Based on this evidence, I hypothesize that APP binds to 27-hydroxycholesterol to initiate an adaptive response that leads to successful rescue of neuronal health. To test my hypothesis, I will characterize the impact of APP on cytotoxicity in response to 27-OHC in cultured cells and assess a range of behavioral and cognitive tasks in APP mouse models subject to different types of cholesterol dysregulation in the brain. Confirmation of my hypothesis would help overcome the theoretical block that has hampered progress in our understanding of pathogenesis in AD, thereby contributing to creating effective, evidence-based approaches to therapy.

GREISHA ORTIZ HERNÁNDEZ

IMSD PARTICIPANT 2017

Growing up on the beautiful island of Puerto Rico (P.R.), I discovered my biggest passion, other than food 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 graduation in biology from Universidad Metropolitana (UMET) in P.R., I was ready to apply for graduate school at Loma Linda University (LLU). But, when doing so, 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. We enjoyed greatly the last days of my Guelo. In this process I learned to enjoy every path in my life and be grateful for that. In spring, 2015, I reapplied for the LLU graduate program, and I was finally accepted and awarded through the IMSD program. Being exposed to my grandpa's death to cancer confirmed my choice of pursuing a career in cancer research.

After completing my first year of required lab rotations, I decided to join Dr. Carlos Casiano's prostate cancer (PCa) research laboratory. Now, in my second year, I chose the Pharmacology program and just finished the required classes for it. My plan for the summer is to divide my time between studying for my comprehensive exam and to start developing preliminary data for my thesis project. My long-term goal in the lab is to explore the contribution of protein-protein interactions to LEDGF/p75-mediated upregulation of stress oncoproteins to tumor aggressiveness and chemoresistance in the context of PCa health disparities.

OPTIMIZATION OF CO-IMMUNOPRECIPITATION PROCEDURES USING HUMAN AND MONOCLONAL ANTIBODIES TO THE STRESS ONCOPROTEIN LEDGF/P75

Greisha Ortiz Hernandez and Carlos Casiano

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

Prostate cancer (PCa) is the most commonly diagnosed and third leading cause of cancer-related death among men in the United States. African American (AA) men show a disproportionate mortality from PCa compared to other racial/ethnic groups. Current therapies for advanced PCa include androgen deprivation therapy and docetaxel (DTX) chemotherapy. Unfortunately, treatment resistance and disease progression are unavoidable, leading to mortality. Consequently, there is a critical need to identify mechanisms contributing to PCa chemoresistance. Our group demonstrated that the stress oncoprotein Lens Epithelium Derived Growth Factor protein of 75 kD (LEDGF/p75) is upregulated in clinical prostate tumors and contributes to DTX resistance in advanced PCa cells. However, very little is known about the mechanisms by which LEDGF/p75 promotes chemoresistance. This study was designed to explore and compare the interactions between LEDGF/p75 and other oncoproteins in DTX-sensitive and -resistant PCa cells in order to elucidate chemoresistance mechanisms. We will first explore the interaction of LEDGF/p75 with MLL-Menin and JPO2. These proteins interact with LEDGF/p75 in leukemia cells but their interactions in PCa have not been explored. We also want to explore the interaction between LEDGF/p75 and other putative interacting partners associated with advanced PCa such as FAPB5. We hypothesize that LEDGF/p75 interactions with these proteins in DTX-resistant PCa cells transcriptionally induces chemoresistant genes. We optimized LEDGF/p75 co-immunoprecipitation procedures using a monoclonal and human antibodies reacting with its N-and C-terminus, respectively. Immunoprecipitation of LEDGF/p75 derived from chemoresistant cells was established by Western blotting. The next step will be to determine if LEDGF/p75 co-immunoprecipitates with a protein complex that includes Menin-MLL, JPO2, and FABP5 in chemoresistant cells. Our long-term goal is to explore the contribution of LEDGF/p75 protein-protein interactions in the context of PCa chemoresistance, and determine if blocking these interactions with small molecule inhibitors attenuate chemoresistance, resulting in reduction of PCa mortality.

HIEL RUTANHIRA

IMSD PARTICIPANT 2017

I am a 4th 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 LLU IMSD program. Our lab's research is on periodontal disease and key microbes, *Porphyromonas gingivalis* and *Filifactor alocis,* which potentiate disease progression. My interest in microbiology began sophomore year in college at Southern Adventist University. There I was able to do research which led me down this career path.

Prior to college, I attended Mount Vernon Academy in Ohio, and there Mrs. C, my science teacher, made me fall in love with biology. This love for biology led me to decide to major in biology with biomedical emphasis. I was born in Zimbabwe, Africa, and my parents had brought us to the United States for a better education, and this move forced me to be focused on school.

During my time at Southern Adventist University, I was inducted into the Tri-Beta Biological National Honor Society which piqued my interests in other areas of biology besides medicine. Upon acceptance into Loma Linda, I began working for Dr. Fletcher where I was partnered with Dr. Yuetan Dou. Dr. Dou has been pivotal to all the knowledge I have gained since the start of my program. My project is titled The Role of Putative Membrane Transporters in Regulation of Virulence in *Porphyromonas gingivalis*. My short term goal is to do my oral proposal in the next few months.

When I'm not in the lab, I'm at the gym, playing sports, or singing for the church praise team. I'm blessed with seven nieces and nephews and get a lot of practice for fatherhood. For now, though, the lab is my priority, and I consider my project my child.

THE ROLE OF PUTATIVE MEMBRANE TRANSPORTERS IN REGULATION OF VIRULENCE IN *PORPHYROMONAS GINGIVALIS*

Hiel Rutanhira, Yuetan Dou, Hansel Fletcher

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

Periodontal disease presents with chronic inflammation, bone destruction, and loss of the supporting structures of the teeth. *Porphyromonas gingivalis*, a Gram-negative anaerobic bacterium, causes periodontal disease in synergy with other oral microbes. The survival of *P. gingivalis* in the periodontal pocket requires a mechanism(s) to overcome oxidative stress in addition to other environmental changes. Extracytoplasmic function sigma factors (ECF) are known to play a role in adaptation to environmental conditions via transcriptional regulation. PG1660, a *P. gingivalis* ECF sigma factor, has been implicated in post-transcriptional regulation of gingipains, a major virulence factor. *In silico* association of PG1660 with the PG1662-PG1663-PG1664-PG1665 gene cluster, which carries putative ABC transporters, suggest that together they may be part of a cell-surface signaling (CSS) system for adaptation in *P. gingivalis*. This gene cluster was further characterized to evaluate its role in response to environmental stress, adaptation, and virulence in *P. gingivalis*. Isogenic mutant FLL500 (ΔPG1662-PG1665) defective in these genes was created by allelic exchange mutagenesis using *ermF* cassette. Similar to the wild-type strain, the mutant formed black-pigmented colonies on blood agar plates. The growth for FLL500 was in contrast to the wild-type as FLL500 displayed a longer generation time. FLL500 showed increased sensitivity to oxidative stress compared to the parent strain in both Brain Heart Infusion media and Tryptic Soy Broth. We observed a significant decrease in gingipain activity in the isogenic mutant FLL500 compared to the wild-type. Results for electrophoretic mobility shift assay show the ECF sigma factor rPG1660, recombinant PG1660, binds to the promoter region of PG1662. Our observations suggest that the putative operon, PG1662-PG1663-PG1664-PG1665, may play a role in virulence regulation and stress adaptation in *P. gingivalis*.

NICHOLAS SANCHEZ

IMSD PARTICIPANT 2017

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 learning the skills 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 several disciplines.
While I have concentrated my efforts on the pathogenesis of neurodegenerative diseases, I have been involved in other projects involving treating superficial bladder cancer and looking for biomarkers for schizophrenia.

My work focuses on copper dysregulation and its involvement in the onset of dementia and how disruption of its transport mechanism can lead to the development of Alzheimer's disease. My project recently earned the Alzheimer's Greater Los Angeles Young Investigators Award, and I'm looking forward to gathering the preliminary data needed for my proposal. Working in such a contested field where each idea is hotly debated and scrutinized is challenging, yet it brings its own excitement from being in a dynamic environment.

Outside of academia, I find my peace in long distance running. Along with everything else in my life, I feel quite fortunate how I am surrounded with friends and family who provide support and to be in an institution that allows me to thrive.

VALDIATING COPPER PROBES FOR USE IN HUMAN PATHOLOGICAL STUDIES: A COMPARATIVE STUDY

Nicholas Sanchez, Jean-Paul Iñesta-Rivera, Wolff Kirsch

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

Alzheimer's disease (AD) is an increasingly prevalent public health issue with one in ten people age 65 and above having been diagnosed. Observations have suggested a correlation between copper dysregulation and the formation of AD. Previous research done in our lab has shown the accumulation of copper in the axons in AD-affected brain samples when compared with control brains, suggesting an abnormality in Cu trafficking. Copper is generally removed from neurons by one of many pathways involving vesicular excretion or cuproprotein transport. Due to the reactive nature of copper in enzymatic reactions, it may promote a neurotoxic environment if not appropriately regulated. We hypothesize that the alteration of Cu chaperone functionality leads to Cu dysregulation and neurotoxicity. In preparing for our first studies in this project, we must first validate our tools and protocols to ensure good data is generated. We focused on comparing two fluorescent monovalent Cu probes (CTAP-3 and TM4-157) in cell culture (neuroblastoma cell line) and brain tissue (human AD, mouse Wilson's disease model for positive control, and respective aged-matched negative controls). Our tests have determined TM4-157 to be the better probe to isolate and display Cu with more consistent signaling and isolation. We plan to move forward and use this probe to track Cu through neurons as we intervene with it to determine their effect on neurotoxicity.

JULIO VEGA-TORRES

IMSD PARTICIPANT 2017

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

I have the privilege of being part of Dr. Johnny Figueroa's laboratory. The lab has been blessed with the contribution of many summer students throughout the years. This summer we have a high school student, Haydee Gallegos, with a great desire to learn and set foundations for her future studies. Her enthusiasm for research motivates me to be an excellent science coach.

Besides being in the lab, I love spending time with my wife and friends, playing the saxophone, 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).

ABNORMAL FEAR LEARNING AND ATTENTIONAL PROCESSING IN JUVENILE RATS EXPOSED TO AN OBESOGENIC DIET AND PSYCHOLOGICAL STRESS

Julio Vega-Torres and Johnny Figueroa

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

Psychological trauma and obesity co-occur frequently and have been identified as major risk factors for stress-related disorders. Despite the epidemiological data showing that 30% of the adolescent population is overweight and obese, no studies have examined how obesity disrupts the ability of the brain to cope with stress later in life. The objective of this study was to determine the impact of an obesogenic Western-like high fat diet (WD) on stress reactivity. We hypothesized that consumption of a WD during adolescence impairs the behavioral reactivity to stress during adulthood. Adolescent Lewis rats were fed for eight weeks with either the experimental WD diet or the control diet. We modeled psychological trauma by exposing rats to a cat odor threat. Fear-potentiated startle (FPS) responses were assessed following psychological trauma exposure to determine fear learning, fear acquisition, and background anxiety. We found that rats that consumed a WD during adolescence exhibited reduced acoustic startle responses suggesting alterations in motivational and sensorimotor processing. Interestingly, the FPS paradigm revealed rats that consumed the WD exhibited marked impairments in fear associative learning while showing increased background anxiety to the acoustic stimuli. These behavioral effects were associated with higher corticosterone levels in the rats that consumed the WD. Altogether, our findings demonstrate that consumption of a WD during critical neurodevelopmental stages has a profound impact in stress-related endocrine and behavioral responses. This study is important because it prepares the ground to delineate the mechanistic links between obesity and stress disorders.

JONATHAN WOOTEN

IMSD PARTICIPANT 2017

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

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

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

ARYL HYDROCARBON RECEPTOR LIGAND 5F 203 INDUCES CYTOGLOBIN EXPRESSION TO CONFER TRIPLE NEGATIVE BREAST CANCER CELL DEATH

Jonathan Wooten, Leah Rowland, Eileen Brantley

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

Triple negative breast cancer (TNBC), characterized by tumors that lack appreciable expression of the estrogen receptor, progesterone receptor, and human epidermal growth factor receptor 2 is associated with a poor prognosis due in part to the lack of clinically available, efficacious, targeted therapy for TNBC. Emerging evidence suggests that small molecules that activate aryl hydrocarbon receptor (AhR) signaling have the capacity to confer anticancer actions. We have previously reported that AhR ligand 2-(4-amino-3-methylphenyl)-5-fluorobenzothiazole (5F 203) potently inhibited TNBC cell growth, induced apoptosis of TNBC cells, and augmented the expression of putative tumor suppressor cytoglobin (CYGB) in TNBC cells. Our primary objective in the current study is to test the hypothesis that CYGB promotes 5F 203-mediated TNBC cell death. MDA-MB-468 TNBC cells were transfected to stably over-express CYGB or transduced to stably knockdown CYGB. Using flow cytometry we evaluated the impact of CYGB on the ability of 5F 203 to effect cell cycle progression, DNA replication and cell death. Our data show that CYGB diminished 5F 203-mediated G1 arrest. In contrast, CYGB enhanced the ability of 5F 203 to inhibit DNA replication and induce TNBC cell death. Collectively, these data suggest that CYGB promotes 5F203-mediated anticancer actions and provide a basis for subsequent studies to develop novel efficacious AhR ligands as part of the arsenal to combat TNBC.

School of Behavioral Health & School of Public Health

Kelly Baek
Simran Brar
Guljinder Chera
Raveena Chera
Semran Mann
Christopher Montgomery
Simone Montgomery
Harinder Pal Kaur
Dipal Patel
Amitoj Randhawa
Navdeep Randhawa
Carmen Soret
Krystle Wiley

KELLY BAEK

BEHAVIORAL HEALTH PARTICIPANT 2017

I am currently a 5th year doctoral student in Social Policy & Social Research, focusing on Korean Americans and mental health views and experiences—in particular, marginalized subgroups such as pastors' wives. My research interests include mental health, developing culturally relevant and sensitive social work curriculum, resiliency, and quality of life issues.

I received my BA in Sociology from the University of Michigan, Ann Arbor, and my Master of Social Work degree from Wayne State University. Before pursuing doctoral study, I worked in the nonprofit sector in Michigan for four years, developing policies, programs, evaluations, resources, recruiting volunteers, and event planning. During this time, I also completed missionary work abroad teaching English for a year in Korea as I knew I wanted to one day focus on the Korean-American population in my doctoral studies.

I am so thankful to all the wonderful people I met in Korea; it was the stories they shared with me that significantly influenced me to focus on the area of mental health and mental well-being. It is my goal to be able to share the stories of struggles and resiliency to help increase awareness of need for resources in addressing the mental health challenges in Korean-American communities in the United States.

EXPLORING MENTAL HEALTH PERSPECTIVES AMONG KOREAN-AMERICAN COMMUNITY LEADERS AND SERVICE PROVIDERS

Kelly Baek, Semran Mann, Larry Ortiz, Qais Alemi, Susanne Montgomery

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

In the United States (US) Korean Americans (KAs) are twice as likely to report higher depressive symptoms than the general population. However, they are less likely to utilize mental health services. Using semi-structured key informant interviews (N = 19), we explored KA community leader and service provider perceptions about KA community conceptualizations of mental health challenges, perceived barriers and facilitators to professional help seeking. Qualitative description methodology with grounded theory undertones guided the analysis. Findings indicate that age, level of acculturation, and gender influenced help-seeking behavior, and that the lack of culturally sensitive services posed a significant barrier towards receiving care. Results also pointed to pastors, pastors' wives, and service providers as specifically vulnerable subgroups. In particular, pastor's wives often serve as lay mental health workers for their KA church community but feel restricted seeking help for themselves or sharing their own personal struggles. Other perceived community needs included increased awareness of mental health, culturally sensitive mental health services, collaborative efforts with Korean churches, and an increased focus on interventions including children and their parents as possible facilitators to increase access to mental health services. Findings support existing literature highlighting the importance of culturally applicable and accessible mental health services for the KA community. Further study on vulnerable subgroups in the KA community is needed.

SIMRAN BRAR

BEHAVIORAL HEALTH PARTICIPANT 2017

This coming year I will attend Riverside Poly High School as part of the senior class of 2018. After high school, I hope to go to George Washington University as a pre-med student while also pursuing my passion of political science as a minor. I have maintained the valedictorian position for the past 3 years as well as being involved with activities such as student body and tennis.

Throughout high school, I have always treasured my Punjabi identity and loved informing others of my culture. Because my parents raised me with both an American and Indian identity, both remain significant in my daily interactions, I hope to pass those values onto future generations. It is for this reason I am excited about my summer internship project which sets out to explore mental health disparities in Punjabi Asian-Indians who are often seen as a model minority but, as it turns out, face challenges associated with the multi-cultural tensions that often accompany immigration from societies with differing social cultures than that in the US.

As I think about what I primarily want to focus on in the medical field, I know I want to help women in third world countries to advocate for their own individual medical rights. I want to thank Dr. Susanne Montgomery and Semran Mann for providing me with this outstanding opportunity to be part of health disparities research and assist with mental health awareness in the Punjabi community.

DESERT HIGHLAND GATEWAY COMMUNITY YOUTH RISK BEHAVIOR SURVEY: EXPLORING RISKS ASSOCIATED WITH THE "SCHOOL TO PRISON PIPELINE"

Christopher Montgomery, Nipher Malika, Simran Brar,
Simone Montgomery, Juan Carlos Belliard

School of Public Health, Institute for Community Partnerships,
Loma Linda University, Loma Linda, CA

In the United States of America over the last 40 years, incarceration has increased by more than 500%. African-Americans (AAs) represent only 13% of the US population but make up 40% of the incarcerated population. Many factors contribute to this enormous disparity, one of which is the "school to prison pipeline." The "school to prison pipeline," as it is often referred to, is the process of funneling students of color out of school (through suspension, expulsion, and law enforcement) into the streets, often followed by their entrance into juvenile correction facilities. This racial disparity of mass incarceration is omnipresent in the US, including the Desert Highland Gateway Community (DHGC) of Palm Springs, a small historically AA community, where it is documented that 40% of the adult population had a previous incarceration and only 43% had graduated high school. To better understand risks associated with this issue, a quantitative needs and assets assessment was conducted utilizing a community-based participatory research methodology. A youth risk behavior survey was created that assessed risk factors in 30 high school students from the DHGC as well as 185 high school students from the Palm Springs Academy for Learning Medicine (PALM) as a comparison group. The data was entered and analyzed using SPSS-24 and descriptive comparative analyses conducted between the two groups. Results show higher prevalence of risk factors associated with the "school to prison pipeline" including mental health (specifically harassment/bullying), disruption in home and neighborhood environments, lower hope scores, and worse perception of school climate. The survey findings suggest that DHGC youth compared to the comparison youth indeed experience higher risks for "school to prison pipeline," calling for urgent attention to break this cycle especially as many of these same youth also present with indicators of strong resilience (good grades, low drug use, high parental protective factors) that need to be supported.

GULJINDER CHERA

BEHAVIORAL HEALTH PARTICIPANT 2017

I am a junior at the University of California, Riverside, pre-med majoring in neuroscience. My goal is to one day serve the Inland Empire since it is such an underserved area. I spent the summer after high school completing my training in Emergency Medical Technician School where I had the opportunity to learn more about what it takes to care for patients on the front line and in critical situations. My work as an EMT eventually led to my working at an urgent care clinic in a rural area of the Inland Empire. There, my duties included checking patients in and triaging. It is an experience that has given me the opportunity to interact more with patients and learn how best to connect and communicate with them. For the past year I have spent time every week in the clinic, working under nurses and doctors, seeing firsthand what it takes to care for patients in an area where the need is the greatest and the resources are minimal. I have seen firsthand what a health disparity truly means in the everyday lives of our patients, and I can attest personally to the urgency for understanding and addressing health disparities in sincerely meaningful ways.

As a future physician, I am keenly interested in gaining all the training, experience, and knowledge I can to do my part to provide quality whole-person care while continuously working with the communities (that I hope to work in) towards alleviating health disparities. I am truly thankful to Dr. Susanne Montgomery for her guidance and giving me the opportunity to work in her lab this summer and to my lab mentor Semran Mann who helped me explore health disparities among Punjabi communities in California.

GENDER DIFFERENCES IN ANXIETY RATES AMONG PUNJABI SIKH ASIAN-INDIANS IN CALIFORNIA

Guljinder Chera, Semran Mann, Rajver Mann, Raveena Chara,
Lisa Roberts, Susanne Montgomery

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

While recent literature has begun to explore mental health challenges experienced by Punjabi Sikh Asian-Indians (AI) in the United States (US), little information exists about anxiety. Our aim was to explore differences on the Generalized Anxiety Disorder 7-item Scale (GAD-7) between men (38%) and women (62%) among a sample of Punjabi Sikh adults (N =350) in the US. The GAD-7 is used in research as a severity measure for generalized anxiety and as a clinical screening tool. Higher summative scores indicate higher levels of anxiety symptoms with cutoff scores of 5, 10, and 15 representing mild, moderate, and severe anxiety, respectively. Results indicated that a majority of the sample completed the survey in English (78%), were married (73%), had a bachelor's degree or higher (53%), were employed (57%), were born in India (84%), and lived in joint-family households (53%). While the overall mean level of anxiety was moderate (M =5.49, *SD* = 5.27), women had significantly higher anxiety (M=6.30, SD=5.30) than the men (M=4.36, *SD*=5.05) who presented in the normal range ($t(287) = 3.12$, $p < .002$). Women, in particular, reported significantly higher frequencies of uncontrollable worrying, worrying too much about different things, trouble relaxing, and being afraid as if something awful might happen. Our results support the existing literature in highlighting the need for addressing mental health among Punjabi Sikh AIs in the US. Our research also points to important gender differences in anxiety symptomatology that healthcare professionals should consider in caring for their Punjabi patients. With limited literature exploring anxiety rates, its correlates, or coping strategies in this population, our findings illustrate a need for a greater understanding of anxiety and related contextual factors among Punjabi Sikh AIs in the US, especially for women.

RAVEENA CHARA

BEHAVIORAL HEALTH PARTICIPANT 2017

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

While I am generally interested in minority mental health, I also have a specific interest in the experiences of the Punjabi community. As an active member of the Punjabi community, I have directly seen how mental health is ignored and rarely considered a priority in care, especially among the women. My goal in continuing my education and training is to be able to reach out to the women of my community, find how I can assist them in their journey towards good mental health and wellbeing, and discover how we as a community can build and maintain a lifestyle that supports mental wellbeing.

My training experience in Dr. Susanne Montgomery's lab has been invaluable. The opportunities I had during this summer have helped me broaden my knowledge and understanding of mental health disparities. Thanks to the guidance of Dr. Montgomery and my lab mentor Semran Mann, 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.

DOES LIVING IN A JOINT-FAMILY IMPACT LIFE SATISFACTION OF PUNJABI WOMEN?

Raveena Chara, Semran Mann, Navdeep Randhawa, Lisa Roberts, Susanne Montgomery

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

Life satisfaction is an important indicator of subjective wellbeing. Recently a few studies have noted an increased risk of negative mental health experiences for Punjabi Sikh Asian-Indian (AI) women in the US. For Punjabi women, the literature points to joint-family households serving both as protective buffers against and risk factors for negative mental health experiences. However, few studies have explored women's level of life satisfaction in this regard. Our aim was to explore differences on the Satisfaction with Life Scale (SWLS) between Sikh Punjabi women (N = 217) who did (60%) vs. did not (40%) live in joint-family households. Results indicated that women had a mean age of 42, lived in the US for an average of 18.5 years, and most women were married (82 %), completed the survey in English (76%), and held a bachelor's degree or higher (54.8%). Women who did not live in joint-family households reported significantly higher life satisfaction (M=26.46, *SD*= 6.85) than women who did (M=22.35, SD= 9.95, p <.000). Specifically, women who lived in joint-families were significantly more likely to report that their life was not close to ideal, their life conditions were not excellent, they were not satisfied with their life, and they had not gotten the important things they wanted in life. These results point to significant lifestyle and cultural nuances that affect the subjective wellbeing of Sikh Punjabi women in the US. While there are a growing number of Punjabi families in the US living in nuclear family households, many still live in joint-family homes. Mental health care professionals working with Punjabi women should be aware of the potential relationship between family structure and life satisfaction and how best to identify and help meet their mental health needs. Further research exploring the influence of family structure on Punjabi women's life satisfaction and other measures of wellbeing is recommended.

SEMRAN MANN

BEHAVIORAL HEALTH PARTICIPANT 2017

I have been involved in social advocacy and community development efforts locally, regionally, nationally, and internationally for over 10 years. Through my work and academic pursuits, I have been able to gain extensive experience in developing and implementing community-based initiatives, translational research, and programming to address social and public health issues affecting culturally and linguistically marginalized populations.

I have a Master's of Public Health in Health Promotion and Education and have a broad background in public health research and practice. During my time working in public health practice, I became increasingly interested in exploring health disparities and, specifically, in examining the interplay of community health within the complex dynamics of culture, language, and gender in ethnic communities. I decided to pursue doctoral studies to further explore and understand mental health disparities from a multi-disciplinary and multi-sectoral perspective.

Currently, I am a PhD candidate in Social Research and Social Policy. Using an intersectional and transdisciplinary approach, my research focuses on gender dynamics and mental health in Punjabi Asian-Indian communities in the United States.

I am able to draw from my training and experience in the fields of public health practice, social research, and policy as a transdisciplinary researcher. I am looking forward to continuing in my commitment to fostering joint research and practice efforts across disciplines to develop new conceptual, theoretical, methodological, and translational innovations that integrate and move beyond discipline-specific approaches in order to address common problems, like health disparities, and promote community resilience.

CROSS-CULTURAL AGING EXPERIENCES, SLEEP QUALITY, AND DEPRESSION

Semran Mann, Kelly Baek, Rajver Mann, Simone Montgomery, Susanne Montgomery

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

Older adults and minorities are among the fastest growing groups in the United States. As America's greying population grows, a better understanding of mental health challenges and the contributing contextual factors among diverse older adults is needed. Depression, along with dementia, is the most common mental health issue for older adults in the US. While depression significantly impacts existing chronic health conditions and overall quality of life of older adults, it remains underdiagnosed and often untreated. Our aim was to understand the mental health care needs and preferences of diverse older adults (ages 55+). We explored aging perceptions, experiences, attitudes, beliefs, and behaviors across three prominent racio-ethnic groups in Southern California's San Bernardino County. Using secondary data (N=401), three separate standard multiple linear regression (MLR) analyses were conducted to predict depression symptoms among African-Americans (n = 99), Hispanics (n = 194), and Caucasians (n = 94). Depression was measured using 8-items (α = .88) from the CESD-10. Scale scores were assessed using a non-weighted summated rating of 0-24 where higher scores indicated higher frequency of depressive symptoms. We found that lower sleep quality significantly predicted higher depression scores across all three groups. Among Hispanics, specifically, more expectations of aging-related changes and collectivistic (vs. individualistic) views of care significantly predicted higher depression scores. Among African-Americans, greater fear of aging, more expectations of aging-related changes, and not being employed were significant predictors of higher depression scores. Our research points to important similarities and differences in depression correlates of African-American, Hispanic, and Caucasian adults. Mental healthcare providers working with these populations should consider patients' potential fears of aging, employment status, and collectivistic vs. individualistic beliefs of care to inform culturally aligned services for older adults. The shared role of sleep quality in impacting depression across all three racio-ethnic groups is especially noteworthy and warrants further research.

CHRISTOPHER MONTGOMERY

PUBLIC HEALTH PARTICIPANT 2017

While playing semi-professional soccer in Germany, I obtained a Bachelor of Science degree in Biology (2016) from the Technical University of Kaiserslautern. I was fortunate to conduct my bachelor thesis research at the Center for Health Disparities and Molecular Medicine working on an interdisciplinary team led by Drs. Susanne Montgomery, Carlos Casiano, and Colwick Wilson that set out to research issues surrounding the high prevalence and mortality of prostate cancer in African-American men. I am currently working on my Master's in Public Health, specializing in Global Health, at Loma Linda University.

As part of my studies I work with adolescents from a low income, African American community in Palm Springs. I also work as a graduate research assistant for the School of Behavioral Health and coach various soccer youth programs in the San Bernardino and Riverside County areas. In addition, I continue to work on Project CHANGE (a prostate cancer research project) helping with the health fairs we organize for data collection and doing data entry and analyses. I feel fortunate to have had a variety of opportunities for health disparities research during my time at Loma Linda University. My plan is to pursue a career in medicine, once I obtain my MPH and the experiences I had here have confirmed my desire to work in the African-American community, addressing various health disparities in medicine.

DESERT HIGHLAND GATEWAY COMMUNITY YOUTH RISK BEHAVIOR SURVEY: EXPLORING RISKS ASSOCIATED WITH THE "SCHOOL TO PRISON PIPELINE"

Christopher Montgomery, Nipher Malika, Simran Brar,
Simone Montgomery, Juan Carlos Belliard

School of Public Health, Institute for Community Partnerships,
Loma Linda University, Loma Linda, CA

In the United States of America over the last 40 years, incarceration has increased by more than 500%. African-Americans (AAs) represent only 13% of the US population but make up 40% of the incarcerated population. Many factors contribute to this enormous disparity, one of which is the "school to prison pipeline." The "school to prison pipeline," as it is often referred to, is the process of funneling students of color out of school (through suspension, expulsion, and law enforcement) into the streets, often followed by their entrance into juvenile correction facilities. This racial disparity of mass incarceration is omnipresent in the US, including the Desert Highland Gateway Community (DHGC) of Palm Springs, a small historically AA community, where it is documented that 40% of the adult population had a previous incarceration and only 43% had graduated high school. To better understand risks associated with this issue, a quantitative needs and assets assessment was conducted utilizing a community-based participatory research methodology. A youth risk behavior survey was created that assessed risk factors in 30 high school students from the DHGC as well as 185 high school students from the Palm Springs Academy for Learning Medicine (PALM) as a comparison group. The data was entered and analyzed using SPSS-24 and descriptive comparative analyses conducted between the two groups. Results show higher prevalence of risk factors associated with the "school to prison pipeline" including mental health (specifically harassment/bullying), disruption in home and neighborhood environments, lower hope scores, and worse perception of school climate. The survey findings suggest that DHGC youth compared to the comparison youth indeed experience higher risks for "school to prison pipeline," calling for urgent attention to break this cycle especially as many of these same youth also present with indicators of strong resilience (good grades, low drug use, high parental protective factors) that need to be supported.

SIMONE MONTGOMERY

BEHAVIORAL HEALTH PARTICIPANT 2017

I am a 2nd year MD/MPH dual degree candidate at Keck School of Medicine at USC. In 2014, I completed my undergraduate education, receiving a Bachelors 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 with the CHDMM in the summers. This summer I am working as a research assistant in Dr. Susanne Montgomery's summer research group at Loma Linda University as well as for Ellen Iverson at Children's Hospital Los Angeles researching transition medicine.

My passion for health disparities and rebuilding broken relationships between medical professionals and marginalized populations led me to pursue a dual degree program in both medicine and public health. Both my summer research projects align with this passion: one seeks to understand barriers to care around cognitive health challenges in older adults of diverse backgrounds, the other to help medically fragile young adults stay engaged with the healthcare they need once they age out of the more protective "integrated child health care" system. While I strive to be a great physician, my passions motivated me to use my public health background to address population health at both the institutional and policy levels to ensure access to culturally-appropriate, quality healthcare for all. I am the Secretary and Events Coordinator for the Keck Student National Medicine Associate group for Black medical students as well as the Keck co-chair heading the 2017 Los Angeles Minority Health Conference. 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.

IEXPLORING COGNITIVE HEALTH NEEDS, PERCEPTIONS, AND BARRIERS TO RESOURCE-SEEKING AMONG SPANISH VS. BILINGUAL LANGUAGE IN HISPANIC OLDER ADULTS

Simone Montgomery, Semran Mann, Christopher Montgomery, Simran Brar, Susanne Montgomery

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

By 2040, the number of Americans above the age of 65 is expected to double and roughly estimate 20% of the population. As this impending demographic shift occurs, it is important for medical and public health professionals to prepare for its impact on the healthcare system. In California, Hispanics comprise 39% of the total population, and research indicates that minorities are more adversely impacted by age-related cognitive decline due to a predominance of pre-existing chronic conditions. The aim of this mixed-methods study is to determine whether language-proficiency impacted cognitive healthcare needs for Hispanic adults qualitatively (N=29) with older Hispanic adults, their caretakers, and providers, and quantitatively (N=204) with older Hispanic adults (ages 55+). Quantitative differences were explored by self-reported language proficiency: only speaking/reading Spanish (n=122) vs. bilingual (Spanish-English; n = 82). We used qualitative description theming and used SPSS v.24 for descriptive and bivariate analyses. Results suggest that Spanish-only speaking older adults experience significantly stronger barriers to receiving cognitive health-related care. Personal barriers include lack of transportation, health insurance/financial ability, access knowledge, cultural barriers, and fear of diagnosis. Importantly, provider barriers (e.g., having a regular healthcare provider), language discordance, inconvenient hours, discrimination, and fear of deportation further contribute to the heightened vulnerability of this subgroup of an already vulnerable elderly, low-income, Hispanic population. Qualitative statements further describe lived experiences of affected older adults. The findings of our study are significant for healthcare providers serving low-income older adults of diverse backgrounds, who need to be aware that not all Hispanic populations present with the same challenges and of the increased vulnerability of Spanish-only speaking populations. Primary care healthcare providers are on the front lines of identifying patients with early cognitive decline, and it is critical for them to identify and preventively refer these highly vulnerable populations.

HARINDER PAL KAUR

BEHAVIORAL HEALTH PARTICIPANT 2017

After graduating from Government Medical College Patiala, India, and working as a general practitioner in India for six years, I moved to California in 2013 for better career opportunities. My passion of becoming a psychiatrist has led me to work with many renowned physicians both in the clinical and the research side. I have had great opportunities to shadow and work in the in-patient and out-patient clinics at Loma Linda University Medical Center with Dr. Serafin Lalas, Dr. Irene Ciovica, Dr. Peggy Chatham, and Dr. Khashayar Dashtipour. Evaluating the emotional needs and easing and comforting the suffering of behaviorally, emotionally, and mentally disturbed patients give me contentment. Since moving to California, volunteering in free clinics as a physician and serving homeless, medically indigent, underinsured, uninsured, and non-residents in Redlands and San Bernardino have given a meaningful purpose to my life. I consider myself really fortunate for acquiring so much knowledge from my vast clinical and research experiences, making it my biggest asset to help me transition smoothly to a residency program.

I have been involved in research projects headed by Dr. Susanne Montgomery at Loma Linda Behavioral Health Institute for over a year now. It feels great to be able to give back to the community by contributing my time and knowledge in return for the learning opportunities of being involved in these projects. I appreciate the support and guidance of Dr. Montgomery and would sincerely like to thank her for allowing me to be a part of her amazing team and trusting me to participate in one of the studies involving elderly people and the mental health challenges they face. I feel proud to be presenting at CHDMM's annual symposium for the second year in a row.

MILD COGNITIVE IMPAIRMENT IN OLDER ADULTS OF DIVERSE BACKGROUNDS: A CALL TO RAISE AWARENESS

Harinder pal Kaur, Semran Mann, Lisa Roberts, Susanne Montgomery

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

Mild Cognitive Impairment (MCI) typically presents as memory impairment and decline in the ability to perform activities, including difficulties in language and perceptual-motor and social skills, although affected individuals are still able to perform these activities without assistance. The conversion rate of those with MCI to dementia is estimated at 23-47% over 2.6 years. Prevalence of MCI is known to increase sharply with age. Early recognition and treatment of MCI could potentially help prevent or delay further deterioration in cognitive impairment, which would confer significant health benefits for an aging US population. The purpose of this study was to explore awareness of MCI across a multi-ethnic sample of older adults in an underserved region of Southern California and describe related health promotion needs. A cross sectional, mixed methods study was conducted with a diverse group of 401 participants. Respondents were primarily female, 50% were Hispanic, 25% each African American and White, and over 50% had a high school education or less. Results showed that while the majority of respondents would discuss brain health with family (78%) and friends (64%), almost 55% were not at all familiar with the term MCI, and 62% feared MCI as they aged. Results support the dire need to raise awareness about MCI, especially among low income, diverse older adults who present disproportionately with MCI. Referral to memory clinics should be considered to warrant timely clinical attention for patients who show signs of MCI as the impairment may be subtle but significant enough to affect their quality of life. In light of an increasing population of older adults from diverse backgrounds, we know little about the risk and protective factors for dementia in these groups. Further research should aim to identify risk factors as well as to develop and evaluate culturally aligned treatment modalities in order to improve quality of life and maintain independence in cognitive decline in affected individuals.

DIPAL PATEL

PUBLIC HEALTH PARTICIPANT 2017

Since I was in high school, I loved science and wanted to enter the medical field and become a physician. I was born in India and both my parents were teachers. They played a major role in encouraging me to pursue the medical field. After many years of hard work, I finally reached this goal.

During my medical school training, I had an excellent exposure to clinical medicine and healthcare. In clinical rotations, I was exposed to patients with different social, cultural, and economic backgrounds including health disparities. This diverse patient population exposure provided me a very valuable experience in understanding the unique needs of the patients and their respective environments. It also taught me the importance of being a good listener and observer. I traveled to villages and worked with medically indigent patients with many diverse healthcare needs. There was much interaction with patients that I found rewarding. It was then that I decided to broaden my career in medicine to also include public health. So, I enrolled in the School of Public Health. I finished my Master's of Public Health (MPH) in Epidemiology at Loma Linda University in June, 2002. During my training in the epidemiology program, I participated in research work in the Diabetes Treatment Center in Loma Linda. Then I worked as a clinical research coordinator at Loma Linda University Medical Center with the surgery team for many different types of clinical trials.

Since I have good experience and knowledge in research and clinical fields, I have decided to pursue my career in research and public health. Through the support of my mentors, Dr. Zaida Cordero-MacIntyre and Dr. Lawrence Beeson, I hope I will succeed in my future career.

THE EFFECTS OF A COLLEGE NUTRITION CLASS ON DIETARY INTAKE AMONG STUDENTS

Dipal Patel, Jimmy Duong, Cody Martinez, Lawrence Beeson,
Zaida Cordero-MacIntyre

Center for Nutrition, Healthy Lifestyle and Disease Prevention, School of Public Health,
Center for Health Disparities and Molecular Medicine, School of Medicine,
Loma Linda University, Loma Linda, CA; Department of Kinesiology and Nutrition,
Whittier College, Whittier, CA

Dietary modification is an important component to any public health strategy aimed at combatting obesity. Nutrition education is used for dietary modification as subjects obtain more knowledge about food and its nutritional content. Several nutrition education programs have led to healthier food choices. The purpose of this prospective three-month study with 23 students from Whittier College (males = 8, females = 15) who were enrolled in an introductory nutrition course was to assess the impact of being in this course and food choices. A validated food frequency questionnaire from the University of Arizona was administered at baseline and at the three month follow-up to assess any significant changes in dietary intake. The results from the frequency questionnaires were sent to the University of Arizona Diet, Behavior, and Quality of Life Assessment Lab to analyze macronutrient and micronutrient intake. Paired t-tests were used to calculate mean differences ($mean_d$) between baseline and 3 month follow-up on dietary intake and physical activity. There was a significant reduction in caloric intake ($mean_d$=-20.46%, p=0.03), total fat intake ($mean_d$= -19.8%, p= 0.03), saturated fat intake ($mean_d$=-18.5%, p=0.03), and total cholesterol intake ($mean_d$=-22.9%, p=0.03). Total carbohydrate intake was reduced ($mean_d$ = -20.3%, p= 0.07) and alcohol intake ($mean_d$=-3.4%, p=0.07) was reduced, too. Total body weight was not significantly altered ($mean_d$ = -0.93 %, p=0.06). Whittier College students enrolled in a nutrition course showed significant decreases in their total fat intake, but notably, their saturated fatty acid intake was reduced. These reported changes may relate to the improvement of healthier food choices as a result of the students' enrollment in a nutrition course that improved their self-care.

AMITOJ RANDHAWA

BEHAVIORAL HEALTH PARTICIPANT 2017

In order to take on the most detrimental health effects in the world, we have to understand the very nature of the people that are affected. Growing up in California's Central Valley, the most valuable lessons and experiences I've gained have been through my individual research and volunteer experiences that allowed me to interact with patients from diverse backgrounds and walks of life.

As a research volunteer in high school, I had the privilege to work with Semran Mann, Dr. Susanne Montgomery, and Dr. Lisa Roberts in their study exploring mental health disparities in Punjabi Asian-Indian communities in the Central Valley. This area of study is particularly important to me because as a member of the community, I have personally seen the detrimental effects of unaddressed mental health. I am specifically interested in exploring the mental health experiences of Punjabi Asian-Indian men. While it has largely been a more elusive area of study, men's mental health struggles throughout the community have certainly been evident in my own experiences.

As a Punjabi male, a member of the community, and a future physician, this work is meaningful to me. By recognizing hidden mental health issues prevalent within the Punjabi community, we are not only able to raise a critical awareness among healthcare practitioners and researchers, but we are also able to shed light on the need for resources and interventions acceptable and accessible to the community.

This summer I had the privilege of working in Dr. Montgomery's lab, and I am incredibly thankful for her mentorship, the guidance of my lab mentor Semran Mann, and the support of my fellow lab-mates. This has been a tremendous learning experience, and I am greatly indebted to everyone in Dr. Montgomery's lab and to the program.

IMPACT OF LANGUAGE PREFERENCE ON LIFE SATISFACTION AMONG PUNJABI SIKH MEN IN CALIFORNIA

Amitoj Randhawa, Semran Mann, Lisa Roberts, Susanne Montgomery
School of Behavioral Health, Loma Linda University, Loma Linda, CA

Preliminary and anecdotal evidence suggest that limited English proficiency (LEP) among Punjabi Sikh Asian-Indian (AI) men in the United States poses a significant risk for mental health challenges. LEP is seen to increase exposure to everyday discrimination and financial strain while it also decreases access to broader social support networks. In the US, Punjabi Sikh AI men are part of an ever-growing population emigrating from India, yet there is little literature on the subjective wellbeing of this subgroup. Our aim was to explore differences on the Satisfaction with Life Scale (SWLS) by Punjabi (23%) vs. English (77%) survey language preference among a sample of Punjabi AI men (N=133). With an average age of 41, results indicated most men were married (62%), held a bachelor's degree or higher (44%), were employed (67%), had a median annual household income of $79,000, were born in India (79%), and resided an average of 19 years in the US. Compared to English survey takers (M = 23.92, *SD* = 8.19), Punjabi survey takers (M = 16.64, *SD* = 8.79) reported significantly lower overall life satisfaction ($t(124) = 3.92$, $p < .000$). Our findings highlight language preference as a barrier to life satisfaction for Punjabi AI immigrant men. For the men who took the survey in Punjabi, it may be that LEP acts as a fundamental obstacle towards being able to achieve the important things men feel are part of the ideal life conditions they may have envisioned by emigrating. Specifically noteworthy is that the inability to express oneself through English was a particularly trying hurdle to overcome for both recent and more established immigrants alike. Given recent evidence of significant discrimination and mental health challenges experienced by Sikh Punjabi US men, our study further underscores a critical need for efforts to better understand and respond to the unique challenges this often ignored minority group faces.

NAVDEEP RANDHAWA

BEHAVIORAL HEALTH PARTICIPANT 2017

I graduated from a small high school in Hemet and went to the University of California, San Diego. I have recently graduated from UCSD with my BS in Cognitive Behavioral Neuroscience. Although I acknowledge my accomplishments in the past, my real journey in pursuing my medical interests is just beginning. I am currently working as a research assistant in a study looking at the mirror neuron system in patients with depression.

Medicine has always been something I have been interested in since watching my family members attend medical school. However, my own motivation was truly sparked when I took a medical trip to Cusco, Peru, and met the beautiful Peruvian culture. The people in Cusco confirmed my direction: to fully drive myself on the medical path. I could see how privileged we (Americans) were living in a westernized society with access to basic medicines, health professionals, and preventative care. Access to healthcare should not be limited for anyone. Through my experiences in Cusco, in a cognitive sciences major, and in this summer internship, I am able to see health disparities from a new perspective. There is more to medicine than identifying and curing illness. Practicing medicine includes being aware of the connection one is making with individuals and communities, not only physically but also mentally and emotionally. I use these experiences and lessons learned as a motivating force to further my academic training and one day be able to help others.

I am excited about the training opportunities given to me throughout the summer research and academic experience. As my knowledge and understanding of health disparities research grows, I look forward to being able to put this knowledge to practice as a future physician.

REPRODUCTIVE DECISION-MAKING AND RELIGIOUS COPING AMONG PUNJABI SIKHS IN CALIFORNIA

Navdeep Randhawa, Semran Mann, Amit Randhawa, Lisa Roberts, Susanne Montgomery

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

Religious coping has been the primary documented strategy for Punjabi Sikh Asian-Indians (AI) in the United States to manage their mental health. Punjabi Sikhs make up a significant portion of a large and growing subgroup of AI immigrants in the US, yet little is known about the role of religious coping in their health care decision-making. Our aim was to explore religious coping among Punjabi Sikh adults (18+) who did (67.5%) and did not (33%) get to choose family planning methods (FPM). Religious coping was measured using the BriefRCOPE scale, assessing levels of positive (PRC), negative (NRC), and overall religious coping strategies employed. Results indicated significant differences in religious coping between those who did and did not choose FPM. For those who did not get to choose FPM, NRC and overall involvement of religion in coping with stress was higher. Especially noteworthy was that there was no significant gender difference ($X(1) = .68$, $p = .41$) between the number of men vs. women who reported that they did (M 71%; W 66%) or did not (M 33%/ W 34%) get to choose FMP. This is an important point of consideration for reproductive and mental health care professionals as well as for Punjabi Sikh community members. In discussions of Punjabi culture and choice in FPM, healthcare professionals and general public alike tend to assume it is primarily Sikh women who do not have a choice. In so doing, Punjabi parents and adults in consensual relationships may be missing critical opportunities to discuss reproductive choices with their male children or significant others. Similarly, healthcare professionals may be overlooking an important need to discuss reproductive planning choices with Punjabi men, and consideration of how ability to participate in choosing FPM may be related to or reflective of coping strategies in dealing with distress among Punjabi Sikh men and women.

CARMEN SORET

BEHAVIORAL HEALTH PARTICIPANT 2017

When I was 12 years old, I was watching TV and stumbled upon a special where Oprah went to Africa on a philanthropic trip focusing on children orphaned by AIDS. I had never seen poverty like this; I had never seen such excitement over soccer balls and backpacks. It may seem cliché, but it was in this moment I decided I wanted to work to help children like the ones I saw on TV and in similarly underserved communities. It should have come as no surprise to me since both my parents were educators motivated by their desire to help others and love of other cultures. My mother, a high school Spanish teacher, modeled compassion for those she saw who suffered injustices. My father, who served as a professor and researcher at the LLU School of Public Health for 21 years, inspired my intellectual curiosities and showed me a field of study through which I could have the kind of impact I longed for.

I received my BA in Global Studies with a minor in Spanish from the University of Southern California. I became fascinated with the connection of international relations and political science with the community perspective from the anthropology basis this degree provided. As a part of this program, I traveled to Huánuco, Peru, two summers ago to serve as a volunteer with the nonprofit organization *Paz y Esperanza* and to conduct research for my senior thesis. My passions lie in maternal and child health and exploring how using intersectional approaches in research and intervention can be of benefit to marginalized communities. I will follow in my father's footsteps and begin an MPH in Global Health in the fall of 2017 at the Loma Linda University School of Public Health.

FAMILY PLANNING METHODS IN HUÁNUCO, PERU: *MACHISMO* AND MISCONCEPTIONS

Carmen Soret, Semran Mann, Susanne Montgomery

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

The limited existing literature on family planning in Peru focuses mainly on the issues related to the introduction of public, government-funded programs in the 1960's and 70's. However, there is little information and research available concerning the relationship between family planning practices in Peru in the 21st century and socio-cultural factors that are negatively impacting women's efficacy regarding their own reproductive health. Therefore, such efforts are critically needed given the historic political, economic, and social dominance of men that pervades Peruvian society and has contributed to high levels of violence regularly perpetrated against Peruvian women. Huánuco, Peru, is one the poorest and least developed regions of Peru, leaving women in this area particularly vulnerable. Our aim was to explore the perspectives of local women of reproductive age in Huánuco about the socio-cultural factors affecting the efficacy of and their autonomy over their own reproductive health. In addition to key informant interviews with mothers of various ages (N=19), further contextual, qualitative data was gathered from service providers and experts on women's health (N=7) over the course of 9 weeks. Quantitative findings indicated that women who had partners that prohibited the use of birth control were younger and less likely to successfully carry a pregnancy to full term. Qualitative findings indicated that sexually related stigmas due to long-standing constructions of gender roles and *Machismo* posed a significant barrier for women to engage in thoughtful family planning including contraceptive use. The results highlight a need for further studies to explore potential facilitators that increase women's access to and autonomy over their reproductive health.

KRYSTLE WILEY

PUBLIC HEALTH PARTICIPANT 2017

I am a first-generation to college student attending Loma Linda to obtain my MPH in Research Epidemiology. Born and raised in Washington, DC, I received a BS in Biology from the University of the DC (UDC) in 2009 and, previously, a BA in Spanish from the University of North Carolina, Wilmington, in 2007. I will obtain my supervisor permit and AA in Early Childhood Education at San Bernardino Valley College and plan to start my own non-profit organization. My goal is to become a bilingual, neuro-developmental disability pediatrician using public health and research to further advance medicine on a more population level.

My volunteer experience includes being a COPE Health scholar at Riverside Community Hospital in numerous departments, a child life volunteer and NICU snuggler at Loma Linda University Children's Medical Center, and a volunteer for Regional Perinatal Programs of California which involves maternal and child health issues. I also volunteered at Jumpstart as an AmeriCorps Member assisting preschoolers to prepare for kindergarten. My community service includes positions such as a Public Health Liaison for LLU Street Medicine which serves homeless populations and a volunteer coordinator for Millennium Momentum Foundation, Inc., a leadership organization.

My research interests are maternal and child health and health disparities in underserved communities. As a UDC research assistant, I conducted and presented my research on how Arsenic modulates the cell proliferation pathways in MCF-7 breast cancer cells. My current LLU research is on the effects of physical activity on Hispanic diabetics in the *En Balance* study. My mentors for this study are Drs. Zaida Cordero-MacIntyre and Lawrence Beeson who both worked diligently to improve my skills as an experienced researcher. With their guidance, I am honored and appreciative that I was given this opportunity.

THE EFFECTS OF PHYSICAL ACTIVITY ON GLUCOSE LEVELS AND NEUROPATHY SYMPTOMS IN HISPANIC DIABETICS IN THE "EN BALANCE PLUS" STUDY

Krystle Wiley, Lawrence Beeson, Anthony Firek, Zaida Cordero-MacIntyre, Marino De Leon

School of Public Health, Center for Health Disparities and Molecular Medicine, Center for Nutrition, Healthy Lifestyle and Disease Prevention, JL Pettis Memorial VA Medical Center, School of Medicine, Loma Linda University, Loma Linda, CA

The purpose of this study is to assess the effects of physical activity and Omega 3-Fatty acids on diabetes control as indicated by hemoglobin A1C levels and neuropathy symptoms in Hispanic diabetics in the "En Balance Plus" Study. The objective of this study is to obtain evidence that the physical activity component of the "En Balance Plus" education program conducted in Spanish is beneficial to lowering glucose levels. This study was for the duration of three months, and participants were examined at the start of the program and three months later at the termination of the program. The En Balance Study is a prospective intervention study that included taking Omega 3 fatty acids in pill form, 12 hours of nutrition instruction and lifestyle choices, including physical activity. To evaluate the physical activity, participants were surveyed using the Arizona Physical Activity Frequency questionnaire. The pain intensity of the participants was measured using the shortest form of the McGill pain questionnaire which displayed a pain diagram. Diabetic pain was described as cramping, aching, sharpening, heavy, and tender. The fasting glucose levels which included the hemoglobin A1C levels were tested at the blood draw clinic and later analyzed at the Loma Linda University Medical Center. Paired T-tests were analyzed and resulted in a significant p value in the A1C levels in the Hispanic population. Neuropathy pain intensity decreased after a 3 month follow-up and was positively correlated with hemoglobin A1C levels. According to the McGill pain questionnaire, after 3 months, subjects reported they had significantly less pain than compared to baseline. Physical activity decreased the A1C levels, therefore decreasing the pain intensity and neuropathy symptoms.

Summer Undergraduate Research Program (SURF)

Adam Bennani
Cody LaCourt
Mindy Lombere
Vanessa Lopez
Simone Moore
Alice Nam
Phoebe Nye
Karndeep Rai-Bhatti
Jessica Reyes
Erwin Stuffle
Evan Thomas
Jonathan Thomas
Natalie Wolske

ADAM BENNANI

SURF PARTICIPANT 2017

In 2014, I graduated from Newport Harbor High School and enrolled at Orange Coast College (OCC). After two years at OCC, I graduated with three associate's degrees in mathematics, chemistry, and physics. I then transferred to University of California, Riverside, where I am currently in my senior year studying bioengineering. In the future, I intend to work in the healthcare industry and then enroll in an MD/PHD program.

Throughout my undergraduate career, I have been active in the community serving as a volunteer at Riverside Community Hospital and Riverside Free Clinic, tutoring underserved youth, and educating the community about constructive ways to help the local homeless population. In my free time, I love to box, play lacrosse, and hangout with family.

This summer I have the privilege of researching in Dr. Ryan Sinclair's lab working on a project that is in conjunction with Dr. Perry's lab. Our project is to develop a method to uniformly distribute bimetallic nanoparticles on an ear tube implant. These nanoparticles, made of gold and silver, inhibit bacteria growth to significantly reduce the probability of infection.

I want to thank Dr. Sinclair for his patience, guidance, expertise, and the opportunity to be a part of his research lab.

EFFECTIVENESS OF VARIOUS NANOMATERIALS IN PREVENTION OF BACTERIAL GROWTH IN PEDIATRIC MYRINGOTOMY TUBES

Adam Bennani, Natalie Wolske, Brittney Springer, Christopher Perry, Ryan Sinclair

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

Silver can act as an antibacterial in biomedical devices and applications such as lab coats and pediatric myringotomy ear tubes. Myringotomy tubes, which permit fluid drainage in the ear, are coated with silver oxide nanoparticles to prevent any bacterial growth that may lead to infection in the ear. Scanning Electron Microscope (SEM) image analysis shows that commercial myringotomy tubes have a small amount of silver. The purpose of the experiment was to test the effectiveness of a myringotomy tube's ability to inhibit bacterial growth. In comparison, alternative solutions such as bimetallic silver-gold, silver nitrate, and silver nanomaterials were also tested to see if they can potentially be used as an antibacterial. The efficacy of such nanomaterials can be tested through examination of the resulting zones of inhibition (ZOI) or circular areas of no visible bacterial growth, signifying bacterial growth inhibition. For this experiment, we cultured *Escherichia coli* ATCC #15597, *Staphylococcus aureus* ATCC #33592, and *Serratia marcescens* on Mueller-Hinton agar (MHA) using a McFarland solution standard with an optical density between 0.08-0.1. Two sets of plates were made; one set had 5 uL drops of newly-prepared nanoparticles while the other had filter paper discs infused with 5 uL of nanoparticles. After 18 hours of incubation, it was found that only silver nitrate produced a zone of inhibition. For the silver nitrate drops treatment, zones of inhibition were observed between 16.82 and 22.22 mm among the bacteria tested. For the silver nitrate infused discs, the zones of inhibition observed were between 9.07 and 17.92 mm in diameter. Our observations show that myringotomy tubes cannot effectively inhibit bacteria growth. Silver nitrate shows the potential as a nanomaterial to be used in biomedical applications like the myringotomy tube to inhibit bacterial growth.

CODY LACOURT

SURF PARTICIPANT 2017

I will be entering my third year at Walla Walla University in College Place, WA, where I am studying physics as a foundation for my greater interests in biophysics. After I complete my undergraduate degree, my goal is to obtain an MD/PhD because of the numerous options these degrees provide for a career dedicated to research. I have enjoyed the opportunity to work with Dr. Reinhard Schulte and expand my knowledge in radiobiology, a field that calls on knowledge from both physics and biology.

I enjoy studying science because there is an inherent uncertainty in all fields of study that requires a certain amount of creativity if it is to be minimized. My physics professors like to say that measurements are only as good as the tools used for measuring. Similarly, the evidence provided during research can only be as good as the experiment someone thoughtfully designed. This summer program has helped me understand that research is very open-ended; it requires critical thinking as well as creative design to be able to contribute in a productive way to one's field.

I would like to thank Dr. Schulte and all the other researchers on his team for the opportunity to work with them and learn about their research.

COMPARISON OF DNA DAMAGE INDUCED BY PROTON CT, X-RAY CT, AND DUAL ENERGY CT

Cody LaCourt, Ying Nie, Reinhard Schulte

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

Proton computed tomography (CT) has many benefits over conventional x-ray CT in the planning stage of proton therapy used for cancer treatment. In this project, we are exploring the DNA damage response of two human cell lines (human umbilical vein endothelial cells and human astrocytes) following exposure to equal doses of radiation in each CT system: proton CT (pCT), conventional x-ray CT (xCT), and dual energy CT (DECT) with x-rays. Cellular DNA damage will be evaluated by observing the formation of γ-H2AX foci where each focus is an indication of an individual double strand DNA break. A range of time periods in between irradiation and fixation will also give insight into the repair time of these double strand breaks. To test the assay upfront in this summer research project, we used U87 cancer cells. After irradiating the cells with a dose of 1 Gy using a cesium-137 source, the U87 cells were incubated for 30 minutes, followed by fixation and staining with primary and secondary antibodies against the phosphorylated histone γ-H2AX. The irradiated stained cells were imaged alongside unirradiated stained cells (control) that had been prepared in the same way. Our results show an increased formation of γ-H2AX foci after irradiation with a mean of 16.10 ± 1.48 (SEM) foci per cell compared to a mean of 7.65 ± 1.31 (SEM) foci per unirradiated cell. These results agreed with published observations using the same assay with two glioma cell lines (T98G, U373). We conclude that the methods used in this research will be suitable for comparing DNA damage response of the three imaging modalities.

MINDY LOMBERE

SURF PARTICIPANT 2017

After several years of working in the dental field, I found myself asking, "As a dental health professional, where else could I go from here?" As an intern, I can recall how excited I was to enter into the healthcare industry. Over the years my interest in the field has never waned as every day in a dental office presents interesting challenges. Now, in my current role as an assistant manager, I have given a lot of thought to my future. Knowing I wanted more for myself, I made the decision to go back to school. I want to sit on the other side of the operatory chair as the dentist.

As a student at CSUSB, I have been fortunate to work with Dr. Daniel Nickerson as a research assistant. I have also enjoyed the experience of taking an animal tissue culture course, which has exposed me to current research techniques. These recent events in my college career have opened my eyes to the possibilities that may lie ahead. I have never felt so relevant as a student of biology as I do now.

My acceptance into the CIRM Bridges program made the idea of being able to enter into the field of stem cell research a reality. However, all of my professional experience is within the dental field. Therefore, my goal is to be a part of research that will lead to therapeutic applications in dentistry. Here at Loma Linda University, working in Dr. Juli Unternaehrer's lab, I have been given the opportunity to do exactly that. My hope is that more personalized treatments involving stem cell-based therapies can be realized for dental patients in the future.

THERAPEUTIC APPLICATIONS OF GMSCS IN PERIODONTITIS: OPTIMIZING OSTEOGENIC DIFFERENTIATION

Mindy Lombere, Hanmin Wang, Alyse Huisken-Hill, Zhe Zhong, Wu Zhang, Juli Unternaehrer-Hamm

Department of Basic Sciences, School of Medicine, Loma Linda University

Periodontal disease is the leading cause of tooth loss and results in damage to supportive periodontal tissues. The periodontium includes the supportive tissues which maintain teeth within the alveolar bone of the oral cavity. Bacterial infection of the periodontium causes inflammation (periodontitis), which results in irreversible bone destruction and gingival deterioration. Using Gingival Mesenchymal Stem Cells (GMSC), we aim to engineer treatment for periodontal disease. GMSCs, which are unique within the periodontium, possess anti-inflammatory properties and are found to play a key role in immunity. GMSCs are multipotent, can regenerate tissues, and have been shown to have a high proliferation rate compared to other types of stem cells. This project utilizes GMSCs isolated from mouse. Initially, cells will be transduced with lentivirally-delivered transcription factors, Oct4 and L-Myc. Cells will then be cultured with osteogenic media, and/or Wnt3A. After culture for three weeks in osteogenic conditions, acquisition of the desired phenotype will be tested. We hypothesize that partially reprograming GMSCs with transcription factors Oct4 and L-Myc provides a more efficient means of inducing an ostegenic lineage than without partial reprograming. Protocols have been established for cell culture conditions and isolation and expansion of GMSCs. pMX-Oct4 and L-Myc retrovirus, along with control pMX-GFP, have been successfully produced. We observe expression of Oct4 and L-Myc after retroviral transduction by qRT-PCR. Conditions for WB to determine expression on the protein level are being developed. The aim of this project is to partially reprogram GMSCs in an effort to ultimately regenerate alveolar bone. Long term, our goal is to regenerate alveolar bone with gingival mesenchymal stem cells which have been induced by Oct4 and L-Myc as well as canonical Wnt signals, in an existing periodontitis mouse model in order to test functionality of cells *in vivo.* Expected outcomes of this research will provide knowledge for new GMSC based methods in the treatment of periodontal disease.

VANESSA LOPEZ

SURF PARTICIPANT 2017

I attend Occidental College, a liberal arts college in Los Angeles, where I am a third-year Biochemistry major. I have some research experience dealing with C. *elegans,* a small yet fascinating creature that has introduced me to the complexity of biology. I am on a pre-med track, intending to go to medical school following my undergraduate degree. As a health geek, I have a love for nutrition and health sciences. Endocrinology, especially, stands out to me as a possible career focus.

In my free-time, I like to sing – Broadway most of all – and dance.
One life approach I stand by centers around the belief that everything happens for a reason. While it is a bit cliché, I do believe that with every closed door there is another brighter and more welcoming door that opens. This belief is reflected in a lot of my projects and research. When faced with scientific obstacles, I like to improvise; changed plans are just evidence I am one step closer to my goals.

This summer, I was fortunate enough to work in Dr. Sean Wilson's lab, exploring metabolomic changes involved in hypoxia, a subject that was very new to me. The most exciting part of my work was connecting metabolites to biological functions as well as clinical applications. As a fairly new topic, metabolomics presented me with a few challenges, but it was a rewarding experience when Dr. Wilson and I had small scientific breakthroughs. I want to thank him for being such a patient and supportive mentor.

HIGH ALTITUDE HYPOXIA IMPACTS OMEGA-3 FATTY ACID METABOLITES IN PLASMA OF FETAL AND NEWBORN SHEEP

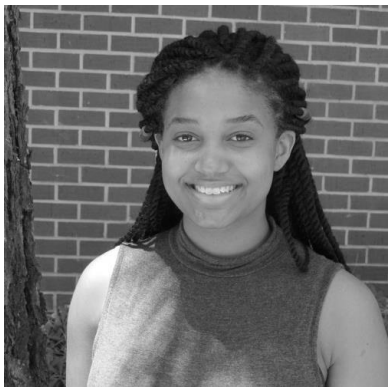
Vanessa Lopez, Michael La Frano, Remy Bosviel, John Newman, Richard Thorpe, Oliver Fein, Lubo Zhang, Sean Wilson

Laurence D. Longo Center for Perinatal Biology, School of Medicine, Loma Linda University Loma Linda, CA

Perinatal hypoxia has profound effect on the infant's pulmonary vascular development with physiological impairment of pulmonary arterial function and structure. The present study explored the effect of chronic hypoxia during gestation and after birth on lipid mediator by measuring the metabolites that foreshadow oxidative stress and inflammation, the primary drivers of pulmonary vascular dysfunction. We tested the hypothesis that chronic hypoxia reduces the amount of oxylipin and endocannabinoid production, which are important mediators of oxidative stress and inflammation. To test this hypothesis, we exposed pregnant sheep and newborn lambs to an altitude of 3,800 meters starting gestation day 30. UPLC-MS/MS analysis was used to investigate the lipid mediator composition in plasma collected from veins of fetal and newborn animals. The results show that hypoxia causes an overwhelming effect on omega-3 fatty acids and their derivatives, which are crucial in late-stage fetal development. We tracked the origin of these changes and traced the pathways of several oxylipins and endocannabinoids. The cytochrome P450 (CYP) pathway enzymes and the subsequent activity of soluble epoxide hydrolase (sEH) are prominent synthesizers of epoxyeicosatrienoic acids (EETs) and epoxyoctadecenoic acids (EpOMEs), which can then be hydrolyzed into oxylipins. Previous studies have suggested the role of EETs and EpOMEs in vasodilation, a feature in inflammation. Based on these findings we demonstrated that a majority of the affected oxylipins were produced from CYP and sEH enzymes, which are important to pulmonary vascular function. These findings provide a novel insight into our understanding of lipid metabolites in hypoxia-induced pulmonary vascular dysfunction in the developing fetus and newborn and may help us develop novel therapies that target inflammatory pathways induced by pre- and post-natal hypoxia.

SIMONE MOORE

SURF PARTICIPANT 2017



I am currently a junior studying biomedical sciences at Oakwood University in Huntsville, AL. During my two years at Oakwood University, I maintained a dean's list academic standing and received the United Giving Scholarship Award. There are many different activities to take part in at Oakwood, and something I take great joy in doing is community service. Voices of Triumph, a music ministry, and R.E.A.C.H., a community outreach ministry, are just some of the activities I participate in.

Along with obtaining a Bachelor of Science in Biomedical Sciences, my goal is to attain a doctor of medicine degree and to work in an area that allows me to find better ways to treat patients. I plan to use my gifts and my platform to change lives for the better with my own practice in an underprivileged neighborhood.

During this summer program, I learned that research could be used in many different areas. What I find to be the most interesting part of research is that there is always something different to learn and discover. I want to thank Dr. Christopher Wilson's lab for giving me an opportunity this summer to learn and explore new areas of science.

"And we know that all things work together for good to them that love God, to them who are the called according to his purpose" (Romans 8:28).

HYPOXIA-INDUCED MICROGLIAL ACTIVATION IN A NEONATAL RAT INFLAMMATION MODEL

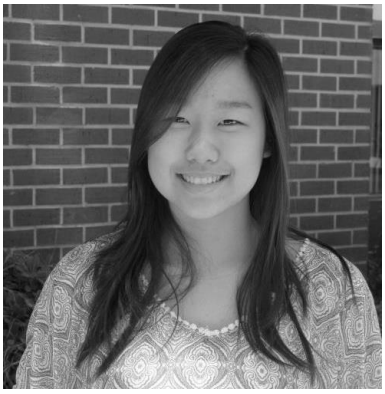
Simone Moore, Rhaya Johnson, Paul Williams, Christopher Wilson

Lawrence D. Longo Center for Perinatal Biology, School of Medicine,
Loma Linda University, Loma Linda, CA

Premature infants are at greater risk for infection due to immature immune systems. We used a lipopolysaccharide (LPS)-induced acute inflammation murine model that replicates the infection seen in preterm infants with chorioamnionitis. My objective was to use immunohistochemical markers and Sholl analysis to quantify the branching of microglial cells as a way to characterize the morphology of the cells. Microglia are immune cells that are part of the nervous system that respond to infection and are also involved in aspects of neuroinflammation. We hypothesize that hypoxia (10% O_2) can induce activation in microglia cells found in the autonomic regions of the brainstem. We gave Sprague Dawley rats, age 10–12 days, a 0.5 mg/kg intratracheal LPS injection. After 90 minutes of recovery, we exposed the rat pups to 10 minutes of hypoxia (10% O_2). We then perfused the pups and harvested the brains. The brain was then frozen and sectioned into 20 micrometer slices using a cryostat. The sections were stained for Iba-1, a selective marker expressed in microglia, using immunohistochemistry techniques. Images of the sections were obtained using the Keyence (BZ-9000) microscope and software. In addition, the branches of the microglia were quantified using the Sholl analysis plugin in *ImageJ* (https://imagej.net/). Our results indicate a significant difference between the LPS and hypoxia (10% O_2) groups. A decrease in the mean of the enclosing radius between the two treatment groups also suggests that microglia from rat pups treated with hypoxia are more activated.

ALICE YOOJUNG NAM

SURF PARTICIPANT 2017



I am a senior at Brandeis University near Boston, MA, majoring in biology and studying Chinese. I grew up in Claremont but decided to go to Boston to escape the California heat. During my freshman year at Brandeis, there was a record blizzard and I am looking forward to coming back to California when I graduate.

In my free time, I like playing tennis, cooking, sleeping, and drawing cartoons. When I was 14 years old, I watched Boston Med on TV and was inspired by the altruistic depiction of doctors and nurses to pursue a career in medicine. However, I soon realized I am too squeamish about seeing blood and live organs to become a doctor, but I knew that I still wanted to help people somehow.

In summer of 2016, I had the privilege of working in Dr. David Hessinger's lab performing Western blots and rt-PCR. With his guidance, I realized I want to go into research in the future. I loved the intellectual challenge, usage of dexterity, and the prospect of discovering something that will help a large number of people. I hope to work as a scientist in industry and work in biomedical science research in the future.

This year, I am once again working with Dr. Hessinger but this time looking at satiety of sea anemones and understanding the mechanisms to study obesity. We are specifically looking at TRP ion channels in a species of anemone called *H. luciae* and trying to connect its function with feeding patterns. Thank you to Dr. Hessinger for his unwavering mentorship and also to Desiree Torres and Selorm Quarshie, ABC participants, for counting hundreds of thousands of shrimp and keeping their sanity.

TRP CHANNELS TRIGGER NEMATOCYST DISCHARGE IN SEA ANEMONES

Alice Nam, Desiree Torres, Selorm Quarshie, David Hessinger

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

While humans can consume food in excess, sea anemones cease ingesting prey when they achieve "fullness" due to a robust satiety response. Because overeating is the major cause of human obesity, studying anemone satiety may illuminate conserved satiety pathways applicable to human health. Among animals, sea anemones possess the simplest nervous systems. They also employ stinging nematocysts to capture and kill prey. Nematocysts are eversible organelles produced by cnidocytes, yet little is known about the mechanism of nematocyst discharge. Because the contact-sensitive mechanoreceptors (CSMs) that initiate nematocyst discharge are likely targets of satiety regulation, the goal of this study is to characterize the CSMs. Since TRP channels can be mechanically gated, we predicted that blocking TRP channels would inhibit triggering of nematocyst discharge. Same-sized, starved, monoclonal anemones (*Haliplanella luciae*) were selected and incubated in different concentrations of non-selective TRP channel blockers, lanthanum [$La(NO_3)_3$] or gadolinium ($GdCl_3$). They were then fed a standardized number of brine shrimp larvae to test if blocking TRP channels decreased prey killing. Both rare earth salts potently inhibited prey killing in a dose-dependent manner consistent with TRP channel blocking. Menthol, a selective TRPM8 channel activator, unexpectedly blocked killing and ingestion in a manner consistent with action on TRPM8 channels while also rendering anemones unresponsive to touch stimuli. Our findings indicate that blocking TRP channels, in general, inhibits nematocyst discharge. The role of TRPM8 channels, along with aminoglycoside-sensitive TRPC1 channels from previous studies, suggests more than one type of TRP channel may be involved. Future studies with additional, selective TRP blockers may identify specific TRP channels as CSMs in triggering nematocyst discharge and their possible role in feeding and satiety.

PHOEBE NYE

SURF PARTICIPANT 2017

I recently graduated from University of California, Riverside, with a Bachelor of Science in Biochemistry. I joined Dr. Richard Hooley's organic chemistry research lab in the beginning of my junior year. I have completed a capstone project for University Honors based on my own research project with a graduate student mentor in the lab.

In addition to the research, I have also been one of the CNAS Science Ambassadors since my sophomore year.

Our responsibilities include participating in outreach events for prospective students; helping at various science fairs; introducing CNAS to students, families and alumni; and sharing our personal experiences at UCR. This was a very rewarding program because I got to talk to different people about how UCR has helped shape me into who I am right now and how it has provided the opportunities I have. In addition, I have volunteered at Riverside Community Hospital as a Health Scholar for about two years, assisting nurses with patient care. Through this program I have learned more about how different health professions work together as a team in the medical field, which I would love to be part of after I graduate.

Currently, I work in Dr. Erik Behringer's lab with two postdoctoral fellows, Mohan Kumar and Md Abdul Hakim. For my summer project, we are interested in studying regulation of cerebrovascular Ca^{2+} and K^{+} ion channels in Alzheimer's disease mice versus normal mice starting with RNA isolation and gene expression analysis using qPCR.

REAL TIME PCR ANALYSIS OF CEREBROVASCULAR ENDOTHELIAL AND SMOOTH MUSCLE CELL BIOMARKERS WITH ADVANCING AGE

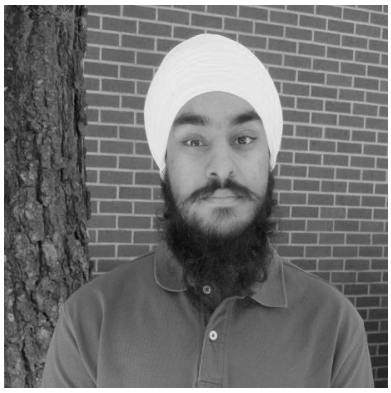
Phoebe Nye, Muthu Mohan Kumar, Md Abdul Hakim, Erik Behringer

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

Alterations in gene expression of biomarkers that regulate blood flow to the brain have not been resolved during aging and development of neurodegenerative disease. This study seeks to resolve expression of genes specific to endothelium and smooth muscle of cerebral arteries (middle and posterior) of young (3 to 7 mo), middle-age (12 to 16 mo), and old (24 to 28 mo) C57BL/6 mice. Based on our functional measurements of intracellular Ca^{2+} and hyperpolarization of membrane potential, we hypothesize that expression of endothelial small and intermediate conductance Ca^{2+}-activated K^{+} channels (SK/Kcnn3, IK/Kcnn4) channels may peak during middle-age and decline in old. mRNA is isolated from respective cell types, transcribed into cDNA, and then analyzed using real-time PCR (or qPCR). SK and IK channels are quantified as target genes in isolated cerebrovascular endothelial tubes and smooth muscle cells. Endothelial (platelet adhesion molecule, cadherin) and smooth muscle (α-actin, myosin heavy chain) biomarkers serve as cell specific reference genes whereas Beta-glucuronidase and β-actin code for general "housekeeping" functions. Also, we will examine mouse models of Alzheimer's Disease (e.g., 3xTg-AD; completely develop pathology by middle age) and mitochondrial-targeted catalase mice (mCAT; readily decompose cellular hydrogen peroxide and live ≈5 months longer vs. normal C57BL/6) as negative and positive controls for healthy aging respectively. These data may provide fundamentally new insight for precision medicine whereby selective treatments are developed for key vascular biomarkers to promote health and cure disease.

KARNDEEP SINGH RAI-BHATTI

SURF PARTICIPANT 2017



I was born in Riverside, grew up in San Bernardino, and have formed a wholehearted connection with my community. For the past six years I have volunteered at Redlands Community Hospital in various departments. Simultaneously and for as long as I can remember, I have been an aid at the Sunday School at my local Sikh temple, helping children learn the Punjabi language as well as more about their own culture and faith. I enjoy being involved with the community and look forward to forming more bonds in the future.

This fall, I will be a senior at University of California, Riverside, finishing my degree in bioengineering. Throughout my university career, I have been an active member of organizations, such as University Honors and Engineers Without Borders, both of which enabled me to constantly pursue excellence in my field. Upon graduation, I aspire to enroll in an MD program and specialize in either pediatrics or family medicine. I chose to study bioengineering due to a passion for both understanding the biology that controls the body as well as an inherent interest in engineering and mathematics. I believe the analytical skills I have gained will make me a better physician. I am passionate about furthering my service to the community through becoming a physician and wish to receive training in the Inland Empire so that I could give back to the community that raised and educated me, making all of my achievements possible.

I would like to thank the members of Dr. Kerby Oberg's lab for welcoming me into their lab this summer and for giving me this wonderful opportunity to learn and apply new skills.

GENES TARGETED BY FGF IN THE POSTERIOR LIMB BUD: CANDIDATES FOR PATTERN COORDINATION BY SHH

Karndeep Rai-Bhatti, Billy Watson, Charmaine Pira, Kerby Oberg

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

Limb development occurs along three axes; the proximal-distal, anterior-posterior, and dorsal-ventral. Growth and differentiation along the proximal-distal axis is regulated by Fibroblast Growth Factors (FGFs) secreted from the Apical Ectodermal Ridge, an ectodermal thickening at the distal edge of the limb bud. Anterior-posterior development is mediated by Sonic Hedgehog (SHH), a protein secreted from the Zone of Polarizing activity, a cluster of mesodermal cells in the distal posterior aspect of the developing limb. These two axes coordinate development through a reciprocal feedback loop between SHH and FGF. Factors involved in the FGF to SHH arm of this feedback loop are still being elucidated. Identifying factors within this loop will provide insights into limb development, wound healing, and regeneration. Implantation of an FGF containing bead into the posterior limb can upregulate SHH after 3 hours. In tissue surrounding the bead, we identified 306 additional genes that were differentially regulated by FGF. We hypothesized that factors involved in the FGF to SHH pathway were likely present in this data set. We analyzed the data using Ingenuity Pathway Analysis (IPA), and the pattern of pathways affected was consistent with embryonic development. To further validate our data, we performed whole mount *in situ* hybridization (WMISH) on several genes with known roles in limb development. We confirmed differential regulation of *SHH*, *LHX2*, *EGR1*, *DUSP6*, *SCUBE3*, *TFAP2C*, and *SHOX*. Our results indicate that these genes are regulated by FGF; their involvement in mediating SHH expression in the developing limb bud is yet to be uncovered.

JESSICA REYES

SURF PARTICIPANT 2017

My journey to the SURF program is one unfamiliar to many and has been accompanied with various accomplishments. To begin, I went through high school with a GPA of 1.7. In order to obtain my high school diploma, which did not look likely, I made up the necessary school credit from an adult/continuation school. College was not part of my vocabulary. Due to economic hardship, I began working with my mother cleaning million dollar homes. Together, we would scrub kitchen counters, floors, and toilets. It was there, in those moments, I developed the energy and aspirations to become the first member of my family to attend and graduate from a four-year college. I went on to working a full-time job while attending a community college full-time. I now find myself in a prestigious four-year institute, UCLA, majoring in microbiology, immunology, and molecular genetics. I am on the road to an accomplishment that was once outside the scope of even a dream.

My aspirations have now grown from graduating with a Bachelor's degree to one day developing a disease-curing medicine. To fulfill my goal, I have participated in Washington University's Genomics Program annotating a fruit fly gene that has not yet been genetically mapped. I am also part of a non-profit organization which removes invasive species from a target area to reintroduce the red-legged frog. Research is the road to discovery; it allows both creative and logical thinking to be expressed. This is the path I plan to take to achieve my ultimate goal.

ROLE OF SNAIL IN OVARIAN CANCER STEM CELLS: SNAIL SILENCING REDUCES INVASIVENESS, CHEMORESISTANCE, AND STEMNESS

Jessica Reyes, Nozomi Hojo, Alyse Huisken-Hill, Sang Nguyen, Christine Castanon, Paul-Joseph Aspuria, Juli Unternaehrer

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

Ovarian cancer has a high cancer recurrence rate, contributing to the five-year survival rate of less than 40%. An important reason ovarian cancer recurs is the presence of chemoresistant cancer stem cells (CSC). For the majority of ovarian cancer patients, tumor cells are eventually chemoresistant, leading to few or no treatment options. A variety of factors contribute to the CSC state, one being a transcription factor, *SNAI1* (SNAIL). SNAIL induces epithelial-mesenchymal transition (EMT) properties in ovarian cancer cells. The objective of this work is to test whether silencing of SNAIL decreased the ovarian cancer cells' chemoresistance and invasiveness. We tested this in OVCAR8 and OVSAHO, two cell lines that accurately reflect aggressive ovarian cancer. We used RNA interference (RNAi) and the CRISPR/Cas9 system to silence Snail. The loss of SNAIL protein expression was confirmed by Western blot analysis. The loss of SNAIL functionality was assessed by invasion and chemoresistance assays. Invasiveness of ovarian cancer cell lines was evaluated by 96-well Boyden chamber assay in which cells are required to digest and migrate through a basement membrane-like matrix to cross a barrier. Boyden chamber assay showed that knockdown of SNAIL in OVCAR8 resulted in less invasiveness. Chemoresistance characteristics were quantified by MTT assay to determine percentage of cells surviving culture with Cisplatin, a commonly-used chemotherapy drug. In conclusion, silencing Snail reduced invasiveness in ovarian cancer lines tested. Furthermore, cell lines in which SNAIL was silenced by knockdown and knockout regained chemosensitivity. The data analysis validates the role SNAIL plays in the induction of EMT and cancer stemness. These results lead to possible novel strategies for treating chemoresistant recurrent, metatstatic ovarian cancer.

ERWIN STUFFLE

SURF PARTICIPANT 2017

Having lived and grown up in the Caribbean island of Barbados for the greater part of my 21 years, coming to the United States to pursue a college education is perhaps the most significant event in my life within the past decade. I am currently a senior biomedical science major at Oakwood University, a small HBCU located in Huntsville, AL. Next spring after I graduate from Oakwood, it is my intention to pursue an MD/PhD.
I'm interested in the fields of microbiology, molecular genetics, and infectious diseases. Back home in the Caribbean, these areas of science and medicine are significantly lacking, and one day I would like to return there to aid in improving the work in these fields.

This summer I had the privilege of working in the lab of Dr. Kylie Watts under the guidance of her postdoctoral fellow Dr. Emilie Orillard. Together, we investigated the interacting partners of the *Pseudomonas aeruginosa* CheY2 and CheA2, chemosensory proteins in the Che2 system of the microorganism. I thoroughly enjoyed the opportunity to work with them, and I am thankful for the experience I gained. This summer my understanding of the multifaceted nature of science and the process of research was strengthened. Though challenging at times, my mentors helped me to focus on the exciting and rewarding parts of being a scientist.

Outside of the classroom and the lab, you can most probably find me at the weight room or out riding my bike. Recently, I have taken to the art of iPhone photography, and I'm currently exploring the extent of my talent in that regard.

IDENTIFYING INTERACTING PARTNERS OF THE *PSEUDOMONAS AERUGINOSA* CHEA2 AND CHEY2 PROTEINS

Erwin Stuffle, Emilie Orillard, Kylie Watts

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

Pseudomonas aeruginosa is a ubiquitous environmental bacterium and important opportunistic pathogen. It relies on four chemosensory systems in order to sense and respond to environmental stimuli. The Che2 chemosensory system was recently determined to contribute to pathogenicity in *P. aeruginosa*; however, its exact function is unclear. Oxygen binding to the Aer2 receptor of the Che2 system modulates autophosphorylation of the CheA2 kinase that, in turn, phosphorylates CheY2, prompting an unknown cellular response. To elucidate the function of the Che2 system, we used a bacterial adenylate cyclase two-hybrid (BACTH) assay to screen genomic libraries of *P. aeruginosa* and identify potential partners of the CheA2 and CheY2 proteins. We cloned *cheA2* into pKT25 and pKNT25CheY2+ (bait vectors), and cloned a *P. aeruginosa* PAO1 genomic library into pUT18 (the prey vector). *Escherichia coli* BTH101 carrying each of the bait vectors were co-transformed with the PAO1 library. Using MacConkey agar we screened for and selected colonies that exhibited functional complementation (dark red-pink colonies, representing reconstitution of adenylate cyclase and lactose fermentation). A total of 45, 000 colonies were screened for each construct. The pKT25CheA2 screen (for CheA2 interacting partners) yielded 218 potential positive hits, while the pKNT25CheY2CheA2 screen (for CheY2 interacting partners) yielded none. Plasmid DNA from potential positives will be extracted and sequenced to identify interacting partners of the CheA2 and CheY2 proteins. Once the function of these proteins is characterized, the role of the Che2 system in *P. aeruginosa* pathogenesis can be clarified.

EVAN LANE THOMAS

SURF PARTICIPANT 2017

I am currently going into my senior year at California State University Maritime Academy where not so long ago I sailed with my class through the Panama Canal towards Europe in order to learn the systems and gain experience working on them. When I was on board, we had a small lab and a group of marine scientists. They were taking ballast water samples from a new ballast water treatment system in order to see which method was the most effective. Since that day, I always wanted to be an engineer on a research vessel and work part-time in the labs on board when sailing abroad discovering new species and tissues.

I have joined the SURF program in order to gain some experience in the labs that I will need when I am at my dream job. Currently, I am working with Dr. Erik Behringer on Western blotting. There I will be taking samples of protein from rats and mice with Alzheimer's disease. The best feeling that I have ever felt is knowing I am helping the human species by doing these studies over the summer. After all, "far and away the best prize that life has to offer is the chance to work hard at work worth doing" (Theodore Roosevelt).

I am looking forward to working in the labs of Loma Linda University, to be a part of something larger than myself, and to be able to say I helped.

EXPRESSION OF THE MITOCHONDRIAL CALCIUM UNIPORTER IN MOUSE HIPPOCAMPUS AND CORTEX WITH ADVANCING AGE

Evan Thomas, Daniel Tsai, Charles Hewitt, John Buchholz, Erik Behringer

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

The mitochondrial calcium uniporter (MCU) is an intracellular transmembrane protein that allows the passage of calcium ions from the cytosol into the mitochondrial matrix. With the aging process, neuronal signaling during exocytosis of neurotransmitters and plasticity becomes increasingly vulnerable to mitochondrial calcium overload, consequences of oxidative stress, and altered membrane potential dynamics. Thus, we are testing the hypothesis that neuronal MCU expression and function may increase with advancing age. Regions of intact cortex and hippocampus are freshly isolated from C57BL/6 mice (age: 3 to 29 months, male and female). Molecular analyses include protein measurements of the MCU via Western blot and immunofluorescence. Physiological assessments (+/- pharmacological stimulation and block of MCU) include simultaneous photometric measurements of calcium and sharp electrode determinations of intracellular membrane potential and cell-to-cell coupling through gap junctions in freshly isolated and intact tissues. These experiments are part of an ongoing study to examine the expression and function of the MCU protein in neurons and vascular cells of mouse models of aging and Alzheimer's disease (e.g., 3xTgAD). Resolving interactions between cardiovascular and neuronal function in the context of mitochondrial calcium signaling will enable our efforts to ameliorate neurodegeneration and a diminished quality of life with aging.

JONATHAN THOMAS

SURF PARTICIPANT 2017

As I see it, life is the pinnacle of ingenuity and beauty within human reality. I cannot express how privileged I feel to have been given the opportunity to examine nature's intricacies. Even the simplest organisms have complex biochemical pathways that require time and dedication to comprehend. My thirst to better understand the world around me drives my passion for research and characterizes my faith: "For the Lord gives wisdom; from his mouth come knowledge and understanding" (Proverbs 2:6).

By committing myself to studying God's creation, I hope to gain the intuition and sophistication required to operate in the clinical and translational sciences. My love for learning, impelled by my trials with chronic pain, fuels my desire to bring relief to those suffering and to improve the science behind medicine as an MD/PhD.

I expect to complete my Bachelor's in Biomedical Science this fall at Adventist University of Health Sciences (ADU) in Orlando where I received the Weniger Fellow Scholarship for outstanding scholastic achievement. At ADU, I work as an organic lab assistant and tutor, guiding students through chemistry/biochemistry and physics. Beyond my scheduled work hours, I regularly mentor those seeking additional help. Previously, I have volunteered as an elementary math tutor and at an adult daycare center assisting the aging and disabled. Currently, I help operate the OFSDA Church livestream, which gives me the opportunity to serve and to explore my love for film production. When I return to Florida, I also intend to continue my involvement with multiple research projects at ADU and Florida Hospital.

This summer I had the honor of studying acute hypoxia under Dr. Sean Wilson. I want to thank both Dr. Wilson and Monica Romero for taking the time to teach and guide me in the lab.

ACUTE HYPOXIA ALTERS RYANODINE RECEPTOR ACTIVITY IN PULMONARY ARTERIAL MYOCYTES OF HIGH ALTITUDE ACCLIMATIZED FETAL AND ADULT SHEEP

Jonathan Thomas, Timothy Yoo, Monica Romero, Jose Puglisi, Lubo Zhang, Sean Wilson

Lawrence D. Longo Center for Perinatal Biology, Advanced Imaging and Microscopy Core, School of Medicine, Loma Linda University, Loma Linda, CA; Department of Pharmacology, School of Medicine, California Northridge University, Northridge, CA

Intrauterine stress, such as long term high altitude hypoxia (LTH), can alter pulmonary function and reprogram fetal pulmonary development, potentially causing respiratory distress and pulmonary hypertension after birth. Our recent data demonstrates that newborn LTH lambs exhibit exaggerated hypoxia-induced pulmonary vasoconstriction; Ryanodine Receptor (RyR) activation is central to this process. Furthermore, LTH disrupts RyR activated Ca^{2+} sparks in pulmonary arterial (PA) myocytes of sheep. Given the relationship between RyR and PA activity, we tested the hypothesis that acute hypoxia and LTH increase RyR activity by measuring the Ca^{2+} spark activity in PA myocytes of full-term fetal lambs and adult sheep residing at either low (335m, LA) or high (3801m, HA) altitude. Ca^{2+} activity was recorded by loading isolated PA tissue with Fluo-4 using line-scan techniques on a confocal microscope. Line-scan images were analyzed using custom software (SparkLab) to determine the number of cells displaying sparks, spark frequency, and spatial- temporal characteristics. Acute hypoxia significantly decreased the prevalence of cells with sparks and spark frequency for both HA fetal and LA adult groups; however, the HA adult sheep exhibited a higher prevalence and frequency of sparks when exposed to acute hypoxia. LTH suppressed spark prevalence and frequency since LA sheep exhibited greater spark activity than the HA groups under most conditions: fetal control, fetal acute hypoxic, and adult control groups. HA adult sheep under acute hypoxic conditions, however, displayed greater RyR activity. Several significant spatial-temporal differences were also identified although it remains unclear how these factors modulate vascular activity. These results provide new insight into the influence of high altitude reprogramming of RyR function in PA of the fetus and adult.

NATALIE WOLSKE

SURF PARTICIPANT 2017

In June 2017, I graduated with a Bachelor of Science degree in bioengineering and a math minor from Walla Walla University. During my college experience, I enjoyed learning about biomaterials, molecular biology and health.

Last summer I was selected to participate in an undergraduate research project by my major professor, Dr. Janice McKenzie, of the Bioengineering Department at WWU, funded by an M. J. Murdock Charitable Trust grant. My role was to manage and facilitate student observations of various parameters and corresponding results of electrospinning nanofibers using a polyurethane polymer. My research team observed the nanofibers produced through exposure to a focusing cone, various voltages, various distances, and other parameters. Presenting our research at the Murdock College Science Research Conference in Spokane, WA, in February was another highlight for me in this undergraduate research experience.

Following this experience, Dr. McKenzie suggested contacting Loma Linda University for any research opportunities available this summer, leading to my current volunteer experience. My program so far at LLU has not been disappointing, opening my eyes to myriad options for Christian professionals working in scientific fields and the positive difference we can make for humanity. I worked with Dr. Ryan Sinclair and appreciated his willingness to include me in his research and explain concepts to improve my understanding of lab techniques. I am also grateful for the opportunity to be exposed to a variety of domains and to interact with individuals pursuing different professional goals and interests. Because of my participation in this program, I am even more convinced my interest in working with biomedical devices and bioengineering concepts can be an instrument in finding solutions to everyday health issues and ultimately improving the lives of others.

EFFECTIVENESS OF VARIOUS NANOMATERIALS IN PREVENTION OF BACTERIAL GROWTH IN PEDIATRIC MYRINGOTOMY TUBES

Natalie Wolske, Adam Bennani, Brittney Springer, Christopher Perry, Ryan Sinclair

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

Silver can act as an antibacterial in biomedical devices and applications such as lab coats and pediatric myringotomy ear tubes. Myringotomy tubes, which permit fluid drainage in the ear, are coated with silver oxide nanoparticles to prevent any bacterial growth that may lead to infection in the ear. Scanning Electron Microscope (SEM) image analysis shows that commercial myringotomy tubes have a small amount of silver. The purpose of the experiment was to test the effectiveness of a myringotomy tube's ability to inhibit bacterial growth. In comparison, alternative solutions such as bimetallic silver-gold, silver nitrate, and silver nanomaterials were also tested to see if they can potentially be used as an antibacterial. The efficacy of such nanomaterials can be tested through examination of the resulting zones of inhibition (ZOI) or circular areas of no visible bacterial growth, signifying bacterial growth inhibition. For this experiment, we cultured *Escherichia coli* ATCC #15597, *Staphylococcus aureus* ATCC #33592, and *Serratia marcescens* on Mueller-Hinton agar (MHA) using a McFarland solution standard with an optical density between 0.08-0.1. Two sets of plates were made; one set had 5 uL drops of newly-prepared nanoparticles while the other had filter paper discs infused with 5 uL of nanoparticles. After 18 hours of incubation, it was found that only silver nitrate produced a zone of inhibition. For the silver nitrate drops treatment, zones of inhibition were observed between 16.82 and 22.22 mm among the bacteria tested. For the silver nitrate infused discs, the zones of inhibition observed were between 9.07 and 17.92 mm in diameter. Our observations show that myringotomy tubes cannot effectively inhibit bacteria growth. Silver nitrate shows the potential as a nanomaterial to be used in biomedical applications like the myringotomy tube to inhibit bacterial growth.

Guest Participants

Marvin Amen
Anna Kwon
Chelsea Lee
Raechel Ospahl
Kari Roberts

MARVIN AMEN

GUEST PARTICIPANT 2017

Since immigrating to the United States in 2004 from Iraq and learning a completely new language, I began my volunteering journey at the age of ten at Loma Linda Broadcasting Network and continue to this day. During high school I began volunteering for the LLUMC East Campus. There I began to learn what science and medicine are. Since then, I have become very fascinated by how the human body's functions are so easily altered by different exposures, and at that point my inquisitive mind began to be directed towards science and medicine.

September, 2012, I began my studies at La Sierra University as a biology: biomedical sciences major. Through several science courses, my love for science, medicine, and research grew stronger, assuring me I am pursuing my correct calling. At La Sierra, I became involved in cancer cell research that studied the effects of electromagnetic waves on glioblastoma cell cultures. After three years, I presented my poster at the annual La Sierra University Research emphasis week and was awarded second place. After I was accepted to LLU School of Medicine and completed my first year of medical school, I became involved in perinatal biology research that investigates effects of high altitude hypoxia on fetal sheep pulmonary artery vasoconstriction that would lead to pulmonary hypertension. This project is currently taking place under the mentorship of Dr. Sean Wilson, assistance of Ashley Vazquez, and work of Carla Blum-Johnston. After completing medical school, I hope to obtain a surgery residency here at LLU.

I want to thank Dr. Wilson for providing me with this incredible opportunity to work and further learn about the hidden mysteries of the human body that we are all blessed with by God.

EFFECTS OF CHRONIC HYPOXIA TO BETA ADRENERGIC INDUCED VASODILATION IN FETAL AND ADULT SHEEP

Marvin Amen, Ashley Vazquez, Brandon Painter, Raveena Jalota, Quinton Blood, Lubo Zhang, Sean Wilson

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

Hypoxia, the lack of oxygenation in tissues, can be associated with high altitude living. Fetuses afflicted with such conditions are subjected to high mortality and morbidity rates. It can lead to developmental abnormalities in vasoreactivity of the pulmonary arteries that may contribute to pulmonary hypertension in fetuses and adults. While the role of beta adrenergic signaling is a major focus for treatment of asthma, far less is known about its role in pulmonary arterial function. Previous evidence illustrates that beta adrenergic signaling pathways hold promise for the treatment of pulmonary hypertension. As Ca^{2+}-activated K^+ channels (BK_{Ca}) are important to beta adrenergic-mediated pulmonary vasorelaxation, their dysfunction may contribute to chronic hypoxia-induced pulmonary hypertension. We hypothesize that beta-AR-mediated vasodilation may be reduced following chronic hypoxia due to the loss of dependency on BK_{Ca} channels. Such channels may therefore provide a powerful therapeutic advancement in the treatment pulmonary hypertension. We isolated pulmonary arteries from adult or fetal sheep that gestated at 700 meters (normoxic) or 3,801 meters for 110+ days. Then, we performed myography to measure isometric tension in pulmonary arteries and studied their vasorelaxation due to the beta-agonist Isoproterenol (ISO) and the methylxanthine phosphodiesterase inhibitor, IBMX. Our data shows that ISO-mediated relaxation was preserved following chronic hypoxia in fetal and adult sheep; however, the effect was greater in arteries from adult hypoxic groups than fetal hypoxic ones. The addition of the BK_{Ca} channel inhibitor, tetraethylammonium (TEA), reduced the effects of ISO-mediated vasorelaxation, suggesting the BK_{Ca} channel is important to vasorelaxation in hypoxic conditions. Overall, these studies provide significant evidence that beta adrenergic pathways rely on BK_{Ca} in fetal groups more than adult hypoxic groups. The BK_{Ca} channel could be therapeutically significant, and alterations in their activity may contribute to the development of disease.

ANNA KWON

GUEST PARTICIPANT 2017

During my undergraduate years at Andrews University, I had the privilege of partaking in research involved with carboxypeptidase O and its effects in colon cancer. I specifically chose that research because of the clinical aspect of cancer, and as a pre-med student, I wanted some clinical exposure before attending medical school. Through that experience, I learned about not only the mechanisms of cancer and carboxypeptidase but also priceless lessons in laboratory techniques. Ever since then, I have always been excited to participate in other research opportunities involving cancer.

Now, as a medical student here at Loma Linda University, I was given the opportunity to join Dr. Salma Khan's and Dr. Steve Lee's research in looking at oncogene overexpression in different subtypes of thyroid cancer. I worked together with a fellow peer, Chelsea Lee, in obtaining data by extracting and purifying RNA and DNA in order to prepare for further tests, such as PCR and immunohistochemistry. The research proved to be rewarding because it allowed me to not only further my laboratory skills but also to explore the multifaceted topic of cancer. We often engaged in discussions about the genetic component of cancer as well as possible risk factors and took time to also review the basic science aspect, thus, giving us more dimension and understanding about cancer and how it affects the human body.

I would like to thank Dr. Khan and Dr. Lee for the honor of allowing me to contribute to their growing research and for being enthusiastic and patient mentors during our time together.

DIFFERENTIAL SUBCELLULAR EXPRESSION PATTERNS OF ENIGMA & ITS BINDING PARTNERS IN WELL-DIFFERENTIATED CANCER TO ANAPLASTIC THYROID CANCER

Anna Kwon, Chelsea Lee, Suneetha Chintalapati, Mia Perez, Li Lei, Alfred Simental, Salvador Ramos, Kari Roberts, Iqbal Munir, Anthony Firek, Marino De Leon, Salma Khan

Division of Biochemistry, Center for Health Disparities and Molecular Medicine, Head and Neck Surgery, Pathology and Human Anatomy, Internal Medicine, School of Medicine, Loma Linda University, Loma Linda, CA

Anaplastic thyroid carcinoma (ATC) is one of the most aggressive solid tumors to affect humans. Despite multimodality approaches, ATC carries a dismal prognosis. This reality motivates us to find a novel strategy beyond conventional methods to combat this lethal disease. For that, it is essential to determine the biological continuum of the disease progression of ATC. ATC can arise *de novo* or from pre-existing well-differentiated thyroid cancer (WDTC). In our previous study, we observed in papillary thyroid cancer (PTC), Enigma colocalized with one of the bone morphogenetic protein (BMP) family, BMP-1, as a candidate binding partner for thyroid malignant calcification. In this study, we analyzed the differential expression of Enigma by immunohistochemistry in ATC, PTC, follicular thyroid cancer (FTC), and poorly differentiated thyroid cancer (PDTC) from patient-derived tissues and the subcellular distribution of Enigma in all these subtypes of thyroid cancer. Furthermore, we analyzed the binding partner of Enigma in ATC, FTC, and PTC. Our results demonstrated that Enigma is disproportionately highly expressed in ATC, and most ATC cells showed a mixed (nuclear and cytoplasmic) type of subcellular localization. In PTC, they were present mostly in the cytoplasm whereas in FTC, Enigma was localized in the nuclei only. Dual staining experiment showed that Enigma colocalized with BMP-1 in PTC. Enigma colocalized with RET and RAS protein in FTC and ATC, respectively. These data suggest the differential pattern of subcellular localization of Enigma expression may play a significant role in disease prognosis and treatment response.

CHELSEA LEE

GUEST PARTICIPANT 2017

From the moment I knew I wanted to go into the field of medicine, I also knew I wanted to be a surgeon. During my first year of medical school at Loma Linda University, my desire to work in the surgical field has grown even stronger after attending wards in the ENT and ophthalmology departments. The quality that draws me to surgery is that it is very proactive in treating illnesses for patients. Like surgery, my experiences working as a research assistant for a year at the University of Illinois in Chicago and now working in Dr. Salma Kahn's lab here at Loma Linda University have demonstrated research is also proactive in attacking illnesses we have yet to find cures or need better methods of treatment for. Even though research can be a slow and long process, I learned its importance especially for medical practice and have come to greatly appreciate those who dedicate their entire careers to research.

I would like to express gratitude towards Dr. Salma Kahn and Dr. Steve Lee for giving me the opportunity to join their research project this summer.

DIFFERENTIAL SUBCELLULAR EXPRESSION PATTERNS OF ENIGMA & ITS BINDING PARTNERS IN WELL-DIFFERENTIATED CANCER TO ANAPLASTIC THYROID CANCER

Chelsea Lee, Anna Kwon, Suneetha Chintalapati, Mia Perez, Li Lei, Alfred Simental, Salvador Ramos, Kari Roberts, Iqbal Munir, Anthony Firek, Marino De Leon, Salma Khan

Division of Biochemistry, Center for Health Disparities and Molecular Medicine, Head and Neck Surgery, Pathology and Human Anatomy, Internal Medicine, School of Medicine, Loma Linda University, Loma Linda, CA

Anaplastic thyroid carcinoma (ATC) is one of the most aggressive solid tumors to affect humans. Despite multimodality approaches, ATC carries a dismal prognosis. This reality motivates us to find a novel strategy beyond conventional methods to combat this lethal disease. For that, it is essential to determine the biological continuum of the disease progression of ATC. ATC can arise *de novo* or from pre-existing well-differentiated thyroid cancer (WDTC). In our previous study, we observed in papillary thyroid cancer (PTC), Enigma colocalized with one of the bone morphogenetic protein (BMP) family, BMP-1, as a candidate binding partner for thyroid malignant calcification. In this study, we analyzed the differential expression of Enigma by immunohistochemistry in ATC, PTC, follicular thyroid cancer (FTC), and poorly differentiated thyroid cancer (PDTC) from patient-derived tissues and the subcellular distribution of Enigma in all these subtypes of thyroid cancer. Furthermore, we analyzed the binding partner of Enigma in ATC, FTC, and PTC. Our results demonstrated that Enigma is disproportionately highly expressed in ATC, and most ATC cells showed a mixed (nuclear and cytoplasmic) type of subcellular localization. In PTC, they were present mostly in the cytoplasm whereas in FTC, Enigma was localized in the nuclei only. Dual staining experiment showed that Enigma colocalized with BMP-1 in PTC. Enigma colocalized with RET and RAS protein in FTC and ATC, respectively. These data suggest the differential pattern of subcellular localization of Enigma expression may play a significant role in disease prognosis and treatment response.

RAECHEL OPSAHL

GUEST PARTICIPANT 2017

I attended Pacific Union College in Angwin, CA, and graduated with a Bachelor of Science in Biology. I have recently finished my first year of medical school at Loma Linda University. It was once said by Albert Einstein, "Intellectual growth should commence at birth and cease only at death." In the past I had always avoided the idea of involving myself in research of any kind. I was only focused on learning material that was already known and nothing more. However, since beginning medical school, I have come to appreciate all of the opportunities and potential advancements that research has to offer. As a result, I made the choice to use my last summer as a chance to acquaint myself with the process of research and experience a short glimpse of all that it entails.

The program has expanded my horizons, helped me develop new skills, and enhanced my understanding of membrane physiology. While my second year of schooling may not allow enough time to continue actively participating in research, it will only be a pause, not an end, to my involvement. I look forward to incorporating research projects into my future aspirations as I continue on the path to becoming a physician.

I would like to sincerely thank Dr. Sean Wilson for his patient instruction and guidance over this summer. He has played an integral part in introducing me to research and the possibilities that it holds for the future.

PULMONARY ARTERIES FROM FETAL SHEEP ARE UNRESPONSIVE TO STIMULATION OF THE ENDOTHELIUM WITH A23187

Varsha Hunter, Lien Hardister, Raechel Osphal, Monica Romero, Sam Murray, Lubo Zhang, Sean Wilson

Center for Health Disparities and Molecular Medicine, Lawrence D. Longo Center for Perinatal Biology, Advanced Imaging and Microscopy Core, School of Medicine, Loma Linda University, Loma Linda, CA

The transition at birth is marked by a large increase in pulmonary vascular blood flow and vessel relaxation is an important part of this process. Previously we showed that pulmonary arteries of fetal sheep were largely unresponsive to vasodilators including acetylcholine and bradykinin. Because the arteries were unresponsive to endogenous agonists, we wanted to test the hypothesis that endothelial vasodilatory pathways are uncoupled from elevations in cytosolic Ca2+. In order to test this hypothesis, we directly increased cytosolic Ca2+ in the endothelium with the calcium ionophore A23187, which was expected to cause dilation. These experiments were performed on fetal sheep extracted from pregnant ewes raised at 700 m. From these fetuses, arteries were harvested from their lung tissue. Endothelial cells were imaged to determine the extent to which A23187 caused calcium responses. Vessel reactivity was measured using wire myography, and contractility was induced using serotonin. Relaxation of the serotonin-contracted arteries was then induced by treating with A23187 or DMSO. Our results show that A23187 caused calcium responses but did not reduce arterial tension. This finding leads us to conclude that fetal arteries calcium responses are uncoupled from vascular relaxation. Thus, our hypothesis was supported by the experiments that followed.

KARI ROBERTS
GUEST PARTICIPANT 2017

I am currently enrolled at Point Loma Nazarene University in San Diego, CA. This fall, I will return to PLNU for my fourth and final year as a student where I will complete my studies as a biochemistry major. In addition to academics, I will continue my part-time job as a teacher's assistant in the biology lab as well as volunteer at University of California San Diego's Medical Center and the San Diego Humane Society. Though I attend college in San Diego, I have grown up in Yucaipa, and that is where I call home. Whenever I am on break or home for summer, I spend my spare time volunteering at Loma Linda University Children's Hospital.

My experiences thus far have been preparing me for my future aspirations. I hope to attend Loma Linda University Medical School in the fall of 2018. I strive to be the type of physician who treats patients beyond the 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 a physician who can provide comfort to others.

It has been a great privilege to work in Dr. Salma Khan's lab and gain insight into a different side of medicine. I have shadowed many doctors in the clinic and seen what goes on during face-to-face appointments with patients. It has been another experience entirely to catch a glimpse of the research that goes into the treatments the physicians prescribe. I'd like to thank Dr. Khan and the rest of my team for helping me learn, grow, and challenge myself this summer.

LINKING HIGH BODY MASS INDEX AND LEPTIN RECEPTOR TO THYROID CANCER HEALTH DISPARITIES

Kari Roberts, Salvador Ramos, Mia Perez, Iqbal Munir, Alfred Simental, Marino De Leon, Salma Khan

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

With regard to global health disparities, Filipino Americans (FP) are at highest risk for the development of thyroid cancer (TC). Our previous study provides evidence that loss of vitamin D binding protein (VDBP) is more frequent in Filipino American (FP) patients with TC than in their European American (EA) counterparts. Thyroid cancer (TC) has been linked to obesity, and obesity has been linked to vitamin D deficiency and high leptin. Vitamin D suppresses Leptin; low vitamin D has been shown to be associated with loss of VDBP, suggesting the possibility of interplay between obesity-linked high leptin and low VDBP-related low vitamin D (VD3) in the development of TC and health disparities in the Filipino population. Obesity increases leptin, a hormone producing visceral adipose tissue associated with cancer. Direct effects of obesity on leptin levels are compounded by the loss of VD3 because VD3 normally aids in suppressing leptin expression. Our preliminary data is the first to suggest a genetic link between obesity, VD3, leptin, and thyroid cancer carcinogenesis in the Filipino population. In this study, we have analyzed the following in both ethnicities: staging of thyroid cancer from our patient demographic data, body mass index (BMI), and leptin receptor expression by immunohistochemistry. Our data provides evidence that FPs present with higher staging than EAs. Expression of the leptin receptor protein is upregulated in thyroid cancers from FPs vs. EAs. Taken together, these data implicate the obesity-leptin pathway as a potential contributing mechanism which produces aggressive thyroid cancer leading to cancer health disparities. These studies suggest that increased leptin signaling contributes to thyroid cancer onco-genesis/progression in thyroid cancer health disparities in Filipinos.

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