LOMA LINDA UNIVERSITY

School of Medicine

Center for Health Disparities and Molecular Medicine

22nd Annual Health Disparities Research Symposium

Education – Development – Health Disparities Research – Community

PROGRAM, BIOS, AND ABSTRACTS

Wednesday, August 2, 2023
2:00 pm – 7:00 pm
Centennial Complex, 4th Floor
Loma Linda University School of Medicine
Loma Linda, California

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

22nd Annual Health Disparities Research Symposium

Wednesday, August 2, 2023
2:00 pm - 7:00 pm, Centennial Complex, 4th Floor Conference Room

Agenda

Poster Session

2:00 pm – 4:45 pm — **Poster Presentations by Research Fellows**

LLU-NIH Initiative for Maximizing Student Development Program (IMSD)
Apprenticeship Bridge to College Program (ABC)
Undergraduate Training Program (UTP)
Medical Training Program (MTP)
Summer Undergraduate Research Fellowship (SURF)
Hispanic Center of Excellence Program (HCEP)
Research Fellows from Other LLU Entities

4:45 pm – 5:00 pm — **Refreshments**

Evening Program

5:00 pm – 7:00 pm

Welcome — **Marino De León, PhD**, Director, CHDMM

Invocation — **Eileen J. Brantley, PhD**, Associate Professor, Basic Sciences

Remarks — **Richard Hart, MD, DrPH**, President, Loma Linda University Health

Remarks — **Tamara L. Thomas, MD**, Dean, School of Medicine

Plenary Panel

Marino De León, PhD - Chair
Director, CHDMM

Jenniffer Licero Campbell, PhD
Assistant Professor, Western University of Health Sciences

Carlos M. Casiano, MD
Assistant Professor, Loma Linda University Faculty Medical Group

Frankis G. Almaguel, MD/PhD
Assistant Professor, Department of Radiology and Basic Sciences

Dequina Nicholas, PhD
Assistant Professor, University of California Irvine

Acknowledgement of Research Fellows

Carlos A. Casiano, PhD
Associate Director, CHDMM

Daisy D. De León, PhD
Professor of Physiology & Director of Medical Training Program

Kylie Watts, PhD,
Associate Professor of Microbiology

Willie Davis, PhD
Associate Dean, LLUSP Student Services and Enrollment

Final Remarks and Acknowledgements

Marino De Leon, PhD
Director, CHDMM

ACKNOWLEDGEMENTS

We would like to acknowledge the contributions of all who were instrumental in making this 2023 Health Disparities Summer Research successful. Teamwork, cooperation, and flexibility are just a few of the skills necessary to successfully implement such a dynamic research program. We also would like to acknowledge the support of the Loma Linda University School of Medicine, the National Institute of General Medical Sciences, NIH (grant 5R25GM060507-22).

2023 Faculty Research Mentors

Frankis G. Almaguel, MD, PhD
Eric Behringer, PhD
Arlin Blood, PhD
Danilo Boskovic, PhD
Eileen Brantley, PhD
Huynh Cao, PhD
Carlos A. Casiano, PhD
Daisy De León, PhD
Marino De León, PhD
Johnny Figueroa, PhD
Mary Kearns-Jonker, PhD
Salma Khan, MD, PhD
William Langridge, PhD
Fayth Miles, PhD
Subburaman Mohan, PhD
William Pearce, PhD
Ryan Sinclair, PhD
Salvador Soriano, PhD
Konrad Talbot, PhD
Julia Unternaehrer-Hamm, PhD
Chi T. Viet, DDS, MD, PhD, FACS
Christopher Wilson, PhD
Sean Wilson, PhD

CHDMM Administrative Staff

Lorena Salto, MPH CHDMM Manager
Flor Sida-Merlos, BS, CHDMM Program Manager
Nannette Nevares, BA, CHDMM General Operations

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.

2023 Student Research Fellow

ABC – Apprenticeship Bridge to College
Frankis Daniel Almaguel
Kelechi Grace Amobi
Benjamin Wolfgang Bello-Soto
Gabrielle Nicole Campbell
Alejandro Cervantes
Isabella Rose Chandroo
Samuel Felix
Juliette Amao Gaytan
Katherine Aimee Granados
Nyana Paige Iniguez
Katie Minh Lam
Solomon Xavier Moore
Valerie Moreno
Joel Mathew Philip
Giara Elle Wright Barcelo

UTP – Undergraduate Training Program
Santiago Emmanuel De La Cruz
Fletcher Alexander Dementyev
Clarissa Dean Do
Isabel Naomi Genovez
Matthew Minh-Tien Le
Diana Carolina Alexa Lozano
Janett Martin
Angel Gabriel Orellana Campana
Abigail Viviana Ramirez
Kristen Laura Whitley

MTP – Medical Training Program
Mina Ramsis Botros
Shahajahan Johir Chowdhury
Aayama Irfan
Paola Fernanda Rivera Morales

Other Participants
Xuelin Gu
Yeonkyu Jung
Collin Robins
Skyler A. Schiff
Arianna Marie Williams

IMSD – PhD Graduate Fellows
Shawnee Angeloni
Natasha Le
Danielle Malivert
Pedro T. Ochoa
Evelyn Sanchez-Hernandez, PhD
Kayla Sanchez
Krystal Santiago
Timothy Simon
Julio Sierra
Francis Zamora

SURF – Summer Undergraduate Research Fellowship
Sharon Asariah
Adya Cherukuri
Elva Garcia
William Geyman
Rowan Glover
Elijah Haynal
Oscar Mena
Stefany Parao
Grace Santrach

HCEP – Hispanic Center of Excellence Program
Diego Aguilar
Ariadna Cervantes
Rita Elhamra
Timothy Streck
Gabriel Viteri

Institutional Affiliations of Student Research Fellows

High Schools

Aquinas High School
Beaumont High School
Bloomington High School
Centennial High School
Citrus Valley High School
Etiwanda High School
Loma Linda Academy
Middle College High School
Patriot High School
Rancho Cucamonga HS
Redlands Adventist Academy
Redlands High School
Riverside STEM Academy

Universities

Andrews University
California State University, San Bernardino
Columbia University
La Sierra University
Loma Linda University School of Medicine
Oakwood University
San Juan Bautista School of Medicine
Southern Adventist University
Universidad Central del Caribe
University of California, Riverside
University of California, San Diego
Victor Valley College
Walla Walla University

LOMA LINDA UNIVERSITY

School of Medicine

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LOMA LINDA UNIVERSITY SCHOOL OF MEDICINE

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

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Plenary Panel

JENNIFFER LICERO CAMPBELL, PHD

PLENARY PANEL 2023

Jenniffer Licero Campbell is the department chair of the Master of Science in Medical Sciences Program (MSMS) and an assistant professor of Anatomy, Physiology, and Biomedical Research at Western University of Health Sciences. She earned her BA in Biochemistry from Baylor University and then transitioned to California where she earned her PhD in Human Anatomy from Loma Linda University. Jenniffer is passionate about minority and URiM education and has taken strong initiatives to increase diversity in healthcare through her program. She strongly believes that representation in healthcare is a pivotal factor in promoting favorable patient outcomes and strives daily to inspire and educate students in aspects of health and health disparities that should be addressed when caring for diverse populations. In addition to her work as an educator, Jenniffer also leads a team of very prolific researchers and is herself a biomedical scientist. Her and her team have been awarded multiple grants and the scope of their research includes innovative discoveries in the fields of microbiology, neuroscience, neuroimmunology and medicine. When she is not leading a team or educating students, Dr. Licero Campbell can be found figuring out how to bring people together (she will be doing this by either singing or cooking). She is usually making sure everyone is having a good time and eating well too. She deeply enjoys hiking and spending time with family and, especially, playing Super Mario 3D World with her six-year-old nephew.

CARLOS M. CASIANO, MD

PLENARY PANEL 2023

Carlos M. Casiano is a California native who has spent most of his life in Southern California. After completing high school in Redlands, CA, he attended La Sierra University in Riverside, CA, where he majored in Biology with an emphasis in Biomedical Sciences. As a high school and undergraduate student, he participated in the ABC and UTP programs at the Loma Linda University School of Medicine's Center for Health Disparities and Molecular Medicine, working with Drs. Daisy De Leon and Kimberly Payne. He attended Loma Linda University School of Medicine and graduated with an MD in 2017. While at Loma Linda University, he took an additional year to obtain an MA in Clinical and Theoretical Bioethics from the School of Religion. Following medical school, he completed a residency in Anatomic and Clinical Pathology at the David Geffen School of Medicine at the University of California, Los Angeles, where he was a chief resident during his fourth year. He then completed a fellowship in Hematopathology based in the Moores Cancer Center at the University of California, San Diego, followed by a fellowship in Pediatric Pathology at Cincinnati Children's Hospital Medical Center. He recently moved back to the Inland Empire, where he will have appointments as an Assistant Professor in the Loma Linda University Faculty Medical Group, Department of Pathology, and as a staff pathologist at the Jerry L. Pettis Memorial Veterans' Hospital.

FRANKIS G. ALMAGUEL, MD/PHD
PLENARY PANEL 2023

Frankis Almaguel is a Nuclear Oncologist with particular interest and expertise in prostate cancer, molecular imaging, and molecular targeted radiopharmaceutical therapy. He graduated from the prestigious NIH-funded Medical Science Training Program, obtaining his MD PhD from Loma Linda University School of Medicine. He subsequently obtained advanced expertise in Radiology, Nuclear Oncology, and Theranostics. Caring for and improving patients' lives is his passion. "My patients become family." He believes translational research will continue to improve patient care. Frankis' contributions to science and medicine are significant. As an active member of various medical societies, he is recognized nationally and internationally in molecular imaging and therapeutics. He chairs the Prostate Cancer Outreach of the Society of Nuclear Medicine and Molecular Imaging and serves on its Board of Directors for Targeted Radionuclide Therapy. Dr. Almaguel serves as the principal investigator in multiple transformational Theranostics clinical trials. As director of the Molecular Imaging and Therapeutics Program at the Loma Linda University Cancer Center, he leads a translational research and precision oncology program. He is committed to providing the best available care to cancer patients by incorporating cutting-edge technology and next-generation therapies in his clinical practice.

DEQUINA NICHOLAS, PHD
PLENARY PANEL 2023

Dequina Nicholas is an Assistant Professor at the University of California Irvine in the Department of Molecular Biology and Biochemistry where her lab studies the intersection of the nutrient environment, the immune system, and metabolic disease using a combination of molecular and cellular biology, transgenic mouse models, cytokine profiling, and flow cytometry. Dr. Nicholas's work focuses on how the immune system and cellular metabolism impacts endocrine diseases, particularly type 2 diabetes and polycystic ovary syndrome. Dr. Nicholas received her PhD. in biochemistry from Loma Linda University and pursued postdoctoral training in the laboratory of Dr. Barbara Nikolajczyk at Boston University, studying the metabolism of immune cells from patients with type 2 diabetes. She also trained in the laboratories of Drs. Mark Lawson and Pamela Mellon at the University of California San Diego, where she established the importance of glucose metabolism in reproduction and discovered a population of immune cells in the pituitary that regulate the reproductive axis. Dr. Nicholas's NIH Director's New Innovator Award from the NIAID funds her "immunoendocrine" lab where her mission is to train the next generation of diverse scientists. She has a passion for first-generation scientists and founded 1stGenInSTEM to curate a resource that demystifies the "Hidden Curriculum" for students who are first in their families to pursue STEM higher education. Dr. Nicholas advocates for bringing your authentic and whole self to science through sharing the ups and downs of being a new PI, a mom, and minority scholar on TikTok (@NicholasLab) and Twitter (@QuinaScience).

Apprenticeship Bridge to College (ABC) High School Program

FRANKIS DANIEL ALMAGUEL
ABC PARTICIPANT 2023

Science has always been a major part of my life, wherever I go I feel called to participate and immerse myself in its endless possibilities. I've always known that I want to commit my life to helping others and the ABC program has helped me realize that science is the path I wat to take to do that. Being a student researcher for the past two summers allowed me to learn from the brilliant minds of my mentors and helped me start developing the skills I need to succeed in a career in the sciences as well as helped me develop a harder work ethic.

As I enter my final year of high school at Redlands Adventist Academy, I am eager to take on the role of leading our campus ministries team, and hope to make a positive impact within my school community. Looking ahead, my goal is to pursue a degree in neuroscience following graduation, allowing me to delve deeper into the complexities of the brain and advance my scientific journey. In my free time, I enjoy playing guitar and reading.

This summer I have had the great privilege of working in Dr. Marino De León's lab, where I have been researching the mechanisms of DHA neuroprotection in Schwann cells in hopes of finding adequate treatment for neuropathic pain. I want to thank my mentors Dr. Marino De León, Francis Zamora, and Dr. Jo-wen Liu for guiding me on this incredible journey.

LIPOTOXICITY INVOLVES REGULATION OF AUTOPHAGY IN IMMORTALIZED SCHWANN CELLS

Frankis D. Almaguel, Francis Zamora, Jo-Wen Liu, Marino De Leon
Center for Health Disparities and Molecular Medicine and Department of Basic Sciences, Loma Linda University School of Medicine, Loma Linda, CA

Palmitic acid-induced lipotoxicity (PA-LTx) is implicated in painful peripheral neuropathy due to its detrimental effects on nerve cells. Our lab's previous studies have shown PA-LTx in Schwann cells involves activation of ER stress, mitochondrial depolarization, and apoptosis. Co-treatment of immortalized Schwann cells (iSCs) with docosahexaenoic acid (DHA) reverses PA-LTx effects. Because autophagy dysregulation is observed in neuropathic pain, this study aims to investigate the role of autophagy during PA-LTx in iSCs. Here, iSCs were treated with 300μM PA: 150μM BSA for 24 or 48 hours to induce LTx. iSCs were also co-treated with 50μM DHA to inhibit LTx, Chloroquine (CQ) to inhibit autophagic flux, or Rapamycin to induce autophagy. Western Blot measured levels of autophagy-related proteins LC3-II and p62/SQSTM1, and stress-response fatty-acid binding protein 5 (FABP5). Real-time qPCR measured expression of autophagy-related gene 12 (ATG 12) and FABP5, and a WST-1 assay evaluated cell viability. We confirmed PA decreased cell viability, while DHA co-treatment fully protected against PA-LTx-induced apoptosis. CQ did not affect cell viability, however, PA+CQ exacerbated PA-LTx effects. Interestingly, CQ, which inhibits autophagosome-lysosomal fusion, slightly reduced DHA's neuroprotection at 24 hours and significantly reduced it by 48 hours, suggesting the importance of autophagic clearance. PA increased LC3-II and ATG 12 expression, indicating autophagy activation. However, PA also dramatically increased p62 levels, suggesting inhibition of autophagosomal content degradation. Conversely, DHA reduced PA-induced elevation of p62 and LC3-II levels. As our positive control, Rapamycin decreased p62 levels. Lastly, PA and CQ increased FABP5 levels, which were suppressed by DHA. These findings suggest PA-LTx causes abnormal autophagic activity. We propose DHA inhibits PA-LTx in part by restoring healthy autophagic flux, which is consistent with DHA's neuroprotective action.

KELECHI GRACE AMOBI

ABC PARTICIPANT 2023

From a young age, I was nicknamed Florence Nightingale (after the British pioneer in statistics and nursing) and "the family doctor" because I showed a keen interest in helping my family when someone needed any form of medical assistance. At the age of nine, I began researching different medical issues and devices and hypothesizing different ways I can cure the disease/condition with an established medical device or one I (realistically) made up. Nevertheless, over the years, my love and passion for medicine, research, and helping others only grew with age and inevitably led me to Loma Linda's ABC Program and Doctor Brantley's lab, which played a pivotal role in my academic and medical career.

I am an incoming senior at Citrus Valley High School in Redlands, California. For the past three years I've been at Citrus, I founded the Multicultural Dance Club, became the secretary of the Black Student Union, treasurer of the Environmental Club, student elected School Site Council board member, was the captain of the Varsity and JV Girls Basketball team, and section leader in the advanced girls choir. Outside of school, I volunteer at the San Bernardino Community Hospital and I'm the secretary and student commissioner for the City of Redlands' Human Relations Commission. My future goals are to attend a University of California and become an Obstetrician/Gynecologist while conducting cancer research.

I sincerely thank Dr. Brantley for mentoring me and molding me into an exceptional future physician/scientist.

TRANILAST AND PRANLUKAST CONFER ANTICANCER ACTIVITY AND SUPPRESS SPHERE FORMING ACTIVITY IN ESTROGEN RECEPTOR POSITIVE MCF-7 BREAST CANCER CELLS

Kelechi Amobi, Eileen Brantley
Center of Health Disparities and Molecular Medicine, Department of Basic Sciences
Cancer, Developmental and Regenerative Biology Program
School of Medicine, Loma Linda University, Loma Linda, CA

Estrogen receptor positive (ER+) breast cancer is a subtype of breast cancer that receives signals from estrogen instructing the cells to grow. As a result, patients with this form of breast cancer receive hormone therapy. However, up to 40% of patients with this subtype of breast cancer will develop resistance to hormone therapy. Therefore, alternative therapies are needed. One key culprit in the development of resistance to hormone therapy is the presence of breast cancer stem cells. Though previous studies show that tranilast and pranlukast demonstrate promising activity against ER- breast cancer cells and their corresponding stem cells, less is known about their anticancer and anti-stemness actions in ER+ breast cancer cells. Using the Alamar Blue and Wound-healing assays respectively, we found that these agents reduce MCF-7 ER+ breast cancer cell viability and inhibit MCF-7 breast cancer cell migration. Using the mammosphere forming assay, we found that both agents and particularly pranlukast decrease MCF-7 mammosphere formation. Our data suggest that both tranilast and pranlukast demonstrate promising anti-cancer actions against ER+ breast cancer cells to warrant further studies to evaluate them as potential agents to treat this breast cancer subtype.

BENJAMIN WOLFGANG BELLO-SOTO
ABC PARTICIPANT 2023

There is more to scientific research than working in wet labs. Starting my summer in 2023 with Loma Linda's ABC program was the best thing I could do as it tested my commitment to the world of research. This program forced me to learn foreign concepts that I otherwise wouldn't know until college; to which I am eternally grateful. Working with statistics made me understand how vital collecting data is when working with surrounding communities.

Entering my senior year at Riverside STEM Academy, I plan on double majoring in Biochemistry and Cognitive Science and minoring in Creative Literature or Comparative Literature. Fueled by my interest in the human brain and human interactions, I plan on applying to Loma Linda University School of Medicine in order to continue my journey to become a neurosurgeon. I have participated in the Mikva Challenge and their first National Youth Summit, joined Riverside Youth Council, and interned here at Loma Linda through the ABC Program. The research I joined observed how cycling affects adolescent psychosocial well-being. Partnering with the Outride organization, our project—Riding For Focus—allows children throughout the nation to ride bikes as we collected data, aiming to prove a positive relationship between riding bicycles and mental health.

A special thank you to Dr. Sean Wilson and his team for taking me in and I hope to join again next year.

EVALUATING THE INFLUENCE OF A MIDDLE SCHOOL CYCLING PROGRAM ON ADOLESCENT MENTAL HEALTH AND WELL-BEING: EXPLORING MODIFIABLE RISK FACTORS

Benjamin W Bello-Soto, Fletcher Dementyev, Starla Murillo, Kai Madison, Esther Walker, Sean M Wilson
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After the COVID-19 pandemic, a notable increase in psychosocial disorders such as ADHD, depression, and anxiety has been observed in adolescent children. This study examines the potential of Outride's middle school exercise intervention program to improve adolescent psychosocial well-being. The R4F program is a 6-8 week cycling education program with at least an hour of bike riding every week. We analyzed anonymous survey data from 3924 youth participants before the R4F program and 3289 adolescent participants after the R4F program. Surveys contained two psychosocial well-being metrics: the Pediatric Symptoms Checklist (PSC-17-Y) and the World Health Organization Well-Being Index (WHO-5), which includes five non-invasive questions to measure depression. This study focused on examining two modifiable risk factors: student sleep habits and screen time. We utilized non-parametric test statistics to compare responses before and after the program. We found that 43% of students failed to meet the daily recommendation of 8 hours of sleep each night and 65% used their devices longer than 2 hours each day. Regression analysis revealed that adolescent mental health was correlated to the hours of both sleep and screen time; less screen time and longer sleep showed better well-being results. The results of these analyses contribute to our understanding of how cycling and the R4F program can positively influence adolescent psychosocial well-being as it relates to the use of electronic devices and sleep patterns.

GABRIELLE NICOLE CAMPBELL

ABC PARTICIPANT 2023

I am truly grateful for the opportunity to have participated in the ABC program. As a rising senior at Rancho Cucamonga High School, my passion for Biology drives me towards earning a bachelor's degree in Biology at UCLA and making a meaningful impact in the healthcare field. In the ABC program, I am actively involved in two research labs. Guided by Dr. Ryu and Dr. Chie Viet, the Gabapentin Lab focuses on evaluating trends in opioid prescription among oral and maxillofacial surgeons, with the aim of reducing opioid use and identifying potential barriers. Furthermore, under the guidance of Dr. Chi Viet, I collaborate with Dr. Zhang, Dr. Hanks, and Dr. Dong to collect crucial data on pain levels in patients with oral cancer. Participating in the ABC program has been an instrumental experience in shaping my career aspirations. Through invaluable mentorship and collaboration with esteemed colleagues, I have gained profound insights into healthcare research and developed essential skills. Beyond research, I actively engage in community service to make a positive impact. These experiences have further honed my leadership and interpersonal abilities. The ABC program has provided a strong foundation for pursuing my dreams. I express my heartfelt gratitude to Dr. Casiano and Dr. De Leon for creating this program and to my mentors for their tremendous impact.

PROSPECTIVE STUDY ON THE PSYCHOSOCIAL FACTORS OF CANCER OUTCOMES

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Psychosocial stress and prior life stressors are known to contribute to outcomes of chronic illnesses, however its effect on cancer outcomes and in worsening cancer symptoms (*i.e.*, pain, opioid tolerance, anxiety, depression,) is unknown. In this prospective multi-institutional study focused on oral squamous cell carcinoma (OSCC) as this diagnosis carries significant symptom burden; we enrolled 114 OSCC patients to determine prior and current psychosocial stressors (using the Adverse Childhood Experience – ACE and Life Events Checklist – LEC-5) and characterize levels of cancer pain, opioid use, depression, and anxiety (using the UCSF Oral Pain Questionnaire – UCSF OPQ, modified Brief Pain Inventory – BPI, and EORTC-QLQ30 HN35). Data were analyzed by a biostatistician using analysis of Variance (ANOVA) and post hoc analysis. Our cohort consisted of 67 males, 47 females, 79 White, 11 Asian, 10 Black, and 14 White-Hispanic. The mean age of the cohort was 64. We showed that OSCC patients who had significant pain (quantified by UCSF OPQ) produced physical and psychological interferences (quantified by modified BPI; $p<0.05$). Interestingly, OSCC patients with financial difficulties had worse clinical pain (UCSF OPQ), independent of their stage at diagnosis ($p=0.0003$). Furthermore, physical interferences were more significant in ethnic minorities compared to White patients. Patients with worse pain also had disturbances in all 5 functioning categories (EORTC-QLQ 30) physical, role, cognitive, social, and global health status ($p<0.05$). When looking at childhood stressors, patients with high ACE scores had worse cancer symptoms in both BPI and EORTC-QLC, showing worse physical and psychological function, and global health status. Lastly, patients with a high LEC-5 score had higher mortality independent of cancer stage ($p<0.05$). Our results demonstrate the significance of prior life stressors in contributing to cancer symptom burden and cancer outcomes.

ALEJANDRO CERVANTES

ABC PARTICIPANT 2023

Throughout my entire life I had always had a greater love for Biological sciences. As I learned more and my understanding of how the body works increased, I knew I wanted to pursue a job in the medical field. I had never done any internship or training regarding this field so when I heard about the ABC program, I knew I had to apply. This program taught me creative problem solving, time management, the growing language of science, and it showed me different routes that I can pursue for my future.

I am currently a rising senior and attend Bloomington High School with plans to major in Clinical Lab Science with a minor in Finance, Real Estate and Law and then obtain my MD. in hopes of becoming a surgeon. This Fall, I will return to BHS and focus on achieving my dreams, of becoming a surgeon and advancing surgical techniques and practices and eventually opening my own practice that will offer lifesaving operations that are accessible to people from all backgrounds. I would love to thank Dr. Arlin Blood for welcoming me into his lab, alongside Karina and Will who taught me with great patience and gave me great learning opportunities where I could learn hands on. It is through the ABC program that not only have I been able to network with people that are changing the world, but also learn something new every day that I can apply in my journey of changing the world.

EFFECT OF THE VAGUS NERVE ON PULMONARY ARTERIAL WALL THICKNESS AND ALVEOLARIZATION IN FETAL SHEEP

Alejandro Cervantes, William Geyman, Karina Mayagoitia, Chris G. Wilson, Arlin B. Blood
Center for Health Disparities and Molecular Medicine, Lawrence D. Longo Center for Perinatal Biology, School of Medicine, Loma Linda University, Loma Linda CA

Interoceptive nerves have sensory receptors that detect and relay information between the organs and the central nervous system (CNS). The developing fetal lung is richly innervated from the first trimester onward. However, what role these nerves play in orchestrating lung or brain development has not yet been determined. The vagus nerve constitutes a key parasympathetic interoceptive link between the lungs and the CNS. In order to determine how the vagus nerve affects lung development, sham and bilateral vagotomy surgeries were performed in preterm fetal lambs at canalicular and saccular stages of lung development. Fetal sheep were then returned to the uterus and allowed to complete gestation. The lambs were then delivered via c-section, anesthetized, and mechanically ventilated, and subjected to a series of respiratory challenges. Fetal sheep were then sacrificed, and lung tissue samples were collected. The tissue was then sectioned, stained with H&E, imaged, and analyzed for morphological differences. Preliminary quantitative analysis based on histological data suggest that the vagotomized group expresses an increased arterial wall thickness compared to sham controls. Additionally, alveolarization was assessed via mean linear intercept and preliminary results suggest there is no significant difference between groups. In conclusion, preliminary results suggest that the vagus nerve may help facilitate proper pulmonary arterial wall development in fetal sheep.

ISABELLA ROSE CHANDROO

ABC PARTICIPANT 2023

I am very thankful for this great opportunity to grow my love in science and learn more about the life of a scientist. Experiencing the life of a researcher showed me the dedication, patience and knowledge that is required inside and outside the lab. I had the pleasure of spending my summer in a perinatal research lab with three other brilliant and hardworking scientists who taught me a great deal of the meticulous work that goes into gathering data that will ultimately create change in our world. As an upcoming senior attending Patriot High School in Jurupa Valley I plan to continue to study hard and take what I learned from this program to the rest of my academic and social endeavors. My future plans include attending UC Berkeley, majoring in biology, and conquering medical school. From then on, I will dedicate my life to help make whole the intricate and fragile part of what it means to be human. This experience grew my excitement for being a Latina woman in science. Thank you to Dr. Pearce's lab for providing me the room to grow as a student and scientist.

HYPOXIC MODULATION OF FETAL CEREBROVASCULAR FUNCTION IS MEDIATED BY CHANGES MITOCHONDRIAL NUMBER, SIZE, DISTRIBUTION, AND RESPIRATORY CAPACITY

Isabella Chandroo, Danielle Lonie Malivert, Desirelys Carreon, James William, William Pearce
Center for Health Disparities and Molecular Medicine, Perinatal Biology, School of Medicine, Loma Linda University, Loma Linda, CA

Fetal hypoxia causes major changes in fetal vascular development and functional maturation that precipitate numerous secondary complications, particularly in the cerebral circulation. Although the causes of fetal hypoxia have been widely studied, the mechanisms that govern fetal cerebrovascular responses to chronic intrauterine hypoxia remain poorly understood. This study tests the hypothesis that hypoxia modulates fetal cerebrovascular structure and function through primary changes in the mitochondria of fetal cerebral arteries. We determined the number of mitochondria per cell by measuring the copy number ratio of mtDNA to nuclear DNA using qPCR. We estimated mitochondrial mass by dividing the cellular mass of Succinate Dehydrogenase, as determined by immunoblot, by the number of mitochondria per cell. Oxygen consumption rate was measured using a seahorse analyzer to determine the respiratory capacity per unit weight. By colocalizing SDHA with smooth muscle myosin heavy chain, mitochondrial distribution was examined to find the fraction of mitochondria at the contractile apparatus. We found that in fresh tissue, there was an initial 6% decrease in oxygen consumption rate implying that hypoxia initially decreases the respiratory capacity per unit mass. We also found that hypoxia decreases mitochondrial copy number by 9% while increasing mitochondrial weight by 50%. The respiratory capacity per cell was calculated from the product of number, mass, and OCR. Hypoxia increased colocalization of SDHa with SM-MHC by 18%, suggesting hypoxic promotion of mitochondrial translocation to the contractile apparatus. Under hypoxic conditions, mitochondrial translocation could improve ATP utilization efficiency, particularly in the context of vasoconstriction. These results support our hypothesis that through primary changes in the mitochondria of fetal cerebral arteries, hypoxia modulates fetal cerebrovascular structure and function.

SAMUEL FELIX

ABC PARTICIPANT 2023

As a kid, everyone asked me what I wanted to be when I grew up; I was unsure what I wanted to be for many years. I was always told I should be something in the medical field because of how much I talked and how I dressed. I knew I wanted to assist others and give them the kindness and respect I was never given but also help take away the pain they have. I looked into becoming a nurse practitioner; becoming one takes work. It takes many years of education and experience through different complex, competitive schooling, but it is possible, and it all starts in high school.

I volunteer at multiple locations like hospitals, assisting kids and distributing food. I also take college classes through my Middle College High School becoming a junior next year, as it is a dual enrollment school with San Bernardino Valley College allowing me to exit with my IGETC and associate's degree in Biology. I'm also in a high school program, Apprenticeship Bridge to College (ABC). The step inside this program and this school will enable me to know myself to the staff and admissions, so I already have something that stands out to other applicants when I apply while also growing my knowledge. I am currently under the fellowship of Dr. Sinclair in environmental microbiology, looking into wastewater. It is tricky and confusing at times, although he is always there for assistance with the help of another student Stefany Alejandra.

INVESTIGATING CUSTOM PASSIVE SAMPLERS FOR WASTEWATER-BASED EPIDEMIOLOGY

Samuel Felix, Michael Pecolar, Ryan Sinclair
Center for Health Disparities and Molecular Science, School of Public Health,
Loma Linda University, Loma Linda, CA

The primary objective of our study is to conduct an intermediate-scale field study to evaluate a passive sampling technique that can be used to sample viruses in sewer systems. It should be user-friendly due to the passive sampler that San Bernardino County uses and can be difficult to program and use. We expect to create a device small and effective that can be put into a manhole without closing off a whole street or even more. We are evaluating three candidate materials for virus absorption properties, ease of use, and virus recovery. We hypothesize that a passive sampler placed in a sewer system can obtain results that can be comparable to the expensive autosampler. We also hypothesize that a passive sampler can be placed in a sewer system, but must be removed after a certain amount of time at a specific flow rate because the passive sampler becomes saturated and then rinsed if left in the pipe for an extended amount of time. The methods use a laboratory-constructed recirculating pipe reactor, pumping sterilized sewage, and a sampling port to place passive samplers. We are using the Bovine Respiratory Syncytial Virus (BRSV), a live surrogate virus that is comparable to SARS-CoV-2, but not pathogenic to humans and can be safely used. We are also using an experimental elution method that will effectively remove the viruses from the sampler material. We are evaluating tampons (proctor Gamble ….), approximately 10cm2 of folded cheesecloth (Fisher Scientific, ….) in an enclosure, and grabbing samples. To achieve this, we are utilizing a uniform concentration of Bovine Respiratory Syncytial Virus (BRSV) in a laboratory-controlled sewage system. In the hope of finding a user-friendly and cost-effective passive sampler that can still bring accurate results.

JULIETTE AMAO GAYTAN
ABC PARTICIPANT 2023

In San Bernardino, the absence of access to healthcare and economic and educational resources are a perceptible discrepancy to the success of minority civilians. Scientist Marie Curie once said, "Nothing in life is to be feared, it is only to be understood." With a passion for knowledge and empowering minorities through educational and healthcare resources, I am entering my senior year in my small, private Aquinas High School with over 300 service hours dedicated to my school's Associated Student Body as now Executive Vice President, shadowing nurses and physicians at Arrowhead Regional Medical Center and Western University of Health Sciences. My goal is to persist with being in the top 1% of my class, with awards such as ALA Girls State and the President's Award of Educational Excellence. Having witnessed health disparities and lack of educational resources in my community, I am forever grateful that the ABC program gave me the opportunity to work in an influential and uplifting perinatal biology lab researching Hypoxic-Ischemic Encephalopathy. I would like to especially thank my mentors: Dr. Christopher G. Wilson, Tyler Hillman, and Nick Iwakoshi.

POSTNATAL DEVELOPMENT THROUGH LPS/HYPOXIA MODEL IN RESPONSE TO PRETERM HYPOXIC-ISCHEMIC ENCEPHALOPATHY (pHIE)

Juliette A. Gaytan, Braeden Jackobson, Tyler C. Hillman, Christopher G. Wilson
Center for Health Disparities and Molecular Medicine, Perinatal Biology, School of Medicine, Loma Linda University, Loma Linda, CA

HIE is a condition emanating from reduced quantities of oxygen transmitted to the neonatal brain. In preterm hypoxic-ischemic encephalopathy (pHIE), 60% of infants develop a range of severe and permanent neurological disabilities including epilepsy, cerebral palsy, or death by 2 years old. Current murine models of pHIE replicate the immediate consequences of neonatal insult, but disregard maternal factors as initiators of or contributors to pHIE. Our laboratory has developed a novel model of pHIE that includes maternal inflammation and other endogenous factors. We use lipopolysaccharide (LPS) and hypoxia to induce pro-inflammatory stress to understand how maternal factors contributes to neurodevelopmental changes from pHIE in mouse pups. Utilizing the Rice-Vannucci (RV) model as well as a novel model created by Lacaille et al. 2019, we replicate the features of pHIE seen in preterm human infants. Our hypothesis is that mouse pups subjected to LPS/Hypoxia (L/H) exhibit impaired neurological and motor function when compared to control and RV pups gestational ages, postnatal days 7 (P7) to 14 (P14). LPS is injected in the dams followed by 6 days of hypoxia exposure (10% O2) for the dams and postnatal pups. We assessed inversion, negative geotaxis, front limb hang, and hindlimb hang—neuromuscular behavioral tests—from P7 to P14 in control, RV, and L/H mice. Our results indicate that pups in the L/H group had blunted neuromuscular performance when compared to control and RV mice. The LH model appears to exhibit delay in recovery from HIE as typically seen in preterm infants suffering from HIE. Further experiments using the developed L/H model must be conducted to better assess its value as a model of human pHIE.

KATHERINE AIMEE GRANADOS

ABC PARTICIPANT 2023

Being able to find something that makes you feel both confident and comfortable when pursuing a career path began when I was introduced to the field of research in 2022. Coming back to Loma Linda in the same lab surrounded by the same mentor, Dr. Daisy DeLeon, has made me feel more confident in the research I will be conducting this year as a recent high school graduate from Redlands High School. As a determined first-generation student, I hope to push forward the field of neurodegenerative diseases to increase awareness and develop optimal treatments for underserved communities.

IGF-II REGULATES MAGMAS, THE MITOCHONDRIAL ROS PROTECTIVE PROTEIN THAT IS REQUIRED FOR CELL VIABILITY

Katherine Granados, Alfonso Durán, Frankis Almaguel, Qianwei Tan, Daisy De León
Center for Health Disparities and Molecular Medicine, Breast Cancer Laboratory, School of Medicine, Loma Linda University, Loma Linda, CA

We have demonstrated that Insulin-like growth factor II (IGF-II) stimulates cell proliferation, regulates mitochondrial proteins, inhibit apoptosis and promotes chemoresistance of Breast Cancer (BC) cells. We have also shown that Triple Negative Breast Cancer (TNBC) cells express high levels of IGF-II which decreases pro-apoptotic proteins while increases anti-apoptotic proteins to prevent mitochondrial cell death. MAGMAS is a strong antioxidant protein that protects the mitochondria from ROS induced-cell death that it is required for cell viability. Thus, MAGMAS is a critical component in the protection from ROS deleterious effects in the mitochondria. The research that we conducted last year showed that high IGF-II levels correlated with high MAGMAS protein levels in TNBC tissues from AA women. In contrast, little or no IGF-II was detected in the normal paired tissues correlating to low MAGMAS levels. To further examine how IGF-II regulates MAGMAS in TNBC we decided to 1) Asses IGF-II regulation of MAGMAS in TNBC cells, 2) To Determine whether different isoforms of MAGMAS are expressed in TNBC cells. 3) Does IGF-II increases MAGMAS intracellular levels or its localization? We examined the CRL-2335 breast cancer cells, a TNBC cell line established from the tumor of an African American woman that produces high IGF-II levels. To address our hypothesis, we used wild CRL-2335 cells (Control, high IGF-II), IGF-II antisense transfected CRL-2335 cells (Treatment 1, blocked or low IGF-II and low MAGMAS?), and transfected cells treated with exogenous IGF-II (Treatment 2, replaced MAGMAS levels?). Our hypothesis is that IGF-II levels will determine MAGMAS levels in the mitochondria. We used cell fractionation and Western blotting (WB) to determine MAGMAS expression and intracellular localization. Furthermore, we utilized immunofluorescence to detect MAGMAS by confocal technology. Preliminary results showed that CRL-2335 cells have lower than expected levels of MAGMAS in the mitochondria in contrast to what was detected in the TNBC tissue. We are currently completing our study comparing MAGMAS in the Control CRL-2335 cells versus MAGMAS in Treatment 1 and Treatment 2 cells. Completion of this study will validate IGF-II as a regulator of MAGMAS. If IGF-II increases the localization of MAGMAS to the mitochondria, it will suggest that this growth factor regulates MAGMAS to protect cancer cells from ROS induced cell death. Comparison between WB of the cell fractions vs confocal analysis of the fractions will further allow us to distinguish if there is any specific MAGMAS isoform preferentially located in the mitochondria. Validation of IGF-II regulation of MAGMAS represents an important new tool for the treatment of TNBC.

NYANA PAIGE INIGUEZ

ABC PARTICIPANT 2023

The Apprenticeship Bridge to College program has made the summer of 2023 the most rewarding and fulfilling experience of my life thus far. During this program, I have witnessed and engaged in scientific events that almost any teenager would be thrilled to do. That being said, I have been so blessed to have the opportunity to do biomedical research here at Loma Linda University. Not only did I learn from this program, but I also made friends and experienced something new every single day.

The ABC program has introduced me to high levels of thinking, studying, communicating, and learning that will forever benefit me in my future career and schooling. As of now, I currently attend Beaumont High School as a rising senior. I plan to major in human biology or nursing while I attend college. My future goals are to become a nurse practitioner specializing in dermatology. During this program, I have been involved in prostate cancer research in which my mentors, Dr. Frankis Almaguel, Dr. Alfonso Duran, Krystal Santiago, and Kristen Whitley have treated me with patience and great kindness. I am immensely grateful for this opportunity and the amazing people I worked with.

ENOLASE-1 AS A NOVEL THERANOSTICS TARGET FOR NEUROENDOCRINE PROSTATE CANCER

Nyana Iniguez, Krystal Santiago, Alfonso Duran, Kristen Whitley, Carlos A. Casiano, Frankis Almaguel

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

Prostate cancer (PCa) is American men's second most common cancer. Although taxane-based chemotherapy is the last line of defense in men with advanced PCa, it fails due to chemoresistance. The protein-specific membrane antigen (PSMA) has been an effective target for the imaging and therapy of advanced PCa. Although PSMA radioligand therapy (PSMA-RLT) is a theranostics option for men with advanced PCa, about 30% have a limited response due to neuroendocrine-like PCa (NEPC), which lacks PSMA expression. A promising alternative is the glycolytic enzyme enolase (ENO), which localizes to the cell surface in advanced tumors. Preliminary studies demonstrate that chemosensitive NEPC PCa cell lines express both ENO-1 and ENO-2; however, docetaxel-resistant NEPC cells only express ENO-1 and have a metabolic vulnerability due to the loss of ENO-2. We hypothesize that ENO-1 is expressed on the surface of NEPC cell lines and can be targeted with small molecule inhibitors (SMIs) that could be used as theranostics agents. Additionally, we have observed changes in the expression and localization of ENO-1 in NEPC cell lines under different glucose concentrations. Our experiments show that under high glucose conditions, found on metabolically active metastatic tumors, ENO-1 is highly expressed on the cell surface, making it an advanced and practical target for theranostics. However, low glucose conditions inhibit the activity of the c-MYC oncogene resulting in decreased production of ENO-1 and increased production of MBP1, the small splice variant of ENO1 that blocks the transcriptional activity of c-MYC. Our efforts to identify ENO-1 surface expression on NEPC cell lines entail using immunofluorescence microscopy, membrane fractionation analysis, and flow cytometry. We are also evaluating the cytotoxicity of SMIs targeting ENO-1 in chemoresistant NEPC cell lines using viability assays and Hoffman Modulation Imaging. Our long-term goal is to identify an alternative treatment for patients with NEPC by establishing ENO-1 as a novel theranostics target.

KATIE MINH LAM

ABC PARTICIPANT 2023

My aspirations in the medical field stemmed from personal experiences where I witnessed the hardships endured by myself and numerous relatives in the face of illness. These encounters fostered my unwavering appreciation for healthcare providers dedicated to treating those in need. Driven by boundless knowledge and a multitude of unanswered questions in science, I plan to major in biochemistry at the University of California, Los Angeles or Irvine, with a future goal of becoming a radiologist. The seamless integration of medicine and technology has sparked my interest and ignited my passion to contribute to this field.

As I enter my senior year at Etiwanda High School in Rancho Cucamonga, CA, I am excited to serve as the editor-in-chief for my school's yearbook committee. Concurrently, I hold leadership positions as the president of Dear Asian Youth and treasurer of the Medical Majors Club. Valuing community service, I actively engage in clubs like National Honor Society and the California Scholarship Federation, while volunteering at my local hospital. I am forever thankful for the opportunity to participate in the ABC program, which has prepared me to excel in future endeavors. I would like to express my heartfelt appreciation to Dr. Salma Khan for graciously welcoming me into her lab, as Kristiana Rood, PhD(c), Romi Yamauchi, Ria Laxa, and Jane Muinde for their invaluable guidance and insight during my research journey.

PDLIM-7 GENE OVEREXPRESSION CORRELATES WITH WORSE SURVIVAL IN THYROID CANCER PATIENTS

Katie Lam, Collin Robins, Celina Yamauchi, Kristiana Rood, Ria Laxa, Gerardo Gomez L., Andrea Shields, Saied Mirshahidi, Mia Perez, Alfred Simental, Salma Khan
Center for Health Disparities and Molecular Medicine, Biochemistry, School of Medicine, Loma Linda University, Loma Linda, CA

The rising incidence of thyroid cancer has drawn attention to its disproportionate impact on minority populations, highlighting the urgent need for innovative treatment approaches to address this healthcare disparity. In a previous study, we investigated the Enigma protein, gene called PDLIM7, as a significant biomarker in thyroid cancer progression. However, stage dependent gene expression is not known. Based on our previous publication, we have analyzed a stage-dependent PDLIM7 gene expression by UALCAN software using 59 normal and 505 thyroid tumor tissues from the TCGA database. We meticulously analyzed the PDLIM7 gene expression in normal versus tumor tissues. Our findings revealed that PDLIM7 gene was overexpressed in tumor tissues compared to normal. We also found that hypermethylation of PDLIM7 promoter in normal tissues whereas hypomethylation in tumors. Females showed more PDLIM7 gene expression than males. A stage-dependent enhanced PDLIM7 gene expression was observed. Out of all histological subtypes, papillary thyroid cancer had the highest expression of PDLIM7 and higher expression was noted in lymph nodes positive compared to node negative cases. Lastly, on overall survival, higher PDLIM7 expression correlated to worse survival. Based on these observations, we propose to use the PDLIM7 gene as an important biomarker for early detection. Our future aim is to use fine needle aspiration (FNA) samples to check the expression level in indeterminate cytology cases. In vitro downregulation of PDLIM7 gene by si-knockdown, tumor cells stopped proliferating. This investigation opens new avenues for groundbreaking therapeutic approaches, particularly for individuals from diverse ethnic backgrounds who are disproportionately affected by thyroid cancer.

SOLOMON XAVIER MOORE
ABC PARTICIPANT 2023

This summer, I have learned so much from the research that I've done in Dr. Erik Behringer's lab. From doing protein isolation and western blotting with Fritz Miot to doing DNA and RNA isolations. There were so many different rules and protocols to learn and follow, but my peers and mentors were patient and always willing to help. My focus this summer was on protein isolation. In doing so, we can find a more accurate picture of what proteins in the body are affected by Alzheimer's disease.

I attend Citrus Valley High School, where I am a Junior. After high school, I plan on majoring in civil engineering at Tennessee State University. In the not-so-near future after college, I want to own an engineering firm. I also plan on taking over my mother's gym/personal training business when she is a lot older and retires. This summer I was able to get a lot of work and research done. In my opinion, the most interesting part of it all was finding things that did not work because that allows me to troubleshoot and dive deeper into each specific component of a protocol to find what went wrong. If everything were to work the first time, there would be no learning or adapting to problems.

Thank you to Dr. Erik Behringer, Fritz Miot, Mary Bishara, and Phoebe Chum for all the help and guidance over the summer.

EVALUATING TECHNIQUES FOR PROTEIN ISOLATION & QUANTIFICATION IN ALZHEIMER'S DISEASE: A COMPARITIVE STUDY IN AGING C57BL/6 & 3xTg-AD MICE

Solomon Moore, Fritz Miot, Mary Bishara, Phoebe Chum, Erik Behringer
Center for Health Disparities and Molecular Medicine, Pharmacology,
School of Medicine, Loma Linda University, Loma Linda, CA

Alzheimer's Disease (AD) is characterized by an elevated level of amyloid-beta, which leads to increased production of reactive oxygen species (ROS), causing damage to brain cells, including cell death. This underscores the brain's vulnerability to ROS as a critical driver of AD pathogenesis. Pre-clinical signs of the disease include proteinopathy, inflammation, and excessive ROS production. Previous research has utilized biochemical techniques like protein extraction and quantification with Western Blot and Enzyme-Linked Immunosorbent Assay (ELISA) to study various proteins. Achieving high-quality protein purification is essential, typically indicated by a 260nm/280nm absorption ratio of 0.6; higher ratios may indicate DNA contamination. We identified the best methods for protein extraction and WB while aiming to detect changes in levels of antioxidant enzymes (e.g., glutathione peroxidase, catalase) in different age groups of mice, specifically the wild-type C57BL/6 and 3xTg-AD models at ages 2- and 18-months. The data collected through protein extraction and quantification will provide insight into the protein expression profiles in regions of the brain (e.g., entorhinal cortex, hippocampus) and other tissues most affected by AD. Following the use of a Tween-based lysis buffer, several nucleic acid removal strategies were applied, such as DNase treatments, column filtration, or organic solvent washes. Thus far, our preferred protocol involves using acetone precipitation, followed by two Phosphate Buffered Saline (PBS) washes, resulting in the most optimal purity ratio for protein extraction. Protein separation was achieved by gel electrophoresis and transferred to a nitrocellulose membrane for imaging. This developing application may contribute to understanding protein expression changes associated with AD pathology and provide valuable guidance for future research in this domain.

VALERIE MORENO

ABC PARTICIPANT 2023

This fall I will be a senior at Bloomington High School. After completing high school, I plan to attend University of California, Irvine (UCI) and major in biology. In the future, I want to attend medical school and specialize in pediatric oncology. I have seen firsthand how children with cancer endure various treatments and how these treatments can impact their ability to perform common childhood activities. I want to help children suffering with cancer and ensure that they receive the best possible treatment options available.

Growing up I have learned that in order to achieve my goals it takes determination and hard work to overcome obstacles in one's path. The summer of 2023 was one to remember because it was filled with new faces, memories, and various challenges. I joined the ABC program knowing I was going to do research but I did not know I would gain a family and knowledge that I will have for the rest of my life. This program assisted with expanding my comprehension on cancer development and progression and the treatments that are available to combat it. The research we conducted allows for new treatment options, in order to increase those patients' life expectancy.

Thank you Dr. Casiano for giving me such a great opportunity to be one of your mentees and leaving me with an abundance of knowledge, experiences, and blessings. I'd also like to thank Pedro Ochoa and Dr. Sanchez-Hernandez for assisting me through the summer with the research process.

DOCETAXEL-RESISTANT PROSTATE CANCER CELLS EXHIBIT SELECTIVE CROSS-RESISTANCE TO DNA-DAMAGING AGENTS

Joel Philip, Valerie Moreno, Pedro T. Ochoa, Carlos A. Casiano
Center for Health Disparities and Molecular Medicine,
Loma Linda University School of Medicine

Prostate cancer (PCa) is the second-leading cause of cancer mortality for men in the U.S, and presents a health disparity in which African American (AA) men have higher mortality rates compared to other racial/ethnic groups. Although the five-year survival rate for localized PCa is nearly 100%, once the disease progresses to later stages patients ultimately develop therapy resistance and the survival rate drops to 30%. Understanding the mechanisms underlying PCa therapy resistance is crucial for developing new treatment options. Cross-resistance, an emerging concern in cancer treatment, is a phenomenon where the molecular mechanisms of resistance to a particular drug confer resistance to another drug. One potential mechanism of cross-resistance is through the Lens Epithelium Derived Growth Factor p75 (LEDGF/p75), an oncoprotein that promotes DNA damage repair and cancer cell survival against environmental stressors including chemotherapeutic drugs such as docetaxel (DTX). This project evaluates the potential for cross-resistance in PCa chemotherapy and the influence of LEDGF/p75 in its development. We hypothesized that DTX resistance in PCa cells confers cross- resistance to DNA-damaging agents. Our findings demonstrated that DTX-resistant PCa cells exhibit cross-resistance to etoposide and doxorubicin, but not to cisplatin. Further studies will focus on targeting LEDGF/p75 to determine its role in cross-resistance, with the goal of resensitizing DTX-resistant cells not only to DTX, but also to etoposide and doxorubicin. Elucidating the mechanisms by which PCa patients develop therapy cross-resistance will help in the development of novel treatment options.

JOEL MATHEW PHILIP
ABC PARTICIPANT 2023

Everything we can and cannot see has come about in some way to shape the world around us. My curiosity for how such mechanisms work led me to my first research experience in the summer of 2021, where I looked at understanding the function of uncharacterized gene LRRC36 using bioinformatic analysis. This experience allowed me to apply my knowledge from my education as well as acquire new skills to develop and test a hypothesis. The process of developing a project from inception to completion captivated me. I applied to the ABC program this summer in the hopes that I could further immerse myself in the research process under the mentorship of established professionals.

I am 16 years old and a senior at Centennial High School in Corona, California. After I graduate from high school, I hope to pursue a neuroscience major as I am fascinated by the intricacy of the brain. I have always been set on becoming a physician, particularly a neurosurgeon, however, the ABC program has offered me insight into the field of research, and I am now considering a career as a scientist as well. Both professions entice me as they offer an intellectually stimulating and constantly developing workplace where I can apply myself to help others.

I would like to thank Dr. Casiano and his laboratory members, especially Pedro Ochoa and Dr. Sanchez-Hernandez, for welcoming me into the lab and for guiding me through the research process as well as supporting me throughout this invaluable opportunity.

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Joel Philip, Valerie Moreno, Pedro T. Ochoa, Carlos A. Casiano
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Prostate cancer (PCa) is the second-leading cause of cancer mortality for men in the U.S, and presents a health disparity in which African American (AA) men have higher mortality rates compared to other racial/ethnic groups. Although the five-year survival rate for localized PCa is nearly 100%, once the disease progresses to later stages patients ultimately develop therapy resistance and the survival rate drops to 30%. Understanding the mechanisms underlying PCa therapy resistance is crucial for developing new treatment options. Cross-resistance, an emerging concern in cancer treatment, is a phenomenon where the molecular mechanisms of resistance to a particular drug confer resistance to another drug. One potential mechanism of cross-resistance is through the Lens Epithelium Derived Growth Factor p75 (LEDGF/p75), an oncoprotein that promotes DNA damage repair and cancer cell survival against environmental stressors including chemotherapeutic drugs such as docetaxel (DTX). This project evaluates the potential for cross-resistance in PCa chemotherapy and the influence of LEDGF/p75 in its development. We hypothesized that DTX resistance in PCa cells confers cross- resistance to DNA-damaging agents. Our findings demonstrated that DTX-resistant PCa cells exhibit cross-resistance to etoposide and doxorubicin, but not to cisplatin. Further studies will focus on targeting LEDGF/p75 to determine its role in cross-resistance, with the goal of resensitizing DTX-resistant cells not only to DTX, but also to etoposide and doxorubicin. Elucidating the mechanisms by which PCa patients develop therapy cross-resistance will help in the development of novel treatment options.

GIARA ELLE WRIGHT BARCELO

ABC PARTICIPANT 2023

I was born and raised in Silver Spring, Maryland, and moved to Redlands, California, at 13. Moving was a tremendous growing and learning experience. As I incorporated into a new place, I gained many unique and valuable relationships and opportunities like the ABC Program. When I am n ot in school, I like trying new and rich experiences. I enjoy playing sports all year and trying local coffee shops and cafes.

In the upcoming year, I will be a senior at Loma Linda Academy and plan to stay local in Southern California for college. I plan on majoring in biochemistry and then going into medical school.

I am grateful to have been matched with Dr. Johnny D. Figueroa. He is a supportive mentor who has believed in me, whether guiding me in the many steps of the application process or teaching me how to contribute to the neuroscience world. Being in Dr. Figueroa's lab has also allowed me to learn and work alongside a fantastic group of people, including neuroscientist (Dr. Perla Ontiveros-Ángel); neuroscientist in training and mentor (Tim Simon), and students Julio Sierra and Arianna De León-Williams. I am confident this experience will allow me to fulfill God's purpose in my life.

SOCIAL ISOLATION STRESS DURING ADOLESCENCE INCREASES ANXIETY AND DISORDERED EATING PATTERNS IN FEMALE RATS

Giara Wright, Timothy Simon, Julio Sierra, Arianna Williams, Perla Ontiveros-Ángel, Johnny D. Figueroa

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

Early-life stress (ELS) contributes to emotional dysregulation and the emergence of eating disorders, particularly in females. Yet, the pathways connecting ELS to disordered eating remain unknown. **We hypothesized that ELS would potentiate the likelihood of anxiety-related behaviors, alterations in eating patterns, and obesity-like phenotypes in female rats**. An animal model of social isolation stress (SIS) was used where adolescent female rats were housed in pairs (n=12), or isolated (n=12). An array of behavioral assessments was monitored weekly during the rat active phase/dark cycle using a home-cage monitoring system (Noldus Phenotyper/Ethovision). An aversive spotlight challenge was performed for 60 minutes at 2300 h to measure avoidance and anxiety-related behaviors. The light would illuminate the area separating the feeding and shelter zones during the dark cycle, generating a conflict between eating or seeking shelter. We found an increase in time spent in the feeding zone and frequency of feeding in the isolated rats relative to controls. Interestingly, isolated animals had a sustained preference for the feeding zone following the aversive spotlight challenge corresponding with increased eating time and frequency. Weekly body weight and food consumption measurements suggest continuous social isolation had divergent effects on early and late adolescence, with pronounced weight gain manifesting in late adolescence. Furthermore, the isolated animals demonstrated residual avoidant interactions with the spotlight area for hours after the spotlight had been terminated. But this effect was inverted during late adolescence, thus revealing dissociable effects of social isolation on different developmental epochs. These results support the link between ELS, anxiety-related behaviors, and maladaptive eating. The results of this longitudinal study highlight the significant contribution of ELS to adolescent behavior and mental health.

Undergraduate Training Program (UTP)

SANTIAGO EMMANUEL DE LA CRUZ
UTP PARTICIPANT 2023

My name is Santiago De La Cruz, a participant in the UTP (Undergraduate Training Program) at Loma Linda University. As a fourth-year Biology major at Cal State San Bernardino, I aspire to attend medical school and become an oncologist, while focusing on cancer research. I am dedicated to addressing healthcare disparities and establishing non-profit clinics in underserved communities, advocating for equitable healthcare provision. As the first in my family to pursue higher education, I understand the challenges faced by underrepresented students. Through mentorship and support, I believe we can empower these individuals to achieve their dreams. In addition to my academic pursuits, I run a mobile detailing business and donate funds to healthcare organizations, furthering my vision of accessible healthcare for all. I am actively involved in biology and AMSA clubs at my university, expanding my knowledge and promoting community wellness. Presently, I am engaged in a research project on osteoporosis under the guidance of Dr. Mohan. Investigating the underlying mechanisms of this prevalent bone disorder has deepened my understanding of the intricate workings of the human body and reinforced my commitment to scientific exploration and patient care.

THYROID HORMONE RECEPTOR BETA SIGNALING INHIBITS ADIPOCYTE DIFFERENTIATION IN A SEX-DEPENDENT MANNER

Santiago De Le Cruz, Subburaman Mohan,
Basic Science Department, School of Medicine, Center for Health Disparities and Molecular Medicine, Loma Linda University, Loma Linda, CA

Obesity is a major health problem in U.S. with a prevalence of over 40% and an annual direct cost of $173 billion. Obesity-related conditions include heart disease, type 2 diabetes, osteoporosis, and certain types of cancer leading to preventable, premature death. Therefore, studies focused on identification of novel strategies for preventing obesity are important to improve quality of life in obese individuals and reduce healthcare costs. One of the common clinical conditions linked closely to obesity is hypothyroidism. Accordingly, we found that fat mass was increased in hypothyroid mice that was rescued by treatment with thyroid hormone (TH) treatment. While TH effects on lipogenesis and browning of white adipose tissue have been well established, systemic TH administration is not a viable strategy for treating obesity as TH exerts a wide range of effects on nearly every tissue in the body, and the adverse effects of thyrotoxicosis are much too dangerous. For this reason, specific downstream effectors in the TH signaling pathway are being targeted to leverage some of TH's beneficial effects while avoiding unwanted adverse effects. TH exerts its physiological effect by binding to specific nuclear receptors, thyroid hormone receptor (TR)α and TRβ. Based on the observation that TRβ, the predominant receptor expressed in liver, mediates the cholesterol lowering effect of TH in hepatic tissue, TRβ-selective thyromimetics have been investigated for the treatment of hypercholesterolemia. In our recent work, we explored the potential of the TRβ agonist, MG-3196, as a therapeutic target for bone-related complications caused by obesity. In a mouse model of high fat diet-induced obesity, we found that MGL-3196 treatment was effective in preventing diet-induced obesity in male but not female mice. Towards the goal of understanding the mechanism for sex-specific effects of activation of TRβ signaling by MGL-3196 in reducing obesity in mice fed with high fat diet, we evaluated in this study if MGL-3196 effects on adipocyte differentiation is dependent on estrogen signaling.

FLETCHER ALEXANDER DEMENTYEV

UTP PARTICIPANT 2023

I was born in LLUMC, and I consider it a great honor to spend a third summer working at the institution, which has been influential in my life from the very start. I grew up around the medical center, and being a student researcher over the last three summers at the CDHMM has allowed me to interact with leading translational researchers spearheading important medical and social issues. Their passion and years of dedication to the advancement of patient care and preventative medicine have moved me to continue my research in higher education. I am a rising sophomore at Columbia University studying neuroscience and business management with the goal of matriculating into MD/PhD. degree program after graduation. I am continually inspired by the work that is being done at LLU and its commitment to building healthier communities as well as caring for individuals.

This summer, I have been privileged to work under Dr. Sean Wilson alongside Starla Murillo, Benjamin Bello-Soto, and Kai Madison. Together, we have navigated a challenging project—analyzing trends in adolescent psychosocial metrics in response to a cycling intervention program. I am grateful for their mentorship, which has had an immense impact on not only my scientific and research abilities but also provided helpful insights into how to thrive in my future career.

R4F AS A PATHWAY TO IMPROVED MENTAL HEALTH IN MIDDLE SCHOOL STUDENTS

Fletcher Dementyev, Starla Murillo, Benjamin Bello-Soto, Kai Madison, Esther Walker, Sean M Wilson

Center for Perinatal Biology Loma Linda University, Loma Linda, CA

Outride, Morgan Hill, CA

Youth mental health remains in a critical state even in a post-COVID pandemic world. Exercise is a well-regarded method to boost mental health and well-being in all age groups. The Riding 4 Focus (R4F) program is a cycling education program designed to equip students with basic cycling handling skills and introduce students to the lifetime physical activity of cycling. A secondary outcome of this program is to improve the behavioral health and well-being of adolescents in middle schools, primarily aged 10-14. The current study examined associations between participating in the R4F program and mental health and well-being in those with specific unmodifiable risk factors including gender, socioeconomic, and racial identity. Anonymous online surveys were collected from 3924 adolescent participants before the R4F program and 3289 students after the cycling program across 31 schools during the fall 2021 and spring 2022 semesters. Psychosocial well-being was quantified using the WHO-5 and PSC-17-Y metrics. Using non-parametric test statistics, the data shows a significant increase in the mental health and well-being of participants after the program. Further analysis revealed that participation in the R4F program was associated with improved psychological health and well-being of minority and low-income adolescents, as well as protective associations for both genders. Although these findings are encouraging, the efficacy of the program depends on a number of factors, and future studies are needed to assess causality.

CLARISSA DEAN DO

UTP PARTICIPANT 2023

Learning and dissecting the unknown had always been encouraged throughout my childhood and it is something I continue to do in my day-to-day life as well as my research. Throughout my high school and college career, I began working as a medical assistant in a hospice clinic, which allowed me to experience firsthand the disparity many underrepresented groups face. This injustice led me to continue my participation in the UTP program in hopes of understanding and making a change toward closing the gap between proper health and income insecurity.

As a returning student, Dr. Huynh Cao and Dr. Yi David Xu never hesitated to push me past my limits and test my capabilities with each experiment. They have both taught me that amazing things can come from the bleak and to have the intent to be meaningful in everything that we do. Because of this program, I was exposed to the beautiful world of medicine and science and how impactful it can be on the community and the world.

This appreciation for the importance and impact of integrating scientific research and clinical medicine has led me to pursue my education at Loma Linda University.

INVESTIGATING HOW LIFESTYLE HABITS (RISKS) AFFECT BLOOD STEM CELLS IN MINORITY POPULATIONS

Clarissa Do, Jeffrey Xiao, Ismael Valladares, Brandon Park, Mark E. Reeves, David J. Baylink, Huynh Cao, David Xu

Divisions of Hematology and Oncology and Regenerative Medicine, Department of Medicine, Loma Linda University, Loma Linda, CA

Underrepresented racial and ethnic minority communities have a disproportionately higher burden of diabetes and nicotine-related complications. This exposure to nicotine and hyperglycemia are both linked to impaired immune function which may result in a higher risk of cancer. This project explores the hypothesis that conditions that disproportionately affect minority groups, such as diabetes and nicotine usage, may affect both the blood system and immune systems by damaging the metabolism of stem cell populations. Mitochondria are a critical component of stem cell metabolism and thus provide the necessary energy needed for stem cells to proliferate. Therefore, we examined the effects of varying nicotine and glucose concentrations on CD3+ T cells and HSCs and developed techniques to isolate and assess mitochondrial damage in T-lymphoblastic and AML blast cells. HSCs treated with nicotine had a 4.54% decrease in cellular concentrations, while CD3+ T cells treated with glucose had decreasing trend in cell clustering with increasing levels of glucose. Altogether, our findings suggest that lifestyle factors such as smoking and uncontrolled blood glucose could impair hematopoietic stem cell production. Further research into the link between mitochondrial function and the impaired hematopoietic stem cell production/ proliferation that arises from nicotine consumption and elevated blood glucose may provide evidence for in-vivo transplantation of genetically modified mitochondria as an effective form of therapy and risk management for cancer in disproportionately affected minority groups.

ISABEL NAOMI GENOVEZ
UTP PARTICIPANT 2023

My interest in research was sparked in the summer of 2021 when I participated in the ABC program. I am grateful for the opportunity to be back for a second summer, now as a UTP student. I am a rising sophomore at Southern Adventist University in Tennessee, majoring in Biology with a Pre-Medicine track and minoring in Chemistry. When I am not studying, I enjoy reading and playing softball.

One of my greatest passions is giving back to my community. Throughout High School, I volunteered at EXCELL through the LLUC UReach program as a tutor. In the height of the pandemic, I volunteered at a Pop-Up clinic with the aim of providing vaccination to underrepresented populations in the Inland Empire. This past May, I participated in a medical mission trip to Costa Rica. As part of the team, we saw over seven hundred patients during a four-day pop-up clinic. I also preached eight sermons at Pacuare Viejo Seventh Day Adventist Church where I was able to connect with amazing people while sharing the Gospel.

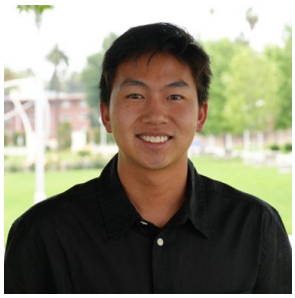
This summer I have had the privilege of working under the guidance of my mentor Dr. William Langridge, PhD student Ryan Fuller, and Tessa Levin. In addition to learning more about immunology and Covid-19, we have specifically been studying the dendritic cell and T-Cell interaction in the immune system. I have learned so much in this short time. My appreciation for immunology and the human body has expanded greatly. I could not think of a better way to further my journey in research and I am truly grateful for the opportunity to continue to learn and grow this summer.

EXAMINATION OF DENDRITIC CELL EXOSOMES AS A MUCOSAL VACCINE FOR THE BETA CORONAVIRUS SARS-COV-2

Isabel Genovez, Tessa Levin, Ryan Fuller, Anthony Firek, Dr. William Langridge
Center for Health Disparities and Molecular Medicine, Division of Biochemistry,
School of Medicine, Loma Linda University, Loma Linda, CA

Since 2020, the Covid-19 pandemic has caused over seven million deaths worldwide. While recent mRNA vaccines reduce mortality, they do not protect against reinfection and are the source of unwanted side effects that include cardiac inflammation, blood clots, cytokine storm, and “long COVID”. To construct a safer, more effective vaccine against the severe acute respiratory syndrome coronavirus (SARS-CoV-2) that is relatively inexpensive and easy to disseminate worldwide, we linked the mucosal adjuvant CTB to the SARS-CoV-2-ACE-2-RBD antigen and produced the vaccine fusion protein in bacteria. After testing vaccine protein efficacy in cell culture and in mice, we transferred the vaccine gene into potato plants to make an edible vaccine that can prevent virus infection through the production of mucosal IgA antibodies. To understand how the vaccine stimulates immunity we incubated the vaccine protein with dendritic cells (DCs), the major antigen-presenting cell in the body. We showed that the vaccine stimulated the maturation (activation) of immature DCs. To understand how vaccine-treated DCs communicate with T cells to stimulate an adaptive immune response to the virus, we isolated 50 – 100 nm exosomal vesicles released from vaccinated DCs and incubated them with naïve T cells to observe by flow cytometry how the exosome cargo stimulates T cell activation. We hypothesize that exosome vesicles deliver virus antigens and other immune-stimulating molecules to activate a T cell pro-inflammatory immune response specific for SARS-CoV-2.

MATTHEW MINH-TIEN LE
UTP PARTICIPANT 2023



I am a rising junior attending UC San Diego in La Jolla, California. I study global health, marine sciences, and business, and work at the Salk Institute for Biological Studies as a lab technician where we study regulatory biology. I also volunteer with a local hospital. I am part of a couple organizations on campus: The Human Development Student Association and the UCSD Moot Court team. In my free time, I enjoy exploring cafes, restaurants, and beaches. I also love to surf, paddleboard, and spend time outdoors. I'm hoping to attend an MD or JD/MD program and serve marginalized communities in the realm of healthcare law, policy, and service. My passion is helping underserved or disadvantaged persons navigate the complexities of our healthcare and educational systems. I am currently working with Tyler Hillman in Dr. Christopher G. Wilson's lab to develop a model to study hypoxic-ischemic encephalopathy in mice. Being in research is exciting because of not only the number of different fields of study, but also the amount of ways one can looks at and interpret data or even a lack thereof. Dr. Wilson and Tyler have been extremely supportive and helpful during my time in the UTP. Their patience, knowledge, and humor are both inspiring and insightful, and I am incredibly appreciative of the opportunity to be a part of this lab.

SEX DIFFERENCE IN RECOVERY IN A NOVEL RODENT MODEL FOR PRETERM HYPOXIC-ISCHEMIC ENCEPHALOPATHY

Matthew M. Le, Braedon Jacobson, Tyler C. Hillman, Christopher G. Wilson
Center for Health Disparities and Molecular Medicine, Perinatal Biology,
School of Medicine, Loma Linda University, Loma Linda, CA

Preterm infants are susceptible to maternal stressors whose subsequent inflammatory response can heavily influence neuronal and motor development over short- and long-term development. Preterm hypoxic-ischemic encephalopathy (pHIE) can occur *in utero*, yet commonly-used rodent models do not accurately mimic the events occurring in pHIE in the developing brain. Our laboratory has developed a novel rodent model that more accurately represents human HIE. In this model, we induced HIE in preterm neonatal mice by producing an inflammatory response in the maternal rodent using lipopolysaccharides (LPS) injection followed by preterm and post-natal exposure to hypoxia (10% O_2). This method incorporates a direct interaction between the maternal inflammatory response and the mouse fetus as opposed to the Rice-Vannucci (RV) model that involves direct insult to the infant mouse brain. Using this model, we assessed differences in pHIE recovery between males and females as is seen clinically. We conducted behavioral tests testing general motor function in preterm mice, by running front- and hind-limb suspension, negative geotaxis, surface righting, and ambulation. We hypothesize *that sex differences in recovery from preterm hypoxic-ischemic injury in neonatal mice will be observed, with females showing a more robust recovery in motor function than male littermates.* Our results, gathered through behavioral analysis of the preterm mice, show no significant sex bias in female and male neonatal mice using our model. This is in contrast to the commonly used Rice-Vannucci (RV) model of HIE. Our results suggest an absence of post-injury recovery in response to the pHIE seen in the RV model. Overall, our behavioral data provides evidence that a pHIE model that incorporates both maternal and neonatal factors more accurately mimics the melange of effects seen in human HIE, further highlighting the importance of involving the maternal inflammatory response in pHIE studies.

DIANA CAROLINA ALEXA LOZANO
UTP PARTICIPANT 2023

I am pursuing a health science degree at La Sierra University. I hope to pursue an MD degree at Loma Linda University in the future to fulfill my dream of becoming a first generation Latina physician. I had the opportunity to shadow various specialties in the medical field and internal medicine has consistently sparked interest and compassion within me. This specialty has provided me encounters with individuals from low-income backgrounds who do not deserve to be judged due to their socio-economic status or race, but are simply seeking health care. I have watched physicians treat these patients with a humble and compassionate demeanor that I hope to make my own in the future.

The UTP program has continually satisfied my intrigue with scientific research while simultaneously providing me with mentors who value diversity in STEM, and while also seeking my best interests. I would like to thank Dr. Casiano for welcoming me into his lab and for all the guidance he has provided me over the summer.

RACE-RELATED DIFFERENTIAL REACTIVITY OF ANTI-ENOLASE AUTOANTIBODIES IN PATIENTS WITH PROSTATE CANCER

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

Prostate Cancer (PCa) is the most prevalent malignancy among men, and the second contributor to cancer-related mortality in the U.S. Based on previous studies, our lab hypothesized that race-related differential anti-enolase (ENO) immunoreactivity in PCa patients is driven by distinct ENO isoforms and has dissimilar inhibitory effects on PCa cells. These studies showed that anti-ENO autoantibodies from African American (AA) and European American (EA) patients with PCa reacted differently against lysates from docetaxel (DTX)-sensitive and DTX-resistant (DR) PCa cell lines by immunoblotting. In addition, anti-ENO antibodies from EA, bot not AA, patients inhibited the migration of DR-PCa cells. Here, we first optimized the reactivity of ENO1 and ENO2 monoclonal antibodies against PCa cellsby immunoblotting. Our results showed that ENO1 antibody strongly reacted in all PCa cell lines tested, while ENO2 antibody showed weaker reactivity in DR cell lines. We also found higher levels of ENO1 reactivity against PCa cells grown in high glucose conditions compared to low glucose. These studies set the foundations for future experiments in which anti-ENO sera from AA and EA PCa patients will be screened against PCa cell lysates and purified ENO1 and ENO2 to determine race-related differences in immunoreactivity. First, we optimized an immunoblotting serum multiscreen system using prototype autoimmune disease sera. We then screened sera from AA and EA PCa patients to confirm the presence of ENO autoantibodies, showing strong to moderate anti-ENO immunoreactivity amongst both AA and EA sera. Further studies are in progress to determine if the PCa patient anti-ENO reactivity is directed against ENO1 or ENO2, and if there are race-related differences in this immunoreactivity. Future studies will analyze if the anti-cancer properties of PCa patient-derived anti-ENO antibodies are influenced by race.

JANETT MARTIN
UTP PARTICIPANT 2023

I attend college at Oakwood University in Huntsville, Alabama. I am studying Biology Pre-Medicine. I have always wanted to study this because of the impact that I have seen doctors, scientists, and researchers have on the lives of the people that I care deeply about. I want to be able to help others the way doctors helped my mother when she was diagnosed with cancer. I participated in research last semester and loved the way that questions were answered, now other questions came up, and seeing the work my group and I did come to fruition at the end.

I am working in Dr. Unternaehrer's lab, researching chemosensitivity and EMT scores regarding ovarian cancer. I am mentored by Daniel Zecena and David Jung. We want to find if there is a correlation between the EMT scores of patient derived cells and their chemosensitivity. This program has challenged me, taught me new research techniques and skills, and has educated me regarding health disparities. I want to thank Dr. Unternaehrer, Daniel Zecena, and David Jung for their patience, kindness, and knowledge that they shared with me. As well as the program coordinators for giving me this amazing opportunity.

EXPLORING THE CORRELATION BETWEEN THE CHEMOSENSITIVITY STATUS AND THE EMT SCORE OF PATIENT DERIVED HIGH-GRADE SEROUS OVARIAN CANCER CELLS

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

High-Grade Serous Ovarian Cancer (HGSOC) is the most malignant form of ovarian cancer. It accounts for 70% of all ovarian cancer cases with a recurrence rate of 80% after treatment for advanced cases. Previous cancer studies have demonstrated that cancer stem cells (CSCs) and epithelial-mesenchymal transition (EMT) cause an increase in cancer aggressiveness, invasion, and metastasis. The aim of this work is to find a correlation between the EMT score of patient derived cells and their chemosensitivity. We tested the hypothesis that the higher the EMT score the less chemosensitive the cells will be. To determine the EMT score, we used epithelial genes such as OCLN, TJP1 (ZO1), CLDN3, and mesenchymal genes such as SNAI1, CDH2, FN1, and VIM. We measured their expression through RT-qPCR to calculate the EMT score. Once the EMT score was determined we used previously acquired chemosensitivity data to test a correlation between the EMT score and the patient derived cells' chemosensitivity. Based on the results we can conclude that there is no correlation between EMT score and the cells' chemosensitivity.

ANGEL GABRIEL ORELLANA CAMPANA
UTP PARTICIPANT 2023

Science and the discovery of new things have always been a big interest of mine, leading me to pursue a degree in Biology, at Andrews University. While taking my first science college classes, my interest in science and the human body, as well as my passion and curiosity for these topics increased greatly. As a result, I decided to apply for the UTP program at Loma Linda University and am very grateful to have been placed in a great lab where my interest and capability for research have increased exponentially.

Apart from my interest in science, my early life experiences and having been the child of humanitarian aid workers, volunteering work is something that I am passionate about. During the 2021-2022 academic year I served as an elementary school teacher in the island of Palau, and when I got back to Andrews, I became especially involved with the Hispanic outreach ministry. I strongly believe that key scientific discoveries along with volunteer work can really impact the most vulnerable communities of our world. Because of this my goals for the future consist of enrolling in LLU's MD program after graduating from Andrews University and work in an underserved community like the ones I grew up in.

I would like to thank Dr. Salvador Soriano for welcoming me to his neurodegenerative diseases research lab, as well as Jacob White and Kayla Sanchez for having patience with me and helping me learn more about the topic.

MITOCHONDRIAL FERRITIN IN FERROPTOSIS AND ITS EFFECTS ON CMT

Angel Orellana Campana, Kayla Sanchez, Salvador Soriano
Center for Health Disparities and Molecular Medicine,
School of Medicine, Loma Linda University

CMT is the most common hereditary peripheral neuropathy, affecting approximately 126,000 people in the United States. Individuals with CMT suffer from demyelination of the peripheral nervous system, which in turn causes progressive motor weakness resulting in limb paralysis by old age. CMT type 1A results from the erroneous expression of the PMP22 gene which encodes for peripheral myelin protein 22 (PMP22). There is no cure or effective treatment available thus far. Several studies have linked ferroptosis, a recently discovered type of iron-dependent cell death, to neurodegenerative diseases including Alzheimer's dementia. Iron is an essential metal for cell processes that allow the cell to function normally. High concentrations of this metal, however, can promote an increase in the rate of Fenton reactions, leading to a rise in lipid reactive oxygen species (ROS) and in turn, ferroptotic cell death. Mitochondrial ferritin, a vital sequestering component of iron metabolism, stores iron in the mitochondrial matrix as species that are not subject to the Fenton reaction; this sequestration reduces the lipid ROS levels in the cell, thus attenuating ferroptosis. Based on previous studies and our preliminary data, we expect to find less mitochondrial ferritin in CMT fibroblasts than age-matched controls. We hypothesize that CMT cells are more prone to ferroptosis, leading to chronic cell death, causing demyelination of peripheral nerves.

ABIGAIL VIVIANA RAMIREZ
UTP PARTICIPANT 2023

It is common knowledge in the world of science that organismal phenotypes are the result of the interplay between genotype and ambient conditions. With that knowledge in mind, I introduce myself: a student, daughter, sister, granddaughter, aspiring epidemiologist, amateur baker, and self-proclaimed sibling lawyer. With a tendency to isolate myself since childhood, I never pegged myself as the type to pursue an opportunity such as the UTP program. Truthfully speaking, I applied on a whim, under the impression that my rejection odds outweighed those of my acceptance. I was convinced that investment in the latter possibility was delusional. Setting foot on campus on Orientation Day felt like a dream, as I saw the medical students, doctors, professors, and hospital staff rush down the streets with a half-filled coffee cup in one hand and a bag in the other, trying their best to beat the time. I intend to become an epidemiologist in the future. Thank you to my mentor, Dr. Fayth Miles, and the rest of the AHS-2 research team for sharing their knowledge.

PLANT-BASED DIETARY PATTERNS MAY PROMOTE KIDNEY FUNCTION AND ATTENUATE KIDNEY HEALTH DISPARITIES

Abigail Ramirez, Gary E. Fraser, Fayth Miles Butler
Adventist Health Study 2, School of Public Health, Loma Linda University, Loma Linda, CA;
Center for Health Disparities and Molecular Medicine, Loma Linda University

One in seven US adults suffers from Chronic Kidney Disease, but a number of biological, socioeconomic, behavioral, psychological, and environmental predispositions make African Americans three times as likely as their White counterparts to experience kidney failure. With Black Americans at an increased risk of kidney-related mortality, the need for practical interventions prevails. Following plant-based or vegetarian dietary patterns may reconcile this disparity. The Adventist Health Study-2 (AHS-2) cohort, with its large representation of individuals following vegetarian dietary patterns, including vegan, lacto-ovo-vegetarian, pesco-vegetarian, semi-vegetarian, and non-vegetarian dietary patterns, may be very valuable in exploring the merits of a diet-centric approach to improved health outcomes. In the current study, we sought to determine if adherence to vegetarian or plant-based dietary patterns was associated with better kidney function and, consequently, attenuation of racial disparities in kidney disease. Serum creatinine was measured in blood samples from nearly 1000 participants of the AHS-2, and the estimated glomerular filtration rate (eGFR) was calculated thereafter to quantify kidney function. Dietary patterns and race served singularly and collectively as exposures of interest, and the response variable was eGFR. Linear regression models were generated to examine associations of distinct vegetarian/plant-based dietary patterns or race with eGFR, with adjustment for confounding variables. Results from linear regression revealed that race was an extremely significant predictor of renal health following adjustment for dietary patterns. A plant-based dietary pattern was associated with higher GFR , which shows a benefit for these diets in prevention of CKD. Larger studies will allow for a more thorough examination of these phenomena.

KRISTEN LAURA WHITLEY
UTP PARTICIPANT 2023

During the summer of 2021, I had the opportunity to perform research in Dr. Kerby Oberg's lab and my wonderful mentors taught me to think like a scientist, questioning what I did and why. I discovered that I love the process of obtaining new knowledge, and I wanted to continue performing research. This past summer, I performed research in prostate cancer therapeutics with Dr. Frankis Almaguel and Dr. Alfonso Durán. This research was the perfect cross between my interest in drug efficacy and my passion for cancer research. I was invited to present my research at the Murdock College Science Research Conference in November where I was awarded the 2022 Murdock Poster Prize for Molecular and Cell Biology. In June, I graduated from Walla Walla University with my bachelor's degree in Biochemistry. During college, I shared my love of the sciences by working as a math and science tutor at Walla Walla High School and working as an Organic Chemistry Lab TA. I also volunteered at a free medical clinic in Walla Walla and witnessed the importance of access to healthcare for individuals from all backgrounds. I hope that someday I will be able to give back to my community in the same way that clinic has.

This summer, I am so grateful that Dr. Almaguel and Dr. Durán provided me with the opportunity to return and continue my research in cancer therapeutics. These doctors have been extremely influential mentors and have guided me in my decision to pursue pharmacy.

INHIBITION OF MITOCHONDRIAL PROTEIN MAGMAS DECREASES DOCETAXEL RESISTANCE IN NEUROENDOCRINE-LIKE PROSTATE CANCER CELLS

Kristen L. Whitley, Alfonso M. Durán, Christian H. Yoo, Krystal R. Santiago, Jennifer D. Tran, Adil S. Mohammed, Carlos A. Casiano, Bhaskar C. Das, Frankis G. Almaguel
Center for Health Disparities and Molecular Medicine, School of Medicine, Loma Linda University Cancer Center, Loma Linda University, CA

Prostate cancer (PCa) is the leading cause of newly diagnosed male malignancy in the United States. Unfortunately, current medical management of the most lethal phenotype, known as neuroendocrine differentiated prostate cancer (NEPC), fails to improve patient outcomes. Recent evidence suggests that targeting the mitochondria may be a critical factor in treating aggressive cancers. MAGMAS is a cytoprotective protein that is overexpressed in several aggressive tumors, including prostate cancer, breast cancer, and glioblastoma. It scavenges reactive oxygen species (ROS) to maintain sufficient levels for cell proliferation while keeping the levels below the threshold that could lead to apoptosis. In our study, we found that drug-resistant PC3-DR and DU145-DR PCa cell lines demonstrated significantly higher levels of MAGMAS than their drug-sensitive parental cell lines. We hypothesized that inhibiting MAGMAS would reduce the aggressive properties of highly proliferative Docetaxel (DTX)-resistant metastatic PCa cell lines and re-sensitize them to DTX. Our results showed that MAGMAS knockdown in DTX-resistant PC3 and DU145 cells, combined with increasing DTX treatments, enhanced sensitivity to DTX. Additionally, pharmacological inhibition of MAGMAS with the novel BT#9 inhibitor in combination with increasing DTX concentrations also enhanced sensitivity to DTX in these cell lines. Our team is conducting further studies to establish MAGMAS as a potential therapeutic target to attenuate the aggressive properties of NEPC. This research is significant in that it could help in the development of new cancer treatments that target MAGMAS to improve patient outcomes. We believe that these findings could provide a promising avenue for future research in the field of cancer treatment.

Medical Training Program (MTP)

MINA RAMSIS BOTROS

MTP PARTICIPANT 2023

Joining the ABC program in the summer of 2016 was a rite of passage that established my aspirations before heading off to college. As I attended the seminars on health disparities found among underserved populations, I couldn't help but think of my own community in the Inland Empire. After graduating from Bloomington High in 2016, I attended UCSD where I received a B.S. in Biochemistry/Cell Biology with a minor in Global Health in the year of 2020. My undergraduate experience exposed me to various healthcare, research, and service opportunities that solidified my passion for medicine. I'm now pursuing that passion as a rising MS2 in the Loma Linda University School of Medicine. This chapter in my life has had its fair share of challenges, but I'm a firm believer this is God's plan to make me the man and physician I'm meant to be. My goal is to become a surgeon who serves the same community that helped me begin this journey. This summer I have been working in the lab of Dr. Erik Behringer. My project involved fecal DNA isolation and tissue dissection to explore the effects of CBD on the gut microbiota and its associations with the pathology of Alzheimer's disease. I give special thanks to Phoebe Chum, Mary Bishara, and Dr. Behringer for the opportunity to learn and grow. I also extend my deepest gratitude to the CHDMM for welcoming me back. I hope to carry their mission with me for the rest of my career.

CANNABIDIOL'S EFFECTS ON GUT DYSBIOSIS IN THE CONTEXT OF ALZHEIMER'S DISEASE PATHOGENESIS

Mina Botros, Rowan Glover, Sarah Meng, Phoebe P. Chum, Mary Bishara, Erik J. Behringer
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Alzheimer's disease (AD) is the most common cause of dementia. Approximately 6.7 million Americans are living with AD; a number that will likely grow to 13.8 million by 2060 barring the development of medical breakthroughs to address this significant public health concern. Previous research has shown that the intestinal microflora takes part in bidirectional communication between the gut and the brain to regulate digestion, metabolism, and inflammation. Hence, imbalances in the gut microbiome may induce inflammation that plays a role in the pathogenesis of AD. Cannabidiol (CBD) has been shown to exhibit inhibitory effects of inflammatory modulators as a potential therapeutic for AD. The aim of this work was to explore whether CBD is able to modulate the gut microbiome composition in AD mice to potentially mitigate intestinal dysbiosis. The Bifidobacterium strain (*Bifidobacterium pseudolongum*) was chosen for its role in reducing pro-inflammatory cytokines. Fecal samples were collected from male wild-type B6129SF2/J and 3xTg-AD animals (age: 4.5-5.5 months) with and without CBD treatment [100 mg/kg daily in raspberry jello, 4 weeks; n=3/group]. Expression of *B. pseudolongum* RNA and DNA, and universal 16s rRNA and DNA were quantified by RT-qPCR. Preliminary results show that *B. pseudolongum* RNA was undetectable throughout groups (average Ct > 38). Further, levels of *B. pseudolongum* DNA were not altered by CBD treatment in either wild-type or AD animal groups. Thus, *B. pseudolongum* does not appear to play a significant role during AD pathogenesis in the mouse model. These data support future application of an -omics approach to comprehensively assess the gut microbiome and which bacterial strains may or may not be impacted by AD pathology while sensitive to cannabinoid treatment strategies.

SHAHAJAHAN JOHIR CHOWDHURY
MTP PARTICIPANT 2023

I'm a Second-Year Medical Student based in Puerto Rico. I am originally from Long Island, NY, where I completed my Undergraduate Degree in Biomedical Engineering at Stony Brook University. I have had a unique experience as a non-Christian intern here at Loma Linda University. I originally heard about this internship through my Seventh-Day Adventist (SDA) friends from medical school. I applied here to enhance my research capabilities as well as to learn more about the SDA culture/faith here. I respect the SDA commitment to maximizing one's health and service to God, and it has been beneficial for myself as a Muslim because for the first time, I did not have to care about dietary restrictions such as Halal Meat given how everything here is vegetarian! Both Faculty and Students are very welcoming and accepting, and I even spent my time here attending Bible Lab and the local Church Service on the Sabbath. I have been offered rides by local Church Members here, and I also attended a game of French Bowling for the first time which was fun! I appreciate how everyone is so passionate to talk about their faith. In fact, I cannot remember the last time I spent so much energy discussing theology in a university-setting. Loma Linda is truly unlike any place on Earth. I am grateful for the mentorship provided by Dr. Danilo Boskovic in investigating platelet inflammation. It has also been a pleasure collaborating with my partners Lidia Malina and Oscar Evan throughout this internship!

LIPOPOLYSACCHARIDE FROM SALMONELLA ENTERICA ALTERS PLATELET FUNCTION IN WHOLE BLOOD

Shahajahan Chowdhury, Oscar Mena, Lidia Malina, Danilo Boskovic
Center for Health Disparities and Molecular Medicine, Biochemistry, School of Medicine, Loma Linda University, Loma Linda, CA

Salmonella enterica is a rod-shaped, gram-negative obligate aerobic bacterium known for causing foodborne illnesses. It is typically found in the mucosal lining of small intestine due to ingestion of contaminated food or water. The innate immune system, including neutrophils and macrophages, represent an early line of defense against foreign pathogens, such as *S. enterica*. In circulation, these leukocytes are functionally dependent on their interactions with other blood components including platelets. Platelets contain multiple receptors associated with a variety of divergent functions including hemostasis and inflammation. Platelets can also release antimicrobial peptides which enhance leukocyte activity. The purpose of this study is to determine how lipopolysaccharides (LPS) derived from *S. enterica* affect platelet functions in whole blood. Whole human blood was drawn by a phlebotomist, from a consented donor, in compliance with the institutional review board (IRB). The blood (80% final) was mixed with varying concentrations of LPS from *S. enterica* (0-300 μg/ml final) in phosphate buffered saline (PBS). Platelet plug closure times were determined by platelet function assay analyzer (PFA-100), using the collagen/ADP cartridges. LPS levels at 0.5 μg/ml and 100 μg/ml were associated with prolonged closure times, while intermediate [LPS]s were associated with less pronounced prolongation. The interactions of this pathogen's LPS with platelets render them refractory to aggregation at particular LPS concentrations, while other concentrations likely lead to different outcomes. Such observations imply the presence of several components in LPS, at least some of which interact with distinct platelet surface receptors. Future work will focus on isolating the particular components of LPS with their specific effects on platelet function, and the identification of the specific platelet surface receptors involved.

AAYMA IRFAN

MTP PARTICIPANT 2023

Driven by a deep-rooted commitment to the field of medicine, I am currently pursuing my Doctor of Medicine degree at the University of California, Riverside (UCR). Building upon a solid foundation in Neuroscience with a Bachelor of Science degree from UCR, I have cultivated a profound fascination with the intricate workings of the human body and the transformative impact healthcare professionals can have on the lives of their patients. Throughout my educational path, I have actively sought out leadership opportunities and engaged in various extracurricular activities that have broadened my horizons and allowed me to contribute meaningfully to my community. Volunteering at an Alzheimer's care center was a pivotal experience that fueled my passion for medicine and research. Witnessing the devastating effects of the disease, I realized the importance of not only alleviating pain but also researching the root causes to prevent such ailments. This led me to join a lab focused on traumatic brain injuries and epilepsy, aiming to understand and prevent neurological diseases from a mechanistic standpoint.

As I continue my medical journey of becoming a physician, I am committed to combining my academic knowledge with the invaluable lessons learned from my service to the Inland Empire. I am determined to contribute to the advancement of medical care, with a special focus on providing compassionate and comprehensive support to patients and their families, particularly those affected by neurodegenerative diseases. I carry the lessons I learned from volunteering experiences with me as I embark on my journey towards becoming a healthcare professional dedicated to providing holistic and compassionate care to those in need.

IMMUNOHISTOCHEMICAL EVIDENCE OF NEURONAL INSULIN SYNTHESIS IN THE HIPPOCAMPAL REGION OF ADULT CYNOMOLGUS MONKEYS (*MACACA FASCICULARIS*)

Aayma Irfan, Tim Distel, Dr. Konrad Talbot
Department of Neurosurgery
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While it has become increasingly clear that some neurons in the adult mammalian brain can synthesize insulin, their frequency and neurochemical identity remains unclear, especially in primates. Answering these questions would clarify if brain-derived insulin has autocrine and/or paracrine functions, different from pancreatic insulin entering the brain. The present study is an initial attempt to clarify that issue by immunohistochemically testing if neurons in the hippocampal region (HR) of the cynomolgus monkey (*Macaca fascicularis*) express not only insulin, but its precursors preproinsulin and C-peptide. Using antibodies selective for these proteins, many neurons in the monkey HR were found immunoreactive for these peptides, especially dentate gyrus granule cells, pyramidal cells of the hippocampal formation, and stellate cells in layer 2 of the entorhinal and perirhinal cortex. Further investigations are required to confirm whether these three proteins are indeed expressed by the same neurons; co-localization studies are essential to establish this relationship conclusively. Subsequent investigations will include testing for insulin gene expression in these cells and ex vivo experiments to explore if depolarization of such cells induces insulin release into the tissue media. Understanding brain-derived insulin could provide valuable insights into the pathogenesis of neurodegenerative diseases like Alzheimer's.

PAOLA FERNANDA RIVERA MORALES
MTP PARTICIPANT 2023

Growing up in Cabo Rojo, Puerto Rico, I encountered a multitude of challenges that stemmed from the daily realities prevalent on the island. Among these challenges were persistent issues like unreliable electricity, frequent natural disasters, an unstable education system, and limited access to healthcare. Through my firsthand experiences, I witnessed the difficulties faced by individuals with limited resources when confronted with these obstacles. It became evident to me that their living conditions profoundly affected their ability to access quality healthcare. This realization deeply compelled me to act. I recognized the urgent need to make a difference and improve the healthcare situation for those in need. My mission took on a deeper significance when I experienced firsthand the impact of illness and the limited access to specialized doctors. As a result, I embarked on my doctoral studies at the Universidad Central del Caribe School of Medicine after successfully completing my Bachelor's degree in Industrial Microbiology at the University of Puerto Rico, Mayagüez Campus. With the guidance of God, I aspire to successfully complete my studies and make a meaningful contribution to accessible healthcare. I am deeply passionate about raising awareness among individuals about preventable diseases and equipping them with the necessary resources to adopt a healthy lifestyle, thus reducing the prevalence of diseases that disproportionately affect the Puerto Rican population.
This summer, I am honored to be a part of Dr. Mary Kearns-Jonker's lab, where we are conducting research focused on studying early cardiovascular progenitor cells. I am immensely grateful for the opportunity to engage in this exceptional research program and extend my heartfelt appreciation to the CHDMM for granting me this valuable opportunity.

COMPARATIVE TRANSCRIPTOMIC ANALYSIS OF ISLET-1+ CARDIOVASCULAR PROGENITOR CELLS: UNRAVELING THE REGENERATIVE POTENTIAL IN NEONATES AND ADULTS FOR ENHANCED CARDIAC REPAIR

Paola Fernanda Rivera Morales, Lorelei Hughes, Mary Kearns-Jonker
Department of Pathology and Human Anatomy
School of Medicine, Loma Linda University, Loma Linda, CA

Considering that heart disease is the leading cause of death worldwide, disproportionately affecting minority groups in the United States, the development of effective cardiac regeneration strategies becomes of utmost importance. To address this pressing issue, the regenerative potential, developmental characteristics, and age-related differences of cardiovascular progenitor cells (CPC) is being studied as a basis for their potential use in cell-based repair. The existing literature acknowledges that neonatal CPC exhibit superior regenerative capabilities compared to adult CPC, yet further investigation is required to fully comprehend the mechanistic basis for their enhanced regenerative ability. In this study, we conducted a transcriptomic analysis of individual Islet-1+ progenitor cell clones isolated from cardiovascular tissue isolated from three neonatal and three adult patients to gain comprehensive insights into age-related transcriptomic differences. We addressed the hypothesis that the transcriptome of neonatal cardiovascular progenitor cells will demonstrate a prevalence of stemness transcripts when compared with the clones derived from adult patients. By comparing lineage markers, spanning from primitive streak to early cardiac progenitors, we were able to determine that our neonatal CPC samples can be staged between day three and day four of cardiac development. Interestingly, the analysis also identified early-stage markers in select adult CPC clones.

Initiative to Maximize Student Development (IMSD)

SHAWNEE ANGELONI
IMSD PARTICIPANT 2023

I have been given the wonderful opportunity of attending the IMSD summer program, which is wonderful throughout the year, however, being able to focus on the program without schoolwork makes it even more manageable. I am a student at Loma Linda University, working on my PhD in the Biomedical Graduate Studies Program. My past education endeavors include a bachelor's degree in microbiology and master's degree in Biology from Cal Poly Pomona. In the future, I hope to work in an industrial research laboratory, preferably working in the field of microbiology on antibiotic resistance research or in a cross-study of microbiology and cancer fields focusing on bacterial-cancer interactions. It is a dream of mine to help contribute towards a treatment or method for helping individuals with antibiotic resistant infections or by expanding our current understanding of microbial-cancer cell interactions. Additionally, my interests have recently expanded to include stem cell research and evaluating their range of plasticity. I work in Dr. Soto's lab focusing on breast cancer research, which includes looking at the role of ITα6 via mammosphere culture and flow cytometric methods. Throughout my academic career I have focused on experiencing new fields in science, so I can be a well-read and experienced interdisciplinary scientist. I want to thank the Soto lab for helping me with my work and helping me learn new techniques in breast cancer research. Without their support I never would have been able to experience all these wonderful opportunities and discover new interests and goals.

THE MICROBIOME AND BREAST CANCER

Shawnee Angeloni, Ubaldo Soto
Division of Microbiology and Molecular Genetics, Department of Basic Sciences, School of Medicine, Loma Linda University, Loma Linda, CA

Recently the importance of the microbiome, defined as microorganisms living in a defined environment, in human health has been demonstrated. Organs or regions such as the buccal space, gastrointestinal tract, and skin have been identified and characterized with several bacteria populations considered to be either healthy or unhealthy, suggesting that some bacteria can be considered positive and others negative for the health of those organs. The role of the microbiome in so-called "sterile organs" is less known, but some data suggest that several have their own microbiome and could play a role in maintaining health. In particular, prostate, pancreas, and breast cancer have identified bacterial signatures that could play a role in cancer development. The effect of the microbiome in "sterile organs" could be dual through bacterial colonization of those organs or by remote signaling coming from the gastrointestinal system. In fact, a bacterial signature has been identified for feces from patients with those cancers. Our laboratory has experience working with breast cancer, including 2D and 3D culture with multiple breast cancer cell line subtypes (luminal, HER2+, and triple negative). In this project we hypothesize that breast cancer cell lines can be influenced by direct and indirect bacterial infection. We are testing our hypothesis *in vitro* by culturing breast cancer cells in 2D and 3D conditions, with direct and indirect presence of bacteria, previously described in literature, as being associated with breast cancer. For that reason, we initially studied the effect of culturing several breast cancer cell lines, directly and indirectly, in the presence of different bacteria to distinguish an *in-situ* from a remote effect. Lastly, we plan to create organoids from normal breast cells and study the effect of bacterial infection in organoid development and potential induction of malignant phenotypes.

NATASHA LE
IMSD PARTICIPANT 2023

I am a fifth year PhD student at Loma Linda University in the Integrated Biomedical Graduate Studies program, with an emphasis in Infection, Immunization, and Inflammation. I graduated with my B.S. in Biochemistry from La Sierra University in 2019, where I was very active in the Chemistry Department as Head T.A., Chemistry Club as Social VP and then President, Spiritual Life Department as a Worship Coordinator, and Music Department as a Percussionist and Pianist for Wind Ensemble and Orchestra. I performed research with Dr. Marco Allard, focusing on exploring salen ligand types inspired from purple-acid phosphatase towards catalyzing pesticides using hydrolysis with zinc complexes.

Here at Loma Linda University, I served as the Worship Music Director for the University for three years and served as Social VP and Vice President of the Basic Sciences Student Council. I perform my research in Dr. Christopher Perry's lab which focuses on translational chemistry and nanotechnology. We are continually working to optimize our protocols for synthesis and characterization of gold nanoparticles, nanorods, and nanostars. We published a paper in the American Chemical Society Omega Journal with our findings. For the rest of my time at LLU, I will continue my research in using nanomaterials for catalysis, antimicrobial activity, and targeted radiation medicine. In the future, I hope to work in industry, specifically in the fields of colloidal nanotechnology or surface chemistry.

GOLD NANOSTARS: NANOPARTICLE TRACKING ANALYSIS AND CATALYSIS

Natasha Le, Christopher Perry
Center for Health Disparities and Molecular Medicine, Division of Infection, Immunity, and Inflammation, Basic Sciences, School of Medicine,
Loma Linda University, Loma Linda, CA

Nanomaterials, regardless of shape, characteristically have at least one dimension limited to <100 nm. At this scale, the physical and chemical properties of the nanomaterial can be drastically affected simply by altering its aspect ratio. Nanomaterials have applications in chemical detoxification, antimicrobial applications, and radiation therapy. Gold nanostars (GNSs) have a high aspect ratio and are of interest for biosensing, catalysis, and therapeutic applications. Our GNS synthesis follows the standard "one-pot" approach whereby a direct reaction in one step is used for the preparation of the inorganic parts while the organic component works as surface capping material or a template. The specific aims of my project are to (1) optimize synthesis and characterization of GNSs, (2) evaluate catalytic activity, and (3) evaluate biocompatibility for future use in targeted radiation-induced DNA damage. Regarding the first aim, the synthesis and characterization have been optimized, the most innovative aspect being the use of a nanoparticle tracking analysis (NTA) instrument for characterization. NTA can measure the GNS concentration, scattering intensity, and hydrodynamic diameter. Size estimates are derived from the particles' Brownian motion based on the Stokes-Einstein equation. The relative scattering intensities as a function of the refractive index can distinguish NPs of comparable diameters. Regarding the second aim, catalytic activity of gold nanoseeds and nanostars is measured using the model reduction of 4-nitrophenol (4-NP) using sodium borohydride. Modifying GNSs with thiolated polyethylene glycol enhanced their catalytic activity. Spectroscopic techniques are used to monitor the catalytic activity. In the future, for the third aim, we will test the biocompatibility of the GNSs with the U87 cell line, performing in vitro experiments.

DANIELLE MALIVERT
IMSD PARTICIPANT 2023

Born to Haitian parents Jean Daniel and Esther Malivert, I am the eldest of three children. I, along with my parents, my younger sister, Daina, and my younger brother, Emmanuel, live in Massachusetts. I matriculated through South Lancaster Academy and Oakwood University where I received a Bachelor of Science in Biomedical Sciences. After I graduated from Oakwood in 2022, I have had the privilege of not only being in the PhD program at Loma Linda University, but also being in the IMSD program. I have learned a lot this past year both in and out of school and lab. I would like to thank the directors of both programs including Dr. Fletcher, Dr. De León, and Dr. Casiano along with Keenan. In addition, I would like to thank the PIs whose labs I have been in, Dr. De León and Dr. Pearce along with their respective lab members, Dr. Jo-Wen, Dr. Alfonso, Francis, Dr. Manuel, Desirelys, James, and Isabella who has been with us in Dr. Pearce's lab this summer. I would also like to thank Lorena, Nannette, and Flor along with my classmates and colleagues in the PhD and IMSD programs.

HYPOXIC MODULATION OF FETAL CEREBROVASCULAR FUNCTION IS MEDIATED BY CHANGES MITOCHONDRIAL NUMBER, SIZE, DISTRIBUTION, AND RESPIRATORY CAPACITY

Isabella Chandroo, Danielle Lonie Malivert, Desirelys Carreon, James William, William Pearce
Center for Health Disparities and Molecular Medicine, Perinatal Biology, School of Medicine, Loma Linda University, Loma Linda, CA

Fetal hypoxia causes major changes in fetal vascular development and functional maturation that precipitate numerous secondary complications, particularly in the cerebral circulation. Although the causes of fetal hypoxia have been widely studied, the mechanisms that govern fetal cerebrovascular responses to chronic intrauterine hypoxia remain poorly understood. This study tests the hypothesis that hypoxia modulates fetal cerebrovascular structure and function through primary changes in the mitochondria of fetal cerebral arteries. We determined the number of mitochondria per cell by measuring the copy number ratio of mtDNA to nuclear DNA using qPCR. We estimated mitochondrial mass by dividing the cellular mass of Succinate Dehydrogenase, as determined by immunoblot, by the number of mitochondria per cell. Oxygen consumption rate was measured using a seahorse analyzer to determine the respiratory capacity per unit weight. By colocalizing SDHA with smooth muscle myosin heavy chain, mitochondrial distribution was examined to find the fraction of mitochondria at the contractile apparatus. We found that in fresh tissue, there was an initial 6% decrease in oxygen consumption rate implying that hypoxia initially decreases the respiratory capacity per unit mass. We also found that hypoxia decreases mitochondrial copy number by 9% while increasing mitochondrial weight by 50%. The respiratory capacity per cell was calculated from the product of number, mass, and OCR. Hypoxia increased colocalization of SDHa with SM-MHC by 18%, suggesting hypoxic promotion of mitochondrial translocation to the contractile apparatus. Under hypoxic conditions, mitochondrial translocation could improve ATP utilization efficiency, particularly in the context of vasoconstriction. These results support our hypothesis that through primary changes in the mitochondria of fetal cerebral arteries, hypoxia modulates fetal cerebrovascular structure and function.

PEDRO T. OCHOA

IMSD PARTICIPANT 2023

As a child I was always intrigued by how things operate which cultivated my passion to learn. I didn't discover my calling in life until a close family member of mine was diagnosed with cancer. I saw my family member go from a healthy individual to a completely different person. Thanks to the hard work of the medical staff and cancer researchers who strive to provide the best treatment for cancer patients, my family member was able to beat cancer. Although this experience was heart wrenching, it ultimately helped in defining my future.

I attended the University of California, Irvine (UCI) where I obtained a Bachelors degree in Biology and Sociology. During my time at UCI, I was fortunate enough to have an opportunity to perform undergraduate research. It was this experience that reminded me of how crucial research is for identifying new treatments. The combination of my previous experience, thirst for knowledge and, passion for cancer biology drove me to pursue my PhD. I am a third year PhD student in the Cancer Developmental, and Regenerative Biology Division in Dr. Carlos Casiano's laboratory. My project aims to further explore the function of the stress oncoprotein LEDGF/p75, and identify inhibitors targeting this protein to determine the effects that this inhibition plays in prostate cancer (PCa) chemoresistance.

SILENCING THE DFS70/LEDGFp75 AUTOANTIGEN REVEALS POTENTIAL ROLES IN LYMPHOCYTE FUNCTION AND IMMUNE EVASION

Pedro T. Ochoa, Evelyn S. Sanchez-Hernandez, Issac Kremsky, Charles Wang, Carlos A. Casiano

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

The dense fine speckled (DFS) antinuclear autoantibody (ANA) pattern is generated by autoantibodies targeting the DFS70 autoantigen, also known as lens epithelium derived growth factor p75 (LEDGFp75). DFS70/LEDGFp75 is a cellular survival protein that is upregulated in cancer cells exposed to environmental stressors, including cytotoxic drugs, and plays an important role in cellular protection against stress-induced cell death. The N-terminus of DFS70/LEDGFp75 contains a PWWP domain which tethers this complex to active chromatin sites. The C-terminus contains the integrase binding domain (IBD), which serves as the binding site for multiple oncogenic transcription factors, such as JPO2, PogZ, Menin, and MLL, that regulate the transcription of cancer-related genes. This study was designed to gain mechanistic insights on the biological functions of DFS70/LEDGFp75 in docetaxel (DTX) resistant prostate cancer (PCa) cells. We silenced DFS70/LEDGFp75 expression in chemoresistant PCa cells via RNA interference, followed by RNA-sequencing analysis. DFS70/LEDGFp75 silencing led to the identification of 970 differentially expressed genes (DEGs), and gene set enrichment analysis (GSEA) analysis revealed a role for this protein in B cell and T cell pathways. We also identified DEGs involved in immune evasion in cancer cells, thus implicating DFS70/LEDGFp75 as a potential target for cancer treatment. As a first step in this direction, we assessed the cytotoxicity of candidate DFS70/LEDGFp75 inhibitors in DTX-resistant PCa cell lines. Our initial results showed increased cytotoxicity upon treatment with specific inhibitors in the presence or absence of DTX. Knowledge of the role of DFS70/LEDGFp75 in immunity may provide new insights into its biological and tumorigenic functions and the significance of its associated autoantibodies.

EVELYN S. SANCHEZ-HERNANDEZ, PhD
IMSD PARTICIPANT 2023

I graduated from California State University, Northridge (CSUN) in 2017 with a Bachelor of Science in Cell and Molecular Biology. Having the opportunity to conduct research as a NIH-MARC scholar at CSUN allowed me to discover my passion for conducting biomedical research. Also, observing my father battling non-Hodgkin's lymphoma in 2014, made me realize the importance of biomedical research in our society. Many patients' lives depend on the answers that scientists seek in their laboratories. I want to contribute to increasing our collective understanding of complex diseases such as cancer, leading to the development or improvement of treatment strategies and ultimately save lives.

I was born in El Salvador and immigrated to the United States at the age of 14. I am the first in my family to pursue a career in biomedical research and earn a doctorate degree. This may I graduated from Loma Linda University School of Medicine with a PhD in cancer biology. My dissertation research project focused on studying the contribution of the glucocorticoid receptor (GR) and LEDGF/p75 to prostate cancer (PCa) chemoresistance. During my graduate studies I've had the privilege to be mentored by scientists that have guided me and encouraged me to become the best version of myself including my PI, Dr. Casiano. I am grateful for the opportunities that the IMSD program has provided for my development as a scientist. I am thrilled to start my post-doctoral training at Sanford Burnham Prebys Institute in La Jolla this September.

GLUCOCORTICOID RECEPTOR REGULATES AND INTERACTS WITH LEDGF/p75 TO PROMOTE DOCETAXEL RESISTANCE IN PROSTATE CANCER CELLS

Evelyn S. Sanchez-Hernandez, Pedro T. Ochoa, Tise Suzuki , Greisha L. Ortiz-Hernandez, Juli J. Unternaehrer, Carlos J. Diaz Osterman, Shannalee R. Martinez, Isaac Kremsky, Charles Wang, and Carlos A. Casiano

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

Prostate cancer (PCa) is the second leading cause of cancer deaths in the U.S. Patients with advanced PCa fail to respond to anti-androgen enzalutamide treatment and docetaxel chemotherapy. The glucocorticoid receptor (GR) is a transcription factor implicated in therapy resistance. Previously, we demonstrated that glucocorticoids, which activate GR, upregulate the chemoresistance-associated transcription co-activator LEDGF/p75 in PCa cells. We hypothesized that GR regulates and interacts with LEDGF/p75 to promote PCa therapy resistance. Genetic silencing of GR in chemoresistant PCa cells decreased LEDGF/p75 expression, and GR upregulation in enzalutamide-resistant cells correlated with LEDGF/p75 upregulation. Additional studies indicated that GR and LEDGF/p75 form a complex in chemoresistant cells, and their co-targeting resensitized these cells to docetaxel. RNA-sequencing of chemoresistant cells revealed a GR-LEDGF/p75 transcriptional overlap linked to therapy resistance. These studies implicate the GR-LEDGF/p75 transcriptional network in PCa therapy resistance and provide a rationale for developing novel therapeutic strategies to treat advanced PCa.

KAYLA SANCHEZ
IMSD PARTICIPANT 2023

I am a third year PhD student at Loma Linda University in the Neuroscience, Systems Biology, and Bioengineering program. Prior to LLU, I obtained my Bachelor of Science in Biochemistry and Molecular Biology from California Baptist University. After my undergraduate studies, I was privileged to work in home health where I specialized in Alzheimer's and dementia care. The experience not only taught me the importance of patience and kindness, but I was able to discover my passion and curiosity for neuroscience. I am grateful for the opportunity to participate in LLU's IMSD and Students for International Missions programs. These opportunities helped me understand the impact of racial disparities in science and health care. It is my goal to continue the mission through pursuing a career in biomedical research while further mentoring students. I am completing my PhD in the laboratory of Dr. Soriano. The lab is focused on Niemann-Pick disease type C (NPC), while my specific project is researching the link between neurosteroid dysfunction and calcium signaling. My deepest gratitude goes out to my primary advisor, *Dr. Salvador Soriano,* who has provided me with guidance, mentorship, and the space to grow as a scientist. My thanks go out to members of the lab, Andrew Tolan and Jacob White, for their continuous support and encouragement.

NEUROSTEROID REGULATION OF MITOCHONDRIAL CALCIUM SIGNALING IN NIEMANN-PICK TYPE C DISEASE

Kayla Sanchez, Jacob White, Andrew Tolan, and Salvador Soriano
Department of Pathology and Human Anatomy, Loma Linda University, School of Medicine, Loma Linda, CA

Niemann-Pick Disease type C (NPC) is a rare neurodegenerative disorder that affects 1 in 120,000 births worldwide. NPC is caused by mutations in either Npc1 or Npc2 genes, with Npc1 mutations accounting for 95% of cases. The Npc1 and Npc2 genes encode for the NPC1 and NPC2 proteins, which are believed to be responsible for cholesterol transport from the late endosome/lysosome to other compartments of the cell. Loss of NPC protein function results in intracellular cholesterol accumulation, calcium dysregulation, oxidative stress, and lipid peroxidation. These mutations contribute to NPC pathogenesis. The mechanisms by which these mutations contribute to NPC pathogenesis are not well understood. Particularly, cerebellar Purkinje cells are sensitive to NPC1 mutations. Purkinje cells serve multiple functions to optimize motor coordination, learning, memory and, uniquely, are one of few types of cells with neurosteroidogenic properties. Within Purkinje cells, neurosteroid synthesis occurs in the mitochondrial inner membrane relying on cholesterol as a precursor. Npc1-/- models demonstrate a decrease in neurosteroid synthesis, due to unavailability of cholesterol. Deficiencies in cholesterol transport are significant because neurosteroids play a critical role in mitochondrial calcium homeostasis. Thus, we hypothesize that impaired neurosteroidogenesis in Purkinje cells may contribute to cell death in NPC through dysregulated calcium signaling in mitochondria. To address our hypothesis, we utilized a genome-wide cerebellum transcriptome analysis of pre-symptomatic Npc1-/- mice and age-matched wild-type mice. We report there Is significant downregulation in the expression of genes involved in neurosteroidogenic and calcium homeostasis pathways in Npc1-/- versus healthy mice. Our findings support a significant role for neurosteroid synthesis dysregulation and mitochondrial calcium dyshomeostasis in NPC pathogenesis.

KRYSTAL SANTIAGO
IMSD PARTICIPANT 2023

I was born in Mayaguez, PR, where my parents taught me that even though success was hard, if I set my mind to it and worked for it, I could achieve it. With this lesson in mind, aiming to obtain academic excellence with the help of God is one of my priorities. Because of this, I have put a lot of effort into becoming the best student I can be. I graduated from the University of Puerto Rico with a BS in Industrial Microbiology and I am now part of the IMSD program as a fourth-year student, where I will further my education by earning a PhD. I learned to play the flute and I also trained my voice which allowed me to be the recipient of different scholarships throughout my undergraduate studies. After Puerto Rico suffered from hurricane Maria, my friends and I helped rebuild houses and feed the homeless. In order to be a force for positive change, I selected Dr. Casiano and Dr. Almaguel, experts in health disparities, to be my co-advisors. This way I could focus my research on diseases that affect underrepresented communities. For my research, I am studying the role of Enolase, a cytoplasmic enzyme, and its effect on the proliferation, migration, invasion and metastasis of Prostate Cancer.

ENOLASE-1 AS A NOVEL THERANOSTICS TARGET FOR NEUROENDOCRINE PROSTATE CANCER

Nyana Iniguez, Krystal Santiago, Alfonso Duran, Kristen Whitley, Carlos A. Casiano, Frankis Almaguel
Center for Health Disparities and Molecular Medicine, School of Medicine, Cancer Center, Loma Linda University, Loma Linda, CA

Prostate cancer (PCa) is American men's second most common cancer. Although taxane-based chemotherapy is the last line of defense in men with advanced PCa, it fails due to chemoresistance. The protein-specific membrane antigen (PSMA) has been an effective target for the imaging and therapy of advanced PCa. Although PSMA radioligand therapy (PSMA-RLT) is a theranostics option for men with advanced PCa, about 30% have a limited response due to neuroendocrine-like PCa (NEPC), which lacks PSMA expression. A promising alternative is the glycolytic enzyme enolase (ENO), which localizes to the cell surface in advanced tumors. Preliminary studies demonstrate that chemosensitive NEPC PCa cell lines express both ENO-1 and ENO-2; however, docetaxel-resistant NEPC cells only express ENO-1 and have a metabolic vulnerability due to the loss of ENO-2. We hypothesize that ENO-1 is expressed on the surface of NEPC cell lines and can be targeted with small molecule inhibitors (SMIs) that could be used as theranostics agents. Additionally, we have observed changes in the expression and localization of ENO-1 in NEPC cell lines under different glucose concentrations. Our experiments show that under high glucose conditions, found on metabolically active metastatic tumors, ENO-1 is highly expressed on the cell surface, making it an advanced and practical target for theranostics. However, low glucose conditions inhibit the activity of the c-MYC oncogene resulting in decreased production of ENO-1 and increased production of MBP1, the small splice variant of ENO1 that blocks the transcriptional activity of c-MYC. Our efforts to identify ENO-1 surface expression on NEPC cell lines entail using immunofluorescence microscopy, membrane fractionation analysis, and flow cytometry. We are also evaluating the cytotoxicity of SMIs targeting ENO-1 in chemoresistant NEPC cell lines using viability assays and Hoffman Modulation Imaging. Our long-term goal is to identify an alternative treatment for patients with NEPC by establishing ENO-1 as a novel theranostics target.

JULIO SIERRA
IMSD PARTICIPANT 2023

My parents immigrated from Mexico looking for opportunities to better their lives and, consequently, my life. As they struggled to acculturate, they instilled in me the importance of education and hard work so that I could successfully overcome the barriers they faced. I enjoy learning, problem-solving, and challenging myself, which motivated me to pursue undergraduate studies in biomedical engineering. During that time, I gained experience collecting data for an animal study, piquing my interest in pursuing research.

I am a first-year PhD. student in the Neuroscience, Systems Biology, and Bioengineering program at Loma Linda University School of Medicine. As a first-generation college student, I understand the difficulties of navigating post-secondary education without a support system. Being involved with the IMSD and the CHDMM programs has provided a sense of community and allows me to play a role in encouraging underrepresented students to pursue higher education. I am grateful to be mentored and encouraged by my PI, Dr. Johnny Figueroa, my peer mentor, Timothy Simon, and many others for helping me develop as a scientist. I will continue utilizing my personal and academic experiences to reduce health disparities. I expect to contribute by investigating how environmental factors, such as diet, affect neurobiological pathways associated with resiliency or susceptibility to stress during adolescence.

ADOLESCENT OBESOGENIC ENVIRONMENT ALTERS EATING PATTERNS IN MALE RATS UNDERGOING HIGH-FAT DIET WITHDRAWAL

Julio Sierra, Timothy Simon, Johnny D. Figueroa
Center for Health Disparities and Molecular Medicine, Department of Basic Sciences,
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Early exposure to obesogenic environments, characterized by access to high-fat diets and stress, increases stress susceptibility, leading to maladaptive coping habits. However, the behavioral alterations connecting obesogenic environments to dysregulated eating still need to be better understood. This study aimed to determine whether early access to an obesogenic diet enhances behavioral vulnerabilities to binge eating in male rats. **We hypothesized that exposure to an early-life obesogenic diet would increase susceptibility to psychosocial stressors and enhance binge-eating-like behaviors**. Male adolescent Lewis rats (n=40) were given *ad libitum* access to either a high-saturated fat Western-like diet (WD, 41% kcal from fat; n=20) or a matched control diet (CD, 16% kcal from fat; n=20). After 4 weeks, each group was further split into exposed (CDE, WDE; n=8) or unexposed (CDU, WDU; n=12) groups. Exposed groups underwent predator exposure followed by 10 days of social instability. Immediately following the psychosocial stress challenge, all groups were switched to a dieting schedule consisting of intermittent access (24 hr/week) to the WD to determine binge-eating-like behaviors. Food consumption and body weight measurements were recorded weekly and analyzed using GraphPad Prism 9 statistical software. We found that acute stress decreased food consumption in WD rats ($p<0.0007$) relative to controls, supporting a heightened susceptibility to stressors following chronic early-life obesogenic diet consumption. While WD rats gained more weight than controls and exhibited increased food consumption after weekly reintroductions to the WD, we did not observe significant binge eating behaviors during the light phase. We conclude that although early access to an obesogenic diet is insufficient to induce a binge-eating phenotype in male rats, it can negatively impact their eating behaviors when challenged with severe acute stress.

TIMOTHY SIMON
IMSD PARTICIPANT 2023

I am a third-year Neuroscience PhD student here at Loma Linda University (LLU). My research focuses on the effects of psychosocial stress and diet on adolescent neurodevelopment and why some individuals tend to be more resilient or vulnerable to stress-induced eating behaviors. Additionally, I am exceedingly interested in applying my newfound knowledge to enhance ethnic diversity in my scientific environment. As I engage in some of Neuroscience's biggest questions, I am continually amazed at how much more there is to learn. Every discovery and scientific discussion with my peers propels my curiosity forward, launching me into a world in need of further exploration.

Currently, my plan is to complete my Neuroscience PhD in 2024 and then transition to a postdoctoral fellowship position enabling me to pursue high-caliber research while refining my teaching skills. My mentor, Dr. Johnny Figueroa, has inspired me to do all things with excellence while eagerly sprinting toward my goals. Apart from research, I greatly enjoy time with family and friends, reading, and finding new breakfast spots. I recognize that the path ahead of me is brimming with twists and turns, and countless uphill challenges, but more importantly, it is likewise abounding in captivating views and people to enjoy them with.

"But he who dares not grasp the thorn, should never crave the rose." – Anne Bronte

SEX-SPECIFIC ALTERATIONS IN EMOTION AND HOMEOSTATIC NEUROCIRCUITS UNDERLYING STRESS-INDUCED BINGE EATING-LIKE BEHAVIORS

T. Simon*, P. Ontiveros-Ángel, B. Noarbe, M. Febo, J.H.P. Collins, A. Obenaus, J. D. Figueroa, Center for Health Disparities and Molecular Medicine, Dept. of Basic Sciences, Loma Linda University, Loma Linda, CA; Pediatrics, University of California, Irvine, CA; Psychiatry Dept., Univ. of Florida, Gainesville, FL; Univ. of Florida, Gainesville, FL

Adolescent stress is a risk factor for frequent and recurrent binge eating episodes later in life. Stress-induced binge eating disproportionately affects females, yet brain circuits underlying this susceptibility are unknown. This study aimed to identify neural circuits contributing to sexual dimorphisms in a rat model of maladaptive eating. We hypothesized that neuroimaging would enhance the detection of stress-induced changes in emotion-related brain circuits driving maladaptive eating. Adolescent Lewis rats (n = 48, half females) were allocated into one of two groups: exposed or unexposed. The exposed group endured a psychosocial stress (PSS) model, including 30 consecutive days of social isolation and two predator exposures. Following PSS, a group of rats was given intermittent access (once weekly for 24 h) to a Western-like high-fat diet (WDI) to promote binge-like eating. Brain tissue was harvested at adulthood and prepared for ultra-high resolution MRI (17.6T)/diffusion tensor imaging (DTI). We found that female rats were more susceptible to stress-induced binge-like eating than males. DTI findings indicated that brain regions regulating food consumption and energy homeostasis, including the hippocampus (HPC) and hypothalamus (HYP), were especially sensitive to adolescent stress, evidenced by significant microstructural changes. Rats exposed to PSS/WDI exhibited divergent changes in the fractional anisotropy of the HPC (decrease in males, increase in females) and the HYP (increase in males, decrease in females) compared to sex-matched unexposed controls. Exposure to adolescent stress negatively affects the maturational trajectories of critical neural circuitry underpinning maladaptive eating. These results deepen our understanding of sex differences in the brain that may link early-life stress to eating disorders.

FRANCIS ZAMORA
IMSD PARTICIPANT 2023

Previous to coming to Loma Linda University, I attained my Masters in Anatomy & Neurobiology from Boston University, where I discovered my curiosity for the neuroscience field. I yearned for the opportunity to continue developing a thorough understanding of the nervous system and to develop the skills needed to make my own inquires, investigate biomedical questions, and contribute to closing the gaps in knowledge in the scientific literature. I am grateful to be part of the IMSD program, as it has provided me with the resources and tools to earn my PhD and fulfill my dream of becoming a neuroscientist. This fall, I will be a fourth-year PhD student in Dr. Marino De León's laboratory. My topic of research focuses on investigating the neuroprotective mechanisms of docosahexaenoic acid (DHA) in Schwann cells during lipotoxicity, which has implications for treating nerve injury and neuropathic pain. I am thankful for Dr. De León and Dr. Jo-wen Liu for their mentorship and guidance as I continue my academic journey.

DOCOSAHEXAENOIC ACID INHIBITION OF PALMITIC ACID-INDUCED LIPOTOXICITY INVOLVES REGULATION OF AUTOPHAGY IN IMMORTALIZED SCHWANN CELLS

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Palmitic acid-induced lipotoxicity (PA-LTx) is implicated in painful peripheral neuropathy due to its detrimental effects on nerve cells. Our lab's previous studies have shown PA-LTx in Schwann cells involves activation of ER stress, mitochondrial depolarization, and apoptosis. Co-treatment of immortalized Schwann cells (iSCs) with docosahexaenoic acid (DHA) reverses PA-LTx effects. Because autophagy dysregulation is observed in neuropathic pain, this study aims to investigate the role of autophagy during PA-LTx in iSCs. Here, iSCs were treated with 300μM PA: 150μM BSA for 24 or 48 hours to induce LTx. iSCs were also co-treated with 50μM DHA to inhibit LTx, Chloroquine (CQ) to inhibit autophagic flux, or Rapamycin to induce autophagy. Western Blot measured levels of autophagy-related proteins LC3-II and p62/SQSTM1, and stress-response fatty-acid binding protein 5 (FABP5). Real-time qPCR measured expression of autophagy-related gene 12 (ATG 12) and FABP5, and a WST-1 assay evaluated cell viability. We confirmed PA decreased cell viability, while DHA co-treatment fully protected against PA-LTx-induced apoptosis. CQ did not affect cell viability, however, PA+CQ exacerbated PA-LTx effects. Interestingly, CQ, which inhibits autophagosome-lysosomal fusion, slightly reduced DHA's neuroprotection at 24 hours and significantly reduced it by 48 hours, suggesting the importance of autophagic clearance. PA increased LC3-II and ATG 12 expression, indicating autophagy activation. However, PA also dramatically increased p62 levels, suggesting inhibition of autophagosomal content degradation. Conversely, DHA reduced PA-induced elevation of p62 and LC3-II levels. As our positive control, Rapamycin decreased p62 levels. Lastly, PA and CQ increased FABP5 levels, which were suppressed by DHA. These findings suggest PA-LTx causes abnormal autophagic activity. We propose DHA inhibits PA-LTx in part by restoring healthy autophagic flux, which is consistent with DHA's neuroprotective action in nerve cells.

Summer Undergraduate Research Fellowship (SURF)

SHARON ASARIAH
SURF PARTICIPANT 2023

I have always been intrigued by the human body's complexities and how diseases are diagnosed and treated; cancer has particularly interested me due to the cell's complex and unpredictable nature. These factors caused me to major in Biomedical Sciences at California Baptist University. While at CBU, I completed a three-semester research project that focused on developing a genetically modified mosquito pesticide that enhanced the toxic properties of two bacterial strains. This experience sparked an interest in lab work, causing me to pursue research at Loma Linda University.

In addition to my major, I am pursuing a minor in music which has allowed me to professionally develop my passion for singing through private voice instruction and choral performances across the Inland Empire. Outside of academics, I serve weekly as a Sunday School leader at my local church and intern at a Sports Clinic where I treat athletes with varying injuries and as I assist in injury recovery, allowing me to gain experience in direct patient care.

I would like to thank Dr. Unternaehrer, Daniel Zecena, and Yeonkyu David Jung for their guidance and willingness to assist in the lab. This experience has allowed me to learn so much about the study of oncology, and I cannot thank Dr. Unternaehrer enough for allowing me to participate in her pioneering research this summer!

DETECTING RADIATION INDUCED AGRESSIVENESS OF GLIOBLASTOMA AND OVARIAN CANCER CELL LINES WITH RT-qPCR

Sharon Asariah, Yeonkyu Jung, Daniel Zecena, Ann Morcos, Antonella Bertucci, Marcelo Vazquez, Tise Suzuki , Aaron Keniston, Ashley Antonissen, Jaqueline Coats, Juli Unternaehrer
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Ovarian cancer is the fifth cancer mortality and the seventh most common cancer in women. Additionally, 70% of patients experience a recurrence following primary tumor treatment. Similarly, glioblastoma is considered one of the most aggressive forms of cancer, as 75% of patients experience a recurrence. Since radiation is the primary treatment for glioblastoma and some advanced ovarian cancer cases, it is necessary to determine if it causes secondary tumors and the characteristics of the cells that could form them. To do this, the glioblastoma cell lines, LN18 and T98G, and the ovarian cancer cell lines, OVCAR8, and OVSAHO, were irradiated and harvested ten days later for RNA extraction. This RNA was then purified, converted to cDNA, and used to complete RT-qPCR to measure the gene expression of EMT *(ZEB1, ZEB2, SNAI1, and TWIST1)* and stemness genes *(POU5F1, SOX2, LIN28A)* in each cell line relative to the mock irradiated cells. It was hypothesized that irradiation would induce aggressiveness via the upregulation of EMT and stemness genes. The results obtained proved this hypothesis. However, an upregulation of the genes was not seen to be dependent on an increase in radiation dosage. LN18 was the sole cell line to exhibit this phenomenon. In the OVCAR8 cell line, most EMT and stemness genes were upregulated, while only EMT genes were upregulated in the OVSAHO samples. Finally, *SNAI1, TWIST1,* and stemness gene expression increased in the 2Gy and 4Gy samples in the T98G cell population. In conclusion, photon radiation administered at 2Gy and 4Gy dosages induces aggressiveness in all cell lines via EMT and stemness gene upregulation.

ADYA CHERUKURI
SURF PARTICIPANT 2023

To say that I have always been interested in science would be a lie. In fact, for the majority of my life, I hated the subject altogether. It wasn't until I reached my junior year of high school that I realized the beauty of biology and began to appreciate the artful way our body systems work together to keep us functioning. To explore the intricacies of biology more in depth, I found myself drawn more and more to research. I am currently a junior neuroscience major and psychology minor at Texas A&M University. My end goal is to become a physician and continue with research throughout my journey in medicine.

Through conducting research, I realized that whether we see our desired results or not, each and every experiment we do contributes to society. There is excitement in success, there is reflection in failure, but all through it, there is a zeal to keep learning. My passion for research is what makes the SURF program so special to me. My research this summer focused on characterizing the effects of two different therapies, administration of heparin-binding epidermal growth factor (HB-EGF) and vagal nerve stimulation, on rodents induced with necrotizing enterocolitis (NEC).

I would like to thank Dr. Chris Wilson's lab for being incredible mentors and colleagues, for teaching me a wide range of new scientific concepts/techniques, and for creating a research experience I will never forget.

THE ROLE OF HEPARIN-BINDING EPIDERMAL GROWTH FACTOR ADMINISTRATION ON TOLL-LIKE RECEPTOR 4 EXPRESSION IN NECROTIZING ENTEROCOLITIS INDUCED LUNG INJURY

Adya Cherukuri, Beverly A. Giang, MD, Christopher G. Wilson, PhD
Department of Pediatrics & Lawrence D. Longo MD Center for Perinatal Biology, Loma Linda University, Loma Linda, CA

Necrotizing enterocolitis (NEC) is a life-threatening gastrointestinal disease that largely affects premature neonates and has a mortality rate between 10–50%. NEC is associated with widespread intestinal inflammation mediated by toll-like receptor 4 (TLR-4) and with lung injury. Heparin-binding epidermal growth factor (HB-EGF) has previously been shown to decrease NEC induced intestinal injury in a murine model. We tested the hypothesis that TLR-4 is more highly expressed in lung tissue exposed to the NEC model and that prenatal administration of HB-EGF affects expression of TLR-4. Mice were divided into three treatment groups: control, NEC only, and HB-EGF. Pregnant mice were given HB-EGF two hours before birth via Cesarean section. Pups in both the NEC and HB-EGF groups were exposed to a NEC protocol consisting of hypoxia, hypothermia, hypertonic feeds, and lipopolysaccharide injection. Pups were sacrificed when they showed clinical signs of NEC. Lung tissue was harvested, and enzyme-linked immunosorbent assay (ELISA) was performed to measure TLR-4 protein levels (ng/mL) across all three treatment groups (n=15). Our results show that TLR-4 expression is significantly greater in the NEC ($p=0.0004$) and HB-EGF ($p=0.0059$) groups when compared to control mice, suggesting that TLR-4 plays an important role in the development of NEC induced lung injury. No significant difference in TLR-4 expression was observed between the NEC and HB-EGF groups. More variability of TLR-4 expression was seen in the HB-EGF group, suggesting that further studies are required to determine the relationship between TLR-4 expression and the role that HB-EGF plays in modulating NEC. Our current findings suggest that administration of HB-EGF to pregnant mothers may reduce risk of developing NEC induced lung injury.

ELVA GARCIA
SURF PARTICIPANT 2023

As a child I was fascinated by childbirth and my dream was to become a "baby doctor". However, in seventh grade, my science teacher motivated me to become a scientist. Although my interests have evolved over time, I am currently a Junior in college, and I still find myself drawn to the idea of being both a doctor and a scientist. I attend La Sierra University as a Biomedical Science and premed major. These courses helped me discover a passion for molecular biology. Although I still plan on going to medical school, this newfound interest has made me consider research-based institutions and the possibility of pursuing an MD/PhD program. Through the SURF program, I had the opportunity to work in Dr. Goulopoulou's lab. Their research revolves around maternal health, particularly preeclampsia and hypoxia. I contributed to a project studying the impact of circulating mitochondrial DNA in pregnant rats. This experience allowed me to combine my interests in maternal health and molecular biology while gaining valuable lab skills. I would like to express my sincere gratitude to Dr. Goulopoulou for welcoming me into her lab, Gabby for teaching me everything there is to know about the lab, Dr. Silva for guiding me throughout my project, and Dr. Hula for patiently answering my questions.

CIRCULATING MITOCHONDRIAL DNA TRIGGERS PLACENTAL INFLAMMATION: IMPLICATIONS FOR PREGNANCY COMPLICATION AND PREECLAMPSIA

Elva Garcia, Renée Oliveira da Silva, Gabrielle Kelly, Styliani Goulopoulou
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Placental inflammation is implicated in various pregnancy complications, including preeclampsia, which is a pregnancy-specific hypertensive disorder. Circulating damage-associated patterns, such as mitochondrial DNA (mtDNA), are released because of tissue damage and cell death and may serve as triggers to placental inflammation. We tested the hypothesis that circulating mtDNA triggers placental inflammation through activation of toll-like receptor 9 (TLR9) signaling. TLR9 is activated by DNA containing unmethylated CpG motifs that are more prevalent in bacterial DNA and mtDNA but rare in nuclear DNA. To test our hypothesis, we treated pregnant Sprague Dawley rats (gestational day: 14-15, term=22-23) with mtDNA or saline (control) via intravenous injection. The rats were euthanized 4 hours after treatment and placental samples were collected. We measured gene expression of inflammatory cytokines and TLR9 using qPCR. In addition, proteins extracted from the samples were subjected to Western blot analysis to evaluate the expression levels of nuclear factor kappa B (NFκB). Our findings reveal that the placental samples of rats treated with mtDNA had higher expression of TLR9 ($p=0.0001$), increased levels of pro-inflammatory cytokines tumor necrosis factor alpha (TNF-α) ($p=0.013$), interleukin (IL)-6 ($p=0.0002$), IL-1β ($p=0.015$), and reduced levels of anti-inflammatory cytokine IL-10 ($p=0.006$) as compared to placental samples from saline-treated rats. Furthermore, the phosphorylated form of NFκB was higher in placentas from the mtDNA treated group compared to controls ($p=0.033$). These results suggest that extracellular mtDNA triggers placental inflammation. On-going studies determine whether this inflammatory response is due to activation of the TLR9 pathway. Understanding of the mechanisms underlying the release of mtDNA and govern the placental inflammatory response may lead to development of new therapeutic interventions aimed at improving maternal and fetal outcomes in pregnancy complications.

WILLIAM GEYMAN
SURF PARTICIPANT 2023

I had the opportunity to explore what it means to be a scientist through LLU's SURF program in 2022. I had no idea the impact this program would have on my future career path and personal life. It is a privilege to continue my journey and be back this summer.

I attend Point Loma Nazarene University (PLNU) in San Diego, where I am studying biology and psychology. It is my professional goal to become a physician and to learn how to properly integrate biology, psychology, and theology into my eventual practice. This is how I see myself contributing to LLU's mission to make man whole.

I am passionate about the connection between science and theology and have had the opportunity to be president of PLNU's science and religion club for two years. We believe, as St. Augustine wrote, that God has provided us with two books: the Book of Nature and the Book of Scripture. We see these speak a single and elegant truth on God's beautiful creation. In my free time, I also love to play music, hike, and read.

I would like to thank Dr. Arlin Blood and his lab for welcoming me back this summer and for challenging me to be a good and truthful scientist. I would specifically like to thank Dr. Karina Mayagoitia for her kindness and mentorship over the past two years.

EFFECT OF VAGAL DENERVATION ON PULMONARY ARTERY CONTRACTILE PHENOTYPE IN FETAL SHEEP

William Geyman, Karina Mayagoitia, Chris G. Wilson, Arlin B. Blood
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Interoceptive nerves detect and relay signals between the organs and the central nervous system (CNS). Interoceptive neural circuits are present in the lung throughout fetal development, potentially contributing trophic input for both lung and brain growth and development. These circuits establish an integral feedback loop between the peripheral system and the CNS. The vagus nerve constitutes a major conduit for interoceptive communication between lung and brain. Proper lung vascularization is important for normal lung physiology and the specific role of the vagus nerve in this process is unknown. Vascular smooth muscle can have either a contractile or proliferative phenotype. One way of assessing this phenotype is by measurement of the colocalization of α-actin and myosin II, a hallmark of the contractile phenotype. To help elucidate the importance of the vagus nerve on contractility in pulmonary arteries in fetal sheep, sham or surgical bilateral vagotomies were performed in canalicular and saccular stages of lung development. Fetal sheep were then returned to the uterus and allowed to complete gestation. The lambs were then delivered via c-section, anesthetized, mechanically ventilated, and subjected to a series of respiratory challenges. Fetal sheep were then sacrificed, and lung tissue samples were collected. Preliminary immunohistochemical analysis of α-actin and myosin II colocalization in pulmonary arteries remains inconclusive on whether vagotomy significantly increases levels of contractile phenotype. Further validation of the colocalization analysis process is underway and will be applied to a larger number of samples from each group in the future.

ROWAN GLOVER
SURF PARTICIPANT 2023

Science has always been a big interest that has only grown with the aid of my family, teachers, and peers. Investigation into developing treatments led to my exploration of research in biotechnology, biochemistry, medicinal chemistry, and biomedical research. This ultimately led me to this summer where I have had the opportunity to work in Dr. Erik Behringer's lab. Participating in the SURF program has taught me new laboratory skills and techniques that I will use in future research. In the fall, I will be starting my senior year at the University of Redlands in Redlands, California where I am majoring in Biochemistry and Molecular Biology. I am also pursuing a minor in Saxophone performance, and enjoy playing in the wind ensemble and jazz band, as well as in quartets. I also enjoy working as an Organic Chemistry tutor at my university. I plan on pursuing a PhD. in Chemical Biology or Medicinal Chemistry in order to work in a lab focused on the synthesis of biologically active compounds that can be used as therapeutic treatments for diseases like cancer. I would like to thank Dr. Erik Behringer for welcoming me into his lab and Phoebe Chum, Mary Bishara, Fritz Miot, Sarah Meng, and Ankita Hooda for their teaching and collaboration over the summer.

CANNABIDIOL INCREASES LIVE *AKKERMANSIA MUCINIPHILA* ACTIVITY DURING EARLY ALZHEIMER'S DISEASE: POTENTIAL THERAPEUTIC INTERACTION OF CANNABINOIDS AND THE MICROBIOME

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Alzheimer's Disease (AD) is the leading cause of dementia, with an estimated 22% of people over 50 years of age exhibiting preclinical, prodromal, or advanced AD. Currently, there is no effective treatment for reversing early or late pathogenesis of AD. Cannabidiol (CBD), a non psychoactive component of the cannabis plant, has emerged as a possible treatment for epilepsy, multiple sclerosis, and other neurological disorders. CBD also modulates interactions among the endocannabinoid system and the gut microbiome as a potential treatment strategy for the development of AD. In particular, *Akkermansia muciniphila* of the family *Verrucomicrobia* may be a potential therapeutic target for AD due to its effects of a protected intestinal epithelial barrier, reduced blood endotoxin levels, and ameliorated insulin resistance. Indeed, mice treated with *A. muciniphila* show a decrease in amyloid-β accumulation and cognitive deficits associated with AD. Thus, our hypothesis is that CBD promotes the activity of *A. muciniphila* in animal models of AD. Fecal samples were collected from male wild-type B6129SF2/J and 3xTg-AD animals (age: 4.5-5.5 months) with and without CBD treatment [100 mg/kg daily in raspberry jello, 4 weeks; n=3/group]. Expression of *A. muciniphila* RNA and DNA, and universal 16s rRNA and DNA were quantified by RT-qPCR. Preliminary results show that CBD elevated *A. municiphila* RNA expression by 1488±932-fold in AD (versus 52±21-fold for vehicle), but not in CBD-treated wild-type mice (36±15-fold versus vehicle, 35±21). *A. municiphila* DNA changes were similar throughout respective wild-type and AD groups regardless of CBD treatment. In conclusion, CBD may be an effective treatment strategy for AD pathology with live *A. muciniphila* of the gut microbiome playing a role.

ELIJAH HAYNAL
SURF PARTICIPANT 2023

During my freshman year of college, my TA for general biology noticed my enjoyment of the lab and suggested that I consider a summer research program with one of the professors at the marine lab. I was lucky enough to be accepted, and I was hooked over that summer. I credit that experience with my continuing interest in research today.

I have lived in Portland, Oregon for most of my life and am currently attending Walla Walla University in southeastern Washington. Next spring, I will graduate after completing my studies in biology and mathematics. My research interests include lab hardware and software design, mathematical modeling, and radiation oncology. After college, I hope to enter medical school in a program that allows me to continue engaging with research. I personally cannot imagine a life away from continued research and learning, I would feel like I was setting aside part of the gift of life if I stopped stretching the boundaries of what I know.

During my time outside of classes I work as a TA in the biology department and a peer mathematics tutor for university students. In my free time, I enjoy playing with the University Men's Volleyball Club, participating in symphony orchestra as a double bassist, skiing, and volunteering at the local hospital.

My special thanks are due to Dr. Schulte for welcoming me into his lab this summer. I have had a great experience and acquired valuable skills that will be useful far into my future.

CHARACTERIZATION OF A 2D IONIZATION TRACK DETECTOR FOR VOLATILE ORGANIC COMPOUND DETECTION

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Volatile organic compounds (VOCs) are an emerging biomarker in cancer detection. Gas chromatography-mass spectrometry is currently used in VOC detection, but a quicker and less expensive method is desirable. This Summer Research project aimed at characterizing an in-house developed VOC ion detector for its ability to detect VOCs in a gas mixture and developing software for detector signal analysis. The detector exposes a low-pressure gas mixture of propane and VOCs to a collimated beam of ionizing alpha particles. The resulting positive gas ions drift in an electric field towards a printed circuit board hole plate, where they are accelerated by a strong electric field penetrating the holes, creating a detectable electric discharge. We collected the discharge signals for pure propane and different mixtures of propane and phenol. After surveying various signal-analysis techniques, we selected methods for cleaning the signals by removing noise and discharges skewed by a recent discharge. We identified 12 signal parameters as useful for analysis of the cleaned signals, including, for example, amplitude, peak width, area under the discharge curve, and fall time. Our results indicate that phenol in the gas mixture produces signals with generally less amplitude, a wider peak, and a longer fall time. Samples of signals in the presence of phenol display more skewed distributions than analogous samples in propane alone. The SURF research time was dedicated to evaluating statistical techniques for their use on detector data. Permutation testing proved well-suited to this analysis, and we developed in-house software for signal processing and testing. The detector needs further study to optimize operating conditions and fully characterize its response to VOC admixtures. This preliminary analysis will be useful to interpret and evaluate future results.

OSCAR CRISTIAN MENA
SURF PARTICIPANT 2023

Life is a journey with unprecedented experiences that influence our character, goals, and passions. Growing up, I had minimal exposure to science and biology. However, my time in the United States Marine Corps challenged me to view life from a different perspective. Additionally, those experiences developed a desire to learn about the intricacies of the human body and how health science aims to understand it.

I'm a Senior at California Baptist University in Riverside, California, majoring in Biomedical Sciences. I'm committed to one day becoming a physician that can utilize aspects of research and medicine to develop innovative care for patients. God has called us to tend to our fellow man, and as a physician, I can utilize my passion for science to care for and share lasting impacts with patients. Growing up, I had very little exposure to medicine; due to the lack of medical insurance. Thus, I want to pursue a medical career because I want to be a part of the generation that bridges the gap in health disparities. Additionally, I'm blessed with the opportunity to inspire my children to pursue their goals and teach them they can accomplish anything their heart and soul desires.

I am honored and privileged to work with Dr. Danilo Boskovic in his Biochemistry Lab this summer alongside my research partners, Lidia Malina and Shahajahan Chowdhury. Our research will focus on factors that affect hemostatic responses, particularly how specific components of the bacteria *Porphyromonas gingivalis* impact platelet plug formation.

CRUDE LIPOPOLYSACCHARIDE FROM *PROTEUS MIRABILIS* INHIBITS IN-VITRO PLATELET PLUG FORMATION IN HUMAN WHOLE BLOOD

Oscar Mena, Shahajahan Chowdhury, Lidia Malina, Danilo Boskovic
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Platelets are anucleate cell fragments produced by megakaryocytes, with a vital role in primary hemostasis and in the formation of responses to inflammation or pathogenic infections. Additionally, platelets possess a wide array of membrane receptors, which activate distinct second messenger pathways within the cell. *Proteus mirabilis* is a gram-negative bacterium with a complex outer membrane including surface lipopolysaccharide (LPS, endotoxin). LPS represents a particular form of pathogen associated molecular pattern (PAMP) that can induce host cellular responses. It is not clear how the surface carbohydrates from various pathogens impact platelet functions. Human whole blood samples were obtained from a consented donor, as approved by institutional review board (IRB), to test the effects of *P. mirabilis* LPS on platelet plug formation. All blood samples were used within four hours of blood drawing. A solution of crude commercially obtained LPS (100 μg/mL final, in phosphate buffered saline (PBS)) was added to donor blood (80% final) and incubated for various time intervals at 37°C. Then, this LPS: blood mixture was loaded into the Platelet function analyzer-100 (PFA-100) system utilizing ADP/Collagen cartridges to determine human whole blood closure time (CT). A prolongation in CT of the 80% whole blood was observed in the presence of LPS with longer incubation time. This implies that LPS from *P. mirabilis*, when added to whole blood, can render human platelets refractory to aggregation and platelet plug formation. Future work will be focused on identifying specific surface receptors involved in the interaction with LPS.

STEFANY PARAO
SURF PARTICIPANT 2023

I am a junior at Southwestern Adventist University in Keene, Texas; majoring in Medical Laboratory Science. I like music and enjoy being in nature. I have always been a curious person; I like to know the meaning behind things, and at a young age, I was exposed to health care for different reasons. Growing up in my country of origin, Venezuela, I have seen firsthand the neglect many people experience because they do not have access to proper analysis and diagnosis. Experiencing these things made me realize that I want to educate myself to help as much as I can. When I applied to this program, I told myself I would use my summer to challenge myself in new ways, and I believe I did. Working with the Environmental Microbiology Research Laboratory allowed me to explore laboratory techniques and expand my knowledge. This experience motivated me to consider obtaining a higher education in biomedical science. This way, I can use my resources to help create ways for people to have better access to diagnosis as well as obtain answers on time. I want to thank Dr. Ryan Sinclair for the opportunity to learn from his project and mentorship. I was highly motivated by his passion for his projects and how they greatly help the people in the community. I would also like to extend my gratitude to participating lab members Samuel, Michael, and Jeremy for their guidance, time, and support during this experience.

INVESTIGATING POTENTIAL RESERVOIRS OF ANTIBIOTIC-RESISTANT PATHOGENS IN HOSPITAL ENVIRONMENTS

Stefany Parao, Hala Nashed, Kelly Bright, Chuck Gerba, Eugene Liu, Ryan Sinclair
Summer Undergraduate Research Fellowship, Environmental Microbiology Research Laboratory, School of Public Health, Loma Linda University, Loma Linda, CA.

Infection control and antibiotic resistance remain pressing challenges in healthcare settings, particularly in hospitals where vulnerable patients are exposed to various pathogens. This study focuses on the sampling of potential reservoirs of bacteria in hospital environments. The aim is to investigate the presence and abundance of select bacteria of concern present on these frequently touched surfaces. Both nurse call phones and bed side rails are important fomites that can act as reservoirs for antibiotic resistant pathogens. Some emerging pathogens of concern can survive for extended periods on surfaces difficult to disinfect, especially in a healthcare setting conditions that support their viability. Swab samples were collected from nurses' call phones and bedside rails at different rooms from the LLU hospital using a 3M sponge stick with DE neutralizer. All the swabbed liquid was squeezed from the sponge and for each selective media, 100µL of swabbed liquid was placed onto the media to determine the occurrence and concentration of pathogens on these surfaces. The LLU Environmental Microbiology laboratory analyzed these two surfaces before and after cleaning for several organisms. The pathogens being evaluated are Vancomycin Resistant Enterococcus (VRE), Methicillin Resistant Staphylococcus aureus (MRSA), *Clostridium difficile*, Carpapenam resistant enterobacteriaceae, Acinobacter baumini and Candida aureus. The lab is also quantifying indicators for contamination being Heterotrophic plate count bacteria (HPC), E.coli and total Coliform. This study uses HPCs to show the efficiency of the cleaning regimen and reports on several important pathogens that are routinely found in nurses' call phones and bedside rails. Ultimately, to safeguard patient safety and highlight the significance of infection control measures and the rise of antibiotic resistance in combating infectious diseases within the hospital setting.

GRACE SANTRACH
SURF PARTICIPANT 2023

While being raised in a STEM focused environment, I have always been interested to know how things work, and engineering, medicine and research fulfill this curiosity. Currently, I attend California Baptist University in Riverside and am working towards my Bachelor of Science in Biomedical Engineering. Presently, I plan to finish my engineering degree and intend to further my education through a PhD program or medical school. After completing my education, I am interested in becoming a surgeon, pursuing research, or both. Eventually, I would love to participate in missionary trips as a doctor and focus on global health.

This summer, I worked in Dr. Kerby Oberg's molecular embryopathy lab where I was paired with a graduate student, Jean Young Kim, to understand the role of ETS transcription factors in CRM-11 regulation of Lhx9. The most interesting part of research is discovery. Very little is known about the role of Lhx9 in limb development, therefore most of our findings about this transcription factor is new. To discover new information and analyze how it fits with what is already known is both exciting and rewarding.

I would like to thank Dr. Oberg guiding and mentoring me this summer. Additionally, I would like to thank Jean Young for teaching me patiently and allowing me to discover alongside her. I would also like to thank Charmaine Pira for showing me the way around the lab.

THE EXPRESSION AND REGULATION OF LHX9 DIFFERS FROM ITS PARALOG LHX2 IN THE DEVELOPING CHICK WING

Grace Santrach, Jean Young Kim, Jessica C. Britton, Charmaine U. Pira, Kerby C. Oberg
Department of Pathology and Human Anatomy, Loma Linda University, Loma Linda

The distal tip of the developing limb is covered by a rim of ectoderm called the apical ectodermal ridge (AER). Fibroblast growth factors (Fgfs) secreted from the AER control limb outgrowth and patterning. *Lhx9,* a LIM homeodomain transcription factor, is expressed in the distal mesoderm, along with its paralog *Lhx2*. In mice, *Lhx9* and *Lhx2* play seemingly redundant roles downstream of Fgf, with both expressed throughout the sub-AER mesoderm (anterior and posterior). In chicken, however, the expression of *LHX9* is anteriorly restricted suggesting differences in regulation despite similarities in the genetic landscape. We suspect that the differential expression is due to differences in the *cis*-regulatory modules (CRMs) regulating *LHX9's* temporospatial expression. Recent work suggests that Fgf uses ETS transcription factors to regulate *LHX2* expression. Previously, CRM(-11) was identified as an enhancer with activity mirroring the differential expression of *Lhx9* in the chick limb. ***We hypothesized that Fgf mediates CRM(-11)'s activity via ETS transcription factors.*** We mapped the *LHX9* mRNA expression pattern during limb development using *in situ* hybridization. *In silico* analysis of CRM(-11) identified a conserved, 10bp ETS binding site. We performed site-directed mutagenesis of the ETS binding site on an CRM(-11)-*tk*-GFP reporter construct. The normal and mutated CRM(-11) constructs were transfected into distal chick limb mesoderm by electroporation at a stage with robust *Lhx9* expression. Activity (fluorescence) was determined 24 hours post-transfection. *LHX9* expression was restricted to the anterior sub-AER mesoderm throughout development, unlike *LHX2.* Interestingly, mutation of the ETS binding site within CRM(-11) did not affect activity suggesting that Fgf does not regulate LHX9 through ETS transcription factors. These data indicate that the chicken expression pattern and regulation of *LHX9* is different from *LHX2*.

Hispanic Center of Excellence Program (HCEP)

DIEGO AGUILAR
HCEP PARTICIPANT 2023

I am a third-year pharmacy student at Loma Linda University. My journey in the pharmaceutical field began over ten years ago. A passion for exercise and nutrition led to an interest in health supplements, which propelled me to become a pharmacy technician; to physically understand medicine. After experiencing various pharmacy settings, I wanted to move away from a physical understanding of medications and into an intellectual level. Becoming a medication expert was my goal, so I went back to school in 2017, and now I am less than two years away from achieving my PharmD degree.

Asides from my background, my proudest accomplishments are being the first member of my family to pursue higher education and being one of the inaugural recipients of the HCEP scholarship. Candidates are chosen based on academic distinction, community dedication, and inspiring future Hispanic professionals. I want to thank all people involved with HCEP, specifically Dr. Willie Davis. He has believed in me since the start of the program.

Drug discovery intrigued me during my studies, which was a prominent topic in immunology and oncology lectures. Cancer research is a complex yet intriguing topic, so I approached Dr. Olivia Francis-Boyle regarding summer research, and she graciously agreed to mentor me. Her lab in the pharmaceutical research department is investigating a promising agent to treat acute myeloid leukemia (AML).

EFFICACY OF DUOCARMYCIN SA IN COMBINATION WITH ETOPOSIDE IN ACUTE MYELOID LEUKEMIA CELLS *IN VITRO*

Diego Aguilar, William A. Chen, Leena So, Yasmeen Jawhar, Nhi Nguyen, Natalie Drew, Terry G. Williams, Carlos A. Casiano, Sinisa Dovat, Kristopher E. Boyle and Olivia L. Francis-Boyle
Center for Health Disparities & Molecular Medicine,
Departments of Pharmaceutical Science, Pathology & Human Anatomy, Basic Sciences,
Schools of Pharmacy & Medicine, Loma Linda University, Loma Linda, CA.

Acute myeloid leukemia (AML) is a blood cancer that is characterized by clonal expansion of myeloid hematopoietic precursors and poor prognosis. Current treatment regimens have been unsuccessful at improving patient survival outcomes. Therefore, the objective of this study was to investigate the efficacy of duocarmycin SA (DSA, an antitumor antibiotic that induces DNA alkylation) in combination with etoposide (a topoisomerase II inhibitor used to treat relapsed/refractory AML) on human AML cells *in vitro*. We hypothesized that DSA in combination with etoposide would exhibit synergistic effects by improving the efficacy of both drugs in AML cells. The human AML cell line (HL60) was used for all studies. The phenotype of the cells was confirmed by flow cytometry and the IC50 of the drugs were determined using MTT assays. Our results showed that the AML cells were CD45+, CD33+, CD13+ and CD4+. The IC50 of DSA alone was ~115 pM. DSA alone induced DNA double stranded breaks in AML cells and significantly decreased the production of colonies in a dose-dependent manner. The IC50 of etoposide alone was ~130 nM. DSA in combination with etoposide showed cytotoxic synergism with CI values < 1 (0.65 and 0.13). In summary, 1) picomolar concentrations of DSA alone is sufficient to significantly reduce AML cell viability; 2) DSA in combination with Etoposide synergistically reduces AML cell viability. Thus, highlighting the potential use of DSA and etoposide as a synergistic drug combination strategy to increase AML patient survival outcomes and possibly reduce off-target toxicity.

ARIADNA CERVANTES
HCEP PARTICIPANT 2023

This summer I was able to participate in the HCEP Research Program which allowed me to participate in the research entitled "Long-term Hypoxia Alters Cytochrome P450 3A4 Activity During Pregnancy in Ovine Species." This research helped me learn a wide range of laboratory techniques that I will carry with me into future research projects. I am currently an incoming second year student at Loma Linda University's School of Pharmacy. In addition to my academics, I also serve as a board member for various organizations including Phi Lambda Sigma, the California Pharmacy Student Leadership Program, and the student chapters for the American College of Clinical Pharmacy and the Student National Pharmaceutical Association. After obtaining my PharmD degree in a couple of years, I would like to pursue a clinical residency and hopefully specialize in oncology. I would like to thank Dr. Adeoye and his lab for providing my colleagues, Rita Elhamra and Timothy Streck, as well as myself with this invaluable opportunity to expand our research experience and knowledge in this field.

LONG-TERM HYPOXIA ALTERS CYTOCHROME P450 3A4 ACTIVITY DURING PREGNANCY IN OVINE SPECIES

Ariadna Cervantes, Rita Elhamra, Tim Streck, Olayemi Adeoye
Department of Pharmaceutical and Administrative Sciences Loma Linda University School of Pharmacy1, Division of Physiology Center for Perinatal Biology Loma Linda University School of Medicine, Center for Evidence-Based Synthesis Loma Linda University

Background: Pregnancies can face complications, including those associated with hypoxia. These complications are disproportionately seen in minority populations due to factors such as smoking, substance use disorders, and medical co-morbidities during pregnancy. Drug treatment of such hypoxia-induced conditions carries risks related to their metabolism by the cytochrome p450 (CYP) system. Whereas there is evidence of a direct effect of hypoxia on pregnancy, its indirect effect via alteration of the CYP system is yet to be fully elucidated. Objective: To explore the effects of long-term hypoxia (LTH) on the expression and activity of CYP3A4 during pregnancy in ovine species. Methods: Four experimental groups were generated. There were Normoxic Non-Preg (NNP), Normoxic Preg (NP), Hypoxic Non-Preg (HNP) & Hypoxic Preg (HP). Normoxic sheep were kept at sea-level, whereas hypoxic sheep were taken to a high altitude for the last 110 days of gestation. CYP3A4 expression and activity assays were conducted on liver microsome samples harvested from the 4 groups. Results: LTH increased CYP3A4 activity in both non-pregnant and pregnant sheep. In normoxic sheep, the pregnant group had a decreased CYP3A4 activity, whereas, in the hypoxic sheep, there was no difference in CYP3A4 activity in the non-pregnant group compared to the pregnant group. Additionally, CYP oxidoreductase abundance increased only in the pregnant groups. A specific CYP reductase inhibitor reversed increased CYP reductase abundance. Conclusion: This study suggests that LTH-induced increases in CYP3A4 activity in pregnant sheep were mediated by a corresponding increase in CYP oxidoreductase. Sponsored by The Health Resources and Services Administration (HRSA).

RITA ELHAMRA

HCEP PARTICIPANT 2023

Participating in the summer research program of 2023 has been a great learning opportunity for growth and development in pharmacy school. Starting research the summer after my first year has been challenging due to my limited knowledge from this year it will be a great chance to show me what I am capable of and gain the extra grain of information. I am very thankful to have gotten the opportunity of working on the "Long-term Hypoxia Alters Cytochrome P450 3A4 Activity During Pregnancy in Ovine Species." I currently attend Loma Linda University and will be part of the graduating class of 2026. As a student pharmacist, it is very important that I obtain any information, knowledge, and experiences that I can expose myself to. My main interest has always been oncology for the patients struggling with cancer at any given age and knowing a pharmacist can specialize in such has been a great motivation. I wanted to extend a huge thank you to Dr. Adeoye for allowing us this opportunity of research experience for my colleagues Ariadna Cervantes, Timothy Streck, as well as myself. He has welcomed us with open arms, taught us to the best of our abilities, and challenged us to be better.

LONG-TERM HYPOXIA ALTERS CYTOCHROME P450 3A4 ACTIVITY DURING PREGNANCY IN OVINE SPECIES

Ariadna Cervantes, Rita Elhamra, Tim Streck, Olayemi Adeoye

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TIMOTHY FRANK STRECK JR.
HCEP PARTICIPANT 2023

I am a second-year pharmacy student attending Loma Linda University School of Pharmacy. I want to continue my education after pharmacy school and apply for residency programs where I can either go into ICU, ambulatory care, total parenteral nutrition, or hemophilia, with a goal of becoming a board-certified pharmacist. Currently, I work as a lead intern pharmacist at Arrowhead Regional Medical Center in Colton, California, in the inpatient pharmacy. When I'm not studying or working, I enjoy fishing, exercising, and learning about nutrition. I also devote some of my time to volunteering at the Riverside Free Clinic, which is situated in the First Congregational Church in Riverside, California. Our study focuses on the "Long-term Hypoxia Alters Cytochrome P450 3A4 Activity During Pregnancy in Ovine Species.", which I find incredibly fascinating. I am grateful to Dr. Adeoye for allowing me to participate in this research project and for providing constant support and guidance throughout the challenging journey we have undertaken.

LONG-TERM HYPOXIA ALTERS CYTOCHROME P450 3A4 ACTIVITY DURING PREGNANCY IN OVINE SPECIES

Ariadna Cervantes, Rita Elhamra, Tim Streck, Olayemi Adeoye
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GABRIEL VITERI
HCEP PARTICIPANT 2023

As I am a First-Generation Immigrant child because my parents came from Ecuador and Mexico. Both sacrificed a lot to help me achieve the level of education that I currently have. They have put me through private high school and college that allowed me to obtain a Bachelor of Arts degree in chemistry from Whittier College. I hope to use what they have given me to benefit others.

In order to help others, I am currently a Pharmacy student attending Loma Linda University hoping to obtain my PharmD in 2025. I am looking forward to everything I must learn for my profession. After pharmacy school I hope to get into a residency program to become a transition of care pharmacist, operating room pharmacist, or obtain a fellowship and enter industrial pharmacy. As a transition of care pharmacist, I would be able to help patients by ensuring that the transition from inpatient care to outpatient care is as smooth as possible. As an operating room pharmacist, I would be able to ensure that patients undergoing surgery will have a smooth procedure by ensuring patient safety. I hope to get into industrial pharmacy to help patients at the source and make drugs more affordable. Overall, I am eager to learn as much as I can in order to narrow down my decision.

HIGH LEVELS OF BREAST CANCER STEM CELL MARKER ALPHA-6 INTEGRIN ARE ASSOCIATED WITH REDUCED FULVESTRANT EFFICACY IN MCF-7 BREAST CANCER CELLS

Gabriel Viteri, Shawnee Angeloni, Ubaldo Soto, Eileen Brantley
Department of Pharmaceutical and Administrative Sciences, Loma Linda University Health School of Pharmacy, Loma Linda, CA
Department of Basic Sciences, Loma Linda University Health School of Medicine Loma Linda, CA

Most women diagnosed with breast cancer have tumors expressing hormones such as estrogen and are prescribed first-line endocrine therapy agents such as aromatase inhibitors. However, up to 40% of these patients will experience relapse due to endocrine therapy resistance. A small population of cells within tumors known as breast cancer stem cells are generally resistant to endocrine therapy and promote patient relapse. We previously found that breast cancer stem cell marker α-6 integrin is expressed at higher levels in cells and mammospheres that are resistant to the antiestrogen tamoxifen and that tamoxifen is less effective in cells overexpressing α-6 integrin. Fulvestrant is another antiestrogen and second-line therapy agent for patients who have relapsed on aromatase inhibitor treatment. Unlike tamoxifen, fulvestrant blocks the action of estrogen in all tissues. We hypothesize that high levels of α-6 integrin correspond to resistance to fulvestrant. Using the Alamar Blue and colony-forming assays, we discovered that cells with enforced α-6 integrin expression were less responsive to the fulvestrant. Using quantitative real-time PCR analyses, we expect to discover that fulvestrant-resistant mammospheres (breast cancer spheroids) show increased α-6 integrin expression and that fulvestrant paradoxically increases α-6 integrin expression in mammospheres. Our data suggest that high α-6 integrin levels are associated with reduced fulvestrant efficacy. Thus, a therapy designed to inhibit this stemness biomarker represents an important strategy to overcome endocrine therapy resistance.

Additional Participants

XUELIN GU
IBGS PARTICIPANT 2023

I am an Integrated Biomedical Graduate Studies (IBGS) PhD student at Loma Linda University in the Neuroscience, Systems Biology, and Bioengineering (NSBB) track. Currently entering my 3rd year at LLU, my research focus is on understanding the role of insulin resistance in the pathogenesis of Alzheimer's disease (AD). Thanks to my mentor, Dr. Konrad Talbot, and in collaboration with my colleague Tim Distel, I have been able to work on post-mortem human hippocampal tissue collected from a variety of AD brain banks to assess the validity of serine-616 phosphorylated insulin receptor substrate-1 as a biomarker of AD dementia.

Prior to joining the PhD program at LLU, I graduated from University of California, San Diego with a Bachelor's of Science degree in Human Biology. I also worked at the University of California, Los Angeles as a research associate in the lab of Drs. Greg Cole and Sally Frautschy, investigating potential interventions such as omega-3 fatty acids and keto diets on animal models of AD, as well as other research studies.

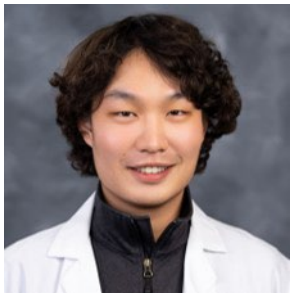
In the future, I hope to continue my research on insulin resistance in AD by investigating the potential repurposing of Type 2 Diabetic drugs for use against dementia, and develop the research into a career to bring new therapeutics and hope to those suffering with AD.

IRS-1 PS616 PATHOLOGY IN HIPPOCAMPUS AS A BIOMARKER OF ALZHEIMER'S DISEASE

Xuelin Gu, Tim Distel, Konrad Talbot
Department of Neurosurgery, School of Medicine,
Loma Linda University, Loma Linda, CA

Alzheimer's disease (AD) is a neurodegenerative disorder affecting 55 million people worldwide in which the cause of cognitive deficits is incompletely understood. Previous studies have linked insulin resistance in the hippocampus with cognitive decline in AD patients. Serine616 phosphorylation of insulin receptor substrate-1 (IRS-1 pS616) is almost exclusively limited to cell nuclei in hippocampal field CA1 of normal humans but accumulates prominently in neuronal cytoplasm in AD dementia (ADd, Talbot et al, 2012). The accumulation of IRS-1 pS616 inhibits normal insulin signaling, resulting in brain insulin resistance. We reconsidered if such IRS-1 pS616 pathology is a biomarker of preclinical AD and ADd when quantified using an artificial intelligence (AI)-based image analysis system on case cohorts from 3 brain banks. Sex- and age-matched normal (n = 81), mild cognitively impaired (MCI, n = 57), and ADd (n = 82) cases were selected, with a subset of normal cases displaying uncommonly high densities of p-tau tangles and Aβ plaques reclassified as preclinical AD. There were no cohorts with a significant difference in density of CA1 neurons with IRS-1 pS616 pathology in MCI vs. normal cases. In contrast, the density of these neurons was significantly greater in ADd than normal cases in each cohort and in the combined data set ($p < 3.1 \times 10^{-13}$). Preclinical cases also showed a significant elevation in density of such neurons in the combined data set ($p < 0.004$). Furthermore, greater than 90% of the ADd cases had larger densities of these pathological neurons than their matched pairs. These findings show that an elevated density of CA1 neurons with IRS-1 pS616 may be a biomarker of preclinical and dementia stages of AD, though not at its MCI stage. This suggests ADd can sometimes develop without a clear MCI stage.

YEONKYU JUNG
CSUSB PARTICIPANT 2023



To briefly introduce myself, I graduated from UC Riverside with an undergraduate degree in biology. During my academic journey, I developed a profound passion for developmental biology and stem cell biology. I am currently pursuing a master's degree at CSUSB

Apart from school, I actively engage in my community. Over the past 7 years, I volunteered for Riverside County Public Health, dedicating more than 2,300 hours. Additionally, I've been creating media content for Coachella Valley Alumnae Panhellenic for the last three years. In recognition of my contributions, I was honored with the Riverside County Volunteer of the Year Award by the Riverside County Board of Supervisors in 2020.

Dr. Juli Unternaehrer played a pivotal role in setting me on my path as a biologist. Currently, I'm involved in studying ovarian cancer and glioblastoma cells, with a focus on exploring radiation-induced cancer aggressiveness

DEFINING THE KEY ATTRIBUTES OF CANCER STEM CELLS IN HIGH-GRADE SEROUS OVARIAN CANCER

Yeonkyu Jung, Daniel Zecena, Tise Suzuki, Aaron Keniston, Ashley Antonissen, Ann Morcos, Jaqueline Coats, Antonella Bertucci, Marcelo Vazquez, Juli Unternaehrer
Department of Biology, California State University San Bernardino, San Bernardino, California
Division of Biochemistry, Basic Sciences, Loma Linda University, Loma Linda, California
Cancer Center, Loma Linda University, Loma Linda, CA
Department of Gynecology and Obstetrics, Loma Linda University, Loma Linda, CA USA
Loma Linda University School of Medicine, Radiation Medicine, Loma Linda, CA

Ovarian cancer is the 7th most common cancer in women globally. High-grade serous ovarian cancer (HGSOC) is a fatal gynecologic cancer with a more than 80% recurrence rate for advanced cases within 24 months after treatment. Understanding the cause of cancer recurrence and optimizing therapy is highly vital. Cancer stem cells (CSCs) are a small subpopulation within the tumor that contribute to tumorigenesis, metastasis, chemo- and radio resistance, and pro-tumor immune traits. The present study utilized primary tumor, ascites, and chemo-resistant cells to examine stemness, epithelial-mesenchymal transition (EMT), and pro-tumor immunity. We hypothesize that in metastatic cells the proportion of CSCs will be higher, as observed by gene expression, mesenchymal traits, and stemness reporter expression. Our data indicate HGSOC ascites cells expressed higher levels of stemness-related genes, POUF1 and SOX2, and an immune checkpoint inhibitor gene, PD-L1, than primary tumor cells. We observed EMT transcription factor genes Zeb1, SNAIL, SLUG, and TWIST were expressed at higher levels in primary tumor cells, while Zeb2 was higher in ascites cells. All mentioned genes were expressed at the highest levels in cisplatin-resistant cells. Furthermore, we incorporated a SORE6-GFP reporter to identify the cell population expressing Sox2/Oct4 and a 3′ UTR-ZEB1-GFP reporter to detect the cell population with mesenchymal traits. To understand the role of CSCs in radiation, we transduced cancer cells with the reporters and then exposed them to 0, 1, 2, 4, and 8Gy of 250 MeV proton and 6 MeV photon beams. We observed that cisplatin-resistant cells had the highest resistance to radiation. We conclude that metastatic HGSOC cells exhibit higher levels of stemness, mesenchymal phenotype, and pro-tumor immunity genes. Studies to determine the role of these attributes in resistance to chemotherapy and radiation are ongoing.

COLLIN ROBINS

MACPHERSON PARTICIPANT 2023

Participating in the Macpherson summer research program has connected me with a deeply rewarding opportunity to work and learn alongside inspiring mentors and colleagues. Working in Dr. Salma Khan's Thyroid Cancer Health Disparities lab has reignited my interest in basic science research from my years studying biochemistry at the University of Washington. Now, entering my second year of medical school at Loma Linda University, I am pleased to appreciate the advancements in patient care and clinical practice that scientific research brings to medicine. It is exciting to consider the potential applications or significance that each new finding can provide.

I have enjoyed living, studying, and working in different areas around the US. Working as a medical assistant in eastern Washington, pursuing a degree in Seattle, conducting genetic research in New Jersey, and now learning and serving in the Inland Empire has shown me the value in diverse academic and professional experiences. Getting to see new places and being a part of the unique communities therein has been one of the best parts of my medical journey. I am grateful to Dr. Khan and her lab for welcoming me onto their team, teaching me, and helping me grow as a future physician scientist.

ENIGMA (PDLIM7 GENE) INTERACTS DIFFERENTIALLY IN THYROID CANCER SIGNALING PATHWAYS

Colin Robbins, Kristiana Rood, Ria Laxa, Romi Yamauchi, Gerardo L. Gomez, Kidianys Sanchez-Ruiz, Amina Khan, Saied Mirshahidi, Alfred A. Simental, Salma Khan
Center for Health Disparities & Molecular Medicine, Loma Linda University School of Medicine, Loma Linda, CA

Due to the rising incidence of thyroid cancer, there is a growing demand for stage-specific diagnostic testing to facilitate accurate and personalized treatment approaches. Our previous studies have demonstrated an association between Enigma protein (PDLIM7 gene) overexpression and thyroid cancer, particularly at different stages. Additionally, researchers are exploring Enigma's links to other known proteins like PI3/AKT, TERT, VDR, DBP and MM2 pathways. However, the precise downstream interactions that contribute to cancer progression necessitate further investigation. This study aims to explore the presence of PDLIM7 and its interactions with other genes involved in signaling pathways that drive cancer progression. To achieve this, we employed UALCAN software analysis using TCGA database. We found that PDLIM7 gene was directly correlated to MDM2, significantly correlated to TERT expression. These findings suggest the potential of PDLIM7 as a biomarker or therapeutic target for thyroid cancer patients. However, further research using in vitro regulation of Enigma expression is necessary to determine the most significant pathways of interaction and their role in cancer progression. This knowledge can pave the way for more effective and targeted treatment strategies for thyroid cancer patients in the future.

SKYLER A. SCHIFF
MACPHERSON PARTICIPANT 2023

My name is Skyler Schiff, and I am currently a second-year medical student at the Loma Linda School of Medicine. I am also currently doing research on ovarian cancer in the lab of Dr. Salma Khan at Loma Linda. Prior to medical school, I obtained a bachelor's degree in business administration from Southern Adventist University in Tennessee. I have always thoroughly enjoyed science, and I also recognized that business is important and present in almost all areas of life, so decided to get a mix of both in my undergraduate education. I also had the wonderful opportunity to spend 5 months in Zambia for a mission trip just prior to medical school. In my free time, I love going on hikes, mountain biking, and just spending time with friends and family.

MIRNAS-LINKED TO ONCOGENES IN OVARIAN HIGH-GRADE VERSUS LOW-GRADE SEROUS CARCINOMA

Skyler A. Schiff, Jane Muinde, Cody S. Carter, Salma Khan
Center for Health Disparities and Molecular Medicine, Department of Pathology and Human Anatomy, School of Medicine, Loma Linda University, Loma Linda, CA

Ovarian cancers as a whole are aggressive cancers for which there are currently no efficient screening methods such as those which have significantly decreased the risk of death from cervical cancer and colorectal cancers. Ovarian cancer comprises about 1% of cancers, and about half of these women succumb to death, in part due to lack of early detection. Therefore, our lab focuses on discovering early molecular biomarkers using gene mutations and miRNA profiling. Many studies have shown miRNAs are dysregulated in ovarian cancer, however, no data showed significant relationships between these miRNAs to the prognosis/overall survival of ovarian cancer patients. **We hypothesize that several miRNAs linked to oncogenes are altered differentially in ovarian low-grade versus high-grade serous carcinoma.** miRNAs can alter oncogenes, and tumor suppressor gene expression levels, therefore they may serve as early biomarkers. To analyze the expressions of oncogenes and miRNAs, we utilized the TCGA database from the University of Alabama at Birmingham (UALCAN) software. We determined the oncogenes with higher statistical significance on survival rates, age, race, cancer stages, tumor grade, and *TP53* mutation status and miRNAs linked to them. Of the genes analyzed, *BRAF*, *CCNE1*, and *MYC* showed statistically significant data on survival rates. *BRAF*/*CCNE1* are amplified in ovarian high-grade serous cancer, whereas *MYC* is upregulated in ovarian low-grade serous cancer. One or more miRNAs-linked to these oncogenes were selected based on their significance in different age, race, and survival rate. Successful identification of early molecular markers in ovarian cancer will potentially allow for earlier detection and decreased mortality rates. Analysis of the appearance and abundance of miRNAs in early and late ovarian cancer can aid in earlier diagnosis. In further study, we hope to verify our results by testing a larger cohort of samples.

ARIANNA MARIE WILLIAMS
CHDMM PARTICIPANT 2023

Surrounded by an environment saturated with inquisitive minds and fervent hearts has inspired me to seek answers to questions regarding the relationship between science, faith, and human purpose. My current neuroscience research amplifies my motivation to pursue a career exploring the scientific and cultural intricacies driving human behavior and how these findings can serve underrepresented communities. My ultimate career goal is to obtain a Bachelor of Science in Psychology and, later, a doctorate in Clinical Psychology and a Master's of Business Administration. I will be a freshman at La Sierra University who has gained focus and dedication due to the summer CHDMM programs. I want to thank the mentorship team under Dr. Johnny Figueroa, especially IMSD students Perla Ontiveros-Angel and Tim Simon for helping me recognize my strengths, enhancing my understanding of the role of research in neuropsychology, and showing me how I can contribute to a growing scientific community. I strive to continue a legacy of care and compassion through research and service in honor of those who have pioneered the way before me.

ROLE OF THE ANTIEPILEPTIC DRUG LEVETIRACETAM IN THE TREATMENT OF BINGE EATING BEHAVIOR

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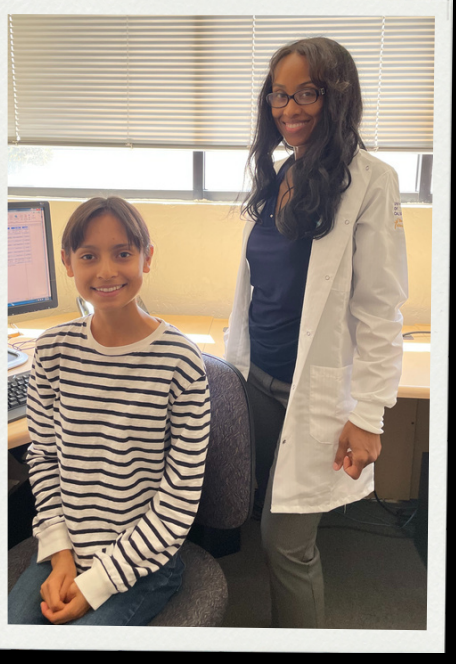
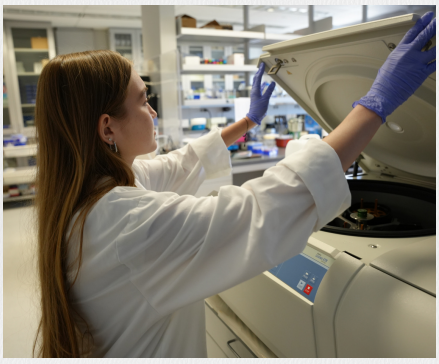
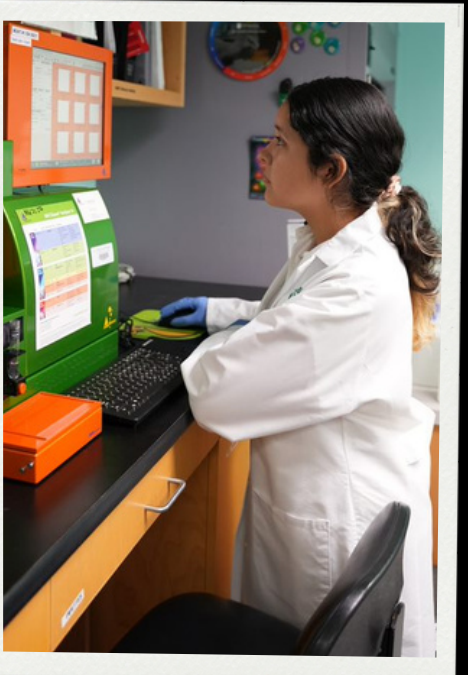
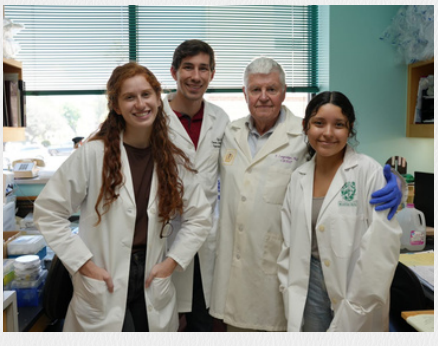
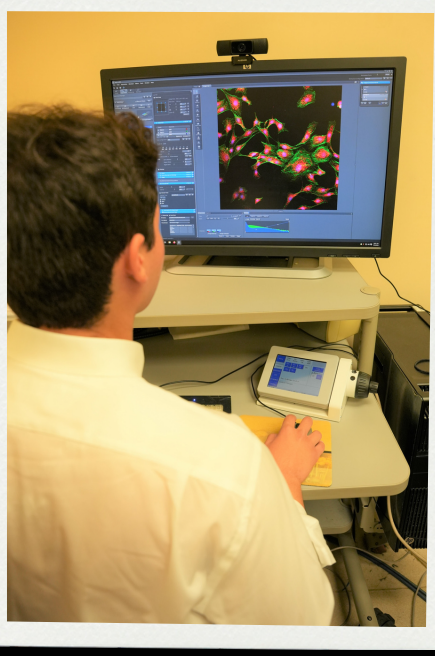
Emotional eating and binge eating are coping strategies in response to social stressors early in life, resulting in overeating, enhanced intake of "comfort" foods high in fats and sugars, and obesity. However, the neurobiological mechanisms that link stress to maladaptive coping and disordered eating remain unclear. Evidence demonstrates that social isolation stress profoundly alters synaptic function, specifically impacting Synaptic Vesicle 2A (SV2A). SV2A modulates neurotransmitter release in the presynaptic terminal of excitatory (E) and inhibitory (I) neurons, regulating the E/I balance in critical brain regions coordinating emotionality and eating. **Therefore, we hypothesize that restoring SV2A levels and synaptic integrity will confer resilience to social isolation and stress-induced binge-eating behaviors.** Adolescent Lewis rats (Male = 32, Female = 32) were randomly housed in Pairs or Isolated. The Paired animals were housed in two rats per cage, while the Isolated animals were single-housed throughout the study. Following adolescence, all animals underwent a battery of behavioral tests to assess startle reactivity, anxiety-like behaviors, and sociability. After the behavioral tests, all the rats completed a binge eating paradigm consisting of three weekly short-term exposures to a Western-like diet (*WD*, 41% kcal from fat). In the third week, the Paired and Isolated groups were subdivided into Vehicle and the anticonvulsant drug, Levetiracetam (LEV) (n = 8). LEV (10 mg/kg via intraperitoneal injection) was administered before the third WD exposure, and food consumption was monitored. Adolescent social isolation stress led to elevated weight gain/food consumption, stress reactivity, and anxiety while reducing sociability in adult rats. LEV administration modulated feeding behaviors and reduced binge-like eating in female rats. This study may aid in developing clinically relevant treatments for stress-related eating disorders.

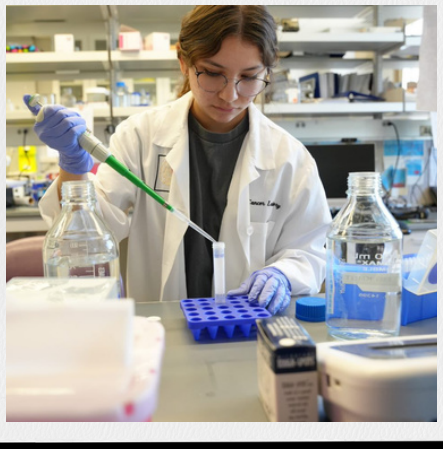


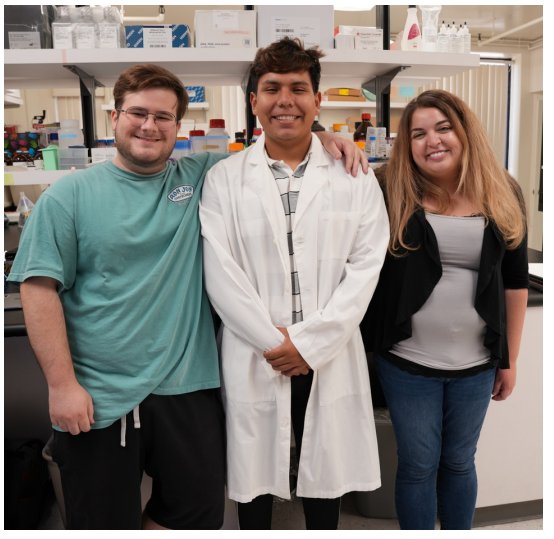


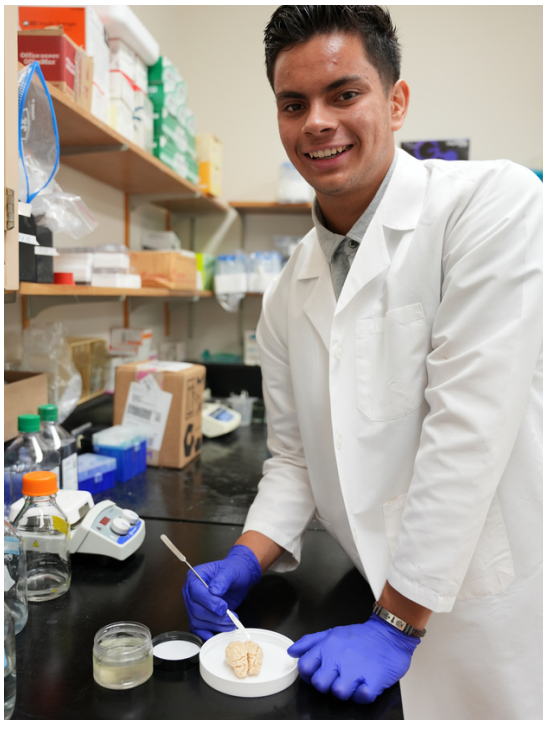


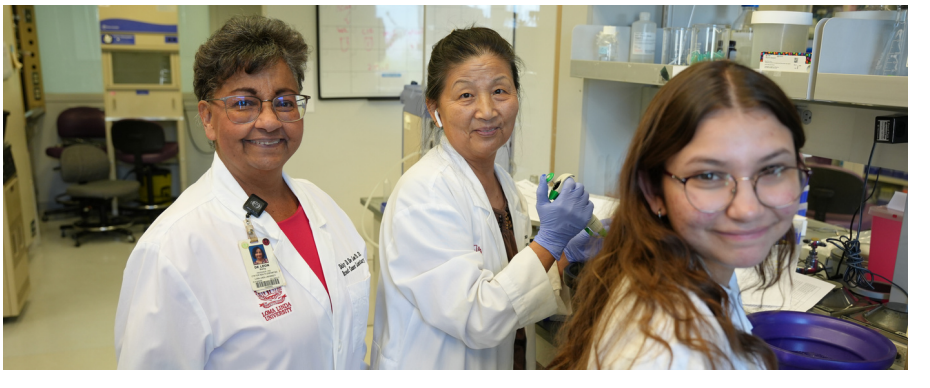


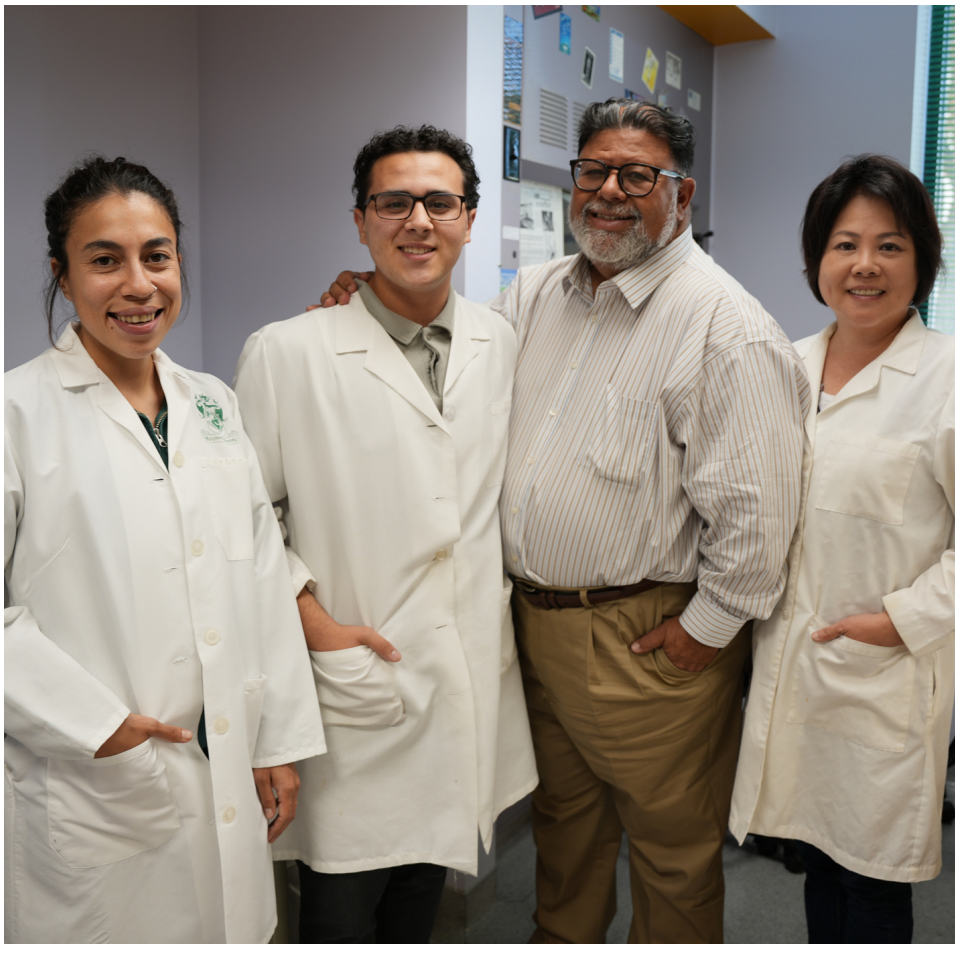


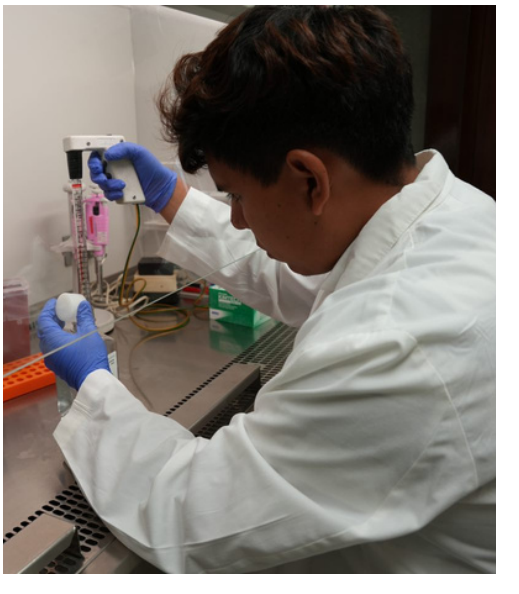


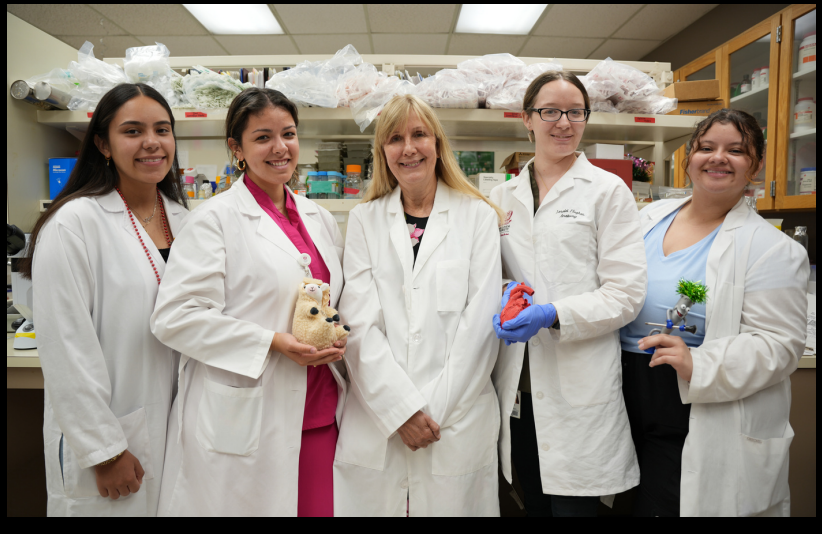


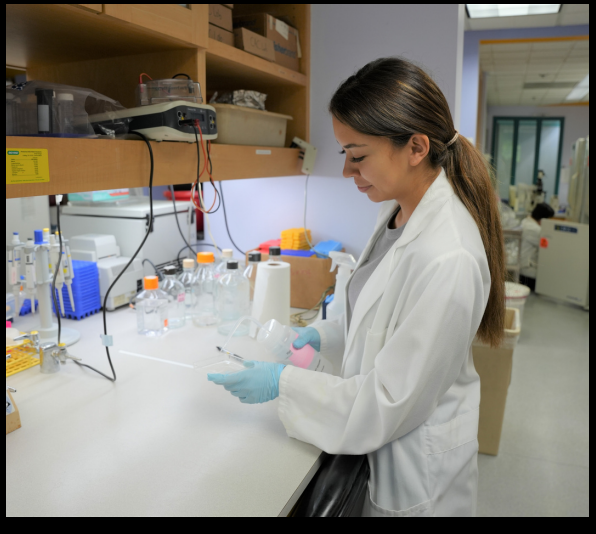


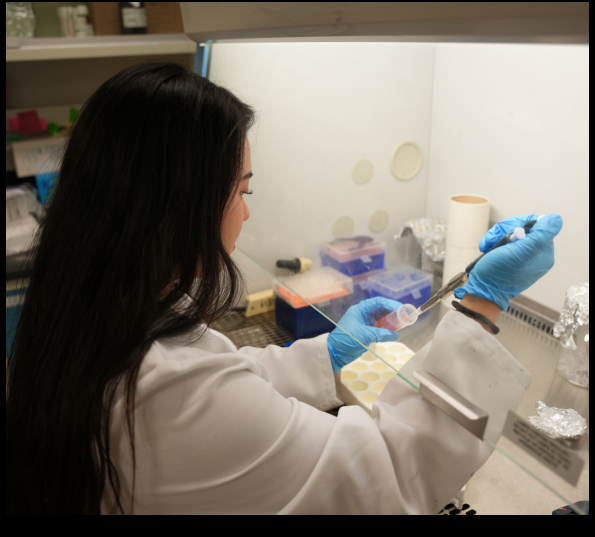


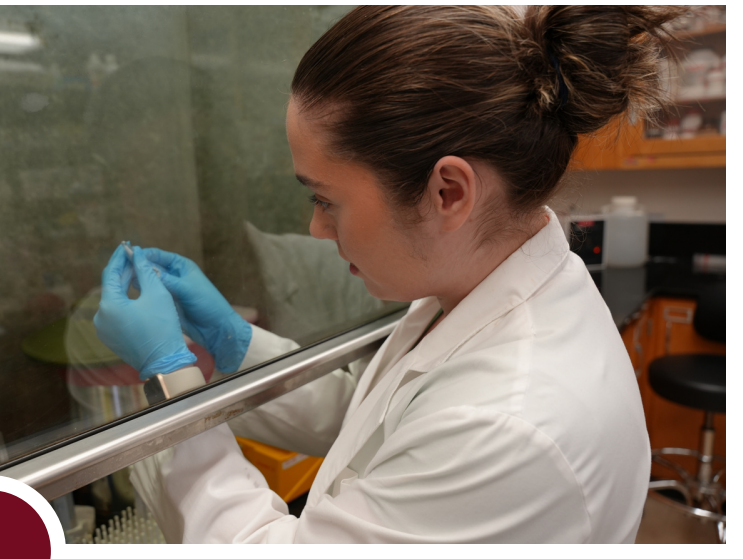


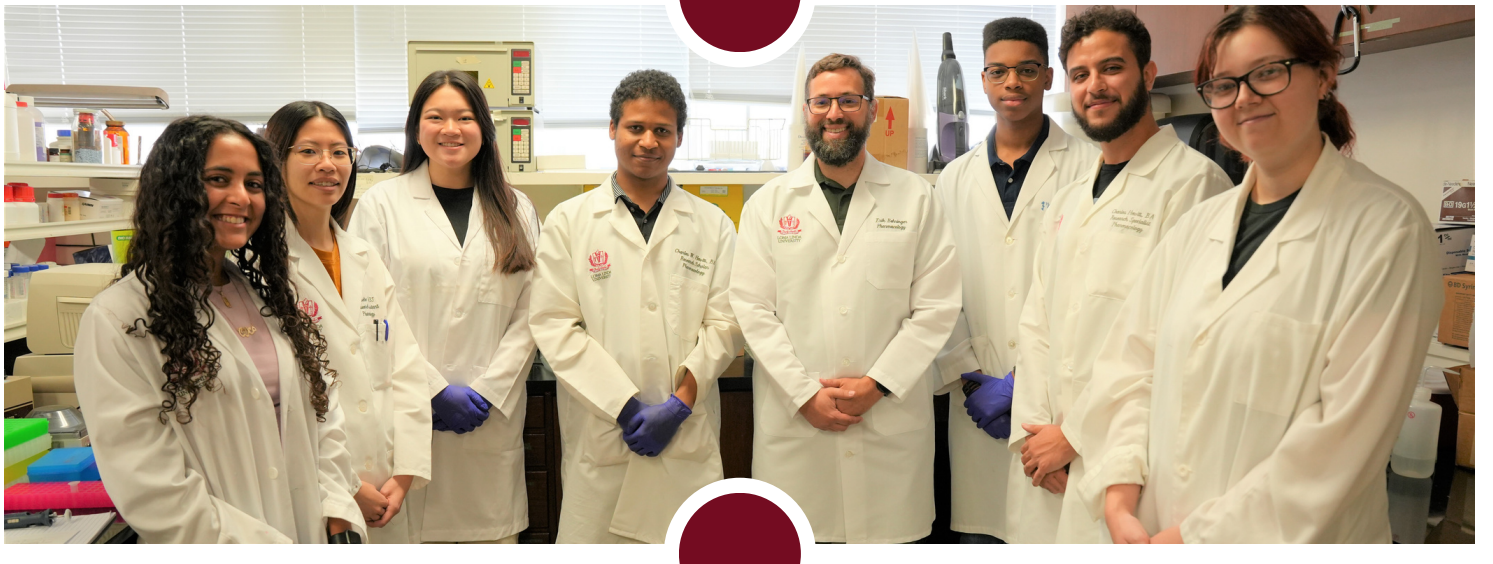


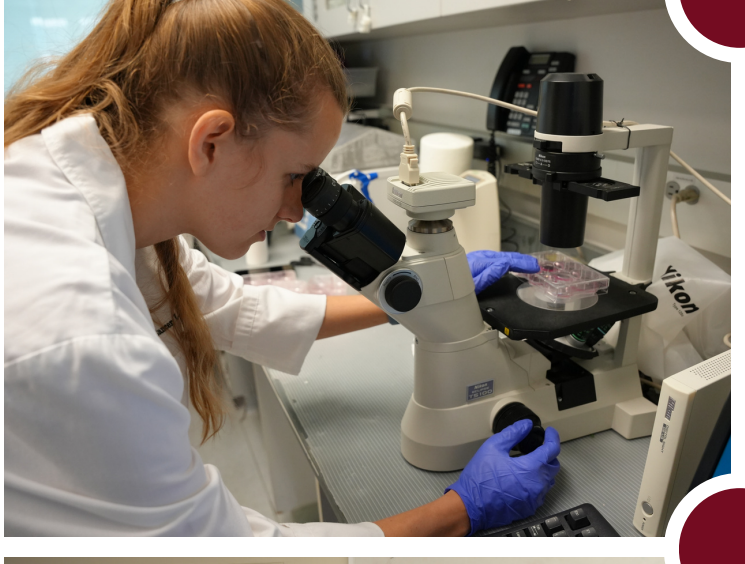








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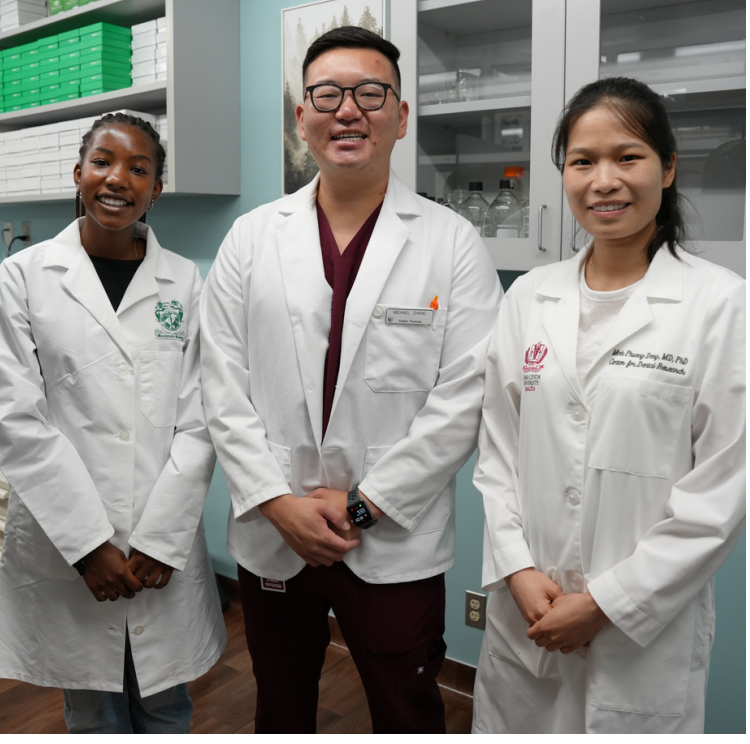


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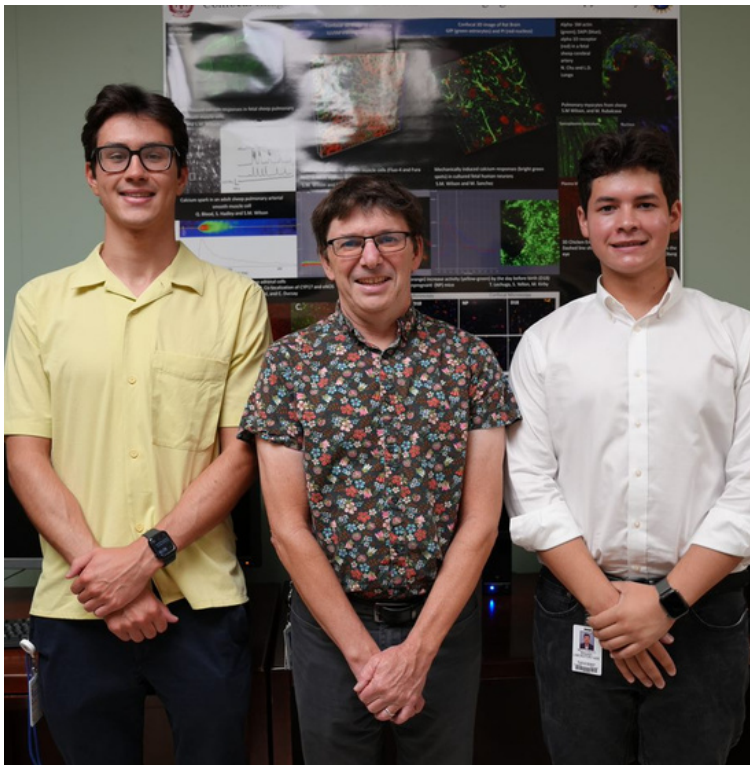

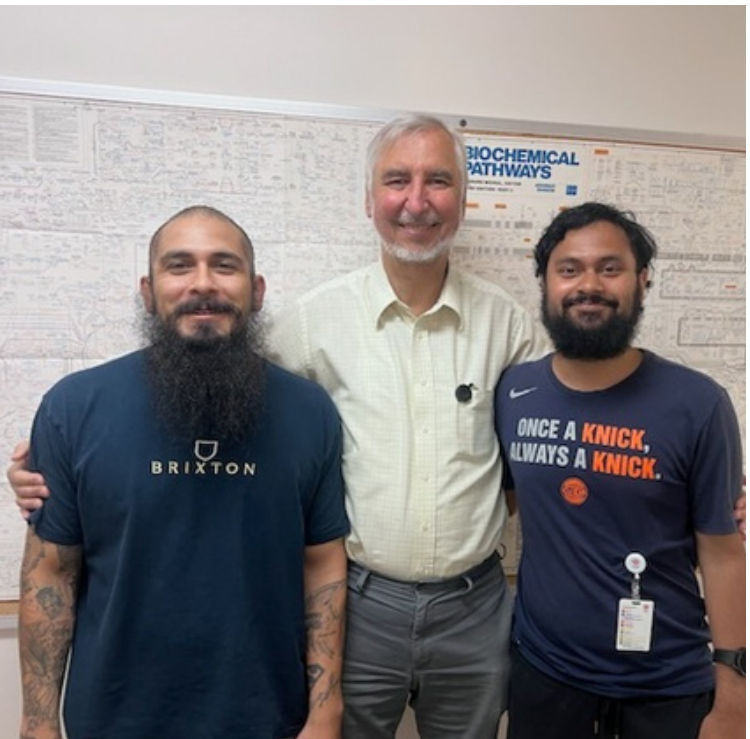
BIOCHEMICAL
PATHWAYS
BRIXTON
ONCE A KNICK,
ALWAYS A KNICK.

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