LOMA LINDA UNIVERSITY

School of Medicine

Center for Health Disparities and Molecular Medicine

2021 Health Disparities Research Poster Presentations

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

PROGRAM, BIOS, AND ABSTRACTS

Tuesday, August 3, 2021
12:00 pm – 4:30 pm
Wong Kerlee International Conference Center
Loma Linda University School of Medicine
Loma Linda, California

LOMA LINDA UNIVERSITY

School of Medicine

Center for Health Disparities & Molecular Medicine

PRODUCTION CREDITS

Cover picture	Jonathan Davidson
Student pictures	Daniela Soto Wilder
Textual editing	Dr. Susan Gardner
Booklet formatting	Daniela Soto Wilder and Venice Walsh
Printing	Printing Connection, Inc.

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

Health Disparities Summer Research Poster Presentations

Tuesday, August 3, 2021
12:00 pm - 4:30 pm, Wong Kerlee International Conference Center

Agenda

12:00 – 1:30 pm **Student Recognition & Certificates**

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

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

Poster Presentations

2:00 pm – 4:30 pm

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

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

Poster Presentations by Research Fellows
LLU-NIH IMSD, MD/PhD Program
Apprenticeship Bridge to College Program (ABC)
Undergraduate Training Program (UTP)
Medical Training Program (MTP)

Lab Group Pictures Each lab is invited to take a group picture by the LLU School of Medicine backdrop

LOMA LINDA UNIVERSITY SCHOOL OF MEDICINE
CENTER FOR HEALTH DISPARITIES AND MOLECULAR MEDICINE
HEALTH DISPARITIES SUMMER RESEARCH POSTER PRESENTATION

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

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

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

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

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

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

ACKNOWLEDGEMENTS

We would like to acknowledge the contributions of all who were instrumental in making this 2021 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.

2021 Faculty Research Mentors

Frankis Almaguel, MD, PhD
Eileen Brantley, PhD
Carlos Casiano, PhD
Daisy De Leon, PhD
Marino De Leon, PhD
Johnny Figueroa, PhD
David Hessinger, PhD
Salma Khan, MD, PhD
Wolff Kirsch, MD
William Langridge, PhD
Eugenia Mata-Greenwood, PhD, PharmD
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William Pearce, PhD
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Christopher Perry, PhD
Julia Unternaehrer-Hamm, PhD
Nathan Wall, PhD
Seth Wiafe, PhD
Christopher Wilson, PhD
Sean Wilson, PhD

Key Personnel

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

CHDMM Administrative Staff

Lorena Salto – CHDMM Manager
Daniela Soto Wilder – CHDMM Program Manager
Nannette Nevares – CHDMM General Operations

School of Medicine Office of Diversity

Venice Walsh – Administrative Assistant

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

2021 Student Research Fellows

ABC – Apprenticeship Bridge to College

Leah Marie Baluyot
Jonah Damian
Fletcher Dementyev
Isabel Genovez
Navaeh Gutierrez
Aidan Lu
Giselle Magana
Julie Nguyen
Taryn Thomas
Andrea-Paula Vargas

UTP – Undergraduate Training Program

Astrid Alvarez de La Cruz
Wendy Chow
Clarissa Do
Aaren Harewood
Caleb McIver
Oasis Perez
Michael Reeves
Samantha Torres
Jennifer Tran
Vivianna Williams

MTP – Medical Training Program

Monique Harding
Claudio Villalobos

IMSD – PhD/MD-PhD Graduate Fellows

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Pedro Ochoa
Perla Ontiveros Angel
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Foluwasomi Oyefeso
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Nicholas Sanchez
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Paul Vallejos
Jonathan Wooten
Francis Zamora

Guest Participants

Casey Curow
Alondra Enciso
Aaron Keniston
Kristiana Rood
Fransua Sharafeddin
Kristen Whitley

Institutional Affiliations of Student Research Fellows

High Schools

Beaumont High School
Beckman High School
Bloomington High School
Chaparral High School
Loma Linda Academy
Martin Luther King High School
Middle College High School
Redlands High School

Universities

Antillean Adventist University
California State University, San Bernardino
La Sierra University
Loma Linda University
Oakwood University
San Juan Bautista School of Medicine
University of California, Irvine
University of California, Riverside
University of California, San Diego
University of Southern California
University of Redlands

LOMA LINDA UNIVERSITY SCHOOL OF MEDICINE

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

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LOMA LINDA UNIVERSITY

School of Medicine

Center for Health Disparities & Molecular Medicine

Apprenticeship Bridge to College (ABC) High School Program

Leah Marie Baluyot
Jonah Damian
Fletcher Dementyev
Isabel Genovez
Navaeh Gutierrez
Aidan Lu
Giselle Magana
Julie Nguyen
Taryn Thomas
Andrea-Paula Vargas

LEAH MARIE BALUYOT

ABC PARTICIPANT 2021

I am currently a sophomore at Chaparral High School (CHS) in Temecula, CA, which recently ranked lowest socioeconomic school in our district with the widest range of racial diversity. Being at CHS combined with my time at Loma Linda University has influenced me to see the world in a different light and encouraged me to use learning about molecular medicine and health disparities to make a positive impact in both my school and local community.

Passionate about addressing diversity and gender disparity in the STEM fields, I founded the Women in STEM program at CHS, part of an international non-profit empowering and inspiring girls to increase female representation in STEM fields. I am on the marketing staff for *Reinvented Magazine*, the first national print magazine for women and girls in science, and vice president of Science Olympiad at CHS.

Besides my passion for science, I am committed to serving my community with a leadership role in Riverside County's Youth Advisory Council addressing youth issues. Despite my rigorous academic schedule, I also enjoy being a varsity cheerleader and working with reptiles in the organization I founded that rehabilitates and rehomes exotic reptiles.

I am extremely grateful to Dr. Carlos Casiano for the opportunity to participate in the ABC program. I also appreciate everyone in Dr. Casiano's lab, especially Dr. Catherine Elix and Pedro Ochoa, for being amazing mentors. Lastly, I would like to thank my parents for their constant love and support.

CYTOTOXIC EFFECTS OF POTENTIAL LEDGF/p75 INHIBITORS IN DOCETAXEL RESISTANT PROSTATE CANCER CELLS

Leah Baluyot, Pedro Ochoa, Catherine Elix, Greisha Ortiz-Hernandez, Carlos Casiano
Center for Health Disparities and Molecular Medicine, School of Medicine,
Loma Linda University, Loma Linda, CA

Prostate Cancer (PCa) is the second leading cause of cancer death in men in the United States. Although the 5-year survival rate of localized PCa is nearly 100%, once the disease progresses into later stages, patients ultimately develop resistance to current cancer treatments, and the survival rate drops to nearly 30%. There are several mechanisms cancer cells can develop to promote resistance to standard PCa therapies. Understanding the mechanisms by which cancer cells develop resistance is essential. One mechanism in which cells acquire resistance is through Lens Epithelium Derived Growth Factor p75 (LEDGF/p75). LEDGF/p75 is a stress oncoprotein that promotes cell survival against environmental stressors such as chemotherapy drugs like docetaxel (DTX), which is used to treat PCa. LEDGF/p75 is upregulated in multiple diseases including PCa, leukemia, and HIV. LEDGF/p75 contains the Integrase Binding Domain (IBD), the binding site for multiple proteins, such as PogZ, Menin, and MLL. These proteins have been shown to regulate the transcription of genes that promote cell viability. Thus, LEDGF/p75 is an optimal therapeutic target. Previously, our lab identified DTX-resistant PCa cell lines overexpress LEDGF/p75 compared to their respective DTX-sensitive PCa cell lines. We hypothesize treatment of LEDGF/p75 inhibitors in conjunction with DTX will increase cytotoxicity in DTX-resistant PCa cell lines. After characterization of the panel of PCa cell lines used in this study, the cytotoxicity of these potential LEDGF/p75 inhibitors in DTX-resistant PCa cell lines were evaluated via MTT assays. Taken altogether, our results show an increase in cytotoxicity upon treatment with the LEDGF/p75 inhibitors, but no difference in the presence or absence of DTX.

JONAH DAMIAN

ABC PARTICIPANT 2021

I was born and raised in the Inland Empire and am now going into my senior year at Martin Luther King High in Riverside, CA. I plan on attending a UC in the future and hopefully majoring in biology. My love for science began my freshman year of high school with an introductory biology class. Due to my affection for science and dexterous activities, I plan on becoming a surgeon in the future.

During my free time, I enjoy volunteering and giving back to the community. Throughout high school I volunteered at blood drives, planned educational community gatherings, helped clean trash from the neighborhood, and joined a youth council for a period of time. Along with being vice president of the medical club at my school, I was also a part of the robotics club.

It has been my pleasure to work under Dr. William Pearce this summer as I have begun studying prenatal biology. Previously to this summer I have had no thorough hands-on experience, let alone education in fetal development. This experience has given me a growth of knowledge as well as a step forward in the direction of my dreams.

I would like to thank Dr. Pearce as well as the other members in my lab including my UTP student for guiding me through this complex process and nurturing my development as both a scientist and student.

INTERACTIVE EFFECTS OF CHRONIC HYPOXIA AND MIR-29C ON MLCK DISTRIBUTION IN FETAL CEREBROVASCULAR SMOOTH MUSCLE

Jonah Damian, Desy Carreon, James Williams, William Pearce
Center for Health Disparities and Molecular Medicine, Perinatal Biology, School of Medicine, Loma Linda University, Loma Linda, CA

Maternal complications such as placental insufficiency, anemia, and preeclampsia can cause chronic in utero fetal hypoxia ultimately accounting for up to 27% of fetal deaths. A frequent consequence of fetal hypoxia is pathologic alteration of vascular structure and function through mechanisms largely unidentified. Recent studies indicate hypoxia can increase vascular expression of miRNA miR-29c, which can influence smooth muscle phenotype, contractility, and extracellular matrix structure. This study tested the hypothesis that hypoxia can act directly, and indirectly through miR-29c, to adversely influence distribution and colocalization of Myosin Light Chain Kinase (MLCK) with its substrate 20 kDa Myosin Light Chain (MLC_{20}) and Smooth Muscle a-Actin. Cerebral arteries from term fetal sheep maintained under normoxic or chronically hypoxic (3820m altitude) conditions underwent in vitro transfection with oligonucleotides coding sequences for Pre-miR-29c, Anti-miR-29c or Scramble control via organ culture for 72h. Immunoblotting determined changes in MLCK abundance, and immunohistochemistry followed by confocal colocalization quantified distribution within cerebral artery smooth muscle. Neither chronic hypoxia nor miR-29c significantly altered colocalization of MLCK with either a-Actin or MLC_{20}. However, in hypoxic arteries, Anti-miR-29c significantly decreased relative proportions of MLCK colocalized with a-Actin and MLC_{20}. Both Pre-miR-29c and Anti-miR-29c significantly increased absolute abundance of MLCK colocalized with MLC_{20} only. Hypoxia attenuated or eliminated effects of miR-29c transfection on MLCK abundance, the effects of Pre-miR-29c on the proportion of MLCK associated with a-Actin only, and the effects of Anti-miR-29c on the proportion of MLCK associated with MLC_{20} only. These findings reveal both hypoxia and miR-29c significantly influence abundance and/or compartmentalization of MLCK, but effects of hypoxia and miR-29c on abundance effectively offset their effects on colocalization, thus preserving the fraction of MLCK in the contractile apparatus and, presumably, contractility.

FLETCHER DEMENTYEV

ABC PARTICIPANT 2021

I was born in LLUMC, and I consider it a great honor to spend this summer working at the institution, which has been influential in my life from the very start. I grew up around the medical center, and through my formative years, I had many opportunities to interact with outstanding healthcare professionals and scientists. As a rising senior at Redlands High School, I am considering a career in the field of medical science and research, and I am confident that my aspirations have been shaped by LLUMC's legacy. Outside of school, I fill my time with music and swimming: I play cello in the Redlands Community Orchestra and am a team captain for the RHS swim team.

This summer I have been privileged to work with Dr. Sean Wilson and his dedicated lab team, including Samuel Murray, Rucha Juarez, Roberto Torres Chavez, and Michael Lee. They have guided me on a challenging project—analyzing trends in adolescent psychosocial metrics in response to different learning systems. Their mentorship 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.

I plan to go to college with a focus in pre-health sciences and public policy, eventually pursuing a dual MD/PhD degree. I am inspired by the work being done at the Center for Health Disparities and Molecular Medicine and its commitment to building healthier communities as well as caring for individuals.

PSYCHOSOCIAL DISPARITIES IN AMERICAN ADOLESCENTS USING PSC-17-Y AND WHO-5

Fletcher Dementyev, Esther Walker, Sean Wilson
Center for Perinatal Biology Loma Linda University, Loma Linda, CA;
Outride, Morgan Hill, CA

Nearly 17 million adolescents (ages 13-17 years old) have been diagnosed with behavior problems, ADHD, anxiety, depression, or a combination of these mental health illnesses. The Riding 4 Focus (R4F) is a cycling intervention program designed to improve the behavioral health and well-being of adolescents in middle schools, primarily aged 10-14. The current study aims to determine whether lower SES, female gender, non-white race, excessive screen time, regular physical activity (PA), lack of sleep, or an Individualized Education Plan (IEP) would result in lower psychosocial well-being scores and increased risk of mental health problems in adolescents before an R4F intervention. Psychosocial well-being was quantified by the WHO-5 and PSC-17-Y using online surveys. Preliminary results were obtained from 1419 students across 20 US schools in 13 states. Statistical analysis was conducted using a non-parametric Mann-Whitney U test to determine differences in psychosocial well-being and Koopman asymptotic scores to examine relative risk. The data showed females had significantly lower well-being scores and a higher clinical risk of depression as did non-whites compared to whites, those who spent more than 2 hours a day on electronic devices, and those of lower SES status as determined by enrollment in school free/reduced lunch programs. However, sleeping at least 8.5 hours per night and participating in 60 minutes of PA at least 4 times a week substantially increased psychosocial well-being and decreased clinical risk. Individuals with an IEP did not experience elevated risk. This data will allow for the examination of the efficacy of R4F programs, selective targeting of schools with at-risk populations, and further investigation into the underlying causes of psychosocial disparities.

ISABEL GENOVEZ

ABC PARTICIPANT 2021

From the time I was little I would dress up in a lab coat and pretend to conduct my own experiments. The ABC program has allowed me to follow my dreams by doing my own real research project. I will be a senior at Loma Linda Academy this fall, and I am planning to major in biology in college. Although my love for science began when I was young, my science teachers and family members in the medical field have continued to contribute to my passion.

Throughout my high school career, I have made sure to keep my studies a priority as well as giving back to my community. I am a volunteer tutor at Excell through Loma Linda University Church's UReach program. I also volunteer as a crew leader every summer at LLUC Vacation Bible School.

This summer I have been lucky enough to work in the Geographic Information System Lab with my mentor Dr. Seth Wiafe and his assistant Lance Pompe. In addition to learning GIS software, we have been studying Covid-19 vaccination trends. I have learned so much in this short amount of time and have grown to love GIS. I could not think of a better way to be introduced to research, and I am truly grateful for the opportunity to grow and learn this summer.

I would like to thank Mr. Pompe for all of his help while I was learning about GIS software. I would also like to thank Dr. Wiafe for teaching me not only about research but about life.

EXPLORING COVID-19 VACCINE DESERTS IN CALIFORNIA WITH GEOSPATIAL TECHNOLOGIES

Isabel Genovez, Seth Wiafe, Lance Pompe
Center for Health Disparities and Molecular Medicine, Health Geoinformatics Lab,
School of Medicine, Loma Linda University, Loma Linda, CA

The COVID-19 pandemic has spread across the world infecting millions and resulting in hundreds of thousands of deaths. In the United States, over 35 million people have tested positive for COVID-19, and over 66% have received the COVID-19 vaccine. Although the vaccine is the best tool to slow down the infection rate, vaccination sites are not equally distributed across the nation. In California, 44% of people have been fully vaccinated, and 53% have received at least one dose of the vaccine as of June 15, 2021. While the state has made tremendous progress in the past six months, there are still thousands of unvaccinated people as the Delta variant cases surge. The purpose of this study was to explore population vulnerability to COVID-19 and identify areas where limited vaccine access may cause "vaccine deserts." Using a set of COVID-19 risk factors, ArcGIS Pro's Getis-Ord Gi* tool was used to identify statistically significant spatial clusters at the zip code level. We also analyzed all available COVID-19 vaccination sites in the state. Spatial query was used to pinpoint all vaccination sites within high-risk areas. Out of 239 high-risk areas, 41% do not have any vaccination sites. To determine population lifestyle in these areas, Tapestry Segmentation data was joined to the high-risk areas with no vaccination sites. Several descriptive maps of areas of greatest need for vaccination were created. These high-risk areas consisted of young homeowners in multilingual and multigenerational households in rural communities. This study helps target areas when planning where future vaccination sites should be located.

NAVAEH GUTIERREZ

ABC PARTICIPANT 2021

This fall I set out to continue my education at the University of California, San Diego, where I will major in biochemistry and with hopes and anticipation to continue my dream of obtaining a PhD in the future. Along with my motivation and curiosity toward science, I find spending the rest of my time baking and listening to true crime podcasts. These hobbies of mine allow me to become mindful and give me a chance to express myself just as the science world does.

In high school I was once told that "science has no limitation." Growing up a Mexican-American in Bloomington, CA, and especially as a female, however, feels as if there *are* limitations in our futures. Through this program I have learned how to break these barriers and express myself through research and learn the values in collaboration.

Thank you to Dr. Frankis Almaguel, Dr. Daisy De León, and Dr. Alfonso Duran for giving me an opportunity to become more knowledgeable about health disparities and helping me find a true passion in research. I also want to thank Christian Yoo and my peers for creating a welcoming environment and giving me valuable advice as I begin my new journey at UCSD. My enthusiasm for science continues to grow because of these individuals and this program.

SHORT TERM STARVATION INCREASES SENSITIVITY TO BT#9 IN TRIPLE NEGATIVE BREAST CANCER CELL LINES

Navaeh Gutiérrez, Christian Yoo, Daisy De León, Alfonso Durán, Frankis Almaguel, Center for Health Disparities and Molecular Medicine, School of Medicine, Loma Linda University, Loma Linda, CA

Triple Negative Breast Cancer (TNBC) is associated with a 13% five-year survival rate and is three times more likely to occur in women of African American descent. Due to the limited therapeutics available for treating TNBC, dietary approaches, such as Short Term Starvation (STS) or the Fasting Mimicking Diet (FMD), have gained traction in the literature for sensitizing cancers to existing treatments. Metastatic TNBC tumours are also associated with elevated Reaction Oxygen Species (ROS) levels, which increases the need of these tumors to scavenge and mediate ROS levels. Magmas, which is a 13.8 kDa mitochondrial protein essential for mitochondria function, has been found in the literature to increase ROS scavenging and mediation. Our research investigated the differential expression of Magmas in African American compared to Caucasian TNBC tumor tissue as well as testing if Short Term Starvation (STS) increases sensitivity to BT#9, a novel boron inhibitor for Magmas in Triple Negative Breast Cancer (TNBC) and HER2 negative (HER2-, estrogen/progesterone receptor positive) cell lines. We treated cell lines MCF-7(HR+/HER2-, Caucasian), CRL-2335(TNBC/African American), MDA-468(TNBC/African American), and MDA-231(TNBC/Caucasian) with varying concentrations of BT#9 over a 48-hour period and compared cell viability compared to 72-hour fasting conditions. Our results attest less cell viability in the CRL-2335, MDA-468, and MDA-231 cell lines due to increased sensitivity to BT#9 inhibitor in combination with a 72-hour STS. This result could be due to the elevated ratio of IGF-2 and the reduction of circulating Leptin, IGF-1, and insulin utilized in growth factor signaling when STS is administered.

AIDAN LU

ABC PARTICIPANT 2021

I first developed an interest in the sciences through my biology class, which I took my freshman year of high school. In the beginning, I was simply just going through the motions, memorizing but not truly appreciating the various concepts. However, as the year progressed, I became increasingly fascinated and invested. I began to truly enjoy the process of learning science in general, and this interest continues to carry on to this day.

I am currently going into my junior year at Beckman High School, and while I am unsure of what college I will be attending, I hope to major in either neuroscience or biology. Overall, my end goal is to contribute to the betterment of human society as a whole through further developed health, whether that be as a physician or perhaps a researcher.

I am greatly thankful for having been given the opportunity to participate in this ABC program. I feel that it has and will continue to satisfy my interest in the sciences as well as help me to attain my future career aspirations. In particular, I would like to thank my mentor, Dr. David Hessinger, who has not hesitated to answer any questions I have had. Already, I have learned so much from him, and I hope the research I am assisting with will help in some way in the future.

BK CHANNELS AND THEIR ROLE IN THE RISE OF THE MODERN NERVOUS SYSTEM

Aidan Lu, Monique Harding, David Hessinger
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Large conductance calcium-activated potassium channels, or BK channels, reverse excitatory calcium currents to terminate calcium influx in excitable and secretory processes. They play a role in several important bodily functions for humans, including regulating blood pressure. However, they can first be traced back to the Cnidarians, specifically, the anthozoans (*i.e.*, sea anemones and coral). Because the simplest nervous systems appear in Cnidaria, and such systems become increasingly complex as species approach *Homo sapiens* phylogenetically, we hypothesize that the advent of BK channels in anthozoans permitted the development of more complex nervous systems. To test this hypothesis, we compared BK isoforms across a wide phylogenetic range of animals. Using NCBI Blast and Clustal, we determined the number of isoforms, splice sites, and alternative exons. We calculated the number of possible isoform combinations and related this to the number of expressed isoforms. We also correlated the number of neurons for each species to the number of expressed isoforms. With this data, we confirmed the following predictions: (i) the earliest alternative splice sites to appear will be the most conserved; (ii) the ratio of isoforms to possible combinations will decrease as the number of alternative exons and splice sites increases; (iii) the number of alternative splice sites and isoforms will decrease in less complex animals; and (iv) the number of isoforms will positively correlate to the nervous system size (*i.e.*, number of neurons). We conclude the diversification of BK channels corresponded with increasingly complex nervous systems. BK channel diversification correlated with the rise of the modern nervous system and possibly directly permitted it.

GISELLE MAGANA

ABC PARTICIPANT 2021

As a small child, I have always embraced science. Throughout my high school education, I always wanted to dive deeper into textbooks and cultivate a vast understanding of the world of atoms, cells, and medical research. I will be attending University of Redlands as a first generation student double majoring in biology and French.

In high school, I volunteered at the San Bernardino Play Date, where I helped give food and school supplies to children. As the Service Coordinator of the National Honor Society, I was also responsible for coordinating donations and food drives to help local underprivileged communities. Additionally, I am very passionate about creating a sustainable environment, especially in my community, by cleaning local parks, such as the Mary Vagle Nature Center.

When I am not studying or volunteering, I am baking cupcakes and dancing around the kitchen. I am captivated with hiking and taking in the wondrous world of nature that I am so privileged to take part in. I enjoy traveling and embracing the different cultures around me. These allow me to learn new aspects about other people and myself. To be alive is an amazing experience that I love sharing with my family, and just taking in one day at a time is unimaginably enlightening.

At Loma Linda University, I am currently an intern in the Unternaehrer lab studying the effects of proton and photon irradiation on the epithelial-mesenchymal transition in ovarian cancer. Being a part of this summer research program has broadened my horizons at such an early start in my path to becoming a scientist. For this, I want to thank my mentor, Alondra Enciso, and my principal investigator, Dr. Juli Unternaehrer, for helping me achieve my dream of mastering a career in medical research.

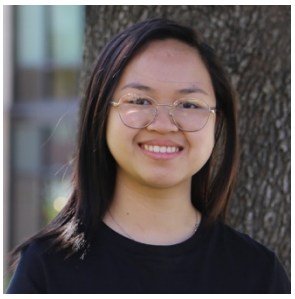
ANALYZING THE ZEB1-GFP 3'UTR EPITHELIAL-MESENCHYMAL TRANSITION REPORTER IN RESPONSE TO PROTON AND PHOTON IRRADIATION

Giselle Magana, Alondra Enciso, Hanmin Wang, Juli Unternaehrer
Center for Health Disparities and Molecular Medicine, School of Medicine,
Loma Linda University, Loma Linda, CA

High grade serous ovarian cancer (HGSOC) is the most lethal gynecological cancer due to the late onset of symptoms. In advanced cases, patients may have the option to pursue radiation therapy; however, many studies have suggested this form of treatment promotes cancer aggressiveness. Epithelial-mesenchymal transition (EMT) promotes these characteristics, and the GFP- Zeb1 3'UTR has been used to detect changes between the epithelial and mesenchymal states. Our lab has previously used this fluorescent sensor system in the T98G glioblastoma cell line to detect EMT in response to photon and proton irradiation. Preliminary results from our lab have shown that proton irradiation increases GFP to a greater degree in ovarian cancer cells than photon irradiation. We furthered our studies by transducing OVSAHO, an established ovarian cancer cell line, with the fluorescence sensor. OVSAHO GFP- Zeb1 3'UTR was exposed to varying doses of proton irradiation (0 Gy, 1 Gy, 2 Gy, 4 Gy and 8 Gy). Cells were harvested after 72 hours and observed by flow cytometry to measure the expression of GFP. Our results show an increase in GFP expression with an increase in dosage of irradiation. We tested the efficacy of the sensor by running qPCR. From these results, we can infer that photon irradiation induces EMT detectable by our reporter system. With the reporter, we plan to then knock down an inducer of EMT, SNA1, to test for resensitization of cells to radiation therapy. In conclusion, changes in EMT status can be detected post irradiation using the GFP-Zeb1-3'UTR in ovarian cancer cells.

JULIE NGUYEN

ABC PARTICIPANT 2021



Being born and raised in San Bernardino, CA, has opened my eyes to the economic, educational, and health disparities that plague my city. Seeing firsthand this city's imperfections has sparked a light inside me to give back to the community I have known all my life. As a result, I have contributed over 200 hours of volunteering to benefit those in my community through free tutoring and Key Club.

I am currently a rising senior at Middle College High School in San Bernardino. As a first-generation college student, I plan on attending a four-year university where I will major in biochemistry. I hope to attend either UCLA or UC Berkeley in the future. After completing my undergraduate education, I intend on attending graduate school for a PhD degree.

Having the opportunity to participate in the ABC program has allowed me to gain an experience like no other. The experience I have gained here directly correlates to my plans of running my own research lab in the future as well. I am extremely blessed and thankful to be invited to work with Dr. Salma Khan and her lab to examine how thyroid cancer affects different ethnic groups, more specifically, how it impacts Filipinos more than Europeans in terms of health disparities.

DIFFERENTIAL EXPRESSIONS OF MIR-323B-3P, PDLIM7 AND C-MYC IN FILIPINO AMERICAN VERSUS EUROPEAN AMERICAN PATIENTS

Julie Nguyen, Kristiana Rood, Celina Yamauchi, Ria Laxa, Mia Perez, Alfred Simental, Salma Khan
Center for Health Disparities and Molecular Medicine, School of Medicine,
Loma Linda University, Loma Linda, CA

The recurrence and mortality rates of thyroid cancer are notably two times higher in Filipino Americans compared to European Americans. However, there is no study to elucidate the biological determinants of health disparities. By using a cutting-edge technique, HiSeq4000, we showed significant downregulations of the top ten non-coding small RNAs when we compared miRNA samples from both ethnicities. Out of them, miR-323b-3p was robustly downregulated in Filipino Americans. By ingenuity pathway analysis, we found that miR-323b-3p interacts with PDZ and LIM domains of an oncoprotein called Enigma. We established Enigma as a biomarker in thyroid cancer staging; it interacts with c-Myc, an oncogene that contributes to the cause of at least 40% of tumors. In this study, we determined whether miR-323b-3p expression correlates to Enigma expression by real time-qPCR in the corresponding formalin-fixed paraffin-embedded (FFPE) thyroid cancer tissues from Filipino American and European American patients. We also determined whether Enigma protein expression correlates to its downstream partner, c-Myc protein by Western blotting from fresh thyroid cancer tissues. We extracted miRNA/DNA from the FFPE, RNA/DNA/protein from fresh tissue samples. Downregulation of miR-323b-3p is inversely correlated to PDLIM7 upregulation determined by RT-qPCR. Enigma protein overexpression directly correlated with c-Myc overexpression in the advanced staging of thyroid cancer in Filipino Americans. Therefore, we concluded that overexpression of the Enigma/c-Myc pathway is induced by miR-323b-3p downregulation. Future study is underway to elucidate the functional consequence of up/downregulation of miR-323b-3p in primary thyroid cancer cells and patient-derived xenograft (PDX) model.

TARYN D. THOMAS

ABC PARTICIPANT 2021

In the black community, the lack of access to quality healthcare is prevalent. I have seen this firsthand as my family is affected with a variety of diseases and at a higher risk. My passion to reduce the medical biases and health inequity minorities consistently face shows in my interest in the medical field. I applied to the ABC program because it would support my passion, enhance my skills and knowledge, and create tangible change beyond myself.

Making a large impact does not end in a laboratory. Albert Einstein once said, "Only a life lived for others is worth living." With over 300 verified hours in volunteer service in California Scholastic Federation and National Honor Society, I desire to make a change within my community to exemplify that change can take place anywhere. I also serve at the statewide level as the Governmental Affairs and Policy Director for California Association of Student Council where we spearhead education reform and legislative campaigns for student representation in key district decisions.

Outside of advocacy and volunteering, I am a senior at Beaumont High School, and academics has been my main priority. My goal is to graduate as valedictorian. Some of my most notable awards include Top 40 Junior Honor Escort and the President's Award for Educational Excellence, where the U.S. Department of Education recognized me for academic excellence. In college I plan to major in neuroscience with a career goal of becoming a neurologist. In my free time, I play varsity basketball and participate in speech competitions.

I would like to thank Dr. Marino De Leon for welcoming me into his lab and my lab colleagues for answering my many questions about research. A special "thank you" to Francis Zamora for guiding me through my summer project.

DHA REGULATION OF FATTY ACID-BINDING PROTEIN 5 (FABP5) IN RESPONSE TO PALMITIC ACID STRESS IN SCHWANN CELLS

Taryn Thomas, Francis Zamora, Marino De Leon
Center for Health Disparities and Molecular Medicine, School of Medicine,
Loma Linda University, Loma Linda, CA

Following nerve injury, inflammation and axonal degeneration contribute to developing hypersensitivity symptoms characteristic of neuropathic pain. Docosahexaenoic acid (DHA), an omega-3 fatty acid (FA), is neuroprotective during neuronal injury by promoting cell survival and inhibiting apoptosis. Previously, our lab showed DHA protects differentiated-PC12 cells and Schwann cells (SCs) against palmitic acid-induced lipotoxicity (PA-Ltx). In non-healthy nerves, SC dysfunction results in compromised myelin sheath integrity. FABP5, an FA shuttle within the cell, is a multi-functional protein involved in neuroprotection. FABP5 is shown to be upregulated by PA-Ltx in neuronal cells and, under these conditions, is protective by its ability to reduce oxidative stress and promote cell survival. We hypothesize that DHA increases FABP5 as one of its neuroprotective strategies. In this study, immortalized SCs were treated with DHA, PA, or DHA+PA for 12 or 24 hours. We used Western blot to determine the levels of FABP5 protein in iSCs cellular extracts (n=4). Our data show that after 12-hour treatment, FABP5 levels were similar between groups. However, iSCs treated for 24 hours with PA showed an 11.2-fold upregulation of FABP5, similar to what is reported during neuronal injury. Treatment with DHA alone also increased FABP5 4.6-fold, suggesting FABP5 also plays a role in DHA's observed neuroprotective role. Interestingly, iSC cultures co-treated with DHA+PA show a similar level of FABP5 compared to control, suggesting DHA activates additional pathways to prevent PA-induced injury. Our preliminary data indicate FABP5 may play a role during SC survival following PA-induced injury, but further experimentation is needed to elucidate potential cellular pathways and the role of DHA.

ANDREA VARGAS

ABC PARTICIPANT 2021

This upcoming school year, I will be a senior at Loma Linda Academy. Having been born and raised in Loma Linda, I have had the opportunity to see the significant and positive impact of biomedical research on my community and others. I joined this program to learn more about the vital and influential work done here at the Center for Health Disparities and Molecular Medicine and how I can contribute to it.

Throughout my academic experience, giving back to my community has been one of my top priorities. During my first year of high school, I took part in the organization of an outreach event at the Helping Hands Pantry, where students had the opportunity to aid their community by sorting food and assisting in the maintenance of the organization's warehouse. Beginning my sophomore year, I joined a community outreach program at my school called Youth to Youth as the Public Relations Secretary. Since then, we have held outreach events and food drives, all of which sought to serve the underprivileged members of San Bernardino County.

This summer, I had the privilege of working in Dr. Nathan R. Wall's lab. Although I had no prior research experience, through the guidance of incredible lab members, I have not only gained a better understanding of biomedical research but discovered a greater appreciation for the wonderfully complex world around us. I admire the dedication, kindness, and prowess exhibited by all those in this lab and hope to one day share in their mission to make a difference in the world of medicine, one Western blot at a time.

EXOSOMAL miRNAs PREDICT PERITONEAL INVASION AND METASTASIS

Andrea Vargas, Paul Vallejos, Ryan Fuller, Nathan Wall
Center for Health Disparities and Molecular Medicine, Division of Biochemistry,
School of Medicine, Loma Linda University, CA

Colorectal cancer (CRC) is the second leading cause of cancer death in the United States with approximately 147,950 estimated cases and 52,980 estimated deaths in 2021. A patient's 5- year survival decreases from 64.7% to 14.3% when the cancer metastasizes. One of the aspects of CRC that makes it so fatal is the threat of developing peritoneal carcinomatosis (PC), a metastatic manifestation considered a terminal diagnosis. Although only 10% of patients present with PC at CRC diagnosis, approximately half will develop PC at recurrence. Metastasis is enabled by a process called epithelial-mesenchymal transition (EMT) through which an epithelial cancer cell becomes a multipotent mesenchymal stem cell by adopting its migratory and invasive qualities, allowing for the metastasis of CRC to other parts of the patient's peritoneum or body. When comparing two colon cancer cell lines, the ascites (peritoneal fluid) cell line (SK-CO-1) was predicted to have greater invasion abilities than the cell line derived from lung metastasis (T84). This hypothesis was supported using a scratch assay performed on both cell lines in which SK-CO-1 was better able to close the scratch or wound than T84. In addition, EMT-associated microRNAs (miRNAs) have been shown to control CRC progression and metastasis. Next-Generation Sequencing (NGS) identified two upregulated miRNAs that are of specific interest to our lab: miR-677-3p in CRC patients and miR-4668 in PC patients. In order to understand their role in invasion, migration, and drug resistance, and to evaluate for therapeutic target potential, these miRNAs will be altered using mimics, inhibitors, and chemotherapy in vivo and in vitro.

Undergraduate Training Program (UTP)

Astrid Alvarez de La Cruz
Wendy Chow
Clarissa Do
Aaren Harewood
Caleb McIver
Oasis Perez
Michael Reeves
Samantha Torres
Jennifer Tran
Vivianna Williams

ASTRID ALVAREZ de LA CRUZ

UTP PARTICIPANT 2021

I am a night owl and hate silence, currently on a quest to find new things I might be passionate about, to keep growing into the person I want to be, and to fulfill my purpose. I am a rising senior majoring in biology at Antillean Adventist University in Mayaguez, Puerto Rico, where I have received integrity, leadership, and oratory awards and have been able to grow academically, spiritually, and socially. In my free time, I volunteer in the local Pathfinders, Adventist Development Relief Agency, and serve as Vice-president of the Student Body. This past year, I was part of the planning and development of diverse scholarships that helped many students. I enjoy exploring things, and, so far, I love spontaneous road trips, music, family, leadership, science, reading on rainy days, and journaling on frustrating days.

This program has been a tremendous opportunity for my professional growth and career advancement. I like the challenges presented by research and how it requires me to think critically. The best part is how every day is a different day and a different problem to solve. I aspire to become an MD or MD/PhD and be able to help innovate, advance, and contribute to the lives and healthcare of underrepresented communities. I know that by putting God in first place and always doing my best, I will accomplish these goals.

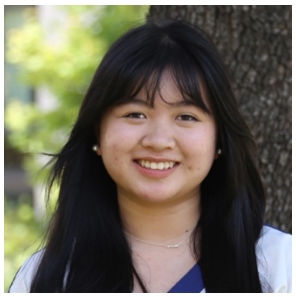
I had the honor and opportunity of working in Dr. Frankis Almaguel's lab this summer where I expanded my knowledge of prostate cancer. I would like to thank my mentor, Krystal Santiago, for her patience and enthusiasm while teaching me many things. I am also very grateful and lucky to have met amazing people who guided, inspired, and motivated me.

TARGETED GLYCOLYSIS INHIBITON WITH NOVEL ENOBLOCK INHIBITORS CAUSE CELL DEATH IN CHEMORESISTANT PROSTATE CANCER CELLS

Astrid Álvarez de La Cruz, Krystal Santiago Torres, Daniel Bazan, Alfonso Durán,
Bhaskar Das, Carlos Casiano, Frankis Almaguel
Center for Health Disparities and Molecular Medicine, School of Medicine,
Loma Linda University, Loma Linda, CA

Prostate cancer (PCa) is the second most common cancer in American men with one in eight men diagnosed annually. Taxane chemoresistance is one of the most common reasons for treatment failure in PCa patients, and evidence links metabolic shifts to this process. A vital glycolytic enzyme, enolase, is over-expressed in PCa. There are three types of enolases with similar glycolytic functions with ENO-1 and ENO-2 implicated in PCa. Enolases regulate the conversion of 2-phosphoglycerate to phosphoenolpyruvate during glycolysis. The absence of enolase interrupts glycolysis and affects cell metabolism. Our preliminary data through immunoblotting demonstrates that drug-sensitive PCa cell lines express ENO-1 and ENO-2; however, docetaxel resistant (DR) PCa cell lines only express ENO-1. The absence of ENO-2 in these cells creates a metabolic vulnerability due to loss of protein redundancy. Thus, ENO-1 could be a novel target for PCa treatment. We hypothesize that DR PCa cells will be sensitive to ENO-1 inhibitors due to their ENO-2 deficiency. Several boron-based enolase inhibitors were identified, and two of them, BT#568 and BT#572, decreased PCa cell viability as assessed by MTT viability assays and Hoffman Modulation Contrast Imaging. Inhibitor efficacy was evaluated by measuring cell viability after treatments with different concentrations. Our results showed cell death starting a 5uM of BT#572, with more pronounced cytotoxicity at 10uM. BT#568 induced cell death at 5uM; however, its potency was lower than that of BT#572. Our results suggest these boron-based ENO1 inhibitors affect glycolysis and cell metabolism leading to cell death in DR PCa cells.

WENDY CHOW
UTP PARTICIPANT 2021



There is something really special in asking a question that's never been answered before and then deciding to take the stage in seeking the answer yourself. That is the alluring beauty of research. Granted a simple choice, I could not resist the opportunity of another exceptional research experience here with CHDMM.

Fall quarter will mark the beginning of my third year attending the University of California, Riverside. With my dreaming heart, I hope to graduate with a BS in Biology and journey into Loma Linda University's or UCR's School of Medicine with a desire of practicing medicine as a primary care physician. I plan to remain in the Inland Empire and give back to the community that has always supported me by emphasizing the importance of preventative care. Dancing is a favorite hobby of mine. Serious disease, however, is like a frightening distant melody that can be prevented and even avoided if signs of a troubling condition are detected and treated early. Rather than dance in fear, dance with peace of mind and confidence in good health is the way an outstanding performance of the body and mind can be continuously achieved.

I am delighted to have been welcomed back to Dr. Eugenia Mata-Greenwood's lab in the Perinatal Department for another enchanting summer. My respect and admiration for her only continues to grow as her zealousness leads to remarkable discoveries for the betterment of our world. Her patience and optimism for my future success pushes me to become an even more passionate physician someday. Thank you, Nana and Charles, for your kindness and guidance in the lab, and thank you, Dr. Mata-Greenwood, for making research one of the most magnificent aspects of science that I have come to love and appreciate.

ROLE OF MATERNAL OBESITY IN FETAL ENDOTHELIAL CELL DEXAMETHASONE-SENSITIVITY

Wendy Chow, Nana Anti, Charles Banda, Eugenia Mata-Greenwood
Center for Health Disparities and Molecular Medicine, Center for Perinatal Biology, School of Medicine, Loma Linda University, Loma Linda, CA

Dexamethasone (DEX) is a drug used to accelerate fetal lung maturation in premature birth, but it has undesirable side effects in vascular endothelial cells (ECs), and drug efficacy is decreased in obese pregnancies. Our aim was to test the in vitro response to DEX in fetal ECs obtained from ewes fed a control or high-fat diet (HFD). Our hypothesis is that HFD increases fetal EC DEX-sensitivity. Sheep umbilical veins, arteries, and fetal aortas were used to isolate endothelial cells by collagenase digestion and then characterized by expression of endothelial markers von Willebrand and CD31. Confluent and quiescent ECs were treated with therapeutic doses of DEX (40 nM, 200 nM, and 1000 nM) for 24 hours to study gene expression by qPCR. DEX-sensitivity was defined as >50% expression changed of control levels in a dose-dependent manner. Four key genes were studied: endothelial nitric oxide synthase (eNOS), vascular endothelial growth factor (VEGF), plasminogen activator inhibitor 1 (PAI-1), and intracellular adhesion molecule 1 (ICAM1). ECs obtained from HFD pregnancies were more sensitive to DEX-induced changes in ICAM1 and VEGF mRNA levels ($p<0.05$). DEX-sensitivity correlated with glucocorticoid receptor (GR) protein levels measured by Western blot and with GR-driven transcriptional activation measured by luciferase assays. Finally, MTT viability assays demonstrated that ECs derived from HFD pregnancies were more sensitive to DEX-antiproliferative effects and to DEX-induced protection against lipopolysaccharide (LPS, 1 ug/mL) apoptotic effects. We conclude that HFD that mimics maternal obesity leads to fetal endothelial cell changes in GR expression and increased DEX-sensitivity.

CLARISSA "NINI" DO
UTP PARTICIPANT 2021

Being the child of two immigrant parents, I was always pushed by them to excel and to live a life they never had. Learning and trying new things were in my blood, and I wanted to make use of that curiosity. Throughout my high school and early college career, I began working as a medical assistant in a hospice clinic which allowed me to experience firsthand the disparity between my patients. This injustice led me to participating first in the ABC program and then in the UTP program in hopes of understanding and making a change towards closing the gap in health disparities.

As a returning student, I found Dr. William Pearce and Desy Carreon never hesitated to push my limits and capabilities with each project. Each mentor has taught me that amazing things can come from the bleak. Thanks to the UTP program, I truly understand the beautiful world of medicine and science and its powerful impact on the community.

An appreciation for the importance and potential impact of integrating basic science research and clinical medicine leads me to hopefully pursue the MD/ PhD program at Loma Linda University in the future.

CHRONIC HYPOXIA AND MIR-29C MODULATE SMOOTH MUSCLE PHENOTYPE IN FETAL CEREBRAL ARTERIES

Clarissa Do, Desy Carreon, James Williams, William Pearce
Center for Health Disparities and Molecular Medicine, Perinatal Biology, School of Medicine,
Loma Linda University, Loma Linda, CA

During early postnatal life, cerebrovascular differentiation is highly vulnerable to injury and stresses such as hypoxia. Main physiological and pathophysiological effects of acute and chronic fetal hypoxia include cerebrovascular remodeling and loss of contractility through mechanisms largely unidentified. Previous studies demonstrated miRNA miR-29c increased by hypoxia and can influence both phenotype and structure of cerebral arteries. The present study hypothesizes chronic hypoxia acts directly on smooth muscle, and indirectly via increases in miR-29c, to alter patterns of differentiation resulting in compromised arterial smooth muscle phenotype, structure, and function in fetal cerebral arteries. Cerebral arteries from term fetuses maintained under normoxic or high altitude hypoxic (3820m) conditions underwent in vitro transfection with oligonucleotides coding sequences for Pre-miR-29c, Anti-miR-29c, or Scramble control via organ culture for 72 hours. Immunoblotting of transfected arteries enabled quantification of contractile protein abundances including Smooth Muscle Myosin Heavy Chain (SM-MHC), Non-Muscle Myosin Heavy Chain (NM-MHC), Myosin Light Chain Kinase (MLCK), 20 kDa Myosin Light Chain (MLC_{20}), and Smooth Muscle α-Actin (α-Actin). Immunohistochemical staining allowed quantification of colocalization via confocal microscopy. Hypoxia promoted colocalization between the cytoskeleton (α-Actin) and SM-MHC but not NM-MHC suggesting contractile differentiation. In turn, inhibition of endogenous miR-29c caused de-differentiation of cerebrovascular smooth muscle through mechanisms absent in hypoxic arteries. MiR-29c had only limited effects on distribution of MLCK in cerebral artery smooth muscle cells, and hypoxia ablated these minor effects. Endogenous miR-29c limited colocalization of MLC_{20} with the contractile apparatus through mechanisms absent in hypoxic arteries. We conclude phenotypic differentiation of fetal cerebrovascular smooth muscle is potently influenced by both hypoxia and miR-29c; hypoxia tends to promote contractile differentiation via mechanisms requiring optimal endogenous concentrations of miR-29c.

AAREN H. HAREWOOD

UTP PARTICIPANT 2021

Sydney Harris once said, "The whole purpose of education is to turn mirrors into windows." Ever since I started my educational journey, my "mirrors" have been changing from a limited view surrounding me to an infinite view that expands my horizon and ability to look beyond my thinking. This view opens my mind to new concepts and ideas that affect our world, enabling me to see there are many who are marginalized. It is this view that has inspired me to make the career choice of becoming a physician. With that as my goal, I am currently a junior at Oakwood University in Huntsville, AL, majoring in biomedical sciences. I plan to enter medical school in the fall of 2023 with the possibility of incorporating research into my future career.

I am a member of the Oakwood Biomedical Sciences Club, the vice president of Oakwood Medical Economics Club, head of academic accelerations for the Kings Mindset Initiative, and historian for the Beta Beta Beta Honor Society. A few of my hobbies are playing the piano, badminton, and relaxing with my family.

This summer I am working with Dr. William Langridge, Mr. Wayne Kelln, and Yumi Munir researching an alternate form of the Covid vaccine through the process of isolating spike proteins. Within this lab, I have been given the opportunity to gain hands-on experience and understanding of the intricate processes by which Covid-19 infects our bodies and how we can prevent it most effectively.

I would like to acknowledge and thank Dr. Langridge, Yumi Munir, and Mr. Kelln for their welcoming hands and for them allowing me to increase my science skills and contribute to a research that will help enhance society.

MUCOSAL VACCINE AGAINST BETA CORONAVIRUS SARS-CoV-2

Aaren Harewood, Wayne Kelln, Tarannum Yumi Munir, Anthony Firek, William Langridge
Center for Health Disparities and Molecular Medicine, Division of Biochemistry,
School of Medicine, Loma Linda University, Loma Linda, CA

The Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV-2) is a highly pathogenic respiratory virus responsible for the respiratory disease COVID-19. Up to the present day, SARS-CoV-2 has caused a worldwide pandemic responsible for 609,000 deaths in the U.S. and 4 million deaths worldwide. Because antiviral treatments are mostly ineffective, the last resort is the construction of an effective vaccine. Presently, three SARS-CoV-2 vaccines have been approved for protection against virus infection. However, none of them protect the *site of virus attack*, the body's mucosal membranes. To overcome this problem, we are developing a mucosal vaccine that produces secretory antibodies (sIgA) and T-cells that protect epithelial cells lining the gut and respiratory tracts. To make the vaccine, the SARS-CoV-2 spike protein was inserted into a pEX-N-His vector, and the vector was transferred into *E. coli* BL-21 cells for amplification of the vaccine protein. Cells synthesizing the protein were lysed by sonication and the homogenate was centrifuged to remove particulate matter. The vaccine protein was separated from other bacterial proteins by acrylamide gel-electrophoresis and identified by Coomassie Blue staining and immunoblotting with a labelled primary antibody specific for the spike protein. Partial purification of the vaccine protein was accomplished by electro-elution and nickel affinity column chromatography. Final purification of the vaccine protein was completed by gel exclusion chromatography (FPLC). The purified vaccine protein will be used to assess vaccine efficacy in animals through antibody titration and virus neutralization studies.

CALEB McIVER

UTP Participant 2021

I am currently a senior biochemistry major at Oakwood University, and I plan to pursue a PhD in Biochemistry. My ultimate goal is to research and develop pharmaceuticals. I have a passion for this field as I have personally witnessed the life-changing effects of medication. I hope to not only develop cutting edge drugs to remedy prevalent problems but also help to destigmatize use of medication in black and brown communities. The prospect of giving others with various conditions the opportunity to live a normal life is extremely compelling to me.

I have a passion for research and have spent time researching *Porphyromonas gingivalis,* a pathogen associated with periodontal disease. I have presented this research on multiple occasions and received a 2nd place poster award at the Annual Oakwood University Symposium and a 3rd place poster award at the NSF-hosted Emerging Research Conference in 2020.

I am a mentee of Dr. Daisy De Leon in the Breast Cancer Lab and am researching IGF II, a growth hormone critical in cell proliferation in cancer, investigating a potential connection between IGF II and Magmas, a mitochondrial protein essential for cell viability. Finding a connection between these could be very impactful in cancer diagnostics as inspecting their levels could indicate the most ideal time to begin chemotherapy. This potential correlation could also be important in providing a better understanding of cancer mechanisms on a cellular level.

I have thoroughly enjoyed my time in the lab and am grateful to my mentors and graduate students for advice they have shared and kindness they have shown. This summer experience has strengthened my passion for research, enriched my knowledge of laboratory techniques, and has overall been a foundational step in my path to becoming an effective researcher.

IGF2 REGULATES MAGMAS, A MITOCHONDRIAL PROTEIN THAT MEDIATES ROS LEVELS IN MCF7 BREAST CANCER CELLS

Caleb McIver, Alfonso Durán, Qianwei Tan, Frankis Almaguel, Daisy De León
Center for Health Disparities in Molecular Medicine, School of Medicine,
Loma Linda University, Loma Linda, CA

Overexpression of Insulin-like growth factor 2 (IGF 2), a mitogenic peptide hormone, is linked to increased cell proliferation, chemoresistance, and higher incidence of tumors. Magmas (Mitochondrial Associated Granulocyte Macrophage Colony Stimulating Factor Signaling Molecule), an inner membrane mitochondrial protein whose mediation of ROS levels makes it essential for cell viability, is overexpressed in malignant tissues. Previous studies have evaluated the role of these molecules separately, but a mechanism associating IGF2 and Magmas has not been identified. This study was designed to determine if IGF2 regulates Magmas since both are downstream signaling molecules of the GM-CSF signaling pathway in the mitochondria. Our hypothesis is IGF2 regulates Magmas and an increase in IGF2 expression will result in an increase in Magmas expression. To test this hypothesis, we used wild type (WT) MCF-7 and IGF2- transfected MCF-7 cell lines to assess Magmas. Whole cell lysates of MCF-7 cells were probed for Magmas and IGF2 by Western blot analysis and ECL, and films were developed and scanned. Our results demonstrated IGF2-transfected cells showed decreased expression of the 13.8kD form of Magmas in comparison to the WT MCF-7 cells. In contrast, a 74kD band was highly expressed in the IGF2-transfected cells as compared to WT MCF-7 cells. We speculate the 74kD band represents a Magmas complex with either Hsp70 or Pam18 & Tim23, all important Magmas partners in the mitochondria. Thus, increased IGF2 expression results in the formation of a Magmas complex, suggesting IGF2 may regulate Magmas' affinity for its binding partners. Our study provides supporting evidence IGF2 regulates Magmas' expression and/or function.

OASIS PEREZ

UTP PARTICIPANT 2021

I was born and raised in the Inland Empire and am currently studying at the University of California, Irvine, pursuing a bachelor's degree in biology. My love for science has been influenced by the shadowing and hands-on experiences I have been fortunate to gain through the Loma Linda University ABC and UTP programs and outside opportunities. My long-term career goals are currently either clinical laboratory scientist or a researcher.

Giving back to my community, both my hometown and university campus, who have provided copious opportunities to learn and grow, is important to me. On my college campus I worked at the Middle Earth dorms as an attendant and was a part of the Active Minds Club, whose focus is reducing the stigma around mental health along with advertising mental health resources on campus. In one of my previous hometown community service groups, the Girls Scouts of America, I was able to complete a mental health promotion-focused gold award project.

Due to the pandemic, I have not been able to have hands-on experience within a campus lab yet, which makes this summer's opportunity crucial for learning through observing and performing rudimentary techniques. During this summer's UTP program, I have been honored to be welcomed with such kindness into Dr. Subburaman Mohan's lab. My project focuses on mechanisms that regulate bone marrow adiposity during conditions such as obesity and diabetes.

I would like to thank my loved ones who have supported me through my academic and personal journey and Dr. Mohan's lab. I want to give a special thanks to my inspirational mentors who taught and guided me—Shelia Pourteymoor, Arul Jothi, and Destiney Larkin—
for their endless dedication to my project and academic success.

HIGH GLUCOSE INDUCES ADIPOGENIC DIFFERENTIATION OF BONE MARROW-DERIVED STEM CELLS

Oasis Perez, Aruljothi Muralidharan, Sheila Pourteymoor, Subburaman Mohan
Center for Health Disparities and Molecular Medicine, School of Medicine, Loma Linda University;
Musculoskeletal Disease Center, VA Loma Linda Healthcare Systems, Loma Linda, CA

Nearly one in ten Americans have type 2 diabetes (T2D) which is associated with increased fracture risk. Bone marrow adiposity (BMA) is known to be increased in patients with T2D. Osteoblasts and adipocytes differentiate from the same mesenchymal stem cells (MSCs), and aging and estrogen deficiency, two major contributing factors for the pathogenesis of osteoporosis, are associated with lower osteogenic and greater adipogenic commitment of MSCs. Since chronic elevated glucose and insulin levels are common features of T2D, we tested the prediction that increased BMA is partly caused by high glucose-induced differentiation of MSCs into adipogenic lineage. MSCs were isolated from long bones of adult mice and cultured in adipogenic media with normal (5.5 mM) or high glucose (30 mM) for 7 days. Oil red staining revealed increased number of adipocytes in MSCs cultured with high glucose compared to normal glucose. Accordingly, expression levels of markers of adipogenic differentiation *Adpn*, *Glut4*, and *Acc1,* measured by real time PCR, were increased to a greater extent in high glucose media. Furthermore, high glucose increased expression of white adipocyte marker *Pat1* but decreased expression of brown adipocyte markers *Ucp1* and *Pgc1a*. We measured expression levels of regulatory factors known to be involved in MSC differentiation into adipocytes. While *Wnt5a* mRNA level was decreased, expression levels of transcription factors *Cepba* and *Srebp1* were significantly increased by high glucose. Based on our data, we conclude increased glucose levels, as in the case of T2D, promotes BMA by directly stimulating expression levels of key transcription factors involved in the differentiation of MSCs into white adipocytes.

MICHAEL REEVES

UTP PARTICIPANT 2021

Growing up, the importance of education was always stressed in our family. My parents emphasized the value of life-long learning and how education helps us understand our world and other people. I had always thought of it as good, respectable advice, but now that I am beginning to make the transition to adulthood, this counsel has become a guiding light for me.

This fall I will be starting my third year of college at La Sierra University with a double major in music and biology: biomedical science. Music has always been a large part of my life. Playing for patients in the hospital is always a joy; seeing their transformation always reminds me why I play the violin: for others to enjoy and be blessed. My love for science, specifically cell biology, has also blossomed in college. My passion for helping people drew me to medicine, but college has shown me that graduate school and research are exciting options that can impact lives as well.

This is my first year in the UTP program, and I am so grateful to have the opportunity to perform research in Dr. Carlos Casiano's lab. I have learned so much in the fields of chemotherapy resistance and autoimmunity. This summer has allowed me to hone my lab skills and techniques while also helping me learn to think critically about science and how to answer some of its questions. I would like to especially thank my mentor, Evelyn Sanchez-Hernandez, for guiding me through my project and the other members of the Casiano lab—Pedro Ochoa, Greisha Ortiz Hernandez, and Catherine Elix—for being available whenever I needed help.

DO ANTI-DENSE FINE SPECKLED AUTOANTIBODIES TARGET THE LEDGFp75/DFS70 PARALOG HRP2?

Michael Reeves, Evelyn Sanchez-Hernandez, Greisha Ortiz-Hernández, Carlos Casiano
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Anti-nuclear antibodies (ANA), biomarkers of systemic autoimmune rheumatic diseases (SARD), are detected in patient sera by indirect immunofluorescence (IIF) microscopy using human HEp-2 cells. Anti-dense fine speckled (DFS) autoantibodies recently attracted much attention because they are considered negative biomarkers of SARD and have been detected in patients with inflammatory disorders, prostate cancer (PCa), and in healthy individuals. These autoantibodies target the lens epithelium derived growth factor of 75 kD (LEDGF/p75), also known as DFS70. Our group has used these autoantibodies as tools to establish a role for LEDGF/DFS70 in PCa. These autoantibodies react with the C-terminal integrase binding domain (IBD) of LEDGF/DFS70, essential for HIV viral integration into host chromatin. Recently, we used these autoantibodies to map the protein interactome of LEDGF/DFS70 and observed that the hepatoma-derived growth factor related protein (HRP2, 100kD) is a member of this interactome and co-localizes with LEDGF/DFS70 in nuclei of drug-resistant PCa cells. LEDGF/DFS70 and HRP2 are considered paralogs since they are the only proteins known to share both N-terminal PWWP and C-terminal IBD domains. We hypothesized that DFS autoantibodies may also recognize HRP2. As initial steps to test this hypothesis, we screened by immunofluorescence and immunoblotting human DFS-positive sera and identified samples that displayed immunoreactivity against protein bands around 75kD and 100kD. Serum pre-absorption with an IBD autoepitope peptide was performed to determine if this immunoreactivity was blocked. HRP2 depletion in PCa cells was also performed to determine if immunoreactivity against the 100kD band was abolished. Determining if HRP2 is also a target of anti-DFS autoantibodies is critical for understanding the clinical and biological relevance of these ANAs.

SAMANTHA TORRES
UTP PARTICIPANT 2021

Thinking about the microscopic world of bacteria, viruses, DNA nucleotides, or even hadrons and quarks leaves new questions as breakthroughs emerge in the scientific community. My intrinsic curiosity leads me to want to know more about the mechanisms of how these microscopic particles work. Particularly, I wish to know more about how this information can then be applied to the macro world of cells, tissues, organs, and organ systems of the body.

Education bolsters formation of new neural connections which is why I want to expand what I know about biology. This fall I'll be a junior at the University of Southern California (USC) majoring in human biology and minoring in health care studies. I aspire to pursue a career as a physician to help mitigate the physician shortage in the Inland Empire while concurrently helping underserved populations.

Addressing health disparities is of vital importance, but with only 6% of physicians identifying as Hispanic, there's a problem of cultural competence and poor physician-patient relationships. USC's Latino Students in Medicine Club is a professional network to increase the number of LatinX health professionals where I facilitated pairing upperclassmen mentors with first and second-year students. Giving back to the community is also of great importance to me which is why I'm part of Trojan Health Volunteers.

This summer I'm thankful for the opportunity to learn in Dr. Kerby Oberg's lab in the Department of Pathology and Human Anatomy. Investigating SOX11 as a transcription factor and its role in regulating limb development allowed me to become immersed in the research world. Notably, I'd also like to thank my mentor Ruth-Love Damoah for her passion in teaching me the intricacies of biological processes, lab techniques, and communicating scientific findings.

IDENTIFICATION OF SOX11-ASSOCIATED *CIS*-REGULATORY MODULES ACTIVE DURING DORSOVENTRAL LIMB PATTERNING

Samantha Torres, Ruth-Love Damoah, Charmaine Pira, Kerby Oberg
Center for Health Disparities and Molecular Medicine, Division of Human Anatomy, School of Medicine, Loma Linda University, Loma Linda, CA

During embryonic development, the Lmx1b transcription factor is necessary and sufficient for limb dorsalization. Nail-Patella Syndrome (NPS), a congenital disorder caused by Lmx1b haploinsufficiency, is characterized by incompletely dorsalized limb joints with abnormal or missing dorsal structures (e.g., nails and patellas). Mechanisms used by Lmx1b to accomplish limb dorsalization, however, remain poorly understood. We previously found Lmx1b up-regulates a joint-associated transcription factor, Sox11, during development. In addition, chromatin immunoprecepitation sequencing (ChIP-seq) detected 3 Lmx1b-bound conserved non-coding regions associated with the *Sox11* locus that may function as *cis*-regulatory modules (CRMs). Hence, we hypothesized Lmx1b regulates *Sox11* expression through one or more of these potential CRMs to dorsalize limb features during their formation. To test the activity of these potential CRMs during joint formation, we cloned each sequence into a GFP reporter plasmid and transfected them into embryonic chicken limbs using electroporation (EP). Activity of each construct was recorded by fluorescence microscopy and compared to *Sox11* and *Lmx1b* whole-mount *in situ* hybridization expression patterns. All three Lmx1b-bound CRMs were active within the *Sox11* expression domain during development, including one with prominent activity in the developing elbow joint. Furthermore, there was a dorsal bias in CRM activity that overlapped with *Lmx1b* expression. The co-localization of CRM activity with *Sox11* and *Lmx1b* expression suggests that these CRMs play a role in the regulation of Sox11 during joint formation mediated, at least in part, by Lmx1b. Further studies are needed to correlate CRM activity with specific joint-associated tissues and confirm Lmx1b's role in regulating Sox11-associated CRM activity.

JENNIFER TRAN

UTP PARTICIPANT 2021

From an early age, I developed an interest in the medical field. I have always been passionate about serving the low-income community in which I reside. This has always been important to me because making an impact fills my heart with joy and satisfaction. Through my past research experience, I realized how much research involves helping people in third-world countries and nationwide. By educating the public about better care within their community, tragedies can be avoided. Throughout my internship, I have learned the value of providing medical care to underserved populations. Income should not be a barrier when it comes to proper healthcare because I believe that everybody deserves to have the utmost quality of life. This view has made me look at life differently.

I am currently a senior at California State University, San Bernardino, majoring in biology. During this summer, I have been fortunate to work with Dr. Daisy De Leon in the Breast Cancer Research Lab. As a returning student for my fourth year in the Loma Linda Health Disparities Research Program, I have seen a whole different perspective of how research plays a role in informing the public, treating people, and pushing science forward.

I am truly grateful to work under Dr. De Leon and my mentor Qianwei Tan and for showing me the essence and passion they have for research. I am fortunate to be in this program, and I will hopefully continue this astonishing experience and use it towards my potential career in the medical field.

IGF2 REGULATION OF MAGMAS IN TNBC TISSUES AND CRL-2335 CELLS

Jennifer Tran, Qianwei Tan, Alfonso Durán, Frankis Almaguel, Daisy De León
Center for Health Disparities and Molecular Medicine, School of Medicine,
Loma Linda University, Loma Linda

Breast cancer is the most common malignancy observed in women. Young African American (AA) women are affected by a higher incidence and mortality rate of triple negative breast cancer (TNBC) compared to Caucasian (CA) women. These patients express high IGF2 and high activation of IGF2 signaling pathways. Our laboratory has shown IGF2 regulates mitochondrial and survival proteins essential for cancer cell survival and chemoresistance. Mitochondrial Associated Granulocyte Macrophage Colony Stimulating Factor Signaling Molecule (Magmas), an inner mitochondria protein, mediates Reactive Oxidative Species. Since IGF2 regulates mitochondrial proteins, we investigated whether IGF2 regulated MAGMAS to use it as a potential target for TNBC Theranostics treatment. Our hypothesis is IGF2 increases Magmas, and since AA women express higher levels of IGF2, they will express higher Magmas levels. We used CRL-2335 AA TNBC cell-line and IGF2 knockdown of these cells. Western blotting and ECL methods were used to detect the specific isoforms of IGF2 and Magmas from cell lysates. Immunohistochemistry (IHC) characterized Magmas' expression in paired, Normal-Tumor, breast cancer tissues. Preliminary results showed Magmas was expressed in the CRL-2335 cells, and IGF2 knockdown significantly decreased Magmas. Re-expression of IGF2 in the knockdown cells increased Magmas levels, too. Breast tissue analysis showed high levels of Magmas staining in the tumor tissue while little or no staining was detected in the normal tissues. Similarly, high IGF2 expression was detected in tumor tissues while little or no IGF2 was seen in normal tissues. Therefore, these results indicate IGF2 expression correlates with Magmas and represents a promising tool for the goal of using Magmas as a Theranostics Marker for TNBC treatment.

VIVIANNA DE LEÓN-WILLIAMS

UTP PARTICIPANT 2021

From an early age, I knew I wanted to pursue scientific knowledge, but it was not until sophomore year in high school that I narrowed it down to neuroscience. After my biology teacher asked us to read and write a report on a scientific non-fiction book, I discovered how passionate I was about the inner workings of the brain and how neurosurgeons play a key role in improving people's quality of life in a lasting way. Today, my goal is to become a neurosurgeon and contribute to alleviating health disparities and educating future generations.

I am thankful to the CHDMM and the opportunity to be part of the ABC and now UTP program, providing me with great insight into compassionate research, as well as equipping and inspiring me to pursue a career in the biomedical field. I have since graduated from Loma Linda Academy and although I was planning to attend the University of California, Davis, God had a different plan. I received a full scholarship to La Sierra University, and this fall I will begin my third year as an Honors pre-med neuroscience major. I am looking forward to seeing how God continues to open doors and blesses me with opportunities to grow.

Over the past year, and this summer, I have had the privilege of working under Dr. Johnny Figueroa's mentorship, studying the interplay and mechanisms between poor diet and stress-related disorders. I want to thank graduate student Perla Ontiveros-Ángel for teaching me everything I need to know, and for providing me with an environment where learning is encouraged. Altogether, this experience has allowed me to pursue my passion for neuroscience without fear of failure, providing the opportunity for my love of neuroscience to reach new heights.

NEUROINFLAMMATION CORRELATES OF COMBINED PSYCHOSOCIAL STRESS AND OBESOGENIC DIET CONSUMPTION DURING ADOLESCENCE

Vivianna De León-Williams, Perla Ontiveros-Ángel, Fransua Sharafeddin,
Yaritza Inostroza-Nieves, Johnny Figueroa
Center for Health Disparities and Molecular Medicine, Department of Basic Sciences
School of Medicine, Loma Linda University, Loma Linda, CA;
San Juan Bautista University, Puerto Rico

Childhood obesity is a significant health challenge with a broad impact on metabolic and mental health. Some individuals are more susceptible to obesity when exposed to psychosocial stress during adolescence. Neuroinflammation is thought to mediate this association; however, the mechanisms that underlie this vulnerability remain unclear. We sought to determine the adverse synergy of an obesogenic diet and psychosocial stress (PSS) on neuroimmune function and behavior. Fifty-six adolescent Lewis rats (PND21) were fed for five weeks with a Western-like high-saturated fat diet (WD, 41% kcal from fat) or a matched control diet (CD, 13% kcal from fat). Subsequently, a group of rats (n = 29) was exposed to a well-established 31-day PSS model of predator exposures and social instability. The effects of the WD and PSS were assessed using a comprehensive battery of standard behavioral tests and assessment of an array of stress and inflammation markers. Stereological and fractal dimension profiling of hippocampal Iba1+ microglia showed various morphological properties in response to the WD and PSS. We found these parameters were associated with decreased sociability, increased anxiety-like behaviors, and dysregulated hypothalamic-pituitary-adrenal axis. *In vitro,* human microglia activities were also disrupted in response to corticosterone and palmitate. Our findings support an adverse synergy between WD and PSS on 1) critical markers of neuroinflammation, 2) stress regulatory pathways, and 3) maladaptive behaviors associated with heightened anxiety. This study contributes to furthering our understanding of potential mechanisms by which obesogenic environments shape resilience networks.

Medical Training Program (MTP)

Monique Harding
Claudio Villalobos

MONIQUE HARDING

MTP PARTICIPANT 2021

I was born and raised in Miami, FL, by parents who emigrated from Jamaica to the US. From a young age, they instilled in me strong moral values and the unyielding willpower to follow my dreams. For as long as I can remember, I have had an intellectual curiosity for the connection between the mind, body, and soul. I explored this during my undergraduate education, including a year abroad in Spain.

In 2016, I graduated from Oakwood University in Huntsville, AL, with a Bachelor of Science in Psychology and a Bachelor of Arts in Spanish. Since then, I have spent the last few years gaining work experience in both clinical and non-clinical settings. My experiences have motivated and empowered me to make a difference. While working as a medical assistant in Huntsville, I was exposed to the socioeconomic issues plaguing healthcare. Firsthand, I have witnessed the challenges people of limited means face and how their living situation can dramatically alter their access to quality care. With a passion for serving the most vulnerable populations, I know God will continue to use me to reflect the healing ministry of Christ as a future physician.

This summer, I will begin my studies at Loma Linda University School of Medicine. I hope to one day be a part of the solution to improving the health and well-being of underserved individuals and communities. I am so grateful to be a part of this amazing program and anticipate that from it, I will gain skills that will facilitate my development into a well-rounded and knowledgeable doctor.

It has been a privilege to work with my mentor, Dr. David Hessinger. I thank him for welcoming me into his lab and sharing his knowledge.

BKα (SLO) ISOFORMS DISPLAY PHYLOGENY CONSISTENT WITH CNIDARIAN ORIGIN

Monique Harding, Aidan Lu, David Hessinger
Center for Health Disparities and Molecular Medicine, Division of Physiology, School of Medicine, Loma Linda University, Loma Linda, CA

BK channels are large conductance calcium-activated and voltage-dependent potassium channels. They function to repolarize the cellular membrane potential by allowing potassium to flow outward in response to depolarization or an increase in intracellular Ca2+. BK channels play a major role in nervous systems. The simplest neuromuscular systems can be found within the Phylum Cnidaria. Because of this, we hypothesize that more complex nervous systems arose from the emergence of BK channels in Cnidaria. To test our hypothesis, we analyzed BK isoforms across a wide range of animals from several different phyla. We utilized NCBI Blast to record the amino acid sequences and exon maps of the BKα isoforms, then performed multiple alignments via Clustal Omega to identify insert sequences, number of isoforms, exons, and splice sites. We then determined the number of neurons for each species and calculated the number of possible isoform combinations. Our findings are consistent with the monophyletic appearance of BK channels in Cnidaria. We found that (I) the number of alternative splice sites and isoforms decrease in less complex animals, (II) the first alternative splice site to appear is the most conserved, (III) the number of possible insert combinations exceed number of isoforms, and (IV) the ratio of isoforms to possible combinations decreases as the number of alternative exons and splice sites increases.

CLAUDIO VILLALOBOS
MTP PARTICIPANT 2021

I have always wanted to become a physician, and although the journey has been arduous, I feel deeply blessed and highly fulfilled by the challenges and opportunities of this goal. Finishing my first year of medical school at San Juan Bautista School of Medicine, my commitment to help others through medicine and science has been solidified.

I come from a family that profoundly appreciates service, especially missionary work. I remember my parents motivating my siblings and me to share time and resources with an indigenous community in the south of Chile. These experiences helped shape my worldview for a life of service. Today, I am preparing myself to actively pursue my parents' vision, resonating with LLU's mission "To further the teaching and healing ministry of Jesus Christ," and contribute to the efforts in "making man whole."

I want to contribute to filling the gaps in knowledge and policy that affect and direct patient treatment and care mainly in communities where social determinants of health disproportionately impact their access to healthcare and diversity of treatments. I look forward to becoming a healthcare provider that implements personalized and comprehensive medical care to patients and communities wherever I am called to serve.

This summer I have had the privilege to be part of Dr. Johnny Figueroa's lab and, alongside his team, research the effects of stress and poor-quality diet in adolescent mental health. I am extremely grateful for the opportunity to participate in cutting edge research and to the CHDMM for allowing me to be part of this outstanding research training program.

FKBP5 EXPRESSION IN THE HIPPOCAMPUS OF ADOLESCENT RATS EXPOSED TO PSYCHOSOCIAL TRAUMA AND OBESOGENICE DIET

Claudio Villalobos, Timothy Simon, Johnny Figueroa
Center for Health Disparities and Molecular Medicine, School of Medicine,
Loma Linda University, Loma Linda, CA

Increase in obesity and psychosocial stress among adolescents raises concerns about their effect on brain development. Studies have shown association between hippocampal atrophy, trauma/stress, obesogenic diets, and aberrant *FKBP5* expression. FK506-binding protein 51 gene (*FKBP5*) is a critical stress biomarker, a co-chaperone regulating stress responses by negatively inhibiting glucocorticoid receptor response. This study aims to expand understanding of *FKBP5*'s role by investigating its spatial expression in the hippocampus of adolescent rats exposed to an obesogenic diet and psychosocial stress. Adolescent Lewis rats (n = 56) were fed a Western-like diet (WD, 41% kcal from fat) or control diet (CD, 13% kcal from fat) beginning at postnatal day (PND) 21 and then subdivided into exposed and unexposed groups. Exposed groups endured a psychosocial stress model (PSS) including 30 consecutive days of social instability (PND 60 - 90) and two predator exposures (at PND 60 and 70). Brain tissue, harvested at PND 107, was prepared for *FKBP5* mRNA expression analysis using RNAscope technique. The dorsal hippocampus CA1 area was chosen for *FKBP5* mRNA quantification. Hippocampal tissue was used for bisulfite conversion to procure *FKBP5* methylation differences. Bisulfite conversion revealed an 8% reduction in *FKBP5* methylation in the hippocampus of WD/PSS rats. RNAscope protocol was successfully optimized to obtain and analyze neurohistological results, which showed altered *FKBP5* mRNA levels in rats exposed to WD and PSS, confirming previous findings from our laboratory. Together, our results indicate obesogenic environments heighten vulnerabilities to early adverse events and contribute to altered brain maturation and unhealthy responses to stress. We identify *FKBP5* as a critical molecular player connecting early psychosocial stress exposure, obesity, and hippocampal development and function.

Initiative to Maximize Student Development (IMSD)

Erika Altamirano
Natasha Le
Jenniffer Licero Campbell
Pedro Ochoa
Perla Ontiveros Angel
Greisha L. Ortiz Hernández
Foluwasomi Oyefeso
Evelyn S. Sanchez-Hernandez
Nicholas Sanchez
Krystal Santiago
Timothy Simon
Paul Vallejos
Jonathan Wooten
Francis Zamora

ERIKA ALTAMIRANO

IMSD PARTICIPANT 2021

"Trust that little voice in your head that says 'Wouldn't it be interesting if...' And then do it," said Duane Michals. This is the philosophy I carry with me in my scientific process. Since my first summer volunteering in a thyroid cancer lab in 2019, I have engaged in many opportunities to learn and fuel my passion for science.

I am now a graduate student in the Neuroscience Systems Biology and Bioengineering (NSBB) program with interests in neuroscience, data analytics, and bioinformatics. I was the previous Treasurer of the Basic Sciences Student Council and look forward to working with my cohort to enrich the Basic Sciences graduate school experience this year as the Public Relations representative.

Throughout my time at Loma Linda, I have not only learned how to properly purify nucleic acids but to perform RNA and DNA-based validation techniques. Some of the most exciting things I've learned here are how to use the LINUX and Unix iOS computer systems to code in command-line, utilize R and Python for data analysis, and learn how to appropriately visualize data.

I am currently in the lab of Dr. Christopher Wilson in the Perinatal Biology Department studying the impact of inflammation and its pathways on biological systems. I would like to apply the skills I am learning towards bioinformatics-related industry positions in the future.

HEPARIN BINDING GROWTH-LIKE FACTOR (HB-EGF) IS A KEY FACTOR IN A NEONATAL MOUSE MODEL OF NECROTIZING ENTEROCOLITIS (NEC)

Adulzir Altamirano, Christopher Wilson
Center for Health Disparities and Molecular Medicine, Division of Neuroscience, Systems Biology, and Bioengineering, Department of Basic Sciences, School of Medicine,
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Necrotizing enterocolitis (NEC) is a gastrointestinal disease that is the leading cause of premature infant death in the NICU with a mortality rate of 20–50%. NEC is difficult to diagnose due to late stage signs such as abdominal distension, blood in stool, microbial imbalance, and gas in intestinal walls (pneumatosis intestinalis) which quickly progresses to local and systemic inflammation, multi-organ failure, and death. Even if the premature infant survives NEC, they may lead a decreased quality of life due to permanent bowel issues and neurodevelopmental delays from NEC exposure. In the field there is no clearly defined pathogenesis, but NEC etiology is linked to altered expression of Heparin Binding Growth-like Factor (HB-EGF). HB-EGF is linked to pro-inflammatory mechanisms of Toll-Like Receptor 4 (TLR4). However, the field still lacks understanding of how HB-EGF is specifically protective against NEC. Preliminary data shows that HB-EGF can significantly attenuate pro-inflammatory markers (IL-1beta, IL-6, and TNFalpha) in an HB-EGF knockout rat model. To evaluate the role of HB-EGF in NEC inflammation, we intend to validate our NEC model in mice and observe the epigenetic effects of endogenous HB-EGF in inflammatory markers. We hypothesize that the development and severity of NEC can be attenuated by exogenous HB-EGF administration in a mouse model. This will be done by RNA sequencing and bisulfite sequencing to observe the changes in gene expression and methylation. We intend to support our findings with mRNA (RT-PCR) quantification, protein (ELISA) quantification, and preliminary in silico analysis to assess NEC inflammatory markers.

NATASHA LE

IMSD PARTICIPANT 2021

I am a third 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 BS in Biochemistry from La Sierra University in 2019 where I was very active in several areas. In the Chemistry Department I was Head TA as well as Social VP and then President of the Chemistry Club. I served as a Worship Coordinator for the Spiritual Life Department, and in the Music Department I was a percussionist and pianist for Wind Ensemble and Orchestra. I performed research as well 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 am the Worship Director for the University and a member of the Basic Sciences Student Council, serving in the position of Social VP. I perform my research in Dr. Christopher Perry's lab which focuses on translational chemistry and nanotechnology. We are continually working to perfect our protocols to synthesize silver nanoparticles, gold nanorods, and gold nanostars. We then immobilize the nanomaterial onto biocompatible titanium dioxide nanofibers and test the effectiveness of these coated nanofibers in different settings, such as inhibiting bacterial growth and dye degradation. In the future, I hope to work in industry, specifically in the fields of bioengineering, nanotechnology, or chemistry.

GOLD NANOSTARS: SYNTHESIS, FUNCTIONALIZATION, AND APPLICATIONS

Natasha Le, Christopher Perry
Center for Health Disparities and Molecular Medicine, Division of Infection, Immunity, and Inflammation, Department of 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 either the shape or the size. The long-term goal of our research is to use novel nanomaterials for chemical detoxification, antimicrobial applications, and radiation medicine targeting. Gold nanostars (GNSs), comprised of a core and multiple spikes, are of interest for biosensing, catalysis, and therapeutic applications. We hypothesize that the large surface area to volume ratio of GNSs and their unique crystallinity enhance their physical and chemical properties, increasing the number of catalytic sites and light harvesting efficiency. Previous approaches for GNS synthesis included seeding solutions with added amino sugars, hydrogen peroxide, or other substances. In our approach, preformed gold nanoparticle (GNP) seeds (~10 nm) were added to solutions (~33-37 °C) of partially reduced (+3 to +1 charge) gold salts to form the GNSs synthesized with a high yield and reproducibility. Increasing the volume of added GNP seeds reduced average spike size. Modifying GNSs with thiolated polyethylene glycol enhanced their catalytic activity. The specific aims were to (1) optimize synthesis and characterization of GNSs, (2) evaluate dental applications (i.e., antimicrobial effects), and (3) evaluate medical applications such as targeting of radiation-induced DNA damage.

JENNIFFER LICERO CAMPBELL

IMSD PARTICIPANT 2021

Jenniffer Licero, a name which some have correlated with the feelings bubbly and happy, is a courageous, humble, hardworking, devoted, focused and happy 31-year-old. I am an incessant questioner of paradigms and theories who daily strives to unearth the unknown through scientific discovery. I am a worshipper. I am God's daughter. I am a Christian. I am Venezuelan, even while recognizing that my grandparent's Colombian blood runs through my veins. I am likely in the smallest of minorities as a Christian, Hispanic, female scientist who wants to change the world and help people live better lives. I am a girl who has defied the odds and looks forward to the challenges ahead. When all is said and done, I would say I am a servant of God that has been used to show that seemingly impossible dreams are not impossible for Him.

My current challenge involves changing paradigms in the field of spinal cord injury with the help of my mentor Dr. Marino De Leon. I am presently conducting studies on inflammation post spinal cord injury and am finding that it takes special skill to coax the unknown out if its comfortable home. In addition to research, I have somehow found the time to complete the major class requirements for a degree in human anatomy. I am excited for what the future holds and cannot wait to continue growing professionally and contribute to the greater body of thinkers who want to learn more about the world and make it a better place.

FATTY ACID BINDING PROTEIN 4 (FABP4) INHIBITION PROMOTES LOCOMOTOR AND AUTONOMIC RECOVERY IN RATS FOLLOWING SPINAL CORD INJURY

Jenniffer Licero Campbell, Miguel Serrano-Illàn, Magda Descorbeth, Kathia Cordero,
Johnny Figueroa, Marino De León
Center for Health Disparities and Molecular Medicine, School of Medicine,
Loma Linda University, Loma Linda, CA

Fatty Acid Binding Protein 4 (FABP4) upregulation in macrophages prolongs macrophage pro-inflammatory behavior and has become increasingly important in the etiology of conditions like cancer, diabetes, and metabolic syndrome. Nevertheless, its function in the context of spinal cord injury (SCI) has not been reported. The inflammatory processes following spinal cord contusion are characterized by marked lipid dysregulation which guide macrophage differentiation and contribute to axonal dieback, neuronal and oligodendrocyte death, and expansion of the injury. As FABP4 plays a critical role in macrophage differentiation and function, we hypothesize that its inhibition will promote locomotor and autonomic recovery following SCI. The present study (1) examines the spatiotemporal expression and functional context of FABP4 in injured spinal cord epicenters, (2) assesses the effects of FABP4 inhibition on locomotor and bladder recovery in rats, and (3) studies the potential role of inhibition on macrophage differentiation. We are the first to report on the significant upregulation of FABP4 mRNA and protein and the effects of its inhibition on macrophage phenotype as well as functional recovery in the injured rat spinal cord. Our data indicates FABP4 is robustly upregulated in the injured spinal cord and its inhibition significantly increased the number of M2 macrophages in the injury epicenter and penumbra which resulted in significant improvements in both locomotor function and autonomic bladder recovery. These findings reveal the importance of FABP4 expression in central nervous system (CNS) injury and provide a novel therapeutic candidate for modulating macrophage responses and promoting recovery following CNS injury.

PEDRO T. OCHOA
IMSD PARTICIPANT 2021

As a child, I was always intrigued by how things operate. I once took apart my father's watch piece by piece just to better understand how it worked. The watch was irreparable, but my passion to learn and understand why and how things function was born. As I progressed through secondary school, I pondered my future and what it held. I knew I wanted to attend college, but I did not feel passionate about any specific field or degree. It was not until a close family member was diagnosed with cancer where I discovered my calling in life and true passion. I saw this family member go from a healthy individual to a completely different person. Thanks to the hard work of the medical staff and to 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, and I knew biology was the undergraduate major I needed to pursue.

I attended the University of California, Irvine (UCI), where I obtained bachelor's degrees in biology and sociology. At UCI, I did research under the supervision of a post-doctorate researcher. This research experience combined with my thirst for knowledge and passion for cancer biology led me to apply and be accepted into the LLU PhD program in 2020. After my lab rotations, I decided to join Dr. Carlos Casiano's lab where I currently work on my thesis project on inhibiting a stress oncoprotein known as LEDGF/p75 and determine the effects this inhibition has on prostate cancer (PCa) chemoresistance. My goal this summer is to identify the effects of potential LEDGF/p75 inhibitors in both chemo-resistant and -sensitive PCa cell lines.

CYTOTOXIC EFFECTS OF POTENTIAL LEDGF/p75 INHIBITORS IN DOCETAXEL RESISTANT PROSTATE CANCER CELLS

Pedro Ochoa, Leah Baluyot, Catherine Elix, Greisha Ortiz-Hernandez, Carlos Casiano
Center for Health Disparities and Molecular Medicine, School of Medicine,
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Prostate Cancer (PCa) is the second leading cause of cancer death in men in the United States. Although the 5-year survival rate of localized PCa is nearly 100%, once the disease progresses into later stages, patients ultimately develop resistance to current cancer treatments, and the survival rate drops to nearly 30%. There are several mechanisms cancer cells can develop to promote resistance to standard PCa therapies. Understanding the mechanisms by which cancer cells develop resistance is essential. One mechanism in which cells acquire resistance is through Lens Epithelium Derived Growth Factor p75 (LEDGF/p75). LEDGF/p75 is a stress oncoprotein that promotes cell survival against environmental stressors such as chemotherapy drugs like docetaxel (DTX), which is used to treat PCa. LEDGF/p75 is upregulated in multiple diseases including PCa, leukemia, and HIV. LEDGF/p75 contains the Integrase Binding Domain (IBD), the binding site for multiple proteins, such as PogZ, Menin, and MLL. These proteins have been shown to regulate the transcription of genes that promote cell viability. Thus, LEDGF/p75 is an optimal therapeutic target. Previously, our lab identified DTX-resistant PCa cell lines overexpress LEDGF/p75 compared to their respective DTX-sensitive PCa cell lines. We hypothesize treatment of LEDGF/p75 inhibitors in conjunction with DTX will increase cytotoxicity in DTX-resistant PCa cell lines. After characterization of the panel of PCa cell lines used in this study, the cytotoxicity of these potential LEDGF/p75 inhibitors in DTX-resistant PCa cell lines were evaluated via MTT assays. Taken altogether, our results show an increase in cytotoxicity upon treatment with the LEDGF/p75 inhibitors, but no difference in the presence or absence of DTX.

PERLA ONTIVEROS-ÁNGEL

IMSD PARTICIPANT 2021

I was born in Tijuana, México, and was always an extremely curious, problem solving, and resilient girl. Today, as a PhD candidate in the Neuroscience, Systems Biology and Bioengineering Graduate program and part of the IMSD initiative at Loma Linda University School of Medicine in training under Dr. Johnny D. Figueroa's mentorship, I get to incorporate all that drive into investigating neuromodulatory effects of psychosocial stress and diet-induced obesity in adolescents exposed to early life stress.

As a first generation, college-educated immigrant to pursue a doctorate, I am proud to represent girls and minorities in the STEM field where gender and racial gaps exist. I am blessed with opportunity to invest my passion for neuroscience and biotechnology in researching health disparities affecting underserved communities. The CHDMM and the IMSD program have provided training and awareness of health equity and whole person care, altogether a true example of the power of scientific pursuit as part of Jesus' mandate of caring for the most vulnerable.

The IMSD program and Fig NeuroLab© have given me the opportunity to mentor great students. This summer, UTP student Vivianna De León-Williams has inspired me with her ability for critical thinking, hardworking attitude, and caring support; MTP student Claudio Villalobos with his thoughtful and compassionate insights; and IMSD student Tim Simon with his dedication and resilience. My long-term goal is to honor God through my research by making an impact in psychological disorders with understanding, diagnosis, and standard of care. Additionally, I want to inspire current and future generations to pursue science to help others in a deep, meaningful, and lasting way.

NEUROPATHOLOGICAL SIGNATURES CONNECTING EARLY-LIFE TRAUMA TO COMPULSIVE EATING BEHAVIOR AND OBESITY

Perla Ontiveros-Ángel, Vivianna De León-Williams, Timothy Simon, Fransua Sharafeddin, John Lou, Johnny Figueroa
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Childhood trauma heightens the risk of severe weight gain and adult obesity. However, neuropathological correlates of increased risk of obesity in individuals exposed to early-life trauma remain poorly understood. Preclinical findings from our laboratory support alterations to cortical structures regulating top-down control of feeding behavior may account for this vulnerability. While both stress-related psychiatric and binge-eating disorders are twice as prevalent in women as men, the neurobiological basis of this disproportionate incidence is not well understood. The present study evaluates neuroadaptations mediating the elevated risk of obesity and aberrant feeding behaviors in adolescents exposed to an obesogenic diet and trauma. Male and female adolescent Lewis rats (n=96, 48M, 48F) were fed for twelve weeks with Western Diet (WD, 41% kcal from fat) or a matched control diet (CD, 13% kcal from fat) and exposed to a novel two-hit model of predator-based psychosocial stress (PSS) followed by intermittent access to WD. Longitudinal assessment of behavioral effects and molecular markers showed female rats were more susceptible to the effects of the PSS and WD. Female rats displayed robust binge eating-like feeding behaviors when intermittently exposed to WD. This phenotype was associated with heightened anxiety-related behaviors. Interestingly, trauma exposure dysregulated estrus cycle length and stage frequency. Our findings demonstrate early-life stress and consumption of an obesogenic WD during adolescence heighten behavioral vulnerabilities associated with risk for anxiety and stress-related eating disorders. Our animal model recapitulates sex differences in traumatic stress responsivity, identifying sexual dysmorphisms linking neuroadaptive responses to early-life trauma, compulsive eating behaviors, and obesity.

GREISHA L. ORTIZ HERNÁNDEZ

IMSD PARTICIPANT 2021

Growing up on the beautiful island of Puerto Rico, I discovered my biggest passion, other than cooking and the outdoors, are the sciences. As Zig Ziglar said: "You don't have to be great to start, but you have to start to be great."

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

Currently, I am mostly finished with my PhD degree requirements and reflect on my years of training under the guidance of Dr. Carlos A. Casiano. My dissertation work focuses on the contribution of protein-protein interactions to LEDGF/p75-mediated upregulation of stress oncoproteins to tumor aggressiveness and chemoresistance. My plans for the summer are to complete my dissertation defense and transition into a post-doc position under a T-32 grant at City of Hope Cancer Center. I am forever grateful for the IMSD program and the excellent training I received in the CHDMM. The tools I acquired during my PhD training will be essential for the development of my career as a scientist who will represent a whole Hispanic community.

CHARACTERIZATION OF THE LEDGF/P75 INTERACTOME WITH HUMAN AUTOANTIBODIES IN CHEMORESISTANT PROSTATE CANCER

Greisha Ortiz-Hernández, Evelyn Sanchez-Hernandez, Pedro Ochoa, Catherine Elix, Carlos Casiano
Center for Health Disparities and Molecular Medicine, School of Medicine,
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Prostate Cancer (PCa) progresses to an advanced stage called metastatic castration PCa (mCRPC) for which, currently, there is no cure in spite of advances in treatment with new generation anti-androgen drugs and chemotherapy with taxanes such as docetaxel (DTX). Our lab demonstrated that the stress oncoprotein Lens Epithelium Derived Growth Factor of 75 kD (LEDGF/p75) is upregulated in clinical prostate tumors and contributes to DTX-resistance in mCRPC cells. However, little is known about the molecular mechanisms by which LEDGF/p75 promotes taxane resistance. The C-terminus of LEDGF/p75 contains a domain called the Integrase Binding Domain (IBD). In non-PCa cells, the LEDGF/p75 IBD interacts with transcription complexes, such as Menin-MLL and the c-MYC binding protein JPO2, to promote cell survival. However, the relevance of these and other protein-protein interactions (PPIs) in the context of PCa chemoresistance has never been explored. This project sought to characterize the interactions between LEDGF/p75 and its IBD-interacting partners in DTX-resistant mCRPC cells and their contribution to chemoresistance. Our results revealed a significant co-upregulation of LEDGF/p75 and its IBD-interacting partners in the DTX-resistant cell lines compared to the parental, drug-sensitive cells. We also observed nuclear co-localization of these proteins by confocal microscopy. Additionally, using an immunoprecipitation approach, we confirmed endogenous LEDGF/p75-IBD interacting partners co-immunoprecipitated with LEDGF/p75 in the DTX-resistant PCa cell lines. Silencing of LEDGF/p75, Menin, or JPO2 effectively sensitized taxane-resistant cells to DTX as evidenced by a significant decrease in their clonogenic potential and tumorsphere formation capacity. These observations suggest that targeting LEDGF/p75 PPIs can disrupt transcriptional activity contributing to DTX resistance.

FOLUWASOMI OYEFESO

IMSD PARTICIPANT 2021

One of the best gifts that life has given me is passion for studying science. While pursuing a BSE in Bioengineering at Walla Walla University, I developed a deeper love and understanding of science while conducting research to develop tissue engineering scaffolds under the instruction of Dr. Janice McKenzie. Our goal to develop a novel construct for regenerative medicine applications by culturing fibroblast cells on polymer scaffolds was produced by optimized 3D printing and electrospinning methods.

My prior research experiences led me to apply for a PhD in Neuroscience, Systems Biology and Bioengineering under the instruction of Dr. Michael Pecaut. Now, continuing four years of progress in the Pecaut lab, I have been fortunate to conduct research under multiple NASA studies; to collaborate with numerous specialists including a world-renowned neuroscientist studying brain organoids, Dr. Alysson Muotri; and to develop and conduct research on the biological effects of human brain exposure to ionizing radiation.

As a PhD candidate, I am thrilled to be studying in a field I feel passionate about and learning something new every day. I am also fortunate to be a student in the IMSD program in the LLU Center for Health Disparities and Molecular Medicine. The remainder of my PhD will be focused on understanding how spaceflight-relevant stressors may contribute to aging-related degenerative diseases which affect the human brain.

Moving forward, next year I plan to enter medical school and continue towards my goal of conducting translational research in regenerative medicine. In the future, I hope to make science and research opportunities more accessible for historically minoritized communities by establishing STEM programs in the Greater Los Angeles area. On my scientific journey I practice the daily mindset captured by these wise words from my mentor, "Life is all about making connections."

BRAIN ORGANOIDS: A NEW TOOL TO CHARACTERIZE MECHANISMS AND BIOLOGICAL DIFFERENCES OF PARTICLE RADIATION-INDUCED NEUROTOXICITY

Foluwasomi Oyefeso, Timothy Simon, Marcelo Vazquez, Antonella Bertucci, Michael Pecaut
Center for Health Disparities and Molecular Medicine, Division of Biomedical Engineering Sciences;
Radiation Medicine, Department of Basic Sciences, School of Medicine,
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Particle therapy (PT) is becoming more widely available for clinical use. For patients with favorable prognoses, particularly childhood brain tumors, proton therapy is increasingly used for treatment. There is also interest in using carbon ion therapy for the treatment of aggressive brain tumors. However, the biological effects of PT (proton and carbon ions) may differ substantially from those of photon radiation. Therefore, there is a need to study the potential mechanisms of particle radiation (PR) neurotoxicity. Three-dimensional (3D) brain organoid cell culture systems have emerged as novel models to simulate the organization and cell diversity of human CNS in vitro. Here, we report the use of human brain organoids to study the cell-specific effects of PR on normal neural tissue as these models recapitulate features of the human brain, such as structural and functional integrity. In this study, we used brain organoids to characterize proton-induced changes to neural cells in vitro. Organoids were exposed to 0, 0.5 and 2 Gy of 250 MeV protons to evaluate changes in cell architecture (i.e., MAP2, GFAP), proliferation (Ki67), apoptosis (Caspase-3), and DNA damage (γ-H2AX) using immunofluorescence and confocal microscopy. Preliminary results from this study support the use of brain organoids as a translational tool to investigate particle-induced cellular and molecular changes as well as identify potential biological differences between photon and particle toxicity in the CNS.

EVELYN S. SANCHEZ HERNANDEZ

IMSD PARTICIPANT 2021

I graduated from California State University, Northridge (CSUN) in May 2017 with a Bachelor of Science in Cell and Molecular Biology. Throughout my undergraduate career, experiences shaped my purpose in life. Having the opportunity to conduct research as a MARC scholar at CSUN allowed me to discover my passion for conducting biomedical research. Observing my father being affected by non-Hodgkin's lymphoma in 2014 also made me realize the importance of biomedical research in our society. Many patients' lives depend on the answers many 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 saving lives.

I am a fourth year PhD candidate at Loma Linda University in the division of Cancer Developmental and Regenerative Biology (CDRB) in Dr. Carlos A. Casiano's laboratory. My dissertation research project focuses on studying the contribution of the glucocorticoid receptor (GR) and LEDGF/p75 axis to prostate cancer (PCa) chemoresistance and its potential role in mortality disparities in PCa that disproportionally affect African-American patients. In particular, I am performing mechanistic studies to better understand how GR regulates LEDGF/p75 and how this axis contributes to chemotherapy resistance.

CONTRIBUTION OF THE GR-LEDGF/p75 AXIS TO PROSTATE CANCER CHEMORESISTANCE

Evelyn Sanchez-Hernandez, Greisha Ortiz-Hernandez, Pedro Ochoa, Christian Gomez, Carlos Casiano
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Prostate cancer (PCa) is the second leading cause of cancer deaths in the U.S., disproportionally affecting African American (AA) men. Glucocorticoids (GCs) administered to PCa patients have been implicated in therapy resistance, which may be critical to AA men with PCa since they have elevated endogenous GCs levels compared to Caucasian American (CA) men. GCs bind to the glucocorticoid receptor (GR) to exert their actions. Mechanisms of GR-mediated chemoresistance and its possible contribution to PCa mortality disparities are unknown. We demonstrated GCs upregulate the chemoresistance-associated protein and transcription co-activator LEDGF/p75 in PCa cells and identified consensus GR binding sites in the promoter region of this protein. Based on our preliminary data, we hypothesized GR transcriptionally upregulates LEDGF/p75 and then interacts with it to enhance taxane resistance in PCa cells. Pharmacological and genetic inhibition of GR in a panel of docetaxel (DTX)-sensitive and -resistant PCa cells decreased expression of LEDGF/p75, confirming its status as a candidate GR target gene. However, silencing of LEDGF/p75 had no effects on GR expression. Immunoprecipitation studies revealed GR and LEDGF/p75 interact in DTX-resistant PCa cells. This interaction was confirmed by confocal microscopy. Immunohistochemical analysis of GR and LEDGF/p75 expression in normal and tumor prostate tissues was performed and the results are currently being analyzed. Our studies use a mechanistic approach to evaluate the potential contribution of the GR-LEDGF/p75 axis to PCa chemoresistance. Evaluating the co-expression of these proteins in racially diverse PCa tissues may also reveal race-related differential expression, providing insights into the potential contribution of this axis to PCa chemoresistance and mortality disparities.

NICHOLAS SANCHEZ
IMSD PARTICIPANT 2021

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

Working in this environment is intimidating yet brings its own excitement from being so dynamic. My project has received an NIH grant, placing it among the fortunate tier of projects that have been recognized with such potential. I am working towards gathering data to test my project's hypothesis and determine the further direction of my work.

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

PROGRESS IN ISOLATING SYNAPTOSOMAL FRACTIONS FROM HUMAN BRAIN SAMPLES

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

"Oxidative stress," particularly instigated by dysregulated transition metal metabolism in the brain, plays an important role in the pathogenesis of Alzheimer's disease (AD). Cycling copper (Cu) between monovalent [Cu(I)] and divalent [Cu(II)] states makes the element potentially neurotoxic by promoting reactive oxygen species production. Preliminary studies show 1) Cu deposits in neuronal axons, 2) decreased Cu in synaptosomal fractions, and 3) reduced Cu transport proteins as emerging diagnostic indicators in AD brains. These findings were not as apparent in patients diagnosed with AD with Cerebral Amyloid Angiopathy (CAA). We hypothesize copper dysregulation is an important step in AD pathogenesis. To study the impact of nonoptimal copper transport, we are working to isolate synaptosomes from human brain homogenate and cell models for measuring downstream effects. We illustrate the attempts to troubleshoot and improve the synaptosome isolation protocol. Additionally, we show work done to confirm siRNA transfections to confirm a working protocol for future experiments regarding downregulating copper transport proteins in a neuronal cell model. This progress is imperative for moving forward with our work and is a step towards a more comprehensive study of the importance of copper regulation in the human brain.

KRYSTAL R. SANTIAGO

IMSD PARTICIPANT 2021

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 view, I have put a lot of effort into becoming the best student I can be. Last summer 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 first-year student where I will further my education by earning a PhD.

Throughout my middle school and high school years, I also attended an after-school academy that is specialized in music and arts. There, I learned to play the flute and I also trained my voice. Because of this musical training, I was able to become one of the few with a scholarship from the Coral Universitaria, a choir that represented the UPRM nationwide. I believe my purpose in this world is to serve others, and I have exemplified this conviction in many ways. After hurricane Maria, my friends and I helped rebuild houses and feed the homeless. I also volunteered as a nanny in a house for abused children.

In order to be a force for positive change, I selected Dr. Carlos Casiano and Dr. Frankis 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.

TARGETED GLYCOLYSIS INHIBITON WITH NOVEL ENOBLOCK INHIBITORS CAUSE CELL DEATH IN CHEMORESISTANT PROSTATE CANCER CELLS

Krystal Santiago Torres, Astrid Álvarez de La Cruz, Daniel Bazan, Alfonso Durán,
Bhaskar Das, Carlos Casiano, Frankis Almaguel
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Prostate cancer (PCa) is the second most common cancer in American men with one in eight men diagnosed annually. Taxane chemoresistance is one of the most common reasons for treatment failure in PCa patients, and evidence links metabolic shifts to this process. A vital glycolytic enzyme, enolase, is over-expressed in PCa. There are three types of enolases with similar glycolytic functions with ENO-1 and ENO-2 implicated in PCa. Enolases regulate the conversion of 2-phosphoglycerate to phosphoenolpyruvate during glycolysis. The absence of enolase interrupts glycolysis and affects cell metabolism. Our preliminary data through immunoblotting demonstrates that drug-sensitive PCa cell lines express ENO-1 and ENO-2; however, docetaxel resistant (DR) PCa cell lines only express ENO-1. The absence of ENO-2 in these cells creates a metabolic vulnerability due to loss of protein redundancy. Thus, ENO-1 could be a novel target for PCa treatment. We hypothesize that DR PCa cells will be sensitive to ENO-1 inhibitors due to their ENO-2 deficiency. Several boron-based enolase inhibitors were identified, and two of them, BT#568 and BT#572, decreased PCa cell viability as assessed by MTT viability assays and Hoffman Modulation Contrast Imaging. Inhibitor efficacy was evaluated by measuring cell viability after treatments with different concentrations. Our results showed cell death starting a 5uM of BT#572, with more pronounced cytotoxicity at 10uM. BT#568 induced cell death at 5uM; however, its potency was lower than that of BT#572. Our results suggest these boron-based ENO1 inhibitors affect glycolysis and cell metabolism leading to cell death in DR PCa cells.

TIMOTHY SIMON

IMSD PARTICIPANT 2021

I am a first-year PhD student in the Neuroscience, Systems Biology, and Bioengineering program. My research focuses on the effects of diet and stress on neurodevelopment. I am particularly interested in the molecular mechanisms of learning, memory, and psychosocial stress in the brain and how different environmental factors (such as diet) affect these processes. A key motivation propelling this research is alleviating the health disparities in populations at risk for chronic stress and childhood trauma.

I am pleased to conduct neuroscience research in Dr. Johnny Figueroa's laboratory where I am encouraged to pursue my scientific passions and creativity. Being a part of this lab has allowed me to engage in research and participate in mentoring a summer medical student. The summer mentoring program has helped solidify my desire to be a university professor and to continue advising students in the future.

Apart from research, I absolutely love hanging out with family and friends, reading, drinking coffee, and camping. Every time I drive to the LLU campus, walk to my lab in the Center for Health Disparities and Molecular Medicine and begin an experiment, I praise God for the opportunities. I really could not have gotten this far by my own strength. As St. Augustine said,
"God provides the wind; Man must raise the sail."

FKBP5 EXPRESSION IN THE HIPPOCAMPUS OF ADOLESCENT RATS EXPOSED TO PSYCHOSOCIAL TRAUMA AND OBESOGENICE DIET

Timothy Simon, Claudio Villalobos, Johnny Figueroa
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Increase in obesity and psychosocial stress among adolescents raises concerns about their effect on brain development. Studies have shown association between hippocampal atrophy, trauma/stress, obesogenic diets, and aberrant *FKBP5* expression. FK506-binding protein 51 gene (*FKBP5*) is a critical stress biomarker, a co-chaperone regulating stress responses by negatively inhibiting glucocorticoid receptor response. This study aims to expand understanding of *FKBP5*'s role by investigating its spatial expression in the hippocampus of adolescent rats exposed to an obesogenic diet and psychosocial stress. Adolescent Lewis rats (n = 56) were fed a Western-like diet (WD, 41% kcal from fat) or control diet (CD, 13% kcal from fat) beginning at postnatal day (PND) 21 and then subdivided into exposed and unexposed groups. Exposed groups endured a psychosocial stress model (PSS) including 30 consecutive days of social instability (PND 60 - 90) and two predator exposures (at PND 60 and 70). Brain tissue, harvested at PND 107, was prepared for *FKBP5* mRNA expression analysis using RNAscope technique. The dorsal hippocampus CA1 area was chosen for *FKBP5* mRNA quantification. Hippocampal tissue was used for bisulfite conversion to procure *FKBP5* methylation differences. Bisulfite conversion revealed an 8% reduction in *FKBP5* methylation in the hippocampus of WD/PSS rats. RNAscope protocol was successfully optimized to obtain and analyze neurohistological results, which showed altered *FKBP5* mRNA levels in rats exposed to WD and PSS, confirming previous findings from our laboratory. Together, our results indicate obesogenic environments heighten vulnerabilities to early adverse events and contribute to altered brain maturation and unhealthy responses to stress. We identify *FKBP5* as a critical molecular player connecting early psychosocial stress exposure, obesity, and hippocampal development and function.

PAUL A. VALLEJOS

IMSD PARTICIPANT 2021

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

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

I would like to thank my mentor Dr. Nathan Wall and laboratory partner Ryan Fuller for all their help and guidance throughout my time in the program. Additionally, I would like to thank the IMSD program and the Center for Health Disparities and Molecular Medicine for their support.

EXOSOMAL PROTEINS AS A SOURCE OF BIOMARKERS IN COLON CANCER-DERIVED PERITONEAL CARCINOMATOSIS

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Peritoneal Carcinomatosis (PC), metastasized from colorectal cancer (CRC), remains a highly lethal disease, especially when significant tumor burden has developed. Diagnosis of PC before tumors have extensive growth and organ infiltration will improve PC treatment and patient outcomes. Using mass-spectrometry-based proteomics, we characterized the protein features of circulating exosomes in the context of CRC PC, CRC with liver metastasis, and CRC without metastasis. We profiled exosomes isolated from patient serum to identify exosome-associated protein cargoes released by these cancer types. Analysis of the resulting data identified metastasis-specific exosome protein signatures, and bioinformatic analyses confirmed enrichment of proteins annotated to vesicle-associated processes and intracellular compartments as well as representation of cancer hallmark functions and processes. Of the 280 proteins identified, 90 had previously been associated to cancer with 50 being directly related to cellular movement. This research yielded distinct protein profiles for the CRC patient groups and suggests the utility of serum exosome proteomic analysis for a better understanding of PC development and metastasis.

JONATHAN WOOTEN

IMSD PARTICIPANT 2021

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

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

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

PLANT ISOLATE DIBENZYL TRISULFIDE INDUCES CASPASE-INDEPENDENT DEATH IN TRIPLE NEGATIVE BREAST CANCER CELLS DERIVED FROM PATIENTS OF WEST AFRICAN DESCENT

Jonathan Wooten, Shaniece Wauchope, Cristina Araújo, Joyce Aja, Nicole Mavingire, Rupika Delgoda, Eileen Brantley
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Patients with triple negative breast cancer (TNBC) possess tumors that lack estrogen receptor, progesterone receptor, and human epidermal growth receptor expression. While these patients traditionally receive chemotherapy to combat this aggressive breast cancer subtype, others use natural remedies. Dibenzyl trisulfide (DTS) is derived from *Petiveria alliacea*, a perennial shrub that grows in tropical regions of the world. Many TNBC patients residing in the tropics are of West African descent. Therefore, we evaluated the anticancer actions of DTS in TNBC cells, including those derived from patients of West African descent. We found that DTS inhibited TNBC cell viability, migration, and proliferation in a dose-dependent manner. Interestingly, DTS blocked the propensity of pro-carcinogen benzo-A-pyrene to induce proliferation of immortalized breast epithelial cells. Moreover, we found that DTS induced early apoptosis in TNBC cells, which was only partially attenuated following pretreatment with pan-caspase inhibitor zVAD-fmk. Though DTS induced pro-apoptotic gene and protein expression along with PARP cleavage, it failed to produce appreciable caspase 3 cleavage and promote significant apoptotic body formation. This finding suggests this plant isolate induces caspase-independent and non-apoptotic death of TNBC cells. Furthermore, DTS promoted lysosomal membrane destabilization and cathepsin B release in TNBC cells. Taken together, DTS exhibits promising chemotherapeutic and chemopreventive ability by inducing non-apoptotic TNBC cell death and thwarting TNBC progression, supporting its evaluation in clinical trials as an agent to combat TNBC among patients of West African descent.

FRANCIS ZAMORA

IMSD PARTICIPANT 2021

Over the course of my academic journey, pursuing a career in medical research became a major goal of mine. Previous to coming to Loma Linda University, I attained my Master's in Anatomy & Neurobiology from Boston University where I discovered my curiosity for the neuroscience field. I yearned to have the opportunity to continue developing a thorough understanding of neuronal mechanisms in order to make my own inquires, investigate medical questions that are yet to be answered, and contribute to closing the gaps in knowledge in the scientific literature.

Thus, I am grateful to be part of the IMSD program at LLU as it provides me with the resources to earn my PhD and fulfill my dream of becoming a neuroscientist. Additionally, being a Hispanic, first generation American woman has always been a driving force to further my education and thus feel proud to represent underrepresented minorities in science.

This fall I will be a second-year PhD student in Dr. Marino De Leon's laboratory. Topics of focus for my research include exploring the mechanisms of docosahexaenoic acid (DHA) in the context of nerve injury and its modulation of neuropathic pain. I would like to thank Dr. De Leon for his mentorship and guidance as I continue my academic journey. I hope that through the research being done in our laboratory, it can one day clinically translate into dissipating health disparities and disease among underserved communities.

DHA REGULATION OF FATTY ACID-BINDING PROTEIN 5 (FABP5) IN RESPONSE TO PALMITIC ACID STRESS IN SCHWANN CELLS

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Following nerve injury, inflammation and axonal degeneration contribute to developing hypersensitivity symptoms characteristic of neuropathic pain. Docosahexaenoic acid (DHA), an omega-3 fatty acid (FA), is neuroprotective during neuronal injury by promoting cell survival and inhibiting apoptosis. Previously, our lab showed DHA protects differentiated-PC12 cells and Schwann cells (SCs) against palmitic acid-induced lipotoxicity (PA-Ltx). In non-healthy nerves, SC dysfunction results in compromised myelin sheath integrity. FABP5, an FA shuttle within the cell, is a multi-functional protein involved in neuroprotection. FABP5 is shown to be upregulated by PA-Ltx in neuronal cells and, under these conditions, is protective by its ability to reduce oxidative stress and promote cell survival. We hypothesize that DHA increases FABP5 as one of its neuroprotective strategies. In this study, immortalized SCs were treated with DHA, PA, or DHA+PA for 12 or 24 hours. We used Western blot to determine the levels of FABP5 protein in iSCs cellular extracts (n=4). Our data show that after 12-hour treatment, FABP5 levels were similar between groups. However, iSCs treated for 24 hours with PA showed an 11.2-fold upregulation of FABP5, similar to what is reported during neuronal injury. Treatment with DHA alone also increased FABP5 4.6-fold, suggesting FABP5 also plays a role in DHA's observed neuroprotective role. Interestingly, iSC cultures co-treated with DHA+PA show a similar level of FABP5 compared to control, suggesting DHA activates additional pathways to prevent PA-induced injury. Our preliminary data indicate FABP5 may play a role during SC survival following PA-induced injury, but further experimentation is needed to elucidate potential cellular pathways and the role of DHA.

Guest Participants

Casey Curow
Alondra Enciso
Aaron Keniston
Kristiana Rood
Fransua Sharafeddin
Kristen Whitley

CASEY CUROW
GUEST PARTICIPANT 2021

My interest and passion for science and medicine have been reinforced over the years. Events revolving around my family started it all, and my undergraduate education, volunteering at Loma Linda University Medical Center, and research at Loma Linda University have only strengthened my career goals.

In April 2021, I graduated from the University of Redlands with a Bachelor of Arts in Biology and minor in psychology. My current goal is to attend medical school to fulfill my dream of becoming a physician. I want to hold the responsibilities of physical and mental healing to have a positive, lasting impact on patients and my community entirely.

Aside from medicine, baseball has been another passion of mine. Baseball played a significant role in my life since I was a toddler and up until I graduated high school. It still remains a big part in my life just not as a player now. I have been a volunteer coach at Canyon Springs High School for the past few seasons and I have enjoyed it immensely. It is always great to see players succeed in school and baseball due to their hard work.

My research in Dr. Juli Unternaehrer's lab began last summer, and I am extremely grateful for the opportunity to continue my project beyond the University of Redland's summer program. Conducting cancer research is exceedingly meaningful to me due to cancer in my family and some of my interactions with cancer patients at Loma Linda University. It is because of Dr. Unternaehrer and her lab that I have been able to connect my research to family and patients. Dr. Unternaehrer's guidance, advice, and help this past year–as well as her deep appreciation for science–have made this research experience one I will never forget.

SNAIL-MEDIATED CHEMORESISTANCE IN OVARIAN CANCER

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Epithelial-mesenchymal transition (EMT) is a crucial mechanism for cancer maintenance and progression in many cancers including high-grade serous ovarian cancer (HGSOC). Chemotherapy is a primary therapeutic strategy, but most HGSOC patients experience recurrence due to chemoresistance. The acquisition of chemoresistance in epithelial cancer cells can arise when EMT is undergone. SNAI1 (Snail), a major EMT transcription factor, initiates EMT thereby promoting resistance to chemotherapeutic drugs. However, little is known about this Snail-induced mechanism. RNA-sequencing results revealed that Snail expression is directly correlated to matrix metalloprotease 1 (MMP1) expression. High MMP1 expression is known to promote invasion and formation of metastases in many cancers. MMP1 is commonly found to be upregulated in chemoresistant cells versus their chemosensitive counterparts as well. Furthermore, in breast cancer, MMP1 has been reported to be a downstream target of Slug, another major EMT transcription factor. Therefore, we hypothesized that Snail utilizes MMP1 to promote chemoresistance in addition to invasion and metastasis. Preliminary data was collected via RT-qPCR to analyze mRNA co-expression of Snail and MMP1 in eight cell lines. There was a positive correlation between Snail and MMP1 mRNA in the seven tumorigenic cell lines used. We also found a direct relationship between Snail and MMP1 levels in two chemoresistant cell lines versus their chemosensitive counterparts. Moreover, the cisplatin-resistance of these cell line pairs were assessed using MTT cell viability assays. Our data indicated that the chemoresistant cell lines were more resistant to cisplatin than their chemosensitive counterparts. Thus, our early findings suggest MMP1 is implicated in Snail-mediated chemoresistance.

ALONDRA ENCISO

GUEST PARTICIPANT 2021

I graduated from California State University, San Bernardino in May of 2021 with a B.S. in Biology. During my time at CSUSB, I developed what I like to call "micropipette phobia" or fear of the lab simply because I lacked confidence in my laboratory skills. With words of encouragement from my mentor Dr. Bournias, I became a CIRM intern and gained confidence in my laboratory and tissue culture techniques. Under this program, I am currently working in Dr. Juli Unternaehrer's lab which studies ovarian cancer. My project entails using a fluorescent reporter to detect changes in cancer cells in response to radiation treatment.

In my free time, I work a part-time job at San Antonio Regional Hospital as an ER medical scribe. My hobbies out of the lab involve working on writing and drawing digital art. My goal in life has been to pursue a career in emergency medicine to help the lives of those in underprivileged communities.

USING THE FLUORESCENT REPORTER, GFP-ZEB1-3' UTR TO DETECT CHANGES IN EPITHELIAL-MESENCHYMAL TRANSITION IN RESPONSE TO IRRADIATION

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High grade serous ovarian cancer (HGSOC) is a lethal gynecological malignancy due to its aggressiveness, compounded by frequent late diagnosis. After standard therapies including surgery and chemotherapy, patient prognosis is poor due to metastasis, tumor recurrence, and chemoresistance. Radiation therapy is used in advanced cases but is known to promote cancer cell aggressiveness. Because cancer stem cells (CSC) are one source of cancer recurrence, CSC-targeted therapies are needed. We aimed to detect radiation-induced aggressiveness, including invasiveness and stemness. Epithelial-mesenchymal transition (EMT) promotes these characteristics, and the GFP-Zeb1-3' UTR reporter (Z-GFP) has been used to observe changes in epithelial and mesenchymal states. Diagnostic tools in identifying CSCs measure cell surface markers such as CD44, CD24, and CD104; however, the expression of these proteins vary in individual patient samples. Alternatively, we detected changes in EMT utilizing a reporter system consisting of green fluorescent protein (GFP) regulated by the presence of the 3’ UTR of Zeb1, an EMT transcription factor. Four different cell lines and one patient derived ovarian cancer cell line were lentivirally transduced with the reporter, and flow cytometry was used for GFP detection 72 hours after they had undergone proton or photon irradiation at 0 Gy, 1 Gy, 2 Gy, 4 Gy, and 8 Gy. We found increasing dosages of irradiation correlated with an increase in cells transitioning to the mesenchymal state. From these results, we can infer irradiation induces EMT detectable by our reporter system. With the reporter, we will develop systems to prevent radiation-induced aggressiveness.

AARON KENISTON

GUEST PARTICIPANT 2021

I am a first-generation college student who graduated with a B.S in Biology from CSUSB. During my time at CSUSB, I designed and developed chemical inhibitors for a malarial metalloprotease known as Falcilysin. When I wasn't busy with research or studying for classes, I peer-mentored first-generation college student through the SAIL program. My undergraduate experience was tough, but I graduated with a 3.8 GPA.

I am currently attending the Master of Science in Biology program at CSUSB, and I am lucky enough to have the opportunity to conduct my thesis research under Dr. Juli Unternaehrer at LLU through the CIRM program. My project involves detecting and modulating ovarian cancer aggressiveness during recurrence. We think aggressiveness is driven by two culprits: the epithelial to mesenchymal transition and cancer stem cells. This experience has been very enriching because I have been challenged by the trial-and-error process that comes along with science which has helped me build analytical skills and strong hand-eye coordination. I plan to employ these skills while reaching my career goal of becoming a dentist.

I am extremely grateful for Dr. Unternaehrer because I would not be able to do this research without her advice and guidance. Her patience and dedication to science inspires me every day to become the best scientist I can be.

During my down time, I enjoy working on my 1964 Volkswagen notchback and going on drives down Pacific Coast Highway. I believe life is about balance and we should work hard but also take time for ourselves. Thank you to everyone who has helped me get this far.

DETECTION OF OVARIAN CANCER STEM CELLS GENERATED BY RADIATION THERAPY WITH SORE6-GFP, A REPORTER OF SOX2 AND OCT4

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Ovarian cancer is the most lethal gynecological cancer with 80% of patients experiencing recurrence within 5 years. The aggressiveness of ovarian cancer during recurrence creates a need to identify and characterize potential therapeutic targets. The cancer stem cell (CSC) -like phenotype has been shown to contribute to cancer aggressiveness, which makes CSCs viable targets for therapeutic intervention. CSC can be detected via surface antigens including CD44, CD133, and CD117. These biomolecules are heterogeneously expressed and require antibodies. As an alternative detection modality of the CSC phenotype, we are analyzing core stem cell transcription factors in which a SOX2/OCT4 response element, designated as SORE6, regulates a GFP reporter system. Our aim was to detect changes in stemness in response to proton and photon irradiation. We hypothesize that proton and photon irradiation will have similar effects on stemness in ovarian cancer. To investigate this hypothesis, four different cell lines and one patient-derived ovarian cancer sample were subjected to 0Gy, 1Gy, 2Gy, 4Gy, and 8Gy dosages of proton and photon irradiation. Seventy-two hours post irradiation exposure, flow cytometry analysis was used to capture SORE6-GFP expression. We found an increase in stemness as radiation dosage increased which suggests radiation is selecting for the CSC phenotype. Proton and photon irradiation seem to have similar effects on stemness, but further trials will be carried out to illuminate any potential differences between the two.

KRISTIANA ROOD

GUEST PARTICIPANT 2021

Growing up, one of my passions was the power of proper nutrition to promote health in almost every way, and this interest helped cultivate my love for science. I am now pursuing a career in science and engineering and am dedicated and inspired to help women in the United States and the rest of the world affected by thyroid cancer through doing research to develop new diagnostic, prognostic, and therapeutic approaches for this disease.

As a graduate student earning my PhD in Loma Linda University's Basic Sciences program, I am working under principal investigators Dr. Salma Khan and Dr. Reinhard Schulte. I earned my bachelor's degree in bioengineering at Walla Walla University in College Place, WA, where I contributed to two different tissue engineering-related projects. My bioengineering background is being used now as my PhD project focuses on diagnosing thyroid cancer using a volatile organic compound ion detector as well as determining patient prognoses through whole genome sequencing and miRNA-signatures in thyroid cancer health disparities to provide appropriate future therapies.

Our team collects fine-needle aspiration biopsy samples from patients and uses these specimens for RNA, DNA, and protein assays. Under the leadership of Dr. Khan, I have been performing laboratory procedures that contribute to the data collection necessary for this project, including miRNA and DNA extraction from paraffin-embedded thyroid tissue, cDNA synthesis, qRT-PCR, and Western blot. I am exceedingly grateful for the knowledge and skills I have had the opportunity to gain thus far, and I am excited to continue working with my mentors to further this work.

DIFFERENTIAL EXPRESSION OF NON-CODING-RNA SIGNATURES IN THYROID CANCER BETWEEN TWO ETHNIC GROUPS

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Filipino Americans show higher thyroid cancer recurrence and death rates compared to European Americans, but the molecular mechanism of this malignancy has not yet been determined. Recent studies demonstrated small non-coding RNAs could be utilized to assess thyroid cancer prognosis in tumor models. Our goal was to determine whether miRNA-signatures are differentially expressed in thyroid cancer in two different ethnic groups. This is a retrospective study of de-identified archival samples from patients with thyroid cancer (both sexes) in the Pathology Division from the last ten years at Loma Linda University School of Medicine. We determined the differential expressions of microRNA in archival samples from Filipino Americans compared to European Americans using the state-of-the-art technique HiSeq4000. By ingenuity pathway analysis, we determined microRNA-targets and the pathways that those targets are involved in. We validated their expressions by real-time quantitative PCR and correlated them with the clinicopathological status in a larger cohort of miRNA samples from both ethnicities. Between Filipino American and European American samples, we identified the differentially upregulated/downregulated miRNA-clusters, some being known to target genes linked to cancer invasion and metastasis. In both univariate analysis and in a multivariate logistic regression model, ethnicity and tumor staging were significant independent predictors of miR-4633-5p upregulation. By contrast, ethnicity remained an independent predictor of significantly downregulated miR-491-5p and let-7 family genes irrespective of tumor staging. We provide evidence that Filipino Americans showed differentially expressed tumor-tissue-derived-microRNA clusters. The functional implications of these miRNAs are under investigation.

FRANSUA SHARAFEDDIN

GUEST PARTICIPANT 2021

My most prominent decision to choose neuroscience as a main direction of my future career is the strong will to help people suffering from devastating consequences of neuropathological diseases and a desire to grow scientifically, having the possibility to conduct different promising research projects.

Neuroscience with its technological advances in medicine, particularly in brain research-oriented areas, provides the possibility to develop as a neuroscientist and fulfill projects that translate into practical medicine, helping create productive treatments beneficial for suffering patients.

My current research interests are related to the neuroanatomical basis of the disease, particularly the prefrontal cortex and hippocampus, and their functions in health and pathology. Disorders affecting the prefrontal cortex and hippocampus have been revealed in diseases such as Alzheimer's, schizophrenia, anxiety disorders, Parkinson's, etc. Despite high morbidity rates, current treatment methods haven't shown to improve outcomes significantly. Failure of current existing treatment modalities to notably improve the results raises the need to develop modern effective therapeutic strategies, which will potentially ameliorate outcomes in patients. Thorough understanding of basic science principles and their implication into translational medicine and pre-clinical studies are key concepts of successful development of novel treatment strategies. In Dr. Johnny Figueroa's lab, we study stress-induced microstructural alterations of the prefrontal cortex and hippocampus, and we aim to reveal potential treatment targets.

CONSUMPTION OF A HIGH-SATURATED FAT DIET DURING ADOLESCENCE LEADS TO HIPPOCAMPAL ATROPHY AND IMPAIRMENT OF COGNITIVE FUNCTIONS POTENTIALLY THROUGH INVOLVEMENT OF TACE/ADAM17

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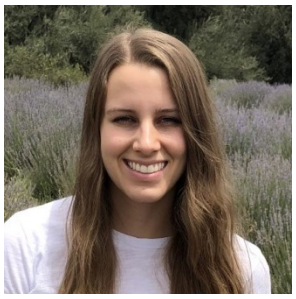
Adolescent obesity is strongly associated with deviant hippocampal maturation. Molecular mechanisms involved in this process are yet unknown. Synaptogenesis and synaptic pruning in the hippocampus during brain development depend on signaling between the growth factor NRG1 and its receptor ErbB4. NRG1-ErbB4 signaling is regulated by proteolysis, particularly by TACE/ADAM17. This study investigates the potential involvement of the TACE/ADAM17-NRG1-ErbB4 pathway in obesity-induced hippocampal atrophy. Adolescent Lewis rats were fed from PND21 to PND49 with either a high-saturated fat diet (WD, 41% kcal from fat) or a control diet (CD, 13% kcal from fat). Behavior was assessed between PND43 and PND49. Animals were euthanized at PND49. MRI was performed and hippocampal tissue was collected to evaluate TACE/ADAM17-NRG1-ErbB4 activities and inflammatory biomarkers. We found that consuming a high-saturated fat diet during adolescence leads to anxiety-like behaviors and hippocampal atrophy, specifically in the CA1 region. Alterations in behaviors were concurrent with changes in hippocampal pro-inflammatory cytokine profiles and microglial morphology. WD consumption increased ErbB4 phosphorylation and TACE/ADAM17 protein levels in the hippocampus. TACE/ADAM17 protein levels were positively associated with pErbB4 and interleukin-6 levels in the hippocampus. TACE/ADAM17 protein levels were associated with reduced ErbB4 and PSD95 protein levels in the hippocampus. We demonstrate that brief exposure to an obesogenic diet during adolescence is sufficient to induce hippocampal dysfunction and structural impairments in rats. We identify TACE/ADAM17-NRG1-ErbB4 pathway as a potential signaling axis linking adolescent obesity with hippocampal atrophy.

KRISTEN WHITLEY

GUEST PARTICIPANT 2021



As a child, I always believed that I would have a defining moment in which I would know exactly what I wanted to do for my career. That moment occurred my senior year of high school. I knew that I was passionate about science, and after talking to a family friend who was a clinical pharmacist, I knew I had found my career. What I didn't know was that I would fall in love with the pursuit of knowledge in the process.

This fall, I will be entering my junior year as a biochemistry major at Walla Walla University. During my first two years of college, I have shared my love of the sciences by working as a math and science tutor at Walla Walla High School. This past spring, I was also fortunate enough to volunteer alongside many health professionals at COVID-19 vaccination clinics. It was really inspiring to see so many people working together for the good of the community and hear their stories. I hope that one day I will be able to provide for my community in the same way these individuals have.

I am so grateful that I had the opportunity to work in Dr. Kerby Oberg's lab this summer. Dr. Oberg and my mentor, Jessica Britton, helped open my eyes to the world of research. While my heart is still set on pharmacy, I am now considering pursuing a PharmD/PhD degree because of my wonderful experience this summer.

REGULATION OF SONIC HEDGEHOG BY LHX2 DURING VERTEBRATE LIMB DEVELOPMENT IS NOT VIA A DIRECT PATHWAY

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In limb development, proximal-distal patterning is controlled by fibroblast growth factors (Fgfs) secreted from the apical ectodermal ridge (AER). Anterior-posterior expansion is coordinated by sonic hedgehog (Shh) released from the zone of polarizing activity (ZPA). Both Fgfs and Shh regulate each other through an autoregulatory loop. The transcription factor LIM Homeodomain 2 (Lhx2) is an intermediate of the Fgf-to-Shh portion of the loop. In the absence of Lhx2 (and its redundant family member, Lhx9), *Shh* expression is markedly reduced. However, the mechanism by which Lhx2 mediates Fgf-regulation of Shh is unclear. Shh is regulated by a limb-specific enhancer called the ZPA Regulatory Sequence (ZRS). Using *in silico* analysis, our lab has identified two putative Lhx2 binding sites within the ZRS. We hypothesize Lhx2 regulates *Shh* expression directly via the ZRS. To determine if Lhx2 directly interacts with the ZRS to regulate activity, we mutated both Lhx2 binding sites within a control tk-ZRS-eGFP reporter construct using site-directed mutagenesis. We electroporated these constructs into the presumptive limb bud of chicken embryos (Hamburger-Hamilton stage 14) and assessed changes in ZRS activity 48 hours post transfection via fluorescence microscopy. We found mutation of both Lhx2 binding sites within the ZRS resulted in fluorescence similar to our control. These results suggest Lhx2 does not bind directly to the ZRS in its regulation of Shh but may instead use intermediary transcription factors. Further experimentation is needed to confirm this connection. Investigating the mechanism by which Lhx2 regulates Shh will provide insight into how the Fgf-to-Shh loop coordinates patterned-limb development.

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