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Children's Hospital Oakland Research Institute

UCSF Benioff Children's Hospitals
Oakland | San Francisco

CHORI

36th Summer Research Symposium 2017

STAND FOR SCIENCE

08.11.17

9 AM–4 PM

August 11, 2017

Welcome to the 36th Annual CHORI Summer Student Research Symposium! We are here to celebrate 36 years of scientific training of young investigators - the future leaders of biomedical research. We are also here to celebrate the wealth of our diversity- which is represented in abundance in this summers' matriculating class. In this years' political environment we are also here to 'Stand up for Science', the theme of our Symposium this year. These young inquisitive minds have been exploring some of the most challenging basic, clinical and ethical questions of our time. This CHORI Research Program provides a short-term education and training to high school and undergraduate students with a broad range of backgrounds and experience. Despite their diverse backgrounds, all these trainees have one common goal- they are considering careers in biomedical research and other health care fields. Today's oral and poster presentations constitute the conclusion of a nine-week long program that has featured a rigorous mentored guided research project and education curriculum.

This summer's program has been unique in that we have overcome many obstacles to achieve our goals. Some students were placed in lab or clinical assignments that required lengthy commutes from their home, others were uprooted from hometowns thousands of miles a way to enter the program, a number of students had family members suffering from life threatening illness and struggled with the balance of daily caregiving, and still others suffered from their own quiet chronic ailments. Yet despite these challenges, these students as a whole have been incredibly strong and resilient, a character trait that will prove invaluable in the future.

We invite you to learn about the various state-of-the-art research topics that the trainees were involved in, ranging from the development of a stem cell model to hopefully cure sickle cell disease, exploration of novel genes in cholesterol metabolism, determination of risk factors for growth failure in children from Mali, to a better understanding of the barriers to the use of opioid medications by our Medical Residents in the treatment of pain. Please mingle and chat with the all the students, as well as the research scientists and physicians who served as mentors for the trainees. We feel truly privileged and honored to have the trainees in our organization and hope that their summer research experience offered a brief glimpse into the exciting world of biomedical research.

Finally, thanks to all of the CHORI, UCSF Benioff Children's Hospital Oakland and San Francisco and UC Berkeley mentors and supervisors who are the backbone of the program. We appreciate their time, effort, and profound commitment to mentor these students. A very special note of appreciation also goes out to David Killilea, Leyna Nguyen, John McDonnell, David Lynch, Phillip Bollinger, Roialle Luckett, Reena Ninan, Kathy Schultz, Jennifer Beckstead, Ken Tse, Jiale Ye, Shar Rauch, Christian Leiva, Peter Chin-Hong, Lily Mirels and all CHORI and BCHO staff, guest seminar speakers and other friends of the CHORI Summer Program for their effort and time, which made this summer's program a huge success. We acknowledge the support and funding provided by the NIH, DDCF, CIRM, the Elizabeth Nash Foundation, the Alex Lucas Memorial Fund and a number of Anonymous donors. We wish the trainees all the very best in their future endeavors and hope that they will keep in touch with us as we would like to know if the program had any impact on their academic and career decisions.

Sincerely,

Bertram H. Lubin, MD
Associate Dean of Pediatric Health, UCSF
Principal Investigator & Co-Director
CHORI Summer Program

Vasanthy Narayanaswami, PhD
Associate Scientist
Principal Investigator
CHORI Summer Program

Ellen B. Fung, PhD RD CCD
Associate Scientist
Principal Investigator & Co-Director
CHORI Summer Program

Contents

Program Advisory Members	5
2017 Program Staff	6
2017 Program Selection Committee	7
2017 Summer Students	14
Rhea Advani	15
Maopeli Ali	16
Natasha Alvarado	17
Christopher Alvarez	18
Emily Beckman	19
Barry Brand	20
Maribel Campos-Hernandez	21
Loralee Chea	22
Jessica Chuang	24
Nina Criswell	25
Brittney Deadwiler	26
Fernando Delgado	27
Aditi Desai	28
Jocelyn Diaz	29
Amber Fearon	32
Meghan Foe	34
Brianna Fredrick	35
Keely Fuller	36
Elijah Goldberg	37
Amira Harara	38
Gopika Hari	39
Lilian Hernandez	40
Sebastian Hurtado	41
Katie Jang	42
Jennifer Juarez	43
Judy Kang	44
Adeleen Khem	45
Franny Kiles	46
Ah Young Kim	47
Andrew Kriozere	48
Philip Lee	49
Kate Lindeman	50
Tyler Lunow-Luke	51
Sharad Mahajan	52
Alishah Momin	53
Julia Nguyen	54
Maria Rodriguez	55
Ali San	56

Contents

Abigail Serrano	57
Jennifer Shearer	58
Abu Sikder	59
Casey Smith	60
Jason Sun	61
Nuhamin Tassu	62
Ricardo Trujillo	63
Adrian Valderrama	64
Juan Valentin	65
Sarah Van Son	66
Amy Wang	67
Anna White	68
Jia Yu	69
Robin Yu	70
Suyi Zhu	71
National Institutes of Health (NIH) Scholars	72
California Institute for Regenerative Medicine (CIRM) Scholars	73
Doris Duke Charitable Foundation (DDCF) Scholars	74
Elizabeth Nash Foundation Scholars	75
Students Presenting Elsewhere	76
This Year's Mentors	78
Notes	80

Support for the 2017 CHORI Summer Research Program was generously supported by the following grants and sponsors:

The National Institutes of Health (NIH), Short Term Research Education Program to Increase Diversity in Health Related Research from the National Heart, Lung and Blood Institute (NHLBI), #R25 HL125451-0

The California Institute for Regenerative Medicine (CIRM), Leveraging Investment in High School Training: Summer Program to Accelerate Regenerative medicine Knowledge: LIGHT-A-SPARK, #EDUC3-08399

The Doris Duke Charitable Foundation (DDCF) Clinical Research Continuum: High School to College Program # 2016143

The Elizabeth Nash Foundation was established in 2003 by her family to honor and perpetuate Liz's lifelong example of giving and to continue her fight against Cystic Fibrosis (CF). The foundation is a donor supported 501(c)3 non profit, public benefit charity operated by a family board.

The UCSF Benioff Children's Hospital Oakland Foundation

National Science Foundation Award No. 1564587
Title: Scholarships for Excellence, Achievement, and Professional Competence in Science, Math, and Engineering
Awarded to: Drs. Mark Wong and Seti Sidharta

The Alex Lucas Memorial Foundation
Various Anonymous Donors

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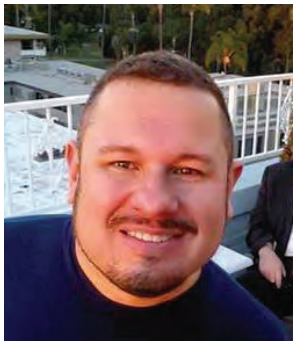

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Program Coordinator
Clinical & Translational Science Institute, Pre-Health Undergraduate Program, University of California San Francisco

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Senior Systems Analyst
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Director, Hemostasis and Thrombosis Program
UCSF Benioff Children's Hospital, Oakland

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2017 CHORI ● UCSF ● UCB Summer Student Research Program Curriculum

Full Program Orientation June 12, 2017
There will be an all-day orientation for summer interns on June 12th. Continental Breakfast and Lunch will be served.

Agenda to include:

- Introduction and overview by Co-Directors and Leadership Team
- Keynote lecture
- Explanation of curriculum
- CHORI tour

Safety Training June 14, 2017
For all students who will be working with mentors in a basic science laboratory, a mandatory Safety Training with CHORI Safety Officer, Miriam Fang. Students are required to complete this training BEFORE beginning their projects.

Meetings with Off-Site Mentors
June 13, 1:00 – 2:30 am Students with mentors at UCSF will travel to UCSF campus along with the Co-Director to meet with their mentors.

June 20, 5:00 pm – 6:00 pm: Students with mentors at UCB will travel to UCB campus along with the Co-Director to meet with their mentors.

Research Project:
The student will conduct research with assigned mentor. The details of project and research plan are left entirely to the individual mentor and each summer intern will follow the procedures, and schedule, laid out by their respective labs.

Submit Written Research Plan Due: June 28, 2017
Students must submit to the Program Coordinator a written Research Plan outlining their project. The Research Plan should be 3 pages long and include:

- Statement of hypothesis
- Specific aims
- Background
- Methods
- Anticipated outcome of project

Students will work closely with their mentor in the preparation of these reports, and mentors should review and approve the reports before submission. Figures, flow charts and schematics may be used to illustrate the research plan. The written report will be sent to: summerstudentprogram@chori.org, and must include student's name, mentor's name and the title of the project.

Weekly Lectures: Current Topics in Health and Disease
Students are required to attend weekly lectures every Thursday afternoon during the program delivered by CHORI, BCHO, UCB and UCSF faculty members. The lectures will cover various scientific topics, as well as discussions regarding women's and minority's issues, career planning, how to read and review literature, scientific ethics and Responsible Conduct of Research.

Abstracts Due: July 19, 2017
Students will work closely with their mentors in the preparation of abstracts concisely summarizing their work. A committee comprised of the Director, Co-Directors and other leading members of the CHORI scientific community will review the abstracts for the Symposium. Abstracts will be considered for either presentation in an oral format or as a poster.

CHORI Summer Student Symposium August 11, 2017
A one-day scientific conference style symposium will be held on the last Friday of the program. All students are required to participate and present the findings of their summer research. Breakfast, Lunch and dessert are served. Family members, teachers, lab members and friends are welcome to attend. At the end of the symposium, students who successfully complete the program are awarded a certificate of completion.

SUMMARY OF IMPORTANT DATES:

November 1, 2016	Applications Available for download
February 10, 2017	High School Applications & Recommendation Letters Due
February 24, 2017	Undergraduate Applications Due
First week of March	High School Award Notification
Mid-March 2017	Undergraduate Award Notification
April 7, 2017	High School Program Orientation (DDCF)
June 12, 2017	Orientation: 8:30 am-4:30 pm (required for all students)
June 14, 2017	Safety Training
June 20, 2017	Safety Training- Make-up
June 28, 2017	Written Research Plan Due by 4:00 P.M
June 29, 2017	Student Photo Day: All Students **must** be present
July 6, 2017	Personal Statement for Program Guide due by 4:00 P.M
July 19, 2017	Abstract due by 4:00 P.M.
August 11, 2017	Summer Student Research Symposium

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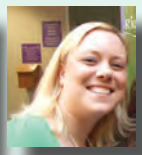
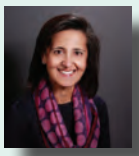
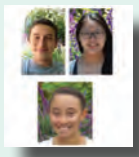
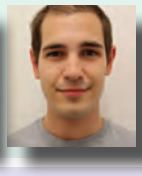
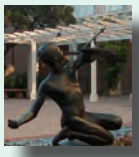
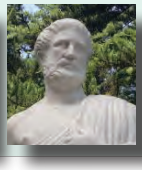
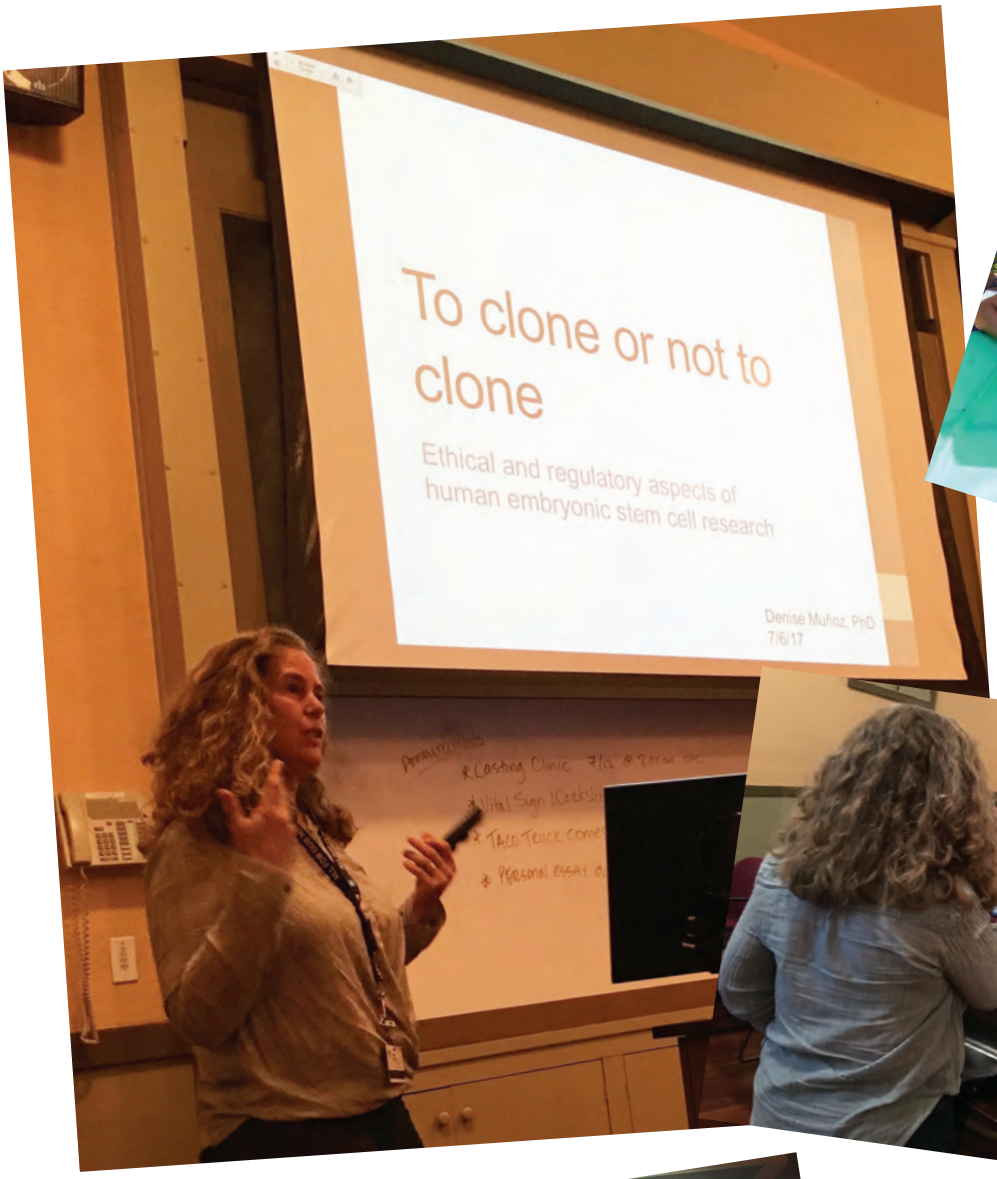
CHORI Summer Student Lecture Series 2017

Refreshments will be provided

Week 1	CHORI Little Theater			
 	Nancy Noonan RN, Marci Moriarty (BCHO)	June 15, 2017 4:00 – 5:00 pm	A Day in the Life of a BMT Patient	
Week 2	UCSF– N217			
 	Alka Kanaya, MD (UCSF) Valy Fontil (UCSF)	June 22, 2017 3:00 – 5:15 pm	Heterogeneity of Diabetes in Asian Americans Learning how to find yourself in academic medicine	
Week 3	CHORI Little Theater			
 	Sebastian Hurtado, Casey Smith, Judy Kang Theo Roth MD PhD Student (MTSP Program, UCSF)	June 29, 2017 3:00 – 5:15 pm	Advice from Your CHORI Peers Careers and Roles as a Physician–Scientist	
Week 4	CHORI Little Theater			
 	Denise Muñoz, PhD (CHORI Staff Scientist) Dayna Long, MD (BCHO)	July 6, 2017 2:00 – 5:15 pm	To clone or not to clone: ethical and regulatory aspects of human embryonic stem cell research Student Presentations Dreaming Big	
Week 5	CHORI Little Theater			
 	Jennifer Below, PhD (U Texas)	July 13, 2017 3:00 – 5:15 pm	Student Presentations PADRE Pipeline: Progress in Predicting Pedigrees	
Week 6	CHORI Little Theater			
 	Vasanthy Narayanswami, PhD (CSU Long Beach)	July 20, 2017 3:00 – 5:15 pm	Student Presentations How We Use Greek Mythology to Overcome Barriers and Stress to Understand the Structure, Function and Application of Apolipoprotein E	
Week 7	CHORI Little Theater			
  	Mark Walters, MD (BCHO) John McDonnell (CHORI IT) Manuel Bramble, MD (BCHO)	July 26, 2017 4:00 – 5:00 pm July 27, 2017 4:00 – 6:00 pm	Curing Blood Disorders Wait, you mean I have to talk? In front of people?? Social Determinants of Health: What They Are and Why We Screen	
Week 8	UCSF – N217			
 	Kirsten Bibbins-Domingo, MD, PhD, MAS (UCSF) Ashkan Ahmadian, Faustine Ramirez (UCSF YIP Program)	Aug 2, 2017 12:00 – 3:00 pm	Health Disparities in Chronic Diseases: How do we study and what must be done?	

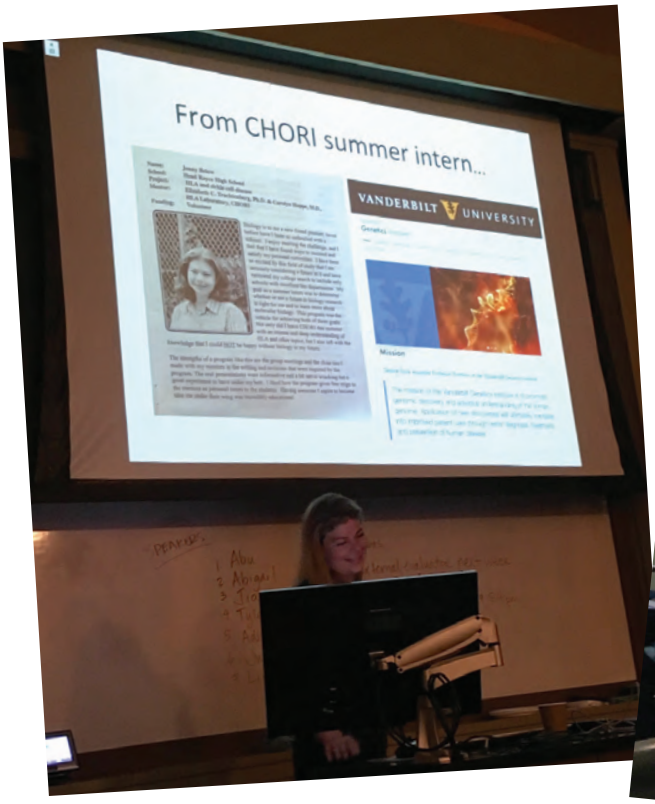

UCSF
C·H·O·R·I
This Week's Talks
Heterogeneity of Diabetes in Asian Americans
Alka Kanaya, MD
(UCSF)
Learning how to find yourself in academic medicine
Valy Fontil, MD, MAS, MPH
(UCSF)
June 22, 2017
3:00 – 5:15 pm
USCF – N217
Implementation Research
Bring it Down San Fr
best practices from Kaise
hypertension manageme
Francisco Safety-net cli
UCSF
EXIT


To clone or not to clone
Ethical and regulatory aspects of human embryonic stem cell research
Denise Muñoz, PhD
7/6/17


Curing Blood Disorders
July 26, 2017
CHILDREN'S HOSPITAL
& RESEARCH CENTER OAKLAND


FIND
WHAT DETERMINES HEALTH?


How We Use Greek Mythology to Overcome Barriers and Stress to Understand the Structure, Function and Application of Apolipoprotein E
Chimera
Trojan Horse
Pandora's Box
Vasanthy "Vas" Narayanaswami, PhD, FAHA
Department of Chemistry and Biochemistry
CSULB, Long Beach, CA
The Beach

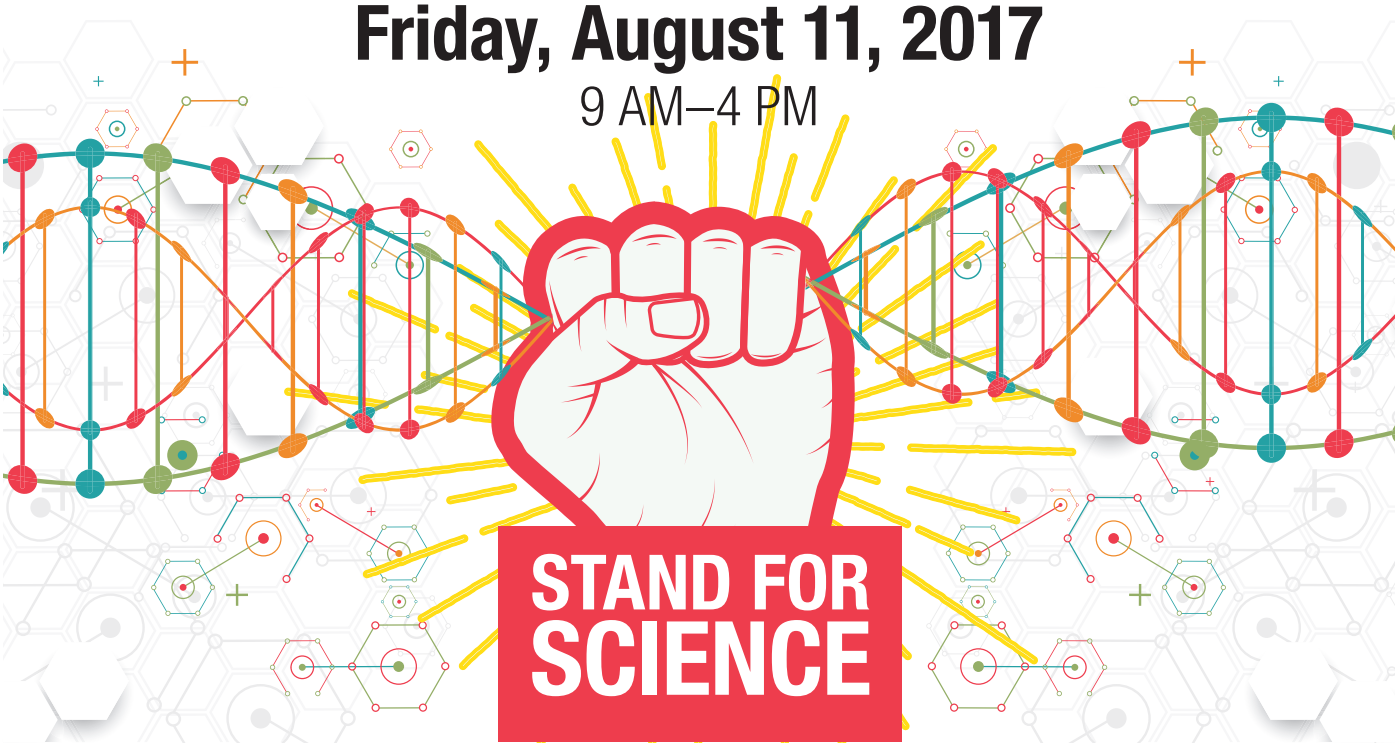

From CHORI summer intern...
VANDERBILT UNIVERSITY
Genetics
Mission

CHORI

36th Summer Research Symposium 2017

Friday, August 11, 2017

9 AM–4 PM



2017 Summer Students

Rhea Advani

Mission San Jose High School

Funded by: Volunteer

Mentor: Mary Jones, MD

Communication Partner Instruction for Parents with Children affected by Rett Syndrome

My name is Rhea Advani and I'm a rising junior at Mission San Jose High School. My desire to be a part of medical research comes from my cousin, Dimpy. Dimpy was diagnosed with Rett Syndrome when she was two, and she turns 20 years old this year. Having lived with her as a young child in Dubai, UAE, I would always wonder why she was unable to talk or walk. This curiosity has remained in me and I am finally getting answers to questions from my early childhood. The sparkle in her eyes when she listens to her favorite Bollywood song leaves me in awe and she is my family's angel. I'm so grateful to have the opportunity to learn more about Rett Syndrome and how we can support parents, lifelong communication partners, of children affected by Rett Syndrome. I am delighted to work with Dr. Mary Jones on this project and to have the privilege of participating in the CHORI Summer Research Program this year. I hope to take all the knowledge and experience I have gained from CHORI to help many more families around the world.

Contributing Authors

Judy Lariviere, AAC Specialist

Introduction

Rett Syndrome is a neurodevelopmental disorder found in mostly females caused by mutation or deletions in the gene MECP2, characterized by the loss of purposeful speech and hand use, difficulty with mobility, and development of stereotypies. Physical symptoms disrupt multiple aspects of the daily lives of families and interfere with the education of girls with Rett Syndrome. The immature connections between neurons result in apraxia, which is the inability to carry out cognitive intent. The inability to verbally participate is demoralizing and frustrating to the girl and to the caregivers who may not know how to respond and aren't able to interpret her communications. The success of interactions with the girl will depend heavily on the interaction skills of the communication partner, however.

Hypothesis

Parents will be better able to recognize and respond to their child's communication attempts after studying a communication module, created by the investigators based on questions previously asked by other parents and input from Rett clinic therapists. Our goal is to empower parents by increasing their ability to demonstrate to others how they communicate with their child with Rett Syndrome and to better articulate their knowledge about Rett and apraxia.

Methods

In this exploratory study, we collected and examined 50 previous intake questionnaires completed by parents seen in clinic to explore questions and concerns about their child's communication. Next, we reviewed videos of five girls with their parents seen in clinic interacting with the AAC specialist. We are creating a curriculum for parents to understand basic information on Rett syndrome, communication challenges of their daughter, and specific communication attempts their daughter makes. The curriculum will be sent to two families to refer to as they review the video of the clinic session. Then, the parents will be asked to complete the post-clinic questionnaire and responses will be recorded.

Anticipated Outcomes

After completing the communication curriculum, parents will have a better understanding of how Rett Syndrome affects a child's controlled speech and how to recognize their child's intent to communicate so that they have more successful exchanges with their daughters in the future.

Acknowledgements

I would like to thank Dr. Mary Jones and AAC Specialist Judy Lariviere for their endless support in the creation and execution of this project.

Keywords

Rett Syndrome, Communication, Apraxia

Maopeli Ali

Kenyon College

Funded by: National Institutes of Health

Mentor: Aimee Medeiros PhD; Polina Ilieva, BS

The Correlation between Social Economic Status and Access to Healthcare at UCSF during the early to mid-20th century

My name is Maopeli Ali and I am currently a sophomore at Kenyon College in Ohio where I am pursuing a major in biology with a minor in Latin. As a child, I have always had a interest in science whether it be in biology, chemistry, or even geology. I always found that science was a place that one could look to for answers that no else could answer. However, this curiosity has made it hard for me to find the perfect career path and focus on one area of science. This curiosity eventually led me to participate in the CHORI summer program back in 2015. I worked under Dr. Swapna Shenvi and Dr. Ellen Fung where we focused on the effects of zinc supplementation on thalassemia. This was the first time that I experienced any kind of lab work or participated in real science. I had a wonderful time in the lab with my colleague discovering new things and coming out the program with more questions than answers. It was this experience that brought me back to CHORI. However, I am going in a very different direction this summer. This summer, I am working in the Archives department of UCSF and digitizing medical records. From the records, I will focus on the social-economic side of medicine. My case study focuses on comparing the types of social groups that UCSF was serving between the early and late 1900's. I will also focus how the payment for medical expenses has changed during this time. The Archives is a new experience for me and I can't wait to explore the social sciences and how they relates to medicine. Hopefully, this experience will bring me one step closer to finding a part of science that I can make a career out of.

Introduction

From the beginning of the 1920's, to the Great Depression, and to the end of World War II, access to medications, operations, and facilities became increasingly difficult for many Americans, especially those from disadvantaged populations. In short, economic class mattered when it came to receiving quality healthcare. The purpose of my study is to further examine how.

Hypothesis

How did one's economic class impact access to quality care during the early 20th century (1920-1950)

Methods

Data set:

The data analyzed are a sample of a larger repository of information currently being digitized from seven million paper-based patient records. The historical patient information (HPHI) I digitized and examined came from a sample of records documenting care received at UCSF during the first half of the 20th century. It was a random selection.

Scanning medical records:

I used the Panasonic KV-S3105C Document Scanner and the Epson Flatbed Scanner to scan and digitize the Medical records. I then use TIF files and adobe acrobat pro to create a master copy of the file.

Metadata collection:

I will then look through the file and collect data on the name, start and end of their medical services, start and end income, race, age, birthday, and notes on the conditions and diseases the patient received treatment for. For my case study, I will focus on the income and their access to certain medical treatment.

Anticipated Outcomes

I anticipate that the data will show a correlation between class and access to healthcare in the US during the early 20th century.

Acknowledgements

I want to acknowledge Dr. Medieros and Ms. Ilieva for teaching me all about the fields of digital medical humanities and history of health sciences and helping me through the process of my case study.
I want to thank Charlie Macquarie for all the help with teaching to handle and document the data from the files.

Natasha Alvarado

Mercy High School

Funded by: Independent/Achieve

Mentor: Marisa Medina, PhD

The Reprogramming Efficiency of Peripheral Blood Mononuclear Cells and Isolated CD34+ Cells into Induced Pluripotent Stem Cells

I am a rising Senior at Mercy High School in San Francisco. I have always found tremendous interest in a variety of scientific subjects. When my grandfather passed away from an undiagnosed degenerative neurologic condition, I knew that I needed to strive for a career as a medical professional. I hope to become not only the first individual in my family to graduate from college, but also the first to become a doctor. I want to help individuals to the best of my ability in the hopes that they can continue to pursue their goals and lead healthy lives.

When the opportunity to participate in the Children's Hospital of Oakland Research Institute Summer Research program presented itself, I was elated and ready to learn. I am very grateful to Mrs. Barbara Bakar and the Achieve Program for making my participation in CHORI possible. CHORI is unlike any program I have ever participated in; it is simultaneously rigorous, challenging, and fun. I have the guidance of Dr. Medina and Tony Munoz to thank for making this experience incredible. They have taught me the ins and outs of peripheral cell reprogramming, stem cell culture, as well as valuable laboratory techniques I hope to apply.

Contributing Authors

Marisa Lin Wong Medina, Ph.D, Antonio Munoz, Natasha Alvarado

Introduction

Stem Cells are capable of self-renewal and differentiation into tissue or organ-specific cells which possess specialized functions. Stem Cells are applicable in biologically personalized treatment and genetically-matched regenerative medicine. In the last decade, scientists have been able to create stem cells by reprogramming adult somatic cells that have already been differentiated, producing cells known as Induced Pluripotent Stem Cells (iPSCs). Traditionally, iPSCs were generated from fibroblasts obtained through a skin biopsy. However, there are many potential sources of somatic cells. In particular, peripheral blood mononuclear cells may be isolated from blood through a minimally invasive procedure; thus, these types of cells can be obtained from individuals who may otherwise be unable to participate in more invasive procedures often required for the harvesting of other cell types. PBMCs comprise a diverse cell population, including CD34+ progenitor cells. Although this cell type constitutes only a fraction of the total PBMCs, these cells are particularly susceptible to reprogramming. One question that remains is whether isolation of CD34+ cells from PBMCs prior to reprogramming increases reprogramming efficiency.

Objective

To test the difference in reprogramming efficiency between isolated CD34+ cells and total PBMCs.

Methods

Preserved PBMC samples from three donors were thawed and suspended in CD34+ isolation/expansion medium. On day 5, another set of PBMC vials from the same donors were thawed and reconstituted for 24 hours. On day 6, both of the cell populations from each donor were nucleofected with a set of plasmids that contain the genes that code for OCT3/4, SOX2, Klf4, and MYC, Yamanaka Factors crucial to reprogramming. Each donor had a total of 3 replicated nucleofection events, with a constant number of PBMC and CD34+ cells used for each nucleofection. IPSC colonies were identified using their morphology and live-action immunohistochemistry. Reprogramming efficiency, as quantified by the number of colonies observed and days required for colony generation, was determined across the 3 donors and within the individual donor sets.

Anticipated Outcomes

We will observe higher reprogramming efficiency in pre-isolated CD34+ cells compared to PBMCs.

Acknowledgements

Marisa Lin Wong Medina, Ph.D, Antonio Munoz, Mrs. Barbara Bakar

Keywords

Induced Pluripotent Stem Cells, Peripheral Blood Mononuclear Cells, Reprogramming

Christopher Alvarez

Madison Park Academy

Funded by: Doris Duke Charitable Foundation

Mentor: Caroline Hastings, MD, Jennifer Michlitsch, MD

Thromboembolism In Pediatric Patients With Cancer

My name is Christopher Alvarez and I am a senior in high school at Madison Park Academy in East Oakland. This summer, I spent my time interning at CHO, and it was the best decision I could have made. This program has exposed me to research, and it has provided me with three different amazing, experienced, giving mentors and the opportunity to shadow their hard work for a period of nine weeks-- no other high school program will offer that! I am very grateful to have this opportunity; CHO is a place I love and hope to work at some day. This will allow me to give back to my community, present a familiar face, and a familiar language, since most patients at CHO are of the same background as I. This program will allow me to solidify my career path, and allow me to identify what it is I want to do in the near future. Thank you!

Contributing Authors

Cheryl Cohler, MD, Caroline Hastings, MD, Jennifer Michlitsch, MD

Introduction

Venous thromboembolism (VTE), which is the formation of blood clots in the vein, though it is rare in children generally, occurs in "...2.1–16% of children with cancer," (Ko RH and Thornburg CD 2017). Children with cancer are known to be "at least 600 times more prone to thrombosis than the general pediatric population" (Athele, 2008). There is limited data for VTE patients with cancer compared to VTE patients without cancer and the clinical characteristics and risk factors in these patients are not fully known. Current information comes primarily from pediatric patients with acute lymphoblastic leukemia the most common cancer in children, but VTE is also recognized as a complication in patients with other cancers such as lymphoma, and sarcoma. There are no specific guidelines for prevention, or monitoring, of children with cancer that have developed VTE, and we aim to identify risk factors for VTE in this population as the first step in creating these guidelines.

Objective

Our objective is to look for a correlation between particular patient characteristics and the development of VTE.

Methods

I am working along with my partner, Sebastian Hurtado, to retrieve data from electronic and paper medical records from 242 patients at UCSF Benioff Children's Hospital Oakland. Spreadsheets have been developed for data capture. Patients, including a control group, were previously identified and this information placed in the spreadsheet. Data collected includes patient age, body mass index (BMI), diagnosis, treatment, surgery, protocol, presence of a central venous catheter (CVC), and number of lumens per catheter. Statistical analysis to consist of comparing and contrasting the particular risk factors to determine defining characteristics and commonalities between these groups.

Anticipated Outcomes

We expect our data analysis will show a positive correlation between the presence of VTE and the following particular variables such as older age, the presence of a double lumen CVC or multiple CVCs, and chemotherapeutic agents such as PEG-L-asparaginase. These findings will provide important information for future studies to address prevention or treatment modification in pediatric patients undergoing treatment for cancer.

Keywords

Thromboembolism, Central Venous Catheter, Cancer

Emily Beckman

Berkeley High School

Funded by: California Institute for Regenerative Medicine

Mentor: Ryo Higuchi-Sanabria, PhD

Identification of Novel Genes Involved in the Mitochondrial Unfolded Protein Response

I became interested in the field of Biotechnology during my freshman year biology class. The idea that all of the features of an organism can be laid out in a four letter code was beyond my comprehension. How can something be so complicated yet so simple? It was then that my curiosity for how genetics are code for life was sparked. In IB (International Baccalaureate) biology, I learned more about the workings of the transcription/translation process and the small complexities of. Nothing was more exciting than hearing "We're still trying to figure that out" and nothing was more annoying than hearing "That's beyond the scope of this course."

I am in the Biotech Academy, which gave me hands on experience with lab techniques; however, I was still curious what the research lab environment. This opportunity with CHORI and the CIRM program allows me to experience the research lab environment while I am still young enough to explore my options.

Introduction

Stress is the pressure and tension, which is experienced by all living organisms. One example of stress is the buildup of unfolded of proteins in the mitochondria; the cell responds to this type of stress through a process called UPR^{MT}. Mitochondria supply a cell with energy (ATP) and helps maintain health and lifespan, so UPR^{MT} has evolved to protect this key organelle. UPR^{MT} is regulated by *atfs-1*. Under normal conditions, healthy mitochondria import and degrade *atfs-1*. However, when the mitochondria are damaged, *atfs-1* translocates to the nucleus where it activates UPR^{MT}. Without mitochondrial regulation, organism can experience decreased life spans and age-related diseases, including neurodegeneration and muscle myopathies. Hyperactivation of UPR^{MT} can actually lead to lifespan extension, however, a hyperactivation of broad UPR^{MT} is damaging to some cells weakens its potential for therapeutic uses. We hope to identify novel interactors and regulators of UPR^{MT}, which can be better targets for hyperactivation.

Hypothesis

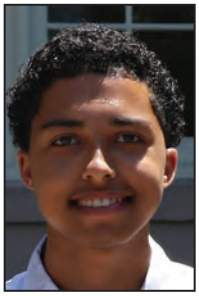
UPR^{MT} is a complex mechanistic pathway, which has pleiotropic effects on organismal health and lifespan. Breaking down this complex pathway will help identify novel therapeutic targets for age-related disease.

Methods

Synthetic lethality screens are performed on *Caenorhabditis elegans* harboring an *atfs-1* mutation, making them incapable of activating UPR^{MT}. RNAi is used to identify genes, that when knocked down, result in lethality of worms lacking functional *atfs-1*, but not for wild-type worms. Worms that lack a functional UPR^{MT} need these genes to survive. To check these gens' specificity to UPR^{MT}, we will take advantage of a GFP-reporter line. GFP expression is driven under the expression of the promoter for the *hsp-6* gene. When UPR^{MT} is turned on we see this by expression and accumulation of GFP. We induce UPR^{MT} by exposing transgenic worms to sodium azide. We will use RNAi to systematically silence our hits and using the GFP—a lack of GFT meaning UPR^{MT} was not activated—identifies the genes which play a role in UPR^{MT}.

Acknowledgements

Dillin Lab
Ryo Higuchi-Sanabria



Barry Brand

Oakland Technical High School

Funded by: Doris Duke Charitable Foundation

Mentor: Ward Hagar, MD

Association Between Common Clinical Cardiac Tests and Transfusional Iron Overload in Patients With Sickle Cell Disease or Thalassemia

My name is Barry Brand. I am a rising senior at Oakland Technical High. For as long as I can remember I have always wanted to do something that would change people's lives and was also curious about the human body. The human body has always fascinated me with how it works and the various parts. As I grew older my curiosity grew and more questions began to form, which set me on the path to become a doctor. I decided to enroll in CHORI to test the waters of what it is like to work in the medical field and it has certainly opened up my mind. CHORI helps me to fulfill my curiosity, also motivating me to learn more about diseases and how one abnormality in an organ affects the rest of the body. My experiences from CHORI will help shape my future in medicine by surrounding me in an environment dedicated to understanding diseases and improving patient health.

Introduction

Patients with sickle cell disease and thalassemia often require lifelong blood transfusions that lead to iron overload. Prior research implicates iron deposition in causing cardiac dysfunction. Current heart iron evaluation requires specialized magnetic resonance imaging (MRI) techniques. There has not been a systematic investigation of common cardiac tests for detecting cardiac iron overload. We investigated whether a predictive model of a combination of findings from common cardiac tests could predict cardiac iron overload.

Objective

To determine the associations between clinical cardiac tests and transfusional iron overload in sickle cell and thalassemia patients.

Methods

Non-identifying demographic and laboratory data were collected from local clinical databases. Electrocardiogram (EKG), MRI, echocardiogram, and liver iron measurements were recorded, along with a transfusion history. Parametric and non-parametric multivariate modeling analyses were used to assess the power of different covariates from clinical cardiac tests to predict cardiac iron loading.

Anticipated Outcomes

We will determine whether cardiac iron loading can be predicted from customary cardiac testing.

Conclusion

This study will help clinical management of patients on transfusions. Whether if the predictive model is validated or not, it can be used to determine best cardiac care or if health policies need to facilitate specialty cardiac MRI evaluations.

Acknowledgements

Doris Duke Charitable Foundation, Ward Hagar, MD, Gregory Kurio, MD, Christine Hoehner, Nurse Practitioner

Keywords

Thalassemia, Sickle Cell, Transfusion, Ferritin, MRI, Echo, EKG, Iron Overload

Maribel Campos-Hernandez

Sonoma State University

Funded by: National Institiues of Health
Mentor: Ellen Fung, PhD, RD

Continual Assessment of Participants in the CHORI Summer Research Program

As a Communications and Media Studies major at Sonoma State University, I'm thrilled to serve as CHORI's Marketing & Program Analyst Intern. This summer I will be working with Dr. Ellen Fung to conduct a continual assessment of the CHORI Summer Research Program, with the purpose of collecting constructive feedback that can be used to ensure the longevity and expansion of the program, determine its increased level of influence on past participants, and to understand the systemic barriers to diversity in STEM education that still persist today. I will be utilizing digital communication to help promote opportunities in the science field that are far-fetched for students.

Despite not majoring in the sciences, being a first-generation college student has allowed me to understand the inequities present in students' educational careers and the lack of resources. I have benefitted from academic/career support programs and believe that there should be some for those students who want to expose themselves to research. The cure for cancer could be out there in the mind of a first-generation college student. Without access to equal clinical and biomedical research they would not be able to prove so, which is why I'm determined to promote this program to its full potential.

Introduction

The CHORI Summer Research Program's mission is to foster generations of under-represented students into STEM careers by exposing high school and college students to a medical system. Allowing students to design independent research projects in clinical or laboratory settings is done with the purpose of increasing student interest in research. Ultimately, the program strives to diversify the STEM field, thus altering the national statistics. To assess how effective the program has been in achieving its mission, we sought feedback from alumni through a cross-sectional survey.

Objective

To systematically assess the long-term effectiveness of the CHORI summer program with reference to alumni's persistence in STEM focused careers. This study originated in 2016 and was expanded this summer to receive more varied opinions of the program, coming from past cohorts.

Methods

A survey was developed online to give alumni the opportunity to share their experiences from the program in a convenient user-friendly format. Questions focused on their past: education level, major, career and the program's impact on career choice (if any). The voluntary survey was distributed to 1994-2007 cohorts as well as to students who did not provide a response to last year's survey. All participants are ≥18 years of age and alumni; they were given a 1-week deadline to complete the survey. Basic demographic data (gender, ethnicity) were collected for statistical interpretation and comparison of the CHORI alumni population to national data on pursuit of STEM careers (US Census Bureau Statistics 2015).

Results

A total of 156 surveys were distributed, of which 11 emails were returned due to address error (7.05% of students). Therefore, the survey was successfully distributed to 93% of the total 156 eligible alumni from the 1994-2007 cohorts. Survey results are pending.

Significance

Feedback gathered from the collection of surveys will allow us to quantify how effective the CHORI Summer Research Program is at influencing its participants to pursue a STEM focused career. Data that reflects that the program is effective in fostering generations of students into STEM majors and careers can be used as a marketing strategy to appeal to prospective participants and potential donors. Data that reflects that the program's curriculum is lacking value and impact can be used to make the necessary improvements.

Keywords

CHORI summer program, alumni, survey, STEM

Loralee Chea

Berkeley City College

Funded by: Volunteer

Mentor: Jin Mei, BS, Robert Yamashita, PhD

Outreach Strategies for Thalassemia, a Genetic Blood Disorder Common Among Southeast Asian Communities

My name is Loralee Chea and I am an undergraduate at Berkeley City College. My ultimate career goal is to become a nurse practitioner. I've done various patient care related volunteer in the past, in which all of these experiences have inspired me to continue my passion in helping others. I applied to be apart of CHORI summer program because I want to take what I can learn from research and apply it to improve clinical health care in the future. This summer I've been working with Children's Hospital Thalassemia Outreach program to raise awareness about Thalassemia. My family immigrated here from Cambodia after a genocide and faced a lot of barriers while living in America. One aspect of my research includes investigating types of barriers in the Asian community in order to improve communication about health. As a future nurse, I am very happy to have been involved with my community

Contributing Authors

Robert Yamashita, PhD, and Elliott Vichinsky, MD

Introduction

Thalassemia is a rare, inherited blood disorder that causes an abnormal form of hemoglobin to be made and can cause severe anemia.There are socio-cultural barriers within the Southeast Asian communities that are preventing them from being tested and asking their providers about thalassemia. Lack of knowledge and awareness of the disease have created a misdiagnosis of thalassemia as anemia. This is due to the fact that they share common symptoms such as, chronic lethargy and tiredness. Western medical doctors have simple ways to test for anemia; however, thalassemia trait looks like anemia and requires further testing.

Objective

An outreach strategy will be created to educate the Southeast Asian community about thalassemia and allow community members to learn more about the health implications of this disorder. After this connection is made, genetic screening and counseling can be introduced and be made available to them.

Methods

Surveys will be administered at health fairs and through local social networks to assess a person's knowledge base on thalassemia. Data will be entered in Excel and summary statistics will be generated. The data will be qualitatively assessed to help develop a baseline understanding of what people know as well as informal interviews with family members and friends.

Anticipated Outcomes

We hope to understand the barriers among the Asian community in order to find an effective approach to educate and encourage people to get tested.

Conclusions

Educating the Southeast Asian community about thalassemia is one part of the equation. The next step would be educating clinicians who sees those patients in order to increase the quality of care.

Acknowledgements

I would like to thank my mentor Robert Yamashita and Jin Mei for guiding me through the process of this research project. I appreciate the time and effort that was given.

Keywords

Thalassemia, Anemia, southeast Asian,

Sarah Chen

University of California, Berkeley

Funded by: Volunteer

Mentor: Tatyana Vayngortin, MD

Adolescents' Acceptance of Long-Acting Reversible Contraception after a Brief Educational Intervention in Emergency Department

As a rising junior majoring in Molecular Environmental Biology, I am frequently troubled by my path toward medicine. Although I have experiences interning in research labs and working as a Mandarin-English interpreter and an Emergency Medical Technician, I always feel like I am not doing enough. Therefore, committing to CHORI for the entire summer was a hard decision to make. But now, as I am half way through the program, I am so glad to work under Dr. Tanya, an emergency pediatrician. Through her mentorship, I simultaneously learned about conducting effective clinical researches and shadowed various doctors in the emergency department. I was able to see what doctors' lives really are about, interact with patients regularly, and most importantly, reinforce my belief in pursuing a medical career. Thanks to CHORI, I not only learned to become a good scientist, but also what a good doctor should be like.

Contributing Authors

Ah Young Kim

Introduction

The rate of teen pregnancy in the United States is higher than those of other developed nations. About 88% of teen pregnancies are unintended and less than one-third of females ages 15-19 consistently used contraception during their last intercourse. The emergency department (ED) is a potentially valuable setting to provide adolescents with education on long-acting reversible contraception (LARC). Studies have shown that adolescents are interested in learning about pregnancy prevention in the ED and same-day initiation of contraception.

Hypothesis

A brief educational intervention during adolescent girls' visit to an urban pediatric emergency department will increase their awareness of contraception and usage of long-acting reversible contraception.

Methods

This is a randomized control trial among sexually active females ages 14-21 that present to an urban pediatric ED. The control group completes a baseline survey, while the intervention group completes the baseline survey, an educational video on LARC, and a post-intervention survey. Follow-ups will be conducted 3 months after the subjects' ED visit through phone calls or chart review to compare differences in actual contraceptive method uptake.

Preliminary Results

Out of all patients approached, about 50% were eligible. About 50% of subjects used condoms at last intercourse, and 12.2% were interested in same-day LARC initiation. Compared to the control group, subjects watching the intervention video were significantly more likely to want an IUD ($p=.002$) or implant ($p=.013$). Among the intervention group, subjects were significantly more likely to want an IUD ($p<.001$) or implant ($p=.004$) after watching the video than before. Hypothesis is currently supported but final result is subject to change.

Significance

This is a pilot study that will potentially be followed up by a larger study to initiate LARC placement in the ED. By removing previously identified barriers such as education, transportation, and access to care, and initiating contraception when adolescents are already in a healthcare setting, the long-term goal of this research is to increase LARC usage among this high-risk population.

Acknowledgements

Special thanks to Dr. Tanya and staff at Benioff Children's Hospital's Emergency Department for all guidance and support. Thank you CHORI for providing this invaluable experience.

Keywords

long-acting reversible contraception (LARC), adolescent pregnancy, emergency department, pediatric, sexual education

Jessica Chuang

University of California, Berkeley

Funded by: Volunteer

Mentor: Grace Wang, PhD, Ervin Epstein, MD

Epithelial to Mesenchymal Transition in Basal Cell Carcinoma

I graduated from University of California, Berkeley with a Bachelor's degree in Integrative Biology and am currently working for Dr. Jean Tang MD, PhD during my gap year. I became interested in human biology in high school and through my courses in college, volunteer experiences, and job shadowing, I realized I wanted to learn more about the intersection of research and medicine. I am a returning research assistant in the Epstein Lab, which studies the Hedgehog signaling pathway in basal cell carcinoma. Through my time at Children's Hospital Oakland Research Institute, I've gain a better understanding of the importance of basic science research and how it connects with clinical medicine. The CHORI Summer Program further cements my interest in pursuing a future career in medicine.

Contributing Authors

John Dolorito, Amy Wang

Introduction

Basal cell carcinoma (BCC) is one of the most commonly diagnosed cancer and is the fifth largest cost of care for Medicare in the United States. Traditionally, BCCs are removed through surgical excision; however, 30-50% of BCCs can reoccur post-surgery and in some area cause severe disfigurements.

The aberrantly activated Hedgehog (HH) signaling pathway plays a critical role in BCC development. In normal tissue, PATCHED1(PTCH1) inhibits SMOOTHENED (SMO) which prevents activation of downstream targets, such as GLI family transcription factors. Approximately 90% of BCC tumors carry loss of function mutation in the PTCH1 gene which then releases its inhibition on SMO. The rest of the 10% human BCCs carry mutations in SMO. Majority of the anti-BCC small molecule drug screens have been conducted focusing on inhibiting SMO.

Even though SMO-inhibitor therapies help shrink tumors and lead to complete clinical remission in some patients, all tumors however eventually reoccur at the original clinical sites after drug withdrawal. Our previous studies have shown that epithelial to mesenchymal transition (EMT), a crucial process in embryonic tissue development and wound healing, is responsible for tumor recurrence.

Objective

In the present study, we further characterize epithelial (E) and mesenchymal (M) BCC cells and evaluate the effects of anti-EMT drugs on these cells.

Methods

In particular, we will identify key genes that differentiate E vs M cell characteristics, measure the efficacy of anti-EMT drug candidates in our BCC cells, and determine the changes of HH, E-, M-markers using immunofluorescence staining.

Anticipated Outcomes

We expect to find key genes that differentiate E vs M cell characteristics and potential drug candidates that will be either be cytotoxic to mesenchymal cells derived from epithelial, induce MET, or reduce the production of mesenchymal cells.

Acknowledgements

Thank you Dr. Grace Wang, Dr. Ervin Epstein, John Dolorito, and Amy Wang in Epstein Lab for helping me through this summer research. Thank you CHORI Summer Program for the opportunity.

Keywords

Basal cell carcinoma, EMT, epithelial to mesenchymal transition, Hedgehog signaling pathway

Nina Criswell

The Urban School

Funded by: Volunteer

Mentor: Janelle Noble, PhD

Type 1 Diabetes: A Study in Population Genetics

My name is Nina Criswell and I am an upcoming high school senior at The Urban School of San Francisco. As the road to college and a career is daunting, one thing that has remained constant is my love for math and science. I was drawn to CHORI not only because it offered an immersion into a career in the sciences but also because I wanted to conduct my own research outside of the classroom setting.

Working in Dr. Noble's lab has not only pushed me to take the initiative in in my own pursuits but also showed me the realities of a research career. Implementing my own personal interests and skills into my research project – such as learning R coding to implement statistical analysis software – also contributed to my devotion to this project. I would like to thank everyone in Dr. Noble's lab for answering every question and enriching me with this transformative experience.

Contributing Authors
Nuhamin Tassu

Introduction
Type I Diabetes (T1D) is an autoimmune disease with a strong genetic component. Genes in the Human Leukocyte Antigen (HLA) region contribute approximately half of the genetic risk. HLA is also extremely polymorphic, meaning that the genes themselves have many different variants. My project, part of a larger study, involved identifying the alleles of the HLA-DRB1 locus and their T1D associations from six countries: Azerbaijan, Haiti, Bangladesh, Pakistan, Sudan, and Mali. We also tested the effect of sample size on statistical significance of T1D association using data from Bangladesh.

Objectives
The primary objective was to identify different allele frequency distributions among six different populations. Secondly, we used these data to identify which alleles drive T1D association in these countries. Lastly, we observed how sample size affected the statistical significance of a study with regards to highly polymorphic HLA data.

Methods
Data sources:
640 subjects taken at birth in Bangladesh
A target of 200 controls and 100 patients for each of the 6 countries.

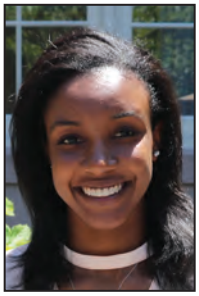
DRB1 data, existing and newly generated, were analyzed using the BIGDAWG package, allowing pairwise comparisons of control frequency distributions to see if any countries were statistically indistinguishable. For each country, patient and control data were analyzed for T1D association. We compared the control samples from Bangladesh to the previously recorded Bangladeshi data to prove that the two data sets are not statistically different. We also conducted a resampling of the combined data to test the effect of sample size on statistical significance of the T1D association.

Results
We found that all six control populations and their overall and DRB1 allele-specific T1D association differed from one another.

Anticipated Outcomes
We expected that the 640 subjects taken at birth and the 200 controls from Bangladesh would be indistinguishable. We predicted that a larger sample size strengthens significance and statistical power.

Acknowledgements
I want to thank Janelle Noble for guiding me during my research process and Steven J. Mack for teaching me everything I know today about BIGDAWG and general statistics.

Keywords
Type 1 Diabetes, HLA, DRB1, polymorphic, BIGDAWG, population genetics, statistical power, Sample Size



Brittney Deadwiler

Harvard University

Funded by: National Institiues of Health

Mentor: Christine McDonald, ScD

Risk Factors for Stunting Amongst Malian Children with Moderate Acute Malnutrition

My name is Brittney Deadwiler and I am a rising junior at Harvard University, studying Neurobiology with a secondary in African American Studies. For as long as I can remember, I have been interested in science and all of its many applications. However, it was not until I started working in the CHORI Summer Student Research Program when I had the opportunity to dive deeper into one of these applications.

One of the first courses I took in college was a freshman seminar researching the history and current issues involving disparities in disease and healthcare in African American communities. It was after this course when I became interested in preventative methods, techniques and programs to help address and end these disparities. I was excited to find out that for my summer research, I would be working with Dr. Christine McDonald on a project researching global health disparities and potential interventions. I would like to thank CHORI for providing me with the resources to have this amazing educational and enlightening experience.

Introduction

Moderate acute malnutrition (MAM) affects about 33 million children under the age of 5 worldwide. It is defined as having a weight-for-height Z score between -2 and -3 or mid-upper arm circumference (MUAC) between 11.5 and 12.5 centimeters. MAM can develop from short-term reductions in food intake or diet quality, and/or recurrent infections that impair the child's nutritional status. Stunting is more prevalent than MAM, affecting approximately 178 million children under the age of 5. Stunting, defined as poor linear growth and a length-for-age Z score < -2, is reflective of chronic undernutrition. Children affected with MAM and stunting are at even higher risk of mortality than children affected by only one condition.

Objective

(1) To identify the risk factors of stunting among Malian children between 6-35 months of age with MAM. (2) To propose potential interventions to address and prevent stunting in this study population based on the risk factors that are identified.

Methods

SPSS software was used to conduct descriptive statistics that describe the study population and logistic regression analysis that identifies significant risk factors for stunting. A series of univariate models were constructed with each potential risk factor as the exposure and stunting as the outcome. A multivariate model will include all variables from the univariate analysis that were significantly associated with stunting at $p < 0.10$. A concluding literature review will analyze other research papers, demographics and health surveys, and government policies to identify gaps in current interventions that address the issue of stunting in children.

Results

In univariate analysis, the odds of stunting were significantly elevated among children from households that did not own a radio, television, or improved sanitation facility. Male sex, older child age, lower weight-for-height Z score, lower MUAC, and living further from a market were also significant risk factors. The multivariate model will provide an adjusted odds ratio that accounts for the effects of confounding.

Acknowledgements

I would like to thank my mentor, Dr. Christine McDonald for her guidance and support throughout my project.

Keywords

Stunting, moderate acute malnutrition, Mali

Fernando Delgado

Arch Bishop Riordan High School

Funded by: Doris Duke Charitable Foundation

Mentor: Lynne Neumayr, MD

Comparison of Sickle-Cell Patients at a Regular State Against the Time of an Acute Pain Crises Using Inflammation And Hemolysis Markers

I am a rising senior at Riordan HS. My curiosity has driven me to question everything. This is why I have always found my interest through science. Exploring ideas and utilizing them to advance technology and medicine to help has sparked my motivation to unimaginable limits. Through CHORI, I have been granted the opportunity to utilize these characteristics for a greater purpose. CHORI, and the assistance of many mentors, guided me through my project allowing me to expand my perspectives. Hopefully, in the future, I will be able to use this experience to make a positive impact.

Contributing Authors

Lynne Neumayr, MD, Anne Marsh MD, Frans Kuypers, PhD, Sandra Larkin, Allysa Kramer, Kacie Smith, Shanda Robertson, Deanna Fink, Elliott Vichinksy MD

Introduction

Sickle-Cell Disease (SCD) a genetic disease resulting from a mutation in the hemoglobin molecule which causes erythrocytes (red blood cells) to become abnormally structured in the shape of a sickle. Hypoxia in the distal circulation leads to polymerization of the hemoglobin and accelerates the sickling of the cell and how adherent it is. This increase in adherence or stickiness of the red cells to the lining of the blood vessels causes red cells to clump together, attracting other cells to adhere as well and cause areas of blockage in blood vessels which can lead to a decrease in the oxygen flow to critical organ systems in the patient's body. This can result in several vaso-occlusive pain crises, acute chest syndrome, stroke and other tissue damage. White blood cells also known as neutrophils, are one of the cell types that can adhere to erythrocytes and potentially damage the vascular endothelium, leading to ongoing inflammation and tissue injury. Another source of inflammation is the destruction of sickle red blood cells (hemolysis) and release of other mediators of oxidation and inflammation like heme.

Objective

Measure markers of Inflammation and Hemolysis of patient with SCD during a steady state in comparison to an acute pain crises.
Determine whether inflammation and hemolysis are related to a patient's age, gender, or hydroxyurea use.

Methods

Baseline samples were gathered from sickle-cell patients who had not experienced an acute pain crises within 30 days prior to the study. These samples were considered steady state markers of inflammation and hemolysis markers. Biomarkers were also collected during acute events when patients received care for a vast-occlusive crisis (VOC), acute chest syndrome, or dactylitis that required need from a parenteral narcotic. Biomarkers of inflammation and hemolysis were plotted and summarized in order to characterize variance within the baseline and acute levels. Changes in biomarkers between steady state and acute events were also analyzed. The statistics were then compared across factors such as age, gender, and hydroxyurea use.

Anticipated outcomes

Results of the study will demonstrate the mean (and median) levels of inflammation and hemolysis biomarkers during an acute pain crisis of a patients with SCD will be elevated compared to a steady state. The results will also determine if factors such as gender, age, or hydroxyurea use play a significant role in relation to inflammation and hemolysis. These preliminary data may be useful to identifying subsets of patients that may benefit from novel targeted therapeutics.

Conclusion

Increasing our knowledge of the changes in inflammation and hemolysis during acute events in patients with SCD can facilitate ongoing research towards the development of new therapeutic approaches to treatment of vaso-occlusive crisis in SCD.

Acknowledgements

Thank you to my mentor Dr. Lynne Neumayr for guidance throughout the project. Thank you to the SCD research team and staff. In addition the Northern CA Comprehensive Sickle Cell Center and the patients who volunteered and consented to participate in the study.

Keywords

Inflammation, Hemolysis, Sickle-Cell Disease, Vaso-occlusive crisis

Aditi Desai

New York University

Funded by: National Institiues of Health

Mentor: Carter Lebares, MD

Effects of Reduced Perceived Stress on Psychological Well-Being and Cognitive Function in Surgical Trainees

My name is Aditi Desai and I am a rising sophomore at New York University. I am majoring in Biology and following the pre-med track. My strong passion for the medical field began with a fascination for my primary care physician's work and has been increasing with exposure to higher-level science courses and lab bench work. This summer, I have had the privilege of working with and learning from my mentor, Dr. Carter Lebares. My first exposure to clinical research has led me to learn an abundance about data processing, effective reading of research articles, practical communication skills, and much more. My fascination with neuroscience is now even greater because of my work in studying the effect of stress on cognition. I am grateful to my mentor and CHORI for allowing such memorable experiences that will shape my medical career.

Introduction

Stress is inherent to surgical training. However, overwhelming-stress levels have a well-established association with burnout and have been shown to increase the risk of depression and impair executive function. In medicine, high burnout and severe stress have been related to increased errors.

Stress is mediated in particular by the hippocampus, amygdala and prefrontal cortex (containing high concentrations of glucocorticoid receptors) which play a central role in the regulation of mood and problem-solving.

Mindfulness Based Stress Reduction (MBSR) is a form of mindfulness training that teaches non-judgemental awareness of thoughts and has been shown to protect executive function in high-stress populations such as marines and felons. Additionally, in non-clinical populations, MBSR has been shown to result in organic neuroanatomic changes in the hippocampus, amygdala, PFC, and connectivity circuits. We propose that training in MBSR can lower perceived stress in surgical trainees and result in improved mood and cognitive function.

Objectives

We will demonstrate that decreased perceived stress in surgical trainees will result in better executive function and changes in neural correlates of problem-solving and decision-making. In surgical interns undergoing mindfulness training or an active control experience, we will evaluate the degree of perceived stress, assess psychologic well-being, analyze cognitive function data for variation in multiple domains, and evaluate neuroanatomic changes in areas believed to subserve cognitive function and affect.

Methods

Twenty-one surgical interns from various surgical specialities at UCSF were put in an active control (relaxed reading) or intervention (mindfulness training), received two hours of training each week for 8 weeks, and asked to practice at home for 20 minutes each day. Data was collected at baseline, after intervention, and one year later. Psychological surveys involved Cohen's Perceived Stress Scale and the Cognitive Affective Mindfulness Scale. The NIH EXAMINER neuropsychiatric battery was used to test working memory, inhibition, and set shifting. Functional neuroimaging involved T1 anatomic scans, with BOLD, and DTI components to observe neuroanatomic changes in areas believed to subserve cognitive function and mood.

Anticipated Outcomes

Through training in MBSR, surgical interns will experience less perceived stress and subsequently have less vulnerability to overwhelming stress. We anticipate that this lower stress state will result in improved psych and cognition scores. Additionally, we expect to find organic changes in regions and circuits of the brain that subserve psychological resilience and robust cognitive function.

Acknowledgements

I would like to thank my mentor, Dr. Carter Lebares and members of our team, Ekaterina Guvva and Amy Hershberger.

Keywords

perceived stress, MBSR, executive function, resilience, mindfulness

Jocelyn Diaz

Holy Names High School

Funded by: Doris Duke Charitable Foundation

Mentor: June Tester, MD MPH

Food Insecurity Among Low-income Families with Diabetes Risk

My name is Jocelyn Diaz, and I am a rising senior at Holy Names High School. For as long as I can remember, science in all its forms has always fascinated me. In fact, it was my great fascination for hands-on science that brought me to apply for the Children's Hospital Oakland Research Institute Summer Program. Before working at CHORI, I had never been involved in a real research project. This program has given me the opportunity to engage in a hands-on research study alongside a fantastic and diligent mentor, Dr. June Tester. CHORI truly has solidified my dream of working in the medical field as a physician. I am very grateful for the opportunities this program has given me this summer. This experience will forever be unforgettable for me, it certainly is one for the books!

Contributing Authors

Maria Rodriguez, June Tester, MD MPH

Introduction

The U.S. Department of Agriculture (USDA) defines food insecurity as a "lack of consistent access to enough food for an active, healthy life". The Food as Medicine study, which included 4-month deliveries of healthy foods to the home, is an example of an intervention designed to address food insecurity and improve health outcomes in low-income families at risk of diabetes.

Objectives

Determine how household food insecurity is related to knowledge and exposure of vegetables and whole grain foods among parents and children at baseline.

Determine how household food insecurity is related to cooking skills and cooking supplies at baseline.

Also, using available preliminary data, explore impact of the program on: household food security, exposure and familiarity with vegetables and whole grain foods, and self-reported frequency of preparation of whole grain foods (e.g brown rice and whole grain pasta).

Methods

The study team recruited 60 low-income families with an obese child (8-17 years) having prediabetes (Hemoglobin A1c 5.7- 6.4). Weekly food deliveries included vegetables and whole grains. Participants completed a survey at baseline and follow up to assess dietary behaviors regarding vegetables and whole grains. Items included the USDA food security module, a score for cooking self-efficacy, a checklist of 40 cooking supply items, questions about whole grain food consumption, and a liking/familiarity score for a list of vegetables and whole grains. We will also be using preliminary data to evaluate change in reported behaviors between food secure and food insecure children and adults. We will use unpaired t-tests of means to compare scores between food-insecure and food-secure families.

Anticipated Results

I anticipate that among 60 low-income families participating in a food-delivery intervention, the families who are food-insecure will have:
Lower scores with respect to familiarity/ exposure to vegetables

- Lower scores with respect to familiarity/ exposure whole grain foods
- Lower cooking self-efficacy
- Fewer cooking supplies

I also anticipate that after participating in the FoodRx Study (Food to Overcome Our Diabetes Risk), a family's level of food insecurity will improve.

Acknowledgements

I would like to thank Dr. June Tester for her help and guidance throughout my research. I would also like to acknowledge the Doris Duke Charitable Foundation for their generous funding that enabled me to participate in this amazing summer program.

Keywords

Food Insecurity, Vegetables, Whole Grains

Azar Dixit

Williams College

Funded by: National Institutes of Health

Mentor: Lorrene Ritchie, PhD, RD

Evaluation of Validity and Reliability of Survey Assessing Current Child Care Nutrition Prior to Implementation of New CACFP Regulations

Coming into the CHORI research program I was completely unsure of what career path would best encapsulate my interests and passions. I wanted to be able to help others directly as a physician but also thought that this would mean I would only be able to address the health of individuals and not broader issues in society that would shed light on more effective, accessible, and equitable methods to improve health. My experience this summer in public health research with the guidance of Dr. Lorrene Ritchie and Danielle Lee at the Nutrition Policy Institute led me to realize the power research has to create and guide public health interventions. In other words, pursuing research can provide unique opportunities to fix and assess a broken system rather than race to keep up with how it impacts the lives of individual people. Thanks to my experiences this summer, I have begun to consider a career as a physician researcher-- concerned with both patient care and related research questions. I am particularly interested in pediatric health and how social factors early on can contribute to the prevalence, development, and treatment outcomes of diseases throughout one's lifetime. I am immensely grateful for the opportunities CHORI has provided to me this summer that have sparked my interest in research and have also given me the necessary skills to pursue it.

Contributing Authors

Adrian Valderrama; Dani Lee, MPH, RD; Klara Gurzo, MA; Lorrene Ritchie, PhD, RD

Introduction

Before the age of five years old, one in four children in the United States is overweight or obese. Excessive body fat at such a young age is likely to persist into adolescence and adulthood and increase risk for many negative health complications throughout a child's lifetime. Child care centers and homes provide care to 7 million young children ages birth to five, and thus provide an optimal setting to assess the current state of children's nutrition and barriers to providing them with healthier foods. This project is the continuation of a study carried out by the Nutrition Policy Institute to examine nutrition in child care prior to the implementation of new federal Child and Adult Care Food Program (CACFP) nutrition standards that will affect more than 5 million young children upon implementation.

Objective

The original study carried out by the Nutrition Policy Institute used a survey to collect data from about 600 child care centers and homes to assess their compliance with the nutrition standards and barriers to implementing them. The goal of this project is to assess the survey used in the original study to reach conclusions regarding its validity and reliability.

Methods

Validity. Twenty child care centers and homes were observed by trained research assistants during lunch time. On the following day, child care providers were asked to fill out the survey tool used in the original study. A comparison of the data gathered using these two methods will be carried out using Kappa statistics to assess if agreement between the data collected from the survey and site observations is statistically significant. Reliability. A group of 50 providers completed the survey tool on two different occasions approximately one month apart. Data will be double-entered and checked for consistency and Cronbach's α coefficients and correlations of responses will be used to determine the reliability of different sections of the survey.

Significance

Children of low-income families are more likely to attend child care that participates in CACFP, where they can receive up to three-fourths of their daily nutrition. Objectively measuring compliance with the CACFP standards will help inform program improvements to improve the health of vulnerable populations. This body of work demonstrates the power that scientifically informed policy development and implementation has to improve lives and promote equity.

Acknowledgements

Many thanks to Lorrene Ritchie, PhD, RD, and Danielle Lee, MPH, RD for their unending support and teaching. Also to Adrian Valderrama, Stella Van Der Eeden, and Tyler Takata for all their help along the way.

Keywords

Nutrition, Child Care, CACFP, Obesity, Children, Infants

Barbara Fairweather

Berkeley High School

Funded by: California Institute for Regenerative Medicine

Mentor: Dario Boffelli, PhD

Developing a Mouse Model System to Analyze the Efficiency of CRISPR/Cas9 Genetic Engineering of the Beta-Globin Gene in Hematopoietic Stem Cells of Sickle Cell Anemia Patients

My name is Barbara Fairweather, and I am entering my senior year at Berkeley High School. Going into high school, I was not interested in science. However, after taking my first biology class, I felt something click. I found the subject to be fascinating, and I understood each mechanism and process we studied. I am very fortunate to attend a school that is rich with scientific opportunities, because the year after, my schedule include AP Biology, and Biotechnology. These classes taught me the subjects of Biology and Biotechnology, but they also amplified my passion in science. During the school year, this internship was presented to me by a mentor, and it sounded like something I wanted. My participation in the CHORI SSRP has been amazing, and I learned more about the workflow, environment and protocol of a research facility than I could in a class.

Introduction

Sickle Cell Disease (SCD) is the most common monogenic disorder. In the United States, SCD affects approximately 100,000 people. SCD is caused by a point mutation in the beta globin (HBB) gene, which results in cells producing deformed beta-globin. This deformity changes the cell shape in a way that can lead to blood clots, severe acute pain, multiorgan failure, and eventually brain damage. The current treatments for SCD do help patients manage their symptoms, but they do not offer a long term solution.

Objective

To test the ability of Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)/Cas9 to target the HBB gene that is responsible for SCD; the longer term goal is to replace the mutation with the wild-type nucleotide, which would produce healthy beta-globin for SCD patients.

Methods

SPLiT-Seq is an RNA sequencing technology that we will use to analyse the genotypes of our samples. It keeps track of individual cells, so that we can later determine how many alleles were edited in each cell. This is in contrast to bulk allele sequencing, which analyses both alleles, but it cannot tell how many of the two alleles were edited per cell.

Anticipated Results

Our anticipations are based on a previous experiment which also used CRISPR/Cas9 to edit genes related to HBB production. In this experiment, it was estimated from bulk allele frequencies that ~70% of cells were not edited, ~15% of cells had one edited allele, and ~15% had two edited alleles. We anticipate that our experiment will be conducted with ~1000 cells. Based on this information, we predict that 700 of our cells will not be edited, 150 of them will have one allele edited, and another 150 will have two alleles edited. Results are still pending on this project.

Acknowledgments

Thank you Fiona Hennig for your guidance all summer. Thank you; Dario Boffelli, PhD, David Martin, MD, Seok-Jin Heo, Fionna Henig, and Wendy Magis for letting me be a part of your research.

Amber Fearon

Rosalind Franklin Chicago Medical School

Funded by: Volunteer

Mentor: Marsha Treadwell, PhD

Pediatric Residents' Comfort Level and Perceived Barriers towards the Use of Opioids in the Treatment of Severe Vaso-occlusive Pain Episodes for Patients with Sickle Cell Disease

My name is Amber Fearon and I chose to do research in my summer between my first and second year at Rosalind Franklin Chicago Medical School. I was lucky enough to join Dr. Marsha Treadwell's team in conducting a needs assessment to inform interventions to improve sickle cell disease (SCD) care. I had early clinical exposure to sickle cell disease when I worked as a medical scribe in an Emergency Department (ED) in Los Angeles after undergrad at UCLA, and have since been intrigued by the social and physiological complexity of the disease. Unfortunately, SCD is a condition commonly surrounded by stigma in the medical community, presenting a myriad of barriers for people with SCD to receive adequate care. I witnessed firsthand how ED providers' false perceptions of patients with SCD could negatively impact their care. Ever since, I have been interested in how I can contribute to the research and broader education to inform providers about SCD. While working within this broader needs assessment, I will focus my research topic on understanding challenges specific to pediatric residents in managing acute pain episodes with opioids in SCD.

Contributing Authors
Anne Marsh, MD; Jennifer Kim

Introduction
Sickle cell disease (SCD) is a genetic condition caused by a mutation in hemoglobin, causing red blood cells to become rigid and "sickle" shaped. Sickled cells can trigger obstruction of blood vessels, causing acute, severe pain episodes, termed vaso-occlusive episodes (VOE). Pain is a major clinical characteristic of SCD, but is often under-treated. Negative provider attitudes towards patients with SCD are documented, but it is not clear if the national "opioid epidemic" contributes further to challenges in SCD management.

Objective
The purpose of this study was to examine whether pediatric residents with differing experiences with SCD varied in concerns and attitudes about the management of VOE.

Methods
Surveys were distributed to 88 pediatric residents at UCSF Benioff Children's Hospital Oakland (BCHO) and could be completed on-line or via paper format. Survey data included demographics, approximate number of patients with SCD seen clinically, attitudes towards patients with SCD, perceived barriers to treatment of VOE with opioids, and comfort level in treating patients with SCD. Descriptive statistics were computed including means, standard deviations, and frequencies. Differences between residents with clinical experience with ≥ 21 patients with SCD compared with those who had seen <21 patients were examined using chi-square analyses.

Results
53 of 88 (60%) residents completed the survey. The majority of respondents were female (69.8%). Residents with greater clinical experience with patients with SCD (45.3%) reported being significantly more comfortable in treating patients with SCD ($p<0.05$) and reported lack of training as a minimal barrier to treatment of VOE with opioids ($p<0.05$) compared with less experienced residents. Less experienced residents reported greater empathy for patients with SCD ($p<0.05$) but greater concern for opioid addiction as a barrier to treatment compared with experienced residents ($p=0.058$).

Conclusion
Pediatric residents with more experience caring for patients with SCD reported greater comfort in treating them, but also showed less empathy towards patients with SCD compared with residents with less experience with SCD. Less experienced residents also reported addiction as a greater barrier to treatment of VOE with opioids, suggesting that increased training and experience with patients with SCD may help to mitigate these concerns.

Acknowledgements
Thank you to my amazing sickle cell research team for all your support and encouragement. Also thank you to the BCHO pediatric residents who took time out of their packed schedules to provide us with invaluable information necessary to this project.

Keywords
sickle cell disease, stigma, attitudes, opioid treatment, vaso-occlusive episodes

Michael Fink

University of California, Berkeley

Funded by: National Institutes of Health

Mentor: Deborah Dean, MD, MPH

Effect of Membrane Trafficking Protein Rab-39A on Ct Inclusion Formation

My name is Michael Fink. I was born and raised in a Mexican-American home in Walnut Creek. I am a rising junior at UC Berkeley. I am majoring in Molecular Cell Biology with a concentration in Biological Chemistry and I am also minoring in Spanish. Since I was a kid, I have always been intrigued by the sciences, but it was not until college that I became interested in the idea of going to medical school. CHORI Summer research helped me get a foot in the door as I become the first in my family to embark on this path to becoming a doctor. I am very excited that I am working in the Dean Lab researching *Chlamydia trachomatis*, which allows me to do the wet lab bench work I wished to do, as well as keeping in mind the clinical significance of these findings to the medical world.

Introduction

Chlamydia trachomatis (Ct) is the world's leading cause of bacterial sexually transmitted infections and of preventable blindness. Ct can be divided into three biovars (strands): urogenitial, LGV, and ocular. Rab proteins are small G-proteins that serve as master regulators of intracellular membrane trafficking. Since each Rab protein associates only with specific organelles, we can use these proteins to track the pathways of each biovar and see how they differ.

Objective

This project focuses on the association between Rab39a and a representative strain of each biovar. We will observe the effects of Dominate Negative (DN), Constitutively Active (CA), and wild type Rab39a proteins in HeLa cells after being infected with each biovar to learn more about the pathways each strain takes.

Methods

Rab 39a wild type (WT) plasmid was mutated into dominant negative (DN) and constitutively active (CA) forms through site directed mutagenesis. Rab 39a WT, DN, and CA plasmids were transformed into E. Coli. Each plasmid DNA was then isolated using a Qiagen MaxiPrep. The plasmids were then transfected into HeLa cells, and infected with each biovar. Finally, the cells were imaged with fluorescence microscopy to determine the number and area of the inclusions for each Rab protein and Ct strain combination.

Anticipated Outcomes

We expect rab39a WT to co-localize with the urogenital and LGV strains, but not with the ocular strain. We expect the CA mutant to have more inclusions for the urogenital and LGV strains in comparison to the rab39a WT.
We also expect there to be fewer inclusions in the urogenital and LGV strains when using the DN mutant in comparison to the rab39a WT plasmid. Lastly, we expect the DN and CA mutants to not differ in number of inclusions from the rab39a WT plasmid in the ocular strain.

Acknowledgements

I would like to thank Amber Jolly, PhD for her guidance and the rest of the Dean Lab for their support.

Keywords

Chlamydia trachomatis, Rab39a, transfection, infection, mutagenesis

Meghan Foe

Brown University

Funded by: National Institutes of Health

Mentor: Marsha Treadwell, PhD, Ashutosh Lal, MD

Factors Related to Adherence to Iron Chelation Therapy for Young Adults with Thalassemia

I am a rising senior studying public health at Brown University. My interest in public health stems from my belief in the need for health equity – for exploring the ways in which we can diminish health disparities and provide accessible health care across various demographic divides. More specifically, I am interested in exploring structural, social, and behavioral determinants as they relate to specific health outcomes and to health equity.

By supporting my research this summer, CHORI has allowed me to pursue my public health passions in a project that is of both immense academic and personal significance to me. Through my work on this project, I have been able to collaborate with a medical team that is at the top of its field both in research and care, as well as develop essential qualitative research skills that I plan to bring with me to future endeavors. I ultimately hope to pursue a career in medicine with a focus on meeting the community health needs of underserved populations.

I would like to thank Drs. Marsha Treadwell and Ashutosh Lal, as well as the thalassemia team for their incredible support and guidance this summer.

Introduction

Thalassemia is a genetic blood disorder that causes severe anemia and requires treatment with frequent blood transfusions. Iron overload from these transfusions must be treated with daily iron chelation therapy (ICT). Adherence to ICT among patients with thalassemia remains suboptimal, despite medical advances that have improved the ease of ICT administration. Young adults with thalassemia are at a higher risk of nonadherence to ICT compared to other age groups, yet research exploring underlying factors to this phenomenon is lacking.

Objective

To identify the barriers and promoters to ICT adherence by qualitatively examining the perspectives of young adults with thalassemia.

Methods

Young adults with thalassemia ages 18-35 years who are prescribed some type of ICT and seen at the UCSF Benioff Children's Hospital Oakland are being recruited for individual, semi-structured interviews. Target enrollment is 10 participants. Interviews cover topics such as the effect of thalassemia on various aspects of life, the experience of transitioning to adulthood with thalassemia, and promoters and barriers to ICT adherence. These interviews are being audio-recorded, transcribed, and imported into the NVivo software for thematic analysis.

Preliminary Results

Preliminary coding passes through the transcripts suggest that promoters and barriers to ICT adherence among young adults with thalassemia are multifactorial and complex. It is expected that the narratives of these young adult patients will provide in-depth information about how the social and emotional experience of thalassemia and the logistical and structural characteristics of chelation interact to inform ICT adherence.

Conclusion

The results from this study will yield an actionable framework that identifies key driving factors to adherence and illustrates the relationships between these factors. This framework will hopefully be used to ultimately improve clinical and self-management approaches to improve adherence for patients with thalassemia during the critical period of young adulthood.

Acknowledgements

Thank you to my mentors, Dr. Treadwell and Dr. Lal, as well as to the rest of the thalassemia team, Dr. Yamashita, Shannon Gaine, Wendy Murphy, and Raquel Manzo, for their support and guidance.

Keywords

thalassemia, iron chelation therapy, adherence, young adulthood, qualitative

Brianna Fredrick

Vallejo High School

Funded by: Doris Duke Charitable Foundation

Mentor: David Killilea, PhD; Kathleen Schultz, MS

The Evaluation of Zinc Status using Hair in Vietnamese Pregnant Women Fed a Nutrient Based Diet

My name is Brianna Fredrick and I am a rising senior at Vallejo High School. Ever since I was young, I have always wanted to work in the medical field because I love helping people. I believe what motivated me was my mother. When I was younger, my mother was a CNA and whenever I visited her job with her, she was always taking care of her patients in such a loving way and you could see the relations she built with them as they were so close. I wanted to feel that same way and I wanted to do something I know I would be happy doing. What also motivates me is that people with my background aren't usually seen within the medical field and I want to show people from Micronesia that they are capable of anything. I applied to the CHORI summer research program because I want to pursue a career in medicine and I believe this summer program is the start of achieving that goal. I hope that my experience here at CHORI makes my path with a career in medicine more clear and reassures me that medicine is meant for me.

Introduction

Zinc is an essential mineral in our bodies that we need just to function correctly. It is needed for our immune systems to work, to synthesize DNA, and the body's healthy growth and development. Although zinc is such an important mineral just to keep us alive, there are many areas in the world that don't have resources to maintain healthy zinc intakes. Zinc deficiency is very common in rural areas, especially in women and children, because of inadequate amounts of zinc-rich foods. In this ongoing study, we will continue analyzing hair samples from a group of 95 pregnant women in rural Vietnam during three gestational time points in their pregnancy. Blood samples were also collected allowing comparison with the hair zinc concentration results.

Objectives

To conclude if the amount of zinc concentration in a woman's body changes over the course of her pregnancy and to compare the effectiveness of hair zinc concentration to plasma zinc concentration, a standard approach used to determine zinc status.

Methods

The amount of zinc in each hair sample will be determined with the inductively coupled plasma optical emission spectroscopy (ICP). Before being tested under the ICP, the hairs will go through a weighing and washing protocol to eliminate any sort of contamination. After being tested on the ICP, the results will be compared to the existing plasma zinc concentration data.

Anticipated Outcomes

We will determine if hair can be used as a target for the measurement of zinc status and hope to clarify how zinc levels may be different in pregnant women than non-pregnant women, especially those that live in rural areas. We hope the zinc content of the hair will correlate with the plasma zinc concentration.

Acknowledgments

I would like to thank the Doris Duke Charitable Foundation for funding me and my mentors Dr. David Killilea and Kathleen Schultz for the guidance they've given me.

Keywords

hair zinc, plasma zinc, pregnancy, zinc deficiency

Keely Fuller

Miramonte High School

Funded by: Volunteer

Mentor: Janelle Noble, PhD, Nancy Keller, PhD

Investigating Ancestry– Based Differences in Clinical Presentation of Type 1 Diabetes Patients

My name is Keely Fuller and I am a rising senior at Miramonte High School in Orinda, California. I am so thankful for the opportunity to participate in the program for a second year. I applied to the CHORI summer research program because my experiences with type 1 diabetes and Celiac disease inspired me to pursue a career in medicine. Someday, I hope to help others with similar illnesses.

I love that I learn something new about diabetes everyday while working on my research project at CHORI, even though I have lived with the disease for over four years now. Participating in this program has solidified my longstanding interest in medicine and clinical research. I am so grateful to Dr. Noble, Dr. Reed, and Dr. Keller for granting me this opportunity and guiding me through my research project. I am also thankful for the administrators who organized such an amazing summer research program!

Introduction

Type 1 diabetes (T1D) is an autoimmune disease caused by T cell mediated destruction of pancreatic beta cells. The T1D population varies in age at diagnosis, diabetic ketoacidosis (DKA) positivity, autoantibody positivity, and C-peptide levels. Ancestry, as the central variable for our study, may offer one possible explanation for these variations.

Hypothesis

Race- and ethnic-based differences exist in: age at diagnosis, presence of DKA autoantibody positivity, and C-peptide levels for T1D patients at the time of disease presentation.

Methods

Intake data from the UCSF Benioff Children's Hospital Oakland endocrine department were analyzed for T1D patients diagnosed between 2010 and 2016. Data collected included patient ancestry, autoantibody titers (IAA, GADA, ZnT8A, and IA-2A), BMI, weight, gender, age, glucose level, and C-peptide levels. Inclusion criteria were: ages 2 to 18, had a BMI calculation within one month of diabetes diagnosis, and had autoantibody titers analyzed at one core laboratory.

Chi squared analyses were performed to examine differences in autoantibody positivity, the presence of DKA, age at diagnosis, and C-peptide levels within and among ancestries.

Results

Mean age of diagnosis in African Americans is lower in patients in DKA versus not in DKA ($p=0.033$). In three out of four groups, C-peptide levels were lower in patients in DKA than in patients not in DKA. C-peptide levels were the same regardless of DKA in Hispanic patients. The proportionality of positive to negative titers for a given autoantibody was compared within each group, but no statistically significant results were found.

Conclusion

Most studies focus on non-Hispanic whites, this study will add information about other populations. Identifying autoantibody profiles among ethnicities may aid in the differential diagnosis process. Since T1D follows a different treatment path than other forms of diabetes, correct diagnosis is crucial for optimal disease management.

Acknowledgements

I want to thank my mentors Dr. Janelle Noble and Dr. Nancy Keller for providing me with this opportunity.

Keywords

type 1 diabetes, autoantibodies, ancestry

Elijah Goldberg

Berkeley High School

Funded by: SD Jr. Bechtel Foundation

Mentor: Ellen B. Fung, PhD RD

Body Composition Effects on Bone in those with Acute Lymphoblastic Leukemia and Eating Disorders

My name is Elijah Goldberg and I'm a rising senior at Berkeley High School. After being diagnosed with Crohn's Disease at the age of nine, I was pushed through hundreds of medical tests. No expense was spared in the attempt to identify and treat the inflammation in my GI tract. During this time, continual proximity to medical staff, technology, and ideas sparked an interest in the field. This led to me working with the Children's Hospital of Philadelphia in a research study attempting to relate thyroid markers to other comorbidities in patients with Down Syndrome, during the summer of 2016. I could not have asked for a better follow up this year; I am so grateful for the amazing opportunity this program has given me. In going forward, my goal is to make a positive and meaningful impact on the lives of as many people as I can.

Contributing Authors

Diane Suchet, MD; Rebecca Peebles, MD; Aenor J. Sawyer, MD; Laura Bachrach, MD

Introduction

Acute Lymphoblastic Leukemia (ALL) and Eating Disorders (ED) are two devastating diseases commonly found in pediatric patients. While the primary morbidities of these diseases are a hardship in themselves, common secondary morbidities include low bone density and increased fracture risk. This study explored body composition factors that may influence bone health in patients with ALL and ED.

Hypothesis

In a retrospective review of Dual Energy X-ray Absorptiometry (DXA) scans, body composition will have pronounced and quantifiable effects on bone density and composition in patients with ALL and ED as compared to healthy control patients.

Methods

DXA scans (spine, hip and whole body) were reanalyzed from 2 pre-existing data sets: ALL-ED (#2006-088), which included two sets of whole body and lumbar DXA scans from ALL, ED, and healthy control patients, and FEDXA (#2013-062), which contained whole body DXA scans of healthy controls. Whole body scans were re-analyzed for visceral fat and spine scans for Trabecular Bone Score (TBS). Data was analyzed by STATA, v9.0, and considered significant at $p<0.05$.

Results

31 patients with ALL (14.4 ±3.5y, 12 M), 74 ED (16.9±2.4, 7 M) and 30 controls (19.8±3.5, 13 M) were assessed by DXA. Visceral fat and total body fat was found to be exceptionally variable in ALL patients, whereas both the controls and ED patients had much lower means and standard deviations. Visceral fat was not associated with any bone outcome in our subject groups. Low BMD and BMC (Z-score≤-2) was most prevalent in ED patients (24.3%, $p<0.01$), while low TBS (<1.2) was found only in ALL patients. Lean mass was significantly correlated with BMD and BMC in all patient subsets ($p<0.05$) except male patients with ALL. Fat mass (appendicular and total body fat) was positively associated with BMD and BMC in males with ALL and ED.

Conclusions

Subjects with ALL have an altered body composition which includes elevated subcutaneous fat, visceral fat, and BMI-Z. The observed relationship between fat and bone mass in males with ALL and ED was unexpected, and should be explored further.

Acknowledgements

I want to thank my mentor Dr. Fung for her unending kindness and patience throughout the program.

Keywords

Acute Lymphoblastic Leukemia (ALL), Eating Disorders (ED), DXA, Visceral Fat, Trabecular Bone Score (TBS), Lean Mass

Amira Harara

Berkeley High School

Funded by: California Institute for Regenerative Medicine

Mentor: Chun Yang, PhD

The Identification of Gene Targets That Functionally Regulate Receptor Clustering In Neurogenesis

My name is Amira Harara and I love science. But this love I speak of, goes further than its ability to interest me for hours. I love science because of the way it changed my family's life. When my sister was only fourteen years old, she passed away from an autoimmune condition known as Chronic Granulomatous Disorder (CGD). It was through her death, however, that the lives of my two brothers were saved, as they later became tested and diagnosed with CGD as well. This life experience inspired me to pursue a career in the STEM field, and one day conduct my own research on conditions like CGD. As a rising senior at Berkeley High School, I made sure to take advantage of every opportunity to immerse myself in the Biotech world. It was for that reason that I was through the roof when I discovered I would be working at CHORI. I know this will be an experience I can never forget, as it marks the beginning of my career as a future scientist.

Introduction

The multivalent binding interaction between ligand ephrin-B2 and its cognate receptor, Eph-B4, triggering Eph-B4 clustering, has shown to play critical roles in neurogenesis. This signal transduction pathway is vital in the central nervous system, specifically with its ability to initiate differentiation of neural stem cells into motor neurons, interneurons, or sensory neurons. Becoming familiar with this interaction, its cell signaling, and the set of genes that mediates receptor clustering, will allow the development of a more potent molecule that can then be utilized to promote neurogenesis. Ultimately, this molecule may be used to help those with neurological damage, or diseases, like Alzheimer's.

Hypothesis

Adult neural stem cells will differentiate into neurons when EphB4 receptors are clustered, and such differentiation will be mediated by a number of critical genes that orchestrate the downstream signaling towards neurogenesis.

Methods

The RNA sequencing data sets was analyzed through a digital portal known as Galaxy, which establishes the target genes that are expressed differently in each condition. Then, a functional annotation tool, e.g. DAVID, was used to perform pathway analysis and further establish the association of the targeted genes. The target genes will then be validated by performing in vitro experiments. The RNA will be isolated and purified, and quantitative RT-PCR will be performed.

Results and Anticipated Outcomes

We have identified a set of genes that are differently regulated by the overexpression of EphB4 and the treatment of the multivalent ligand conjugates based on the RNA sequencing analysis. Pathway enrichment analysis was also performed to select the genes that were related in neurogenesis. We will then perform in vitro experiments and use qRT-PCR to verify these gene candidates. We anticipate the expression profile of these gene candidates to be consistent with the RNA Seq. results. Overall, we expect to identify critical gene regulators that are mediating the neurogenesis through EphB4/ephrin-B2.

Acknowledgements

Chun Yang, PhD, Schaffer Lab, CHORI Summer Student Program, California Institute for Regenerative Medicine

Keywords

Differentiation, Overexpression, Transduction, Mediation, Neurogenesis.

Gopika Hari

Virginia Commonwealth University

Funded by: Elizabeth Nash Foundation

Mentor: Beate Illek, PhD

Defective Response to Prostaglandin-E_2 Contributes to Cystic Fibrosis Airway Disease

My name is Gopika Hari and I'm a junior at Virginia Commonwealth University. I was a SSRP participant in 2014 – the opportunity to continue the work we had started earlier has been incredibly rewarding. Through Dr. Illek's mentorship, I've engaged in various aspects of the research experience, from designing experiments to presenting research results. Learning these skills has sharpened my understanding of the scientific process and its relevance to clinical medicine. Having worked with a Cystic Fibrosis (CF) organization for many years, it meant a lot to be able to contribute to the work the lab was doing with CF bench research and personalized medicine. I'd like to thank Dr. Illek and Dr. Sellers for their guidance, as well as my lab members for the great memories.

Introduction

Prostaglandin-E_2 (PGE_2) is a hormone-like lipid compound produced by epithelial and inflammatory cells. PGE_2 is known to facilitate mucociliary clearance (MCC) involving the secretion of chloride and bicarbonate into the airway surface liquid. In airways of patients with the genetic disease cystic fibrosis (CF), defective function of the cystic fibrosis transmembrane conductance regulator (CFTR) protein leads to insufficient secretion of the chloride and bicarbonate anions. The resulting build-up of acidic, dehydrated mucus impairs proper MCC. PGE_2 has demonstrated increased chloride and bicarbonate secretion in intestinal cells of the duodenum and increased MCC in tissues from the trachea. Preliminary chloride transport studies found minimal PGE_2-stimulated Cl-secretion in CF bronchial epithelial cells homozygous for the F508del CFTR mutation as compared to CFTR-corrected bronchial epithelial cells, indicating that PGE_2 may function through a CFTR-dependent pathway. However, the specific impacts of PGE_2 on HCO_3^- secretion, as well as the prostaglandin-E_2 receptors (EP_3 and EP_4) and signaling pathways involved, have yet to be determined.

Objective

Aim 1 is to determine the regulatory role of PGE_2 on CFTR-mediated Cl^- and HCO_3^- transport. Aim 2 is to test the involvement of EP_3 and EP_4 receptors. Aim 3 is to determine the specific intracellular signaling pathways involved.

Methods

CFBE41 and CFBE41+CFTR cell lines were grown on Snapwell inserts at a density of $1x10^5$ cells/filter. Ussing assays were used to measure chloride currents following addition of PGE_2, as well as EP_3 and EP_4 receptor agonists (sulprostone, CAY10598) and antagonists (L-798106, AH23848). Additionally, inhibitors of PKA (H-89) and intracellular Ca^{2+} levels (thapsigargin, BAPTA-AM) were applied to determine involvement of intracellular cAMP and Ca^{2+}, respectively. PGE_2-stimulated bicarbonate secretion was measured with pH-stat.

Outcomes

PGE_2-stimulated Cl^- and HCO_3^- transport in CFBE41+CFTR cells but not CFBE41 cells. PGE_2-stimulated chloride conductance was inhibited 74% by H-89 (n=5), 34% by BAPTA-AM (n=2), and 36% by thapsigargin (n = 1), indicating that PGE_2 may work mainly through a cAMP-dependent mechanism. It is expected that inhibition of the EP_4 receptor will block PGE_2-mediated phosphorylation of CFTR, while the EP_3 receptor involved in increasing intracellular Ca^{2+} will have no significant effect.

Acknowledgements

The Elizabeth Nash Foundation

Keywords

Cystic Fibrosis, Prostaglandin-E_2, electrolyte transport

Lilian Hernandez

Contra Costa College

Funded by: National Science Foundation

Mentor: Ronald Krauss MD, Sarah King, PhD

Testing the Effects of Statins on Mitochondrial Function in Patient-derived LCLs

Growing up in a small Guatemalan town that lacked adequate medical access has spurred my desire to assist people to gain access to quality medical care. Ultimately, this desire has served as the inspiration to pursue a career in the medical field. This research opportunity marks the first step to pursuing my aspirations of changing the world. My newly acquired knowledge will be used to help improve the lives of others for the better. I am certain that the experiences I have gained this summer will serve as guidance towards becoming a well-rounded student in the medical field, as I approach my junior year as a transfer student at UC San Diego where I will be majoring in Global Health.

I would like to thank the CHORI Summer Program for this wonderful opportunity that will aid me in achieving my goals. CHORI has provided me with a great research experience that created a great opportunity to meet amazing people. Thank you to my mentors Dr. Krauss and Dr. King for their valuable knowledge and guidance. I would also like to thank Brendan Neilan for always helping during lab and also the entire Krauss lab for their support.

Introduction

Statin drugs are widely used to reduce plasma low-density lipoprotein (LDL) cholesterol and heart disease risk. However, with the use of statins, a small but significant risk of muscle damage, known as myopathy, has been reported. Myopathy is a neuromuscular disorder in which the primary symptom is muscle weakness due to dysfunction of muscle fibers.

Muscles contain the highest mitochondrial content of any tissue in the body due to the large amounts of ATP required for muscle movement. Because of the role of mitochondria in muscles, studies have shown that mitochondria may play a part in the development of myopathy in patients on statin treatment. Furthermore, since mitochondrial oxygen consumption is recognized as the fundamental measure of mitochondrial function, assessing the oxygen consumption rate (OCR) in lymphocyte-like cells (LCL) will provide an indication of metabolic stress associated with statin usage.

Objectives

To assess the degree of variation of mitochondrial function in LCLs.
To investigate if simvastatin has adverse effects on mitochondrial function in cultured LCLs

Methods

I will treat patient-derived LCLs with simvastatin, which has been found to cause myopathy in humans. I will be using the Seahorse XF Analyzer with the Mito Stress Kit to measure the mitochondrial function in LCLs. This assay measures the key parameters of mitochondrial function by directly measuring the OCR of cells. Additionally, this kit uses modulators of cellular respiration that target components of the electron transport chain (ETC) to reveal key parameters of metabolic function.

Results

We treated 3 LCL lines with 2μM simvastatin for 24 hours. Statin-treatment reduced the viability of the cells, but did not change the basal respiration rate. We anticipate that changing the statin dosage and including a larger number of cell lines might reveal a statin effect on basal respiration.

Acknowledgments

I would like to thank Dr. Krauss and Dr. King for their mentorship throughout the summer. I'd also like to thank Brendan Neilan for the lab assistance. Lastly, I would like to thank the CHORI Program for this wonderful experience.

Keywords

Mitochondria, Statin, LCLs

Sebastian Hurtado

University of California, Los Angeles

Funded by: Doris Duke Charitable Foundation

Mentor: Jennifer Michlitsch, MD, Caroline Hastings, MD, Cheryl Cohler, MD

Risk Factors for Venous Thromboembolism in Children with Cancer

My name is Sebastian Hurtado and I am a rising third-year at UCLA. My ultimate goal is to serve children either by becoming a pediatric physician or by focusing on psychiatry, epidemiology, or global healthcare. As a psychobiology major and pre-med student at UCLA, I have enjoyed interning at UCLA Ronald Reagan Hospital, shadowing nurses and helping patients of all ages by volunteering on several hospital units. These experiences, coupled with my partaking in clinical research at CHORI both in 2014 and this summer, have instilled in me a deep fervor for working face-to-face with people. Ultimately, I hope to serve the children of the world by mitigating suffering, promoting effective patient care, and bridging the gap in health disparities that exist in the modern world. My time at CHORI has highly enriched my experiences in and out of the classroom, and I am so grateful for the staff and directors at CHORI, the Doris Duke Charitable Foundation, and my kind-hearted and dedicated mentors, who have all taught me so much and gifted me with unforgettable opportunities.

Introduction

Venous thromboembolism (VTE), the obstruction of a vein due to a blood clot dislodged from a blood vessel elsewhere in the circulatory system, has recently been shown to be increasing in incidence in children with cancer. VTE is most commonly noted in patients with acute lymphoblastic leukemia, lymphoma, or soft tissue sarcoma/bone tumors. Previous studies have identified several potential risk factors that lend to the multicausal occurrence of VTE: genetic predisposition, disease classification, and type of treatment, such as chemotherapy, as well as presence of a central venous catheter.

Hypothesis

Previous research has found certain demographic and physiological factors that have predisposed pediatric patients suffering from blood cancers and other malignancies to venous thromboembolism (VTE) and related diseases. We hypothesize age, malignancy type, body mass index (BMI), specific agents of chemotherapy, and presence of a central line to be the most significant risk factors for development of thromboembolism.

Methods

We accessed the UCSF Benioff Children's Hospital Oakland's Meditech medical database, as well as physical paper charts, to conduct a retrospective chart review analysis on pediatric patients treated for cancer from 2000-2009. Subsequently, we collected data on age, BMI, sex, ethnicity, malignancy type, chemotherapies, major surgeries, complete blood count, and details of patients' central venous catheters (CVC). A spreadsheet database was created compiling this data, consisting of 200 control patients with pediatric malignancies but no history of VTE, and of 42 patients who had both a malignancy and history of VTE. The data were then analyzed using statistical analyses programs, to locate trends in the hypothesized risk factors. Finally, a risk stratification strategy was created to better identify specific populations at risk for developing VTE and to ascertain specific risk factors for VTE in cancer patients in order to better handle and determine subsequent routes of treatment.

Anticipated Outcomes

We expect to find a correlation between type of cancer and incidence of VTE, with patients suffering from acute lymphoblastic leukemia or other blood cancers having a higher incidence of VTE than patients suffering from non-blood malignancies. Furthermore, we expect patients who received chemotherapy, specifically with the chemotherapeutic drug of PEG-L-asparaginase, among others, to be more vulnerable to developing VTE. Finally, we expect to detect a positive correlation between numbers and types of CVCs used, as well as the number of lumens in these central lines, to an increased risk of developing VTE. Overall, we anticipate presenting these findings to the medical field in order to better patient healthcare and affect prognosis by applying preventative measures.

Acknowledgements

I am extremely grateful to my dedicated mentors, Dr. Cheryl Cohler, Dr. Jennifer Michlitsch, and Dr. Caroline Hastings; to my funding organization, The Doris Duke Charitable Foundation; and to my co-researcher, Christopher Alvarez.

Keywords

venous thromboembolism, acute lymphoblastic leukemia, lymphoma, cancer, deep vein thrombosis

Katie Jang

University of California, Berkeley

Funded by: Volunteer

Mentor: Kathleen Schultz, MS, David Killilea, PhD

Measuring Phytic Acid Levels in Nordic Wheat to Identify the Most Nutritious Strains for Growth in the US

Hello, my name is Katie Jang and I am a rising Junior at the University of California, Berkeley. Since coming to college, I became more aware of how integral nutrition is in our lives. For this summer, I will be researching phytic acid, a paradoxical compound found to prevent the absorption of zinc in the body. Phytic acid levels of flour samples will be used as a factor in determining the ideal strains of flour to use for farmers.

This opportunity to work in a laboratory setting would not be possible without the help of mentors and staff. I would like to thank my mentor Dr. David Killilea. His guidance and his genuine willingness to pay it forward cultivated my curiosity for science. I am amazed at the complexity of nutrition and the human body processes from working in this environment. Dr. Killilea has been extremely helpful in my journey in STEM in securing my passion for science by creating a lab setting that is open to ask questions. I would also like to thank Kathy Schultz for encouraging me and supporting me in the lab. I am eager to translate what I have learned at CHORI into my future work and encourage others in my community to pursue STEM

Introduction

Phytic acid is a natural compound found in plants composed of an inositol ring surrounded by six highly charged phosphates that often bind minerals. These phosphate groups and minerals function as an important nutrient store for plants. When consumed, phytic acid can be a nutritional concern because it interferes with the absorption of minerals, including zinc. Zinc is one of the most common nutrient deficiencies in the world, affecting approximately 2 billion people. Unfortunately, phytic acid intakes are often higher in communities where zinc deficiency is common. Recently, agricultural scientists are introducing wheat varieties adapted to Nordic climates into northern regions of the US to bolster nutrition and local agronomies. It is unclear if these wheat varieties will have a positive mineral-to-phytic acid balance when grown in this country.

Hypothesis

Wheat phytic acid levels will vary between different strains. We seek to determine which wheat varieties have highest mineral content and lowest phytic acid to recommend to farmers.

Methods

Phytic acid levels in 44 varieties of Nordic wheat will be measured using the Megazyme Phytic Acid kit. Total phytic acid will be extracted by acid hydrolysis and degraded by recombinant phytase and alkaline phosphatase. The resulting phosphate levels will then be measured by spectrophotometry using the dye molybdenum blue. Modifications to the phytic acid analysis kit will be made in order to improve sensitivity and robustness. The levels of zinc and other mineral will also be measured by inductively-coupled plasma spectroscopy.

Anticipated Outcomes

We will identify the strains with highest zinc and the lowest phytic acid ratio. The endogenous mineral and phytic acid levels may differ when Nordic strains are grown in the US under different conditions. The optimal strains for nutritional criteria will then be recommended to the agricultural scientists for testing growth characteristics, baking performance, and taste.

Acknowledgements

Dr. Steve Jones and Bethany Econopouly from Washington State University. Brianna Fredrick and Brittney Deadwiler from the CHORI SSRP.

Jennifer Juarez

Sonoma State University

Funded by: National Institutes of Health

Mentor: Cindy Leung, ScD MPH

The Effects of Food Insecurity on Cognitive Development and Eating Behaviors of Children – The Role of Toxic Stress

My career in medicine began when I witnessed chronic illness among my family in a village in Guatemala. I observed the scarce access to basic survival resources and adequate healthcare. The history of chronic illness and the lack of appropriate medical care abroad and in the U.S to underserved communities created the desire in me to advocate for lives that suffer and to improve the laws that affect my community's access to primary care and treatment by following a MD/MPH route.

My participation in the CHORI/UCSF Research Program was remarkable because I familiarized myself with the process of conducting community-based research. It allowed me to work closely with participants as an experimenter and to understand the impact of food insecurity. I thank my amazing and supportive mentor, Dr. Cindy Leung for the chance to work with her. I also thank Dr. Tester for the opportunity to shadow her at the pre-obesity clinic which taught me significant healthy habits. Through CHORI, I have become better, driven to positively impact the greater community.

Introduction

Food insecurity is an issue of lacking access to enough resources to obtain nutritious aliments. The psychological impact that food insecurity brings upon children, usually involves feelings of embarrassment, sadness, or anxiety and a lack of food choice. This follow-up quantitative study will examine whether food-insecure children differ from food-secure children based on cognitive development and eating behaviors.

Objective

To examine the relationship between household food insecurity and cognitive processes and eating behaviors in children and parents and the extent to which the toxic stress of food insecurity mediates the associations between them in relation to overeating.

Methods

The study has 2 parts:

1. A 15-minute survey that the parent completes at home in English or Spanish, and
2. A 90-minute lab visit of parent and child at UCSF at Laurel Heights.

130 children between the ages 7 and 14 years will be recruited from the Bay Area through flyers, websites and other agencies. The study will involve 65 food-secure and 65 food-insecure children. They will complete the eating in the absence of hunger paradigm, tasks that measure cognitive function, complete questionnaires, and interact with research assistants. We will take anthropometric measures after parent and children are reunited. The rate of discounting (impulsivity), the rate of elasticity (food reinforcement), and consumption of calories, saturated fat (g), sodium (mg), and sugar (g) from the eating in the absence of hunger task will be the primary study outcomes.

Anticipated Outcomes

We expect food-insecure children and parents to have lower performance on cognitive tasks that measure various decision-making abilities, have higher levels of impulsivity, find food more reinforcing, and would consume more calories even when not hungry than their food-secure counterparts. We anticipate food insecure participants to most likely experience toxic stress which partly intervenes in the cognitive development (decision-making) of children. This can influence the eating patterns that families develop which can lead to negative consequences such as obesity.

Acknowledgements

Cindy Leung, Scd, MPH, Elissa Epel, PhD

Keywords

Food Insecurity, Stress, Cognitive Development, Children

Judy Kang

University of Southern California

Funded by: National Institutes of Health

Mentor: Nahal Lalefar, MD

Association Between Hyponatremia and Induction Therapy in Pediatric Patients Diagnosed with Acute Lymphoblastic Leukemia

Hello! I am a rising sophomore at University of Southern California and studying human biology in the pre-med track. This is my second summer at CHORI. My first time at CHORI was when I was a high school senior in 2014. However, a rare congenital arteriovenous malformation in my brain burst and caused a hemorrhagic stroke that caught me unawares, just the week before the CHORI Symposium. A brain surgery saved my life, but the damage left me as a semi-paralyzed, illiterate, speechless 16-year-old. Through physical and speech therapy, it took about four months to be able to walk and about a year to relearn and recover the ability to speak, read, and understand language. I am now given the opportunity to learn science once again through CHORI. CHORI has given me an unforgettable learning experience that I am grateful to be a part of.

Introduction

Acute Lymphoblastic Leukemia (ALL) is a type of fast-growing blood cell cancer that originates in the bone marrow. There are 2 types of ALL, T-cell or B-cell. ALL is the most common type of cancer that occurs in children. Patients diagnosed with ALL receive multiple cycles of chemotherapy in order to go into and stay in remission. The first phase is called induction therapy, and it lasts to 35 days after start of treatment.
It is observed that many of Children's Hospital patients undergoing their induction phase therapy develop hyponatremia, an electrolyte imbalance condition where there is less sodium in the blood. Severe sodium deficiency can lead to dangerous consequences, such as seizures; so early intervention is important. Chemotherapy can cause hyponatremia but this has not been studied closely for pediatric patients undergoing induction therapy for ALL.

Objective

To assess and evaluate the possible association between hyponatremia and induction therapy for pediatric patients diagnosed with acute lymphoblastic leukemia (ALL) and determine the risk factors for developing hyponatremia.

Methods

We performed a retrospective chart review of 102 patients who were diagnosed with B-cell or T-cell ALL between December 1, 2013 to May 31, 2017 at UCSF Benioff Children's Hospital, Oakland. The induction therapy for B-cell and T-cell lymphoma is identical to ALL induction therapy, so patients with B or T-cell lymphoma are included. The patient background information collected include: age at diagnosis, gender, race and ethnicity, and genetic disorders (Down Syndrome). Information collected at time of diagnosis include the type of ALL, risk levels (standard versus high risk leukemia), central nervous system (CNS) involvement, and which steroids (dexamethasone versus prednisone) used for induction therapy. The sodium, potassium, and albumin levels are also collected during 35 days of induction. There will be a statistical analysis to evaluate risk factors in patient's background, diagnosis, or treatment that are associated with hyponatremia.

Anticipated Outcome

Once data collection and analysis is complete, it is expected that we will find some association between induction therapy and hyponatremia for patients diagnosed with ALL. If certain factors are found to be associated with high risk of hyponatremia in pediatric patients undergoing induction therapy for ALL, physicians can initiate early interventions to prevent hyponatremia or treat it early to prevent further complications.

Acknowledgements

Ginny Gildengorin, PhD

Keywords

Acute Lymphoblastic Leukemia, Induction phase, Hyponatremia, Chemotherapy

Adeleen Khem

Bishop O'Dowd High School
Funded by: Volunteer
Mentor: Elliott Vichinsky, MD

Alpha Thalassemia Outreach

My name is Adeleen Khem and as I look ahead on what career path I want to go down, I know that I want to pursue medicine and work with children, thanks to CHORI. As a rising senior at Bishop O'Dowd High School, I want to continue to explore what the medical field has to offer and bring my passion for learning and being a resource to my community.
I had the privilege of being mentored by Dr. Elliott Vichinsky, and I learned about blood diseases, such as Thalassemia, which is highly populated in the Southeast Asian community. I have been exposed working in a clinic and developing a survey and I will take this experience and utilize them in my future experiences. This summer solidified what I want to pursue in college and beyond and so I'd like to thank Dr. Vichinsky and Dr. Yamashita for the continuous support and mentorship.

Introduction

Thalassemia is the most common genetic disorder affecting seven percent of the world.
There are two major versions of the disorder: Alpha thalassemia and Beta thalassemia, and Beta is the better known one, consisting changes in the beta chain. On the other hand, four genes affect alpha thalassemia. Carriers with one or two gene mutations have a generally mild anemia and microcytosis. They are often misdiagnosed and treated as iron deficiency resulting in iatrogenic iron overload; a three gene mutation causes hemoglobin H, a worldwide public problem with are an estimated 50,00 cases in California most of whom have not been identified or have received care. They are often not diagnosed because special laboratory tests are needed, and they are not referred to a thalassemia center. A four-gene deletion causes the inability of the fetus to make functional blood. Without early identification and an intrauterine transfusion, most of these pregnancies result in miscarriages or stillborn. As the patient's approach adulthood, their disease progresses, resulting in organ failure and death. However, parents can be carriers of this disease and not be aware they have this disease until they have a child. Early identification can result in intrauterine transfusions with a healthy yet transfusion dependent baby. The most important factor of this project is to identify carriers of alpha thalassemia so they can make educated decisions and for people with moderate disease hemoglobin H to obtain preventive therapy.

Hypothesis

We hypothesize that if we can ID the key knowledge gaps, then we can construct target interventions that can begin to address weakness in the information base of both at-risk couples and healthcare providers that can begin to improve the healthcare provided to these groups.

Methods

1) A questionnaire will be piloted to understand its strength and weakness utilizing **four groups.**
2) The data from the finalized questionnaire will be entered into a database that exists for the thalassemia data collection program. Two new approaches will be selected and piloted, pamphlet and video in Khmer to an at risk community. Following the video, an assessment from the audience is concluded. Similarly, a bilingual pamphlet will be made available to three physician offices and will assess the acceptance and the utilization of the pamphlets by voluntary communication of the person who reads the pamphlets.

Anticipated Outcomes

1) We will identify the major obstacles to providing information to the Cambodian community about thalassemia. 2) I will learn how to effectively communicate complex health issues to communities that have the least access to basic health issues.

Acknowledgements

Thank you to Dr. Vichinsky and Dr. Yamashita for mentoring me and encouraging me to become a better scientist and a health advocate to my own community. This has been an invaluable summer experience for me and my family.

Keywords

Alpha Thalassemia, Anemia, Hemoglobin, Questionnaire

Franny Kiles

Tufts University

Funded by: Elizabeth Nash Foundation

Mentor: Beate Illek, PhD

Personalized Medicine for Rare Mutations in Cystic Fibrosis

I am a rising sophomore and biochemistry major at Tufts University. My experience doing Cystic Fibrosis (CF) research in Dr. Beate Illek's lab this summer was very special, because I was diagnosed with CF when I was two months old. All of my life I have only learned about and dealt with CF from a patient's perspective, and this summer I got to look at CF from a scientist's perspective as well. I understand the struggles that people affected by CF go through every day, and I am so thankful that I had this opportunity to try and make a real difference in the lives of those suffering from the disease.

The CHORI Summer Research Program was my first experience doing lab work. I am still unsure of what career path I would like to follow when I graduate, but am grateful that I got to immerse myself in research and take another step toward figuring that out. Thank you to everyone here at CHORI for doing inspiring work every day and for making this program possible.

Introduction

Cystic Fibrosis (CF) is a genetic disease that results from a defect in the Cystic Fibrosis transmembrane conductance regulator (CFTR) protein, which regulates salt and water transport in epithelial cells. It affects 30,000 Americans and there are currently 2019 known mutations. The CFTR modulators are new drugs that target the underlying channel defect in CF. VX-770 and VX-809/VX-770 have been approved by the U.S. Food and Drug Administration (FDA) and VX-661/VX-770 is undergoing Phase 3 clinical trials. CFTR potentiator VX-770 activates residual mutant CFTR function in the cell membrane. CFTR corrector VX-809 aids in the folding of CFTR in order to fix the F508del defect. VX-809/VX-770 is approved for patients homozygous for the mutation F508del, the deletion of phenylalanine at amino acid 508 that results in protein degradation. The modulator VX-661/VX-770 has shown positive results in patients who are heterozygous for F508del and another residual CF mutation. The project aims to test these modulators on two ultra-rare CFTR genotypes, F508del/S1159P and F508del/c.850dupA. It is imperative to test these modulators on ultra-rare mutations so that no patient is overlooked.

Hypothesis

Ultra-rare Cystic Fibrosis mutations may respond to FDA approved CFTR modulators.

Methods

Nasal epithelial cells of two CF patients were obtained by nasal brushing. The cells were conditionally reprogrammed using irradiated 3T3-L1 fibroblasts and ROCK inhibitor in order to expand the number of cells. Differentiated cells at passage 1 were incubated with either VX-809 or VX-661, and the acute response of VX-770 was tested with the Ussing assay. Data was recorded (DI710, DataQ) and analyzed (SigmaPlot, Version 11.0).

Anticipated Outcomes

The CFBE41o- cell line, homozygous for F508del, showed promising results when incubated with VX-661 and VX-809. ATP was used as a positive control to induce chloride transport across a calcium activated channel and test the functionality of the cells. The F508del/S1159 cells responded to acute VX-770 when incubated with VX-809 and with no treatment. The S1159P mutation occurs near the end of the protein, and may have residual protein function. It is less likely that c.850dupA leads to residual CFTR function, since the mutation induces a stop codon early in the sequence at membrane spanning region 4 (MSR 4). VX-809 and VX-661 could lead to some residual function by correcting the F508del mutated CFTR.

Acknowledgements

Dr. Beate Illek, Dr. Dennis Nielson, Lorna Zlock, Dr. Walter Finkbeiner

Keywords

Cystic Fibrosis, conditional reprogrammed cells

Ah Young Kim

University of California, Berkeley

Funded by: Volunteer

Mentor: Tatyana Vayngortin, MD

Adolescents' Acceptance of Long-Acting Reversible Contraception After a Brief Educational Intervention in the Emergency Department

Having lived in South Korea, China, Mexico, Texas, and California as part of both the majority and minority cultures around the world, I grew up with a curiosity about the interconnection of people's behaviors and minds. Focusing my studies in Psychology, Social Welfare and Education at UC Berkeley, I had the opportunity to work with the Developmental Psychology Lab. The deeper I explored into the field, the deeper my concern for children's mental and emotional problems grew. Although I am still brainstorming my future goals, I am determined to help others. Participating in CHORI's Summer Research Program enhanced my knowledge in clinical research and the medical field. I worked with Dr. Tanya on a research project on women's health in the emergency department, which definitely introduced me to new perspectives in research and medicine. I am grateful to pursue this remarkable opportunity to shape my future journey.

Contributing Authors

Sarah Chen

Introduction

According to the National Survey of Family Growth, about half of unintended adolescent pregnancies are due to contraceptive failure from incorrect use of contraception or non-use. Despite the safety and efficacy of Long-Acting Reversible Contraception, only about 5% of adolescents are using these methods. The emergency department is a potential valuable setting for educating adolescents about the efficacy of Long-Acting Reversible Contraception. Studies have found that adolescents are interested in receiving pregnancy prevention education and initiating contraception in the emergency department (ED).

Hypothesis

A video intervention for female adolescents in the pediatric emergency department will increase their awareness and use of long-acting reversible contraception.

Methods

This is a randomized control trial of sexually active females 14-21 years old presenting to a pediatric emergency department. The control group will complete a baseline survey, and the intervention group will complete a baseline survey, watch an educational video about contraception made by UCSF Bixby Center for Reproductive Health, and complete a post-video survey. The subjects will be followed 3 months after their ED visit by e-mail, phone call, or chart review to determine contraceptive usage.

Preliminary Results

Compared to controls, teens who watched the video were significantly more likely to want an IUD (p=.002) or Implant (p=.013). Among teens who watched the video, they were significantly more likely to want an IUD (p<.001) or Implant (p=.004) after watching the video. About12.2% adolescents were interested in same-day Long-Acting Reversible Contraception initiation.

Significance

The intention of the research is to provide more information and resources about Long-Acting Reversible Contraception and to access the unmet contraceptive needs of teenage girls in the emergency department. Our long-term goal of the study is to increase the rates of Long-Acting Reversible Contraception use among adolescents in the high-risk population.

Acknowledgements

Thank you Dr. Tanya, UCSF Benioff Children's Hospitals, and the CHORI summer research program for the opportunity.

Keywords

Long-Acting Reversible Contraception, Emergency Department, Adolescent Pregnancy, Pediatric, Sexual Education

Andrew Kriozere

Miramonte High School

Funded by: Independent

Mentor: Flora Ting, BS, Marisa Medina, PhD

The Effect of *Tmem55b* and *Ldlr* on Hepatic Triglyceride Levels

Hello, my name is Andrew Kriozere and I am a rising senior at Miramonte high school. I was diagnosed with Ulcerative Colitis as a 12 year old. My experience with the disease, combined with my love for science and math, spurred my interests towards biomedicine and biotechnology. These interests pushed me in search of opportunities to work with biotechnology and eventually led me to CHORI. This program has helped me determine the major I want to study in college. The invaluable lab work I have experienced over the course of this program has taught me the importance of being methodical and paying attention to details. Under the mentorship of Marisa Medina and Flora Ting, I have learned about the entire research process including reading scientific journals, writing research proposals, planning experiments, and analyzing results. In the future, I want to use this valuable experience to help others with diseases.

Introduction

Non-alcoholic fatty liver disease (NAFLD) is the leading cause of liver failure in the United States. The disease initially presents as accumulation of fat within the liver (i.e. fatty liver or hepatic steatosis) and in some individuals, progresses leading to liver cancer or failure. Other than diet and exercise recommendations, there is currently no treatment for NAFLD. Impaired triglyceride secretion from the liver is one mechanism that causes accumulation of liver fat. In previous studies, the Medina lab found that inhibiting hepatic expression of Transmembrane Protein 55B (*Tmem55b*), a gene recently implicated in cholesterol metabolism, leads to increased levels of plasma cholesterol as well as severely reduced triglyceride secretion in mice fed a high-fat Western Diet. Additional studies in cellular and animal models have shown that TMEM55B protein functions in part through regulation of the low density lipoprotein receptor (LDLR), the primary receptor responsible for transporting low density lipoproteins out of circulation. However, to date it is unclear if the ability of TMEM55B to inhibit triglyceride secretion and potentially alter hepatic triglyceride levels is dependent on LDLR. Thus, in this study, we will test if *Tmem55b* knock-down in *Ldlr* knockout (KO) mice will alter triglyceride secretion and levels of hepatic triglyceride.

Hypothesis

Tmem55b knock-down in *Ldlr* KO mice will lead to impaired triglyceride secretion and accumulation of hepatic triglyceride.

Methods

Male and female *Ldlr* KO mice were fed 4 weeks of a high-fat Western Diet and injected weekly with one of two antisense oligonucleotides (ASOs) dosed by weight: one ASO treatment effectively silences expression of *Tmem55b* while the other is a non-template control. At the end of 4 weeks, tissues were collected and hepatic lipids were quantified using Wako kits (cholesterol, free cholesterol, triglycerides, and free fatty acids) and normalized to protein concentrations by Bradford assay. The efficacy of *Tmem55b* knockdown was quantified by qPCR.

Anticipated Outcome

Tmem55b knockdown in *Ldlr* knockout mice will have impaired triglyceride secretion and thus have higher levels of hepatic triglycerides.

Conclusion

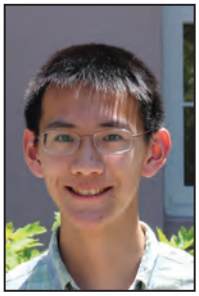
Identification of molecular pathways, such as *Tmem55b*, that contribute to hepatic steatosis may inform the development of drugs for the treatment and prevention of NAFLD.

Acknowledgement

Thank you Flora Ting and Marisa Medina, PhD, for your time, effort, and endless patience.

Keywords

Ldlr, Tmem55b, antisense oligonucleotides, knockdown, triglyceride secretion



Philip Lee

Albany High School

Funded by: Volunteer

Mentor: Amber Jolly, PhD

Effect of Membrane Trafficking Protein Rab-8A on *Ct* Inclusion Formation

My name is Philip Lee, and I will be starting my senior year at Albany High School this fall. I have always had an interest in learning new things and making a positive impact on the world. During my freshman year of high school, I developed a strong interest in biology, especially protein modeling. However, I was unsure about what career path I wanted to take. The CHORI program gave me a taste of what life is like for a research scientist. I am very grateful for the opportunity to work in the Dean Lab, and I really enjoyed experiencing the exciting nature of science and research.

I worked on a project that studied the role of intracellular vesicle trafficking proteins known as Rabs in *Chlamydia trachomatis* infections. I would like to thank Dr. Deborah Dean, Dr. Amber Jolly, and Dr. Ellen Fung for organizing this amazing experience for all of us. I would also like to thank Michael and Sheila for working (and struggling) with me and making me laugh throughout the summer.

Introduction

Chlamydia trachomatis (*Ct*) is one of the most common sexually transmitted bacteria, and its complications include non-congenital blindness, pelvic inflammatory disease, infertility, and anorectal infection.

Rab proteins are small GTPases that help to control intracellular membrane trafficking. Rab proteins are also heavily involved in the *Chlamydia* life cycle. Therefore, examining how *Chlamydia* inclusions hijack a host cell's Rab proteins and vesicular transport system will broaden our understanding of the *Chlamydia* inclusion mechanisms. In addition, due to the specific nature of the Rab binding mechanisms, Rab proteins can be used to track the pathway of *Chlamydia* inclusions.

Objectives

This project will be focused on the Rab-8A protein and the *Ct* strains Ba, E, and L2. The overall goal of this project is to observe the effects of the wild type, constitutively active (CA), and dominant negative (DN) Rab-8A proteins in HeLa cells infected with the three different strains of *Ct*.

Methods

Mutant Rab-8A genes inserted in plasmids will be generated using a process called site-directed mutagenesis, creating plasmids that contain CA or DN Rab-8A genes. Host HeLa cells will be transfected with WT and mutant plasmids. Once inside the cells, a CMV promoter will drive the expression of a fusion protein that contains Rab-8A and GFP. The GFP will mark the location of the recombinant Rab-8A proteins inside the cells.

The cells will be imaged with fluorescence microscopy to determine the number and area of the inclusions for each Rab protein and *Ct* strain combination.

Anticipated Outcomes

It has been shown that Rab-8A protein in HeLa cells co-localizes with *Ct* inclusions formed by the urogenital strain E and the LGV strain L2, but it is not present in *Ct* inclusions formed by the trachoma strain Ba. I therefore anticipate that the Rab-8A protein will increase the *Ct* inclusions in both size and number in the E and L2 strains.

Acknowledgements

Thanks to Dr. Amber Jolly for her guidance, and Michael and Sheila for their support.

Keywords

Chlamydia trachomatis, Rab-8A, mutagenesis, transfection

Kate Lindeman

Bentley High School

Funded by: Volunteer

Mentor: Rachel Kuperman, MD

EEG Serves as a Reliable Biomarker of Impending Infantile Spasms in Children with a History of Neonatal Seizures

Hello, my name is Kate Lindeman, and I am a rising junior at Bentley High School in Lafayette, California. I was very excited about participating in the CHORI program this summer to gain greater understanding about applied scientific research. I had several areas of interest when I applied and am grateful that I was offered a chance to work in neurology. I have been around discussions of research throughout my life. But, I have never applied the rigor of developing and pursuing a research protocol that can actually affect people.

I am extremely grateful to Dr. Rachel Kuperman for her opening new opportunities for me to investigate aspects of neurology that I was not aware. I am especially thankful for Dr. Burt Lubin for faith in me as a rising junior to explore possible areas of interest for my college study and career. His encouragement to pursue research related to children's health and his passion for this area is opening up new possible career paths.

Introduction

Hypoxic-ischemic encephalopathy (HIE) is one of the most commonly occurring causes of neonatal seizures. There is a quiet period right after the neonatal seizures prior to the development of epilepsy and the subsequent onset of acute seizures. These seizures primarily present in the form of infantile spasms. The development of chronic seizures occurs through the process of epileptogenesis, for which there currently is no biomarker. Electroencephalograms (EEGs) conducted over a period of time could provide a means of predicting the likelihood of a child developing infantile spasms. Given that this is a routine and non-invasive form of assessment, sequential EEGs could be an innovative and safe biomarker for detecting which children will develop epilepsy.

Objective

The objective of this study is to determine if a longitudinal analysis of EEGs can be a biomarker to predict which children with a history of neonatal seizures will develop infantile spasms.

Methods

- Looked at Video EEG log books and pulled out neonates less than 5 days old.
- Recorded the de-identified patients that had neonatal seizures secondary to HIE or other etiologies
- Reviewed and recorded EEGs done after day 5
- Then looked at medical records to see if they developed infantile spasms in the clinical notes
- Analyze the babies that had neonatal seizures to the ones that did not to determine if EEG abnormalities predict development of infantile spasms

Anticipated Outcome

Abnormal EEG after acute neonatal seizures predicts the development of infantile spasms.

Keywords

Hypoxic Ischemic Encephalopathy (HIE), neonatal seizures, epileptogenesis, EEG, biomarkers

Tyler Lunow-Luke

University of California, Berkeley

Funded by: National Institutes of Health

Mentor: Lisa Lavrisha, PNP, Kevan McCarten, MD

Predictive Factors of Traumatic Brain Injury in Cranial Computerized Tomography Scans

Being raised in Hawaii, I appreciate a spirit of adventure and connection to nature. Perhaps more importantly, I understand the wisdom from my favorite Disney characters, Lilo and Stitch, that "ohana means family, and family means no one gets left behind." This value of inclusivity drives my passion for medicine and inspires me to leverage my education for the benefit of others. The ability to treat illness fascinates me and provides an outlet to challenge myself. Furthermore, my mixed-race provides unique insight to barriers that prevent communities from seeking and providing healthcare. The CHORI Summer Student Research Program has affirmed my interest in the medical field and aligns perfectly with my core passion of promoting equity among people and communities. My role in the emergency department at CHO supported my enthusiasm and pursuit of a career in medicine.

Introduction

Over the last decade, there has been a drastic improvement in the clinical ability to diagnose and treat traumatic brain injuries (TBIs) through the use of computerized tomography (CT) scans. It has been demonstrated that the use of cranial CT imaging has greatly surpassed the number of treatable TBIs in the population (Fenton et al. 2004). This indicates a general overuse of CT imaging in head traumas which can increase financial burden for both care-providers and patient populations. A set of clinical decision rules were recently derived to help identify pediatric TBIs and optimize CT use (Kupperman & Holmes 2009). These decision criteria are currently being validated in a multiple site study.

Hypothesis

There are several patient and physician factors in diagnosing traumatic brain injury that are associated with abnormal findings in cranial CT scans.

Specific Aims

Identify patient and physician factors that are most predictive of traumatic brain injury on cranial CT (computerized tomography) scans.
Identify patient and physician factors that are least predictive of traumatic brain injury on cranial CT (computerized tomography) scans.

Methods

Symptoms linked to TBI and cranial CT scan results were collected from electronic medical records for trauma patients at UCSF Benioff Children's Hospital Oakland (BCHO) who received a cranial CT scan and participated in the Pediatric Emergency Care Applied Research Network (PECARN) validation study. Both raw data and statistical calculations were conducted in a Microsoft Excel file. Binomial statistics were applied to each symptom and evaluated based on their correlation to TBI in trauma patients. The measure of a successful trial (p) was defined as an abnormal finding on a CT scan. This analysis helped determine the symptoms most associated with TBI in trauma patients.

Anticipated Outcomes

It is anticipated that more severe symptoms such as a low GCS (Glasgow Coma Scale) score, skull fracture and neurological deficits are more indicative of brain injury than common symptoms such as headache, seizures and vomiting.

Acknowledgement

Thank you to Lisa Lavrisha, PNP, Dr. Kevan McCarten, and Dr. Nisa Atigapramoj for supporting all logistical aspects and mentoring this study with patience, dedication and enthusiasm.

Key Words

computed tomography, traumatic brain injury, trauma, pediatrics

Sharad Mahajan

Head Royce High School

Funded by: California Institute for Regenerative Medicine

Mentor: Kevin Tharp, PhD

Yes-Associated Protein (YAP)/ WW Domain-Containing Transcription Regulator Protein 1(TAZ) Role in Adipocyte Growth and Thermoregulatory Capacity

Hi, my name is Sharad Mahajan, and I am a high-schooler at The Head-Royce School in Oakland, California. This summer I wanted to explore and further my knowledge in biology. This past junior year I took Advanced Placement Biology and absolutely loved the course; however, doing research in a lab is very much different than reading about biology in a classroom. I am very lucky to have a mentor like Dr. Tharp because of how hard he pushes me. Whenever we do an experiment, I have to fully understand how the experiment gets the results. In doing so, I have already learned so much. In addition, we talk about all facets of science. This summer, I really wanted to learn about the careers based upon science. Being in a lab allows me to see the frustrations and triumphs in this career path. The summer program has also brought great seminar speakers to talk to us about their career paths, and why they have chosen science. Overall, I am lucky to be part of such a great program.

Introduction

YAP/TAZ are transcriptional co-activators that play a role in determining stem differentiation decisions. Reduced YAP/TAZ levels results in a higher proportion of Mesenchymal Stem Cells (MSC) becoming adipocytes. Additionally, YAP/TAZ has been found to regulate Uncoupling Protein 1 (UCP1) expression. UCP1 is found in brown adipose tissue (BAT), and dissipates the proton gradient generated by oxidative metabolism to create heat and maintain core body temperature.

Objectives/Hypotheses

Our objective was to study adipogenic outcomes in vivo when levels of YAP/TAZ are altered. We hypothesized that lowered YAP/TAZ activity will lead to increased adipogenesis and decreased thermoregulatory capability.

Methods/Results

We used conditional heterozygous deletions of YAP/TAZ in UCP1Cre and AdipoQCre animal models to assess the role of YAP/TAZ in thermogenic and non-thermogenic adipocytes.
We expect increased adipose mass due to reduced energy expenditure and increased adipogenesis. Both the UCP1Cre and AdipoQCre mice seem to have higher body fat percentages and body mass indexes (BMI). Based on a Triglyceride Assay (TGA) and Bicinchoninic Assay (BCA) there seems to be increased adipogenesis in the subcutaneous white adipose tissue of the AdipoQCre. In the BAT, because of higher normalized lipid content, we expected hypertrophy in both the UCP1Cre and AdipoQCre; however, from immunohistology, it appears that while the UCP1Cre tissue exhibited hypertrophy, the AdipoQCre tissue looked very similar to the wild-type. More lipid in BAT seems to be the result of a slowed metabolic rate, and in the AdipoQCre there seems to be more adipogenesis overall, resulting in an increase in adipose mass.

Conclusions

Decreased YAP/TAZ activity leads to increased adipose mass due to reduced energy expenditure and increased adipogenesis. Despite a higher body mass index (BMI) and higher body fat percentages, lowered levels of ectopic normalized lipid content in the liver of the AdipoQCre^/- relative to the wild-type suggest that decreasing YAP/TAZ levels enables more lipid storage in appropriate organs (eg. expanded adipose mass). Reduced thermoregulatory capacity promotes nutrient storage, decreasing temperature homeostasis.

Acknowledgements

Thank you Stahl Lab

Keywords

Temperature homeostasis, YAP/TAZ, adipogenesis, Mesenchymal Stem Cells, thermoregulatory capacity

Alishah Momin

Pomona Collge

Funded By: National Institutes of Health

Mentor: Tariq Ahmad, MD, Ashutosh Lal, MD

The Prevalence of Endocrinopathies in Patients with Transfusion-Dependent Beta-Thalassemia Major

My name is Alishah Momin and I am a rising junior and Pomona College, majoring in Molecular Biology. I first became interested in health when my younger brother was diagnosed with Cerebral Palsy at birth. My role as his primary caregiver has exposed me to the varying applications of medicine and revealed its immeasurable social implications, especially for the marginalized communities I identify with. My experiences growing up as a first-generation, low-income, and a Muslim immigrant scholar have shown me how dental healthcare is often inaccessible & unaffordable for many underprivileged communities. After my undergraduate career, I see myself pursuing a joint degree in Dentistry and Public Health to ultimately work in underserved communities.

Throughout the course of my college education thus far, I have only participated in basic science research. However, I had been craving a more immersive and different research experience. As a participant in the CHORI program, I was granted the opportunity to participate in clinical research in endocrinology and hematology/oncology. Throughout this experience, I discovered that clinical research is an impactful, exciting, and a challenging field of work to pursue. Under the guidance of my auspicious mentors, I have honed my skills, learned about the research process more broadly, and gained invaluable advice. I am greatly thankful to CHORI, my mentors, and everyone who has helped make this summer unforgettable.

Introduction

Beta thalassemia major is an autosomal recessive blood disorder in which individuals with two deficient copies of the beta globin gene are unable to properly synthesize hemoglobin. Consequently, these patients become severely anemic and require periodic blood transfusions every 2 – 4 weeks to survive. Without adequate chelation therapy, chronic transfusions can lead to progressive iron overload in which excess iron causes cell death through redox reactions. Iron deposition in the pancreas and the pituitary gland impair the secretion of specific hormones, leading to many endocrinopathies. As the survival of patients with transfusion dependent thalassemia has increased, the quality of life of these individuals has been affected by subsequent development of various endocrinopathies. The prevalence of these endocrinopathies may be changing however, as treatment of iron overload has evolved over the last 2 decades.

Hypothesis

We hypothesize that age-specific prevalence of endocrinopathies secondary to iron toxicity has declined in the last 10 years with the availability of new options to control iron overload. Sub-analyses can also look to differentiate between the prevalence of endocrinopathies between those on newer chelation therapies compared to older treatment modalities.

Methods

The Comprehensive Thalassemia Center has an accruing database that started approximately 10 years ago. Laboratory studies obtained as part of the routine care for those with transfusion dependent beta thalassemia have been collected over the course of each patient's care and criteria for specific endocrinopathies were defined individually based on normative data respective of where the laboratory study was done. Prevalence of endocrinopathies was determined by the number of individuals with abnormal laboratory studies in the context of all those who were tested. Cohorts were also divided based on history of chelation therapy and compared to look for significant disparities

Preliminary Results

Of the 166 patients who had thyroid function (TSH and Free thyroxine) evaluation, 28.3% had values consistent with primary hypothyroidism and 23.5% with central hypothyroidism. The average IGF-1 z-score for patients between 3 and 19 years old was is -1.2, whereas patients less than 3 and older than 19 were -2.1 z-scores away, indicating most tansfusion-dependent beta-thalassemia patients have IGF-1 levels significantly below the mean and by our definition, x were GH deficient.

Anticipated Outcomes

By comparing our prevalence rates with those from previous studies done, we anticipate our findings will demonstrate a significant impact of current therapy on prevalence rates of endocrine complications secondary to iron overload. Given the large number, and diverse thalassemia population at our institution we hope to strengthen and bring awareness to the association of iron deposition and subsequent endocrinopathies.

Keywords

Thalassemia, endocrinopathies, hypothyroidism, growth hormone deficiency, hypoparathyroidism

Julia Nguyen

Rocklin High School

Funded by: California Institute for Regenerative Medicine

Mentor: Katie Carlberg, MD; Sandy Calloway, PhD

The Effects of Storage Temperature and Duration on the Extraction Yield of Cell-free DNA

My name is Julia Nguyen. I am a rising senior at Rocklin High School. One of the few certainties I have about myself at this age is that I want to pursue a career as a physician. Because I am adventurous and dynamic, I am interested in many different practice settings, including hospital systems, military, law enforcement, government, and of course, research and academic institutions. CHORI has given me the chance to experience the latter, and I am so grateful to have been able explore research, learn new skills at the bench, and peer into the prospect of becoming a physician-scientist.

My experience in research at CHORI was intellectually stimulating. My tasks were challenging and my schedule was demanding. This is certainly a very important step in shaping my future in medicine, and it is one I will remember and cherish forever. Thank you to CHORI, CIRM, and the Calloway Lab for an awesome and transformative summer!

Introduction

Analysis of circulating cell-free fetal DNA (cfDNA) in maternal plasma has enabled non-invasive prenatal testing (NIPT). NIPT, which poses no risk to a fetus when performed, is a more expedient method of screening for and diagnosing genetic disorders in fetuses than current tests like amniocentesis and chorionic villus sampling, both of which present the risk of miscarriage. Applications of NIPT for autosomal recessive disorders, like sickle cell disease and thalassemia, require very precise quantitation of cell-free DNA in order for such testing to be accurate. Therefore, it is crucial that cfDNA yield is optimized.

Objectives

This project intends to determine the relationship between temperature and duration of plasma storage and the stability of cell-free DNA. It also aims to determine the ideal temperatures and acceptable durations of plasma storage for optimal yields of cfDNA.

Methods

Whole blood is collected in Streck tubes and centrifuged to separate the plasma. Then, the spun plasma is aliquoted into 1.5 mL tubes and stored at 4˚C, -25˚C, and -80˚C. For control purposes, cfDNA extraction is performed in triplicate using the QIAamp Ciculating Nucleic Acid Kit immediately following plasma separation. Subsequent cfDNA extractions are performed after 1 week, 2 weeks, and 4 weeks. After each extraction, cfDNA concentration is measured using the Quant-iT PicoGreen Assay and recorded.

Anticipated Outcomes

The outcome of this experiment will be the demonstration of how cell-free DNA levels in plasma change with storage time and temperature. It will also determine the optimal storage conditions of plasma for producing the greatest yield of cell-free DNA.

Acknowledgements

Thank you to my mentors and the Calloway Lab for taking me under their wing and assisting me with my project. Thank you to CIRM for providing me the funding to embark on this journey and thank you to CHORI for giving us high school students this wonderful opportunity to explore scientific research.

Keywords

Cell-free DNA, NIPT, plasma storage, autosomal recessive, QIAamp Circulating NA Kit, Quant-iT PicoGreen

Maria Rodriguez

Contra Costa College

Funded by: National Science Foundation

Mentor: June Tester, MD MPH

Readiness for Change in Food As Medicine

My family and I migrated to United States when I was only 3 years old, in pursuit of a better educational future. I am now approaching my junior year at UCB as a molecular environmental biology major– and hope to go on to medical school afterward. All of my professional interests are driven by my personal experiences– my mothers walk with triple negative breast cancer. I choose medicine because I am determined to help those who are given no hope when battling a terminal illness. There's a lot that I can learn about the effects of the environment on human health– I want to further understand the mechanisms that the human body undergoes in the presence of a teratogen– to one day find better treatment and prevention for environmental caused illnesses.

When I learned about the CHORI program, I knew it would be a great opportunity and learning experience for me because it would give me the opportunity to work along a physician scientist which is something that I was extremely interested in doing– but at the time did not know existed. Working with Dr. June Tester– taught me what it took to do research meanwhile serving a community. It was such a rewarding experience to see how agencies around Oakland– worked together to conduct a study that could potentially better health out comes for an underserved community. I enjoyed witnessing the excitement of both the staff and patients during this intervention study. I know that science comes in all shapes and sizes– but this program reassured the stance I want to take in STEM and that is– to one day become a physician scientist and help find answers and preventative measures to unanswered questions and illnesses in medicine.

Introduction

The Food as Medicine study, which included 4-month deliveries of healthy foods to the home, is an intervention designed to improve health outcomes in low-income families that have a child with pre-diabetes. The Stages of Change (SOC) model is a way of identifying an individual's level of motivation for lifestyle change. Parents take on a huge role in their children's health behaviors, and researchers have modified the SOC to apply to a parent's readiness to change lifestyle-related behaviors in their child.

Hypothesis

We hypothesize that parental SOC regarding readiness to offer their child vegetables and to offer whole grains, respectively, will predict baseline diet behaviors as well as degree of consumption by the completion of the study.

Methods

The study team recruited 60 low-income families an obese child (8-17 years) having pre-diabetes (Hemoglobin A1c 5.7- 6.4).They received weekly food deliveries of vegetables and whole grains (WG). Participants were asked to fill out a survey at baseline and follow up to assess dietary behaviors regarding vegetables and WG. Items included readiness to serve the age-appropriate amount of vegetables or whole grains to (rated in 5 stages), knowledge about WG, and liking/familiarity of vegetables and WG. We plan to conduct a unpaired t-test to look at the means among parents with higher SOC compared to those with lower SOC at baseline and also a paired t-test to compare responses within the same individual.

Anticipated Outcomes

We anticipate that participants who have a larger understanding of WG and vegetables will be more ready to change behavior at baseline and therefore reduce their risk of chronic illness after intervention. We anticipate that lack of understanding about what constitutes a WG will contribute to lower SOC regarding serving WG. SOC for serving WG will be positively associated with: knowledge of whole grain foods, exposure to, and liking of WG.

Conclusions

Among low-income families at risk for diabetes, parental motivation to change will correlate with their children's diet behaviors at baseline and at completion of the program.

Acknowledgements

Funding in part from Alameda County ALL IN initiative and the Tom Long Foundation.

Keywords

Readiness for change, Stages of Change (SOC), low income, whole grains, diabetes

Ali San

University of California, Berkeley

Funded by: National Institutes of Health

Mentor: Carolyn Hoppe, MD

Lack of Association Between the Hb F–Modifying XmnI –158 Polymorphism and Stroke Risk in Sickle Cell Disease

My name is Ali and I am a first generation college student and rising junior at UC Berkeley majoring in molecular environmental biology. My childhood has primarily shaped my current aspirations. At the age of eight, I witnessed an obscene event that still haunts me. I encountered an old man in the hospital with a cane who looked sick and needed help, but the nurse did not allow him to see the doctor because his insurance had expired. I remember feeling the pain of that elder man and wondered how people could be that inhumane by letting those in need suffer when they could help. At that moment, I promised myself that I would become a doctor and travel to developing countries to combat urgent health disparities. From this point, I started to pursue my interest in medicine further. In Southern Turkey, thalassemia is the most inherited genetic life threatening disorder. I have family members that are affected by the blood disorder and thus started to research further. As I learned more, I became interested in the heterogeneity of sickle cell disease, which led me to research the genes that affect Hb F in order to create predictors of disease severity. CHORI gave me an outlet to assist and spearhead my own investigation into these topics.

Introduction

Sickle cell disease is a hereditary blood disorder characterized by painful vaso-occlusive episodes, acute chest syndrome, cerebrovascular disease, and progressive multi-organ dysfunction. With the exception of stroke, Hb F is an independent predictor of nearly every complication of SCD. Advances in molecular genetics have resulted in an increased focus on identifying genetic modifiers of the phenotypic expression of sickle cell disease. One means by which such genetic variants may affect disease expression is through their influence on Hb F expression. Restriction enzyme analyses have uncovered particular variants associated with Hb F expression, such as the XmnI polymorphism located in 5'HBG2 promoter and several others, both within and outside of the beta globin gene locus, including the BCL11A and HBS1L-MYB genes.

Objective

The association between the XmnI polymorphism (-158 C>T) in the promoter of the Gγ-globin and elevated Hb F levels has been well documented, and together with other Hb F modifying polymorphisms confers protection from most SCD complications, except stroke. The objective of this study is to confirm an association between the XmnI SNP and Hb F levels and evaluate this association with stroke risk.

Methods

Using an allele-specific PCR assay specific for the XmnI polymorphism, we genotyped 99 archived blood samples from a well-characterized SCD population. We reviewed clinical information related to cerebrovascular complications, imaging data, and baseline Hb F levels. Statistical analyses were used to determine genetic associations between XmnI polymorphism and baseline Hb F, and stroke.

Results

21% of the patients were observed to be heterozygous for the XmnI polymorphism, while none showed homozygosity. 23% of the study population showed stroke/abnormal MRA. The XmnI polymorphism was associated with an increased Hb F level by a mean difference of 3.41% (p=0.006) compared to patients without the SNP. No associations were found between Hb F levels or the polymorphism and stroke risk (p=0.29, p=0.94).

Conclusions/Discussion

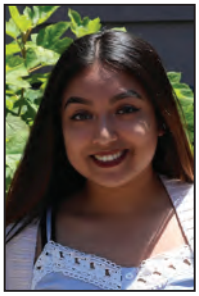
These findings suggest that, although increased Hb F is protective of SCD-related complications, such as VOC and ACS, it is not predictive of stroke. It is possible that biological pathways other than Hb F modulation are involved. The results of this study and Hb F variations caused by other SNPs in the genome can help create a genetic score for predictors of complications caused by SCD; this can help us understand the underlying heterogeneity of SCD. Early identification of high-risk patients would provide a rationale for early interventions.

Acknowledgments

I want to thank my mentor Dr. Hoppe, and Dr. Hagar and Dr. Marsh of the hematology/oncology clinic and wonderful staff of the Hemoglobinopathy Reference Lab (Mahin Azimi, Shabnam Tavassoli, Adriane Fung) who have also been alongside me during the program.

Keywords

Sickle Cell Anemia, Stroke, Hemoglobin F Levels, XMNI Polymorphism, Disease Severity



Abigail Serrano

Contra Costa College

Funded by: National Institutes of Health

Mentor: Mindy Benson, PNP, Karen Daley, MA, MFTI

Pediatric ACEs Screening and ResiLiency Study (PEARLS)

My name is Abigail Serrano and I am a transfer student from Contra Costa College getting ready to enter my junior year of college at UC Davis. I am majoring in Physical Anthropology with a minor is Global Disease Biology. I did not become interested in medicine until my junior year of high school when I traveled to Guatemala for community service. While I was there I worked at an orphanage and a rural elementary school. Though my tasks as a volunteer consisted of construction and maintenance, I felt more inclined to aid the children medically. While there, I observed a group of medical students who provided the children with basic medical checkups and awareness of prevention of illness by means of nutrition. Like those medical students, I want to be able to serve the public as a pediatrician with a complete and profound knowledge of the study of humans; how the live, how they interact, their biological structure and genomes.

Being part of the CHORI Summer Internship Program has given me the opportunity to gain the skills necessary to work in a field that could potentially be my career in the future. I believe research is always an important field especially when it relates to the well-being of a child. My understanding and knowledge for research has significantly expanded in the couple of weeks that I have participated in the program. I love that the CHORI Summer Internship Program challenges me to dig deeper into health-related issues concerning children that I could have never possibly thought about. I am inspired by the people who work hard to create a better and healthier future for children. That is why I chose to be a part of CHORI.

Introduction

ACEs (Adverse Childhood Experiences) are traumatic events experienced in childhood that have been associated with poor health outcomes that can extend into adulthood. The term ACEs was created in 1998 following the publication of the Adverse Childhood Experiences Study. This study found that ACEs common within the population were also associated with negative health outcomes in adulthood (Felitti et al. 1998). However, to date, the pediatric medical community does not have a validated screening tool to identify children at risk.

Hypothesis

Caregivers willing to disclose/discuss the social determinants of health with their provider, could assist in the prevention of health-related problems.

Methods

The ACEs screening consists of questions that cover a broad spectrum of ACEs that a child may have faced. Families with one or more ACEs are randomly assigned to one of two interventions: care-coordination or the Resiliency Clinic.

Care-Coordination is based on the Family Information & Navigation Desk (FIND) Program model to assist a family with their basic social needs. Based on ACEs screener results, families are connected to appropriate resources.

The Resiliency Clinic is a monthly, mindfulness-based, caregiver-child group intervention focused on understanding toxic stress, the development of self and co-regulation skills in caregivers and children identified as exposed to ACEs.

Bio-specimens are collected on all patients enrolled, to study the correlation between ACEs, stress physiology and health outcomes.

Results/Anticipated Outcomes

The willingness of caregivers to be open about ACE scores allows pediatricians to further assist in the physical and emotional well-being of the child. We hope the screener will facilitate a richer patient-medical provider relationship that mitigates the effects of toxic stress.

Conclusions

We hope this study helps to advance ACEs screening in the pediatric clinic setting, offer families and providers further direction in choosing ACEs-related interventions, provide insight into the underlying biochemical patterns associated with ACEs, and lay a strong foundation for future work.

Acknowledgments

Bay Area Research Consortium, Dayna Long, MD, Mindy Benson, NP, and Karen Daley, MFTi #87525

Jennifer Shearer

University of California, Berkeley

Funded by: Volunteer

Mentor: Nikita Ikon, PhD Candidate; Robert Ryan, PhD

The Effect of Calcium on Cardiolipin Membrane Structure and Cytochrome C Release

My name is Jennifer Shearer, and I am a Molecular and Cellular Biology major at UC Berkeley. I am thrilled to be part of the CHORI Summer Symposium and to share my Honors Thesis with the CHORI community. Having spent the last two years in the Ryan Lab, this research represents the culmination and application of all that I have learned as student at Cal and as a researcher at CHORI. I have worked on a variety of projects studying cardiolipin, reconstituted high–density lipoproteins, and a novel treatment for Barth Syndrome. CHORI has been the most welcoming environment to a young researcher, and my passion for scientific research has only grown: reading papers, brainstorming protocols, and discussing my hypotheses. As graduation approaches, and I look towards a future in medicine, I am confident that research will continue to be a vital piece of my education and my career.

Contributing Authors

Jennifer Shearer, Nikita Ikon and Robert Ryan, PhD

Introduction

Calcium flux from the endoplasmic reticulum (ER) to the mitochondria and the subsequent release of cytochrome c from the mitochondrial inner membrane (MIM) are important, but poorly understood steps in the instinsic apoptosis-signaling cascade. Under normal conditions, cytochrome c is bound to the membrane through its interaction with cardiolipin (CL), a conical phospholipid unique to the MIM. However, studies have shown that, in vitro, calcium (Ca^{2+}) causes CL to undergo a phase transition from an organized lipid bilayer to a polymorphic hexagonal phase.

Objective

Herein, we examined the effect of Ca^{2+} on an *in vitro* model of the MIM in an effort to further illuminate the interaction between cytochrome c and CL, as well as the role of Ca^{2+} in apoptosis.

Methods

A cardiolipin bilayer was formed via reconstituted high-density lipoprotein (rHDL) to model of the MIM. These rHDL were incubated with varying levels of calcium and other cations, with and without cytochrome c, and membrane disruption was evaluated via light scattering.

Results

Exposure to 10 mM Ca^{2+} resulted in membrane disruption, with maximum disruption achieved at concentrations of 40mM and above. This effect appeared to be CL and Ca^{2+}-specific, as monovalent cations did not have this disruptive effect, nor did calcium cause disruption of membranes consisting of <50% CL. Membrane disruption also resulted in cytochrome c release.

Conclusions

These results suggest the release of cytochrome c from the CL bilayer may be caused—in part—by the Ca^{2+}-dependent disruption of the CL-rich MIM

Acknowledgements

Thank you to Bruce Ames, PhD, for allowing me to complete my research in his lab this summer, and James Hurley, PhD, for sponsoring my thesis.

Keywords

cytochrome c, cardiolipin, calcium flux, high-density lipoprotein

Abu Sikder

University of California, Berkeley

Funded by: National Institutes of Health

Mentor: Felipe Jain, MD

Application-Based Psychotherapy for Dementia Caregivers

Hello there, my name is Sab Sikder. I come from a small rural village in Bangladesh where there is no running water, electricity, or access to medicine. So from a young age I became fascinated with what I didn't have in Bangladesh—medicine and technology.

I believe that the fruitful marriage between medicine and technology will help progress our state of medical care both concerning access and diagnosis. Therefore, my mission is to heal others through medicine using technology as a medium. My life has been surrounded by this mission and I fight for it everyday. From studying Medical Biology and Physiology at UC Berkeley, to running my own technology company, all while taking care of my father who is slowly and painfully recovering from a liver transplant.

I have struggled a lot financially, emotionally, and physically as a low-income first generation college student with a huge familial burden. However, great people and opportunities like this have helped me accomplish astonishing things—which is why CHORI is so important to me. Thanks to brilliant and altruistic people like Dr. Jain, Dr. Fung, and everyone else from CHORI we will be piloting a med-tech study that can possibly change the world.

Background

Family caregivers of dementia patients carry a significant physical, socioeconomic and psychological burden—which has been shown to increase their risk for physical and psychiatric illnesses. They suffer from a higher prevalence of depressive and anxiety disorders, compromised immune function, and possibly increased mortality. Mentalizing Imagery Therapy (MIT) is a group psychotherapeutic intervention that promotes emotion regulation skills and empathetic perspective taking, using mindfulness and guided imagery techniques. Pilot studies of MIT in caregivers have demonstrated promising improvements in symptoms of depression and anxiety. However, the current intervention methods utilize in person technologies that limit treatment delivery to local catchment areas and reduce accessibility to care.

Hypothesis

MIT delivered via a mobile application ("App") is feasible and will improve symptoms of depression, anxiety and quality of life in family dementia caregivers.

Methods

Procedures:
Ten primary family caregivers of dementia patients will be given access to a 4-week lesson plan. The subject will utilize the teaching material, and practice meditation and mindfulness for a minimum of 30 minutes a day.

Measures:
App usage data including amount of time spent practicing meditations, immediate improvements in mood after practicing meditation, and overall frequency of use, will be recorded. Pre to post measures will include the Quick Inventory of Depression Symptoms, Positive and Negative Affect Scale and Quality of Life and Enjoyment Scale – Short Form. A structured narrative interview will be conducted at post assessment.

Statistical Analysis:
For quantitative pre-post measures, a paired t-test will be used to determine whether the App had a statistically significant effect using the self-reported psychometric scales.

Anticipated Outcomes

We expect App delivery of MIT will be feasible based on frequency of usage and immediate mood changes. Based on previous research with MIT, we expect to see an improvement in depression, anxiety and quality of life. Narrative interviews will demonstrate increased perspective taking after MIT.

Conclusion

Application based psychotherapy may be a feasible delivery method for MIT for caregivers and improve psychological symptoms. Our results may provide justification for larger, controlled trials.

Keywords

Dementia, Psychotherapy, CMIT

Casey Smith

Wellesley College

Funded by: Doris Duke Charitable Foundation

Mentor: Greg Moe, PhD

Role of de-N-acetyl Polysialic Acid (dPSA)-modified Nucleolin in Cancer Cell Adhesion/Migration

I have been interested in neuroscience for the past 6 years, since I was given the freedom to choose my own research project in the 7th grade. Even with as limited as middle school research could be, I found interest in the evolution, organization, and communication within the brain. I began reading books about neuroscience, and participating in more STEM classes and programs. I built upon my curiosity in high school as I began to pursue a career in health science, when I participated as a summer research student in 2015.

After performing a retrospective study on Acute Chest Syndrome (ACS), a leading cause of death in sickle cell patients, with Dr. Hagar in the department of hematology, I gained a better understanding and appreciation of the patient side of research. Now, as a neuroscience major and rising sophomore at Wellesley College, I have an even greater interest in biomedical research. I returned to CHORI after participating as a high school student in a clinical research setting to increase my research knowledge with bench side experience. I am glad to have had the opportunity to work in Dr. Moe's lab this summer, learning techniques to study cancer cell adhesion and migration. Although I am still in the beginning of my journey, I plan to continue with biomedical research as a career.

Introduction

The homopolymer, Polysialic acid (PSA), consists of nine-carbon sugar, N-acetyl neuraminic acid (sialic acid) residues with α2-8 linkages. PSA is expressed mainly during fetal development and a few regenerative areas of adult tissues. Although few proteins are known to be modified with PSA, it is overexpressed in several human cancers, and is associated with metastasis. The Moe laboratory has described a derivative of PSA containing a mixture of de-N-acetyl and N-acetyl neuraminic acid residues (dPSA), that is expressed at much higher levels on the cell surface of many human cancer cell lines and tumors. Recently, the lab found that dPSA is linked to nucleolin. Nucleolin is normally found in the nucleus, but in cancer cells it is present on the cell surface. The purpose of this study is to determine whether dPSA-nucleolin is present in cellular structures associated with cancer cell adhesion and motility, whether there are differences in dPSA-nucleolin expression patterns in adherent versus non-adherent cells, and how anti-dPSA antibodies affect cell adhesion and migration in cell culture.

Hypothesis

dPSA-nucleolin will be localized in structures associated with cancer cell adhesion and migration, and anti-dPSA antibodies will affect how cancer cells migrate in models of human basement membrane.

Methods

Laser Scanning Confocal Microscopy
Corning® BioCoat™ Matrigel 3D Invasion Assay
Cytoselect™ Wound Healing Assay

Results

dPSA-nucleolin was concentrated in invadopodia and lamellipodia structures associated with cell adhesion/migration. The distribution of dPSA on non-adherent cells and cells migrating through Matrigel was polarized in the direction of cell movement. Anti-dPSA inhibited migration in the wound-healing assay.

Conclusion

Cancer cell adhesion and migration has a central role in metastasis, which is the primary reason cancer can be a life-threatening disease. This study establishes, for the first time, a role for cell surface dPSA-nucleolin in this process.

Acknowledgements

I would like to thank Dr. Greg Moe, Adarsha Shivakumar, and Nyle Almeida for assisting me in developing my laboratory skills.

Keywords

Polysialic acid, dPSA, nucleolin, adhesion, migration, metastasis

Jason Sun

College Preparatory School

Funded by: Volunteer

Mentor: Julie Saba, MD PhD; Joanna Lee PhD

Establishing the Effect of Vitamin B6 on Sphingosine Phosphate Lyase Protein Abundance, Stability and Activity

My name is Jason Sun, and I'm a rising senior at The College Preparatory School. I've always had an interest in science, and during my junior year of highschool, I took Advanced Placement Biology. I really grew to love biology while taking this course. I find learning how living things function really interesting. During the school year, I don't really have a lot of time since I am part of a crew team, so I wanted to pursue biology more this summer. I had never really had any lab experience before the CHORI program. Researching and trying to solve real problems intrigue me. My time at CHORI has allowed me to delve deeply into research, and I am currently working with Dr. Saba and Dr. Lee. While learning about biology in a classroom is very interesting, I am fascinated by the real world applications of biology. Although I am still unsure as to what career to pursue, I think it will be in a science field. My experience at CHORI has been incredible, and I will be forever thankful.

Introduction

Mutations in the SGPL1 gene, which encodes an enzyme called sphingosine phosphate lyase (SPL), were identified in patients with a hereditary form of nephrotic syndrome. The mutation segregated with the disease state in seven separate kindred. Nephrotic syndrome is a condition affecting the glomerulus, which is the main filtration unit of the kidney and is needed to filter the blood. Dysfuncion of the glomerulus in nephrotic syndrome causes patients to lose key blood proteins in their urine. The mutations were shown to be inactivating and led to poor SPL protein stability, reduced SPL abundance and loss of enzyme activity. SPL depends on the cofactor pyridoxal-5'-phosphate, also known as vitamin B6. Vitamin B6 is a cofactor for many different enzymes. In some conditions caused by mutations in enzymes that require vitamin B6, patients have shown improvement on high-dose vitamin B6 supplementation. This is thought to be due to the ability of vitamin B6 to help the mutant protein fold better by acting as a chaperone. Utilizing immortalized B lymphocytes from patients with SGPL1 mutations and from healthy individuals, we can compare the effect of vitamin B6 on the protein abundance, half-life and activity levels of mutant and wild type SPL.

Hypothesis

I hypothesize that vitamin B6, which serves as a cofactor for the enzyme sphingosine phosphate lyase (SPL), will act as a chaperone to increase the abundance and half-life of SPL proteins present in the cells of patients harboring inactivating mutations in SGPL1, the gene that encodes SPL.

Methods

Utilizing immortalized B lymphocytes from patients and controls grown in standard RPMI culture media, custom made vitamin B6 free RPMI, or vitamin B6 free RPMI plus the addition of vitamin B6 vitamers, we compared the effect of vitamin B6 on SPL protein abundance using western blotting. For determining half-life of SPL proteins, cycloheximide will be employed to halt new protein synthesis, and SPL abundance was measured over time by western blotting. If time allows, SPL activity will be measured using a novel LCMS method.

Results

Vitamin B6 increased the abundance of SPL protein in the B cells of the patient with SGPL1 mutation and did not have any effect on the control. Vitamin B6 add back studies and half life studies are on going.

Conclusions

Our results provide promising evidence that vitamin B6 supplementation may improve the abundance of mutant SPL. On going studies should help to confirm these findings.

Acknowledgements

I would like to thank Julie Saba and Joanna Lee for mentoring and guiding me, as well as the CHORI summer research program for providing me with such a great opportunity.

Keywords

Vitamin B6, SGPL1, nephrotic syndrome, SPL

Nuhamin Tassu

Holy Names High School

Funded by: Doris Duke Charitable Foundation

Mentor: Janelle Noble, PhD

Type 1 Diabetes Genetics: A Study in Understudied Countries

My name is Nuhamin Tassu, and I am a rising senior at Holy Names High School. Throughout my childhood, I always had an interest in medicine and science. When I went to hospitals and saw doctors dressed in their white coats, I was inspired. I would always go up to my family members and say "I want to become a doctor and save lives." This dream is still very much alive. So, when I heard about the CHORI program, I was excited because I knew this was a great opportunity for me. Before this summer, I was never a part of any research projects, so I thought maybe this experience would show me a new side of science that I could embark on in the future.

I know that after the CHORI program, I will finally know if I want to have a future in medicine and that, if I do, it will be for all the right reasons. This experience will also give me new skills that I could take with me wherever I go. So, thank you because these past three months have been an enjoyable experience.

Contributing Authors

Nina Criswell

Introduction

Type 1 diabetes (T1D) is an autoimmune disease that is characterized by T-cell mediated destruction of insulin-producing beta cells in the pancreas. Human Leukocyte Antigens (HLA) play an important role in initiating immune response. The HLA region (chromosome 6) contains genes, including *DRB1*, which encode HLA proteins. This summer, my project was part of a larger project, which studies the risk factors of T1D for many populations. The project is centered around collecting *DRB1* data from six different countries: Azerbaijan, Haiti, Sudan, Mali, Pakistan, and Bangladesh.

Hypothesis

DRB1 frequency distributions and T1D associations differ among countries.
Countries that are closer together geographically will have more similar allele frequency distribution and disease association patterns than those that are farther apart.

Methods

Help generate *DRB1* genotypes on 100 patients and 200 controls to supplement the data that have been collected from each country using high resolution genotyping and next generation sequencing.
Nina Criswell, a fellow summer student, analyzed the genotyping data using a software program called BIGDAWG to assess *DRB1* allele frequency distribution and *DRB1* disease association.
Data from online sources, for example, Britannica and Humanitarian Forum were used to look for historical, demographic, and environmental data for each country to identify potential reasons for similarities and differences in *DRB1* allele frequency distributions and *DRB1* association for T1D.

Results

The *DRB1* allele frequency distributions and T1D association differed among countries, even those that were geographically proximal like Pakistan and Bangladesh.

Anticipated Outcomes

We anticipate that historical migration patterns may help explain why countries have similar or different patterns of *DRB1* allele distribution and type 1 diabetes association.

Acknowledgements

I would like to thank Dr. Janelle Noble for her mentorship, time, and support throughout this summer. I would also like to thank Keely and Nina for helping me during this summer. Finally, CHORI and DDCF for giving me this fantastic opportunity.

Keywords

Human Leukocyte Antigen (HLA), type 1 diabetes, *DRB1* genes

Ricardo Trujillo

University of California, San Diego

Funded by: National Institutes of Health

Mentor: Marcela Weyhmiller, PhD

Standardizing Techniques to Measure Pancreas Geometry with MRI in Transfusion Dependent Thalassemia Patients

My name is Ricardo Trujillo and I am a senior at UCSD. I am majoring in cognitive science with a specialization in human cognition and am minoring in music. Previously, I was completely disinterested in pursuing a career in health and promised myself I would never come back to this hospital because of how long I stayed here as a child. However, the older I got, the more appreciative I became of those who helped me. Now, I've decided to pay it forward by dedicating my life to ensuring the health and happiness of others. I became a part of the CHORI program in hopes of attaining invaluable research experience while assisting with important advancements in medical science. I'd like to thank Dr. Marcela Weyhmiller for being such an incredible and supportive mentor, to CHORI for giving me this amazing opportunity, and to my family for supporting me on my academic journey. `

Contributing Authors

Marcela Weyhmiller, PhD, Ashutosh Lal, MD, Eric Padua, MD, Tariq Ahmad, MD

Introduction

Thalassemia is an inherited erythrocyte disorder that decreases the patient's ability to produce hemoglobin, requiring frequent blood transfusions and putting patients at risk for iron overload. Extended exposure to high iron levels lead to iron loading in the pancreas which may be linked to the onset of diabetes mellitus in thalassemia patients. Analysis of iron, fat content, size and shape of the pancreas with MRI can elucidate the relationship of iron and diabetes in thalassemia. However, the analysis can be laborious as iron and fat can cause analysis to become more complex. Techniques are needed to standardize the analysis of pancreas geometry for a wide range of conditions in an efficient manner.

Objectives

To develop standardized measurement techniques that allow us to efficiently assess the length and volume of the pancreas, as well as to accurately identify the head, body, and tail.

Methods

Coronal T2, Axial T2, and Dual Phase MRI sequences were used to measure pancreas geometry from retrospective clinical abdomen exams of 20 thalassemia patients. Pancreas length and volume as adjusted by fat content were measured. Reproducibility of measurement techniques was accomplished through two separate analyses by independent investigators.

Results

The axial sequence required fewer slices for analysis and provided a clearer image of the pancreas. Both the coronal and axial sequences were required to identify the boundaries of the pancreas. Low amounts of iron or high fat concentration made analysis difficult. Body surface area, iron content, fat concentration, splenectomies, and age contribute to pancreas geometry. Age and history of splenectomy were positively correlated with pancreas length. One patient with high pancreatic fat content was not analyzable. The pancreas of 5 splenectomized patients extended into the space previously occupied by the spleen. The dual sequence was collected with a slice gap too large to assess pancreas volume.

Acknowledgements

Kevin Lofton, National Institutes of Health, CHORI

Keywords

Thalassemia, Diabetes Mellitus, MRI

Adrian Valderrama

University of California, Berkeley

Funded by: National Institutes of Health

Mentor: Lorrene Richie, PhD RD

Pilot-test of a Grocery Receipt Protocol to Assess Food Expenditures in Family Child Care Homes

After completing my freshman year at UC Berkeley I knew that I had an interest in hard science, but I also wanted to explore my interest in public health. Fortunately, I had the privilege of joining the Nutrition Policy Institute (NPI) and helping to assess the state of childhood nutrition in family childcare homes in California. This population has been overlooked in many academic evaluations of childhood nutrition, and I find it fascinating that I was able to assist in exploring this new territory. It was empowering to know that I was contributing to research that could have significant effects on my community. Furthermore, I was able to participate in the process of data collection and analysis, and fully understand and appreciate how formal research can be used to answer a scientific question. My mentors during this process, Danielle Lee and Dr. Lorrene Ritchie, were extremely helpful and supportive; I learned a tremendous amount of information about nutrition, health policy, and my community. As a result of my experience this summer, I strive to conduct more research during my studies and eventually in my career as a physician.

Contributing Authors

Lorrene Ritchie, PhD, RD, Danielle Lee, Adrian Valderrama, Azar Dixit

Introduction

Childhood nutrition is a critical issue in the United states, where the percentage of children with diabetes has more than tripled since the 1970's, and about 1 in 5 school children is obese. Especially from ages 0-5, nutritional foods are vital for healthy development and establishing good habits early on. In California, many parents choose family child care homes as their primary form of childcare. This population has been overlooked in many academic evaluations of childhood nutrition, despite the fact that over a third of a million children receive up to three fourths of their daily nutrition there. With recent health guidelines established, it is important to understand what barriers are preventing providers from following these guidelines.

Objective

Create and pilot-test a grocery receipt collection tool that can be used to assess food expenditures before and after the implementation of nutrition standards for children aged 0-5 in family child care homes.

Methods

Ten family child care home providers will participate in a pilot-test, which includes following the proposed protocol and giving feedback about the clarity of the tool. Once data is collected, a data entry and analysis protocol will be created to allow future researchers to easily access and analyze the data.

Anticipated Outcomes

We expect that providers will give feedback that will allow researchers to further optimize the grocery receipt collection tool, and that this tool will allow food expenditures to be more easily and accurately measured. This tool will then be used in a state-wide study of food expenditures in family child care homes. This will allow researchers to identify obstacles preventing the full implementation, particularly food cost, of nutrition standards.

Acknowledgements

Thank you to Lorrene Ritchie, Danielle Lee, and Nutrition Policy Institute for welcoming me and guiding me through my first research endeavor. Also thanks to Azar Dixit as well as the National Institute of Health for helping make this project possible.

Keywords

family child care homes, nutrition, food expenditures, pilot-test

Juan Valentin

Vallejo High School

Funded by: California Institute for Regenerative Medicine

Mentor: Vlad Senatorov, PhD

The Role of Blood–Brain Barrier Disruption and Astrocytic Inflammatory Signaling in the Rodent Hippocampus After Epileptogenic Insult

I've been interested in the human body since I was a kid. I loved learning facts and trivia about the body from T.V or Books that I would read in my local library. I took Biotech and a Anatomy and Physiology course in the past years of high school. All three of those classes I passed with decent grades and learned a lot in those years. I'm going to take chemistry and AP Physics in my senior year.

My main goal is to get into the medical field and become a paramedic. I do well under pressure and I feel like I would do great in a setting of a paramedic. I also love helping people and would put anything on the line to save a life. My dream is to become a cardiologist one day. I was interested on the way the heart works. My mother has a heart condition and when I was younger I would always listen to it. I was curious on why it sounded like it was whispering to me and eventually learned that she had a heart murmur. My mom always has to take care of herself and I want to help her and others that have the same problems as her so they can have a healthy life. I joined this program because it will help me with the experience I need to become a doctor. It is showing me the proper way to be in a lab and the techniques they use on a daily bases. Currently I am learning a lot in the Kaufer lab and I'm loving every moment in it.

Introduction

A single injury to the brain can lead to chronic neurological brain disease that afflicts patients for their entire lives. The most common of these secondary diseases is post traumatic epilepsy (PTE). †Around 10-40% patients go on to develop epilepsy after brain injury, which can appear weeks or months after the original injury (Verellen and Cavazos, 2010).

Under healthy conditions, the brain is protected by the blood-brain barrier -- a lining of cells that surround blood vessels and maintains the brain environment by filtering the blood that enters. The Kaufer lab has found that after injury, the BBB becomes disrupted and blood signaling molecules enter the brain to induce an injury response leading to pathological changes. Astrocytes are among the first responders to epileptogenic injuries -- they take up serum albumin, the main serum protein that causes pathology after BBB damage -- and subsequently activate a transforming growth factor beta (TGFfl) signaling cascade to induce an inflammatory response (Cacheux et al., 2009; Ivens et al., 2007). Our previous research suggests that this sets in motion events that represent the earliest stages of post-traumatic pathology.

Methods

Within 3 groups of 3 mice, 1 group got saline injected into their hippocampus, and were perfused 7 days after surgery. Another group was injected with kainic acid, and perfused 7 days after surgery. The last group had kainic acid injected into their hippocampus, but were perfused after 1 day of surgery. Here, we evaluate the astrocytic inflammatory response and albumin infiltration in the rodent hippocampus in a model of acute epileptogenesis, by analyzing the spatial and temporal dynamics of astrocytic TGFfl signaling and albumin uptake after acute epileptogenic insult. †

Objective

To see how the Brain and the Blood-brain Barrier disruption reacts to an neurological injury, and how the Blood Brain Barriers functions stop working in between the time the kainic acid was injected into the brain.

Anticipated results

By understanding when and where post-injury inflammatory signaling occurs, we can begin to design target and novel therapeutic approaches to prevent or even reverse neuropathology after brain injury.

Sarah Van Son

Washington University

Funded by: National Institutes of Health

Mentor: Andréa Dosé, PhD, Marisa Medina, PhD

Confirming the Role of Novel Genes Implicated in Cholesterol Metabolism

As a rising junior at Washington University in St. Louis, it has been wonderful spending my summer back home in California. I am currently studying Biochemistry and Global Health through the school of Arts and Sciences and could not be more grateful to have my first research experience here at CHORI.

I grew up in a small town near the Los Padres National Forest, and my considerable time outdoors has instilled in me a fascination for natural science. Whether backpacking, spending time on the Pacific Ocean, or working on the John Muir Trail in the Sierras, I have always been drawn to how nature and its systems work together. Throughout high school, I shared my love for biology and chemistry with classical voice, and while music continues to be a large part of my life, my studies have increasingly attracted me to the medical field. Though I am still determining my place in this field, I am looking forward to a summer of exploration into this world that I hope to soon enter.

Contributing Authors

Ke Liu, PhD and Elizabeth Theusch, PhD

Introduction

High cholesterol is one of the largest risk factors associated with cardiovascular disease. Cholesterol is synthesized in the liver by a network of genes whose expression levels are regulated by transcription factors in response to changes in cellular cholesterol. Using gene expression data and various statistical analyses, the Medina lab has identified eleven genes, not previously implicated in cholesterol metabolism, that are sterol-regulated and have expression levels that are highly correlated with genes encoding the cholesterol biosynthesis pathway. Confirming the role of these genes may lead us to a better understanding of genetic variation on cholesterol regulation.

Hypothesis

Since many genes that play a role in cholesterol metabolism are negatively regulated by cholesterol levels, we hypothesize that some (or all) of 11 identified genes may play a role in cellular cholesterol metabolism.

Methods

One way to determine whether the elected genes hold a role in cholesterol metabolism is to silence their expression and monitor changes in cellular cholesterol levels. HepG2 cells were reverse transfected with either an siRNA fragment targeting one of each of the 11 genes or a non-targeting control (NTC) in replicate (n=6). Three of these samples were used to document the efficacy of knock-down; the others were used to quantify cellular cholesterol levels.

Expression levels of each of the target genes was quantified by qPCR with all measurements performed in triplicate. Values were normalized against CLPTM using the $\Delta\Delta$CT method. The gene was considered effectively silenced if expression levels decreased by at least 70%. The remaining samples were solubilized in an organic solvent, allowing for the isolation of cellular cholesterol. Total cholesterol, free cholesterol and cholesterol ester levels were quantified, and two-sided t-tests were used to identify statistically significant differences in cholesterol levels between NTC and siRNA-treated cells.

Anticipated Outcomes

Despite initial difficulties, we anticipate that our siRNA fragments will effectively knock down the majority of the genes in question. Moreover, we expect that one or more of these successful knock downs will show alterations in cellular cholesterol levels.

Acknowledgements

I would like to thank Andréa Dosé, Marisa Medina, and the Medina lab for their guidance and support.

Keywords

Cholesterol metabolism genes

Amy Wang

California State University, East Bay

Funded by: Volunteer

Mentor: Grace Wang, PhD

Studies of anti-EMT drugs in BCCS

I am a rising junior at California State University East Bay, majoring in Biology with an Option in Physiology. In high school, I was never attracted to the sciences, however, I took a chance and decided to major in biology when I went to college. Now, in college, I have learned to appreciate all the different aspects of the subject as well as how it interacts with the other sciences such as chemistry, physics, etc. I became really fascinated with my biology and chemistry lab classes because doing hands-on lab work helped to solidify my knowledge of a certain concept or method of that particular branch of science. I am taking this opportunity at the CHORI Summer Research Program to see if I would like to go the research route. I did benchwork during my time at CHORI. I have learned incredibly useful skills, working alongside amazing scientists and doctors, that I could not have gotten anywhere else. I would like to thank everyone in the laboratory for giving me such an incredible opportunity, especially Dr. Grace Wang, and teaching me so many fascinating methods and tasks that will surely prove useful in the future.

Contributing Authors

John Dolorito, Jessica Chuang, Grace Wang, PhD, Ervin Epstein, MD

Introduction

Basal cell carcinoma (BCC) is the most common form of cancer in humans of European ancestry. There are over 4 million cases of this cancer in the US alone every year. They rarely metastasize; however, they may invade locally and cause severe disfiguration. Environmental insults, such as ultraviolet or ionizing radiation can increase the risk of developing BCCs. Aberrant activation of hedgehog (HH) signaling pathway plays a pivotal role in BCC carcinogenesis. There are 2 HH inhibitors that have been approved by the FDA, vismodegib (Roche) and sonidegib (Novartis). Despite a promising clinical response (i.e. rapid tumor shrinkage), tumor regrowth occurred at their original clinical sites once treatment was stopped. Our previous studies have shown that epithelial to mesenchymal transition (EMT) is responsible for tumor recurrence.

Hypothesis

In the present study, we will further investigate our hypothesis by evaluating the effect of anti-EMT drugs on BCC cells in vitro.

Methods

We will culture BCC cells in vitro and use cell proliferation assay (WST-1 reagent) to assess the efficacy of anti-EMT drug candidates on these cells.

Results

In particular, we will evaluate the effects of statin, RSL3 (GPX4 inhibitor), and Wnt inhibitors (LGK-974, XAV-939) in combination with HH inhibitor (XL-139) on our cells and choose the most potent one for in vivo assessment in the future studies.

Acknowledgements

I would like to thank the Epstein Lab, particularly Dr. Grace Wang, PhD, John Dolorito, Jessica Chuang, and Dr. Ervin Epstein, MD, for all their incredible help, support, and encouragement while I was in their care this summer.

Keywords

skin cancer, basal cell carcinoma (BCC), epithelial to mesenchymal transition (EMT), cell proliferation assay

Anna White

Oakwood University

Funded by: National Institiutes of Health

Mentor: Roberto Mok, Dayna Long, MD

Effect of Caregiver Employment on Asthma Control in Pediatric Patients in the UCSF Benioff Primary Care Clinic

I aspire to become a medical doctor as well as a researcher and am currently in my senior year at Oakwood University, pursuing a biomedical sciences degree. Throughout my various research experiences, I did not have the opportunity to engage in clinical research. Thus, I decided to participate in the CHORI Summer Research Program, where I could gain invaluable experience and a greater understanding of performing research in a clinical setting. My involvement with CHORI has enabled me to see how practicing medical professionals can play an integral role in research development. I would like to thank the team members of CHORI, as well as, the wonderful people in my lab, who played an important role in my success.

Contributing Authors

Roberto Mok

Introduction

Affecting over 300 million people worldwide, asthma is a chronic disease commonly diagnosed in children. Although its cause is unknown, asthma can be exacerbated by a variety of environmental and social factors, termed social determinants of health. Social Determinants of Health (SDoH) are the circumstances in which people live, grow and earn their livelihood (eg: food, housing, education, employment, discrimination, quality health care).

Previous studies have found that SDoH have been linked to health outcomes in children and adults. Research has found that changes in parental employment have correlated to differences in health outcomes in children; thus, exploring the impact of caregiver employment on asthma control could provide more understanding of the factors that contribute to effective treatment and control of a chronic disease, such as asthma.

Objectives

1. To determine if there is a correlation between caregiver employment and asthma control of pediatric patients.
2. To explore the effect of existing Social Determinants of Health (SDoH), specifically, housing and access to food on asthma control in different caregiver employment situations of pediatric patients.

Methods

Data will be collected from current studies in the clinic about the children, ages 2-17, and their primary caregivers who answered 'yes' to a Health Assessment survey question, "Has your child ever had asthma?" To assess asthma control parameters in the pediatric patients, the physician's notes will be used. A telephone survey may be conducted to confirm information on the household and employment status of the primary caregivers of the pediatric patients. Data will be analyzed to determine if there is a relationship between different caregiver employment statuses, other existing social determinants of health, and asthma control in the pediatric patients.

Anticipated Outcomes

We anticipate that there will be a positive correlation between asthma control and caregiver employment. In addition, we anticipate that households with identified food insecurity or housing issues will have poor asthma control, regardless of parental employment.

Conclusions

Caregiver employment could potentially lead to higher income, causing better housing situations and access to food for the entire household. Because of its role in these factors, caregiver employment could indirectly affect asthma control.

Acknowledgements

I would like to thank my mentors, Dr. Dayna Long, Karen Daley, and Roberto Mok, and all the staff of the UCSF Benioff Primary Care Clinic.

Keywords

asthma, asthma control, social determinants of health, caregiver employment

Jia Yu

New York University

Funded by: National Instituites of Health

Mentor: Sunita Ho, MS PhD

Correlative Mapping of Lipids and Biominerals Within a Human Renal Papilla

In high school, I did my internship at AEMTEK Inc., a company that does food analysis. In my project, I used back titration to determine the concentration of salt in food. I learned that excessive salt consumption leads to high blood pressure, which damages blood vessels. It was this experience that inspired me to study medicine and research.

To delve deeper into medicine, I shadowed a hematologist–oncologist in college. Seeing difficult clinical cases everyday strengthened my resolve to enter the biomedical fields. I want to demystify the hidden secrets in medicine.

I'm very grateful for CHORI for giving me this research opportunity to work with Dr. Sunita Ho and her lab at UCSF. This research experience trained me to learn new material quickly and think critically and independently. It is truly exciting to be involved in cutting–edge research, and seeing the impact of those advances on real people in clinics.

Contributing Authors

Scott Wiener, MD, Neelanjan Bose, PhD, Ling Chen, PhD, Michelle Reyzer, PhD, Ryan Hsi, MD, Marshall Stoller, MD

Introduction

Idiopathic calcium oxalate nephrolithiasis (kidney stones) is increasing in prevalence in the United States. Precipitation of calcium oxalate has historically thought to begin at a calcium phosphate lesion of the distal renal papilla known as Randall's Plaque. Our group has utilized advanced imaging modalities to localize upstream microcalcifications to the proximal aspect of the papilla. The different morphology of these site-specific minerals in human renal papilla may be related to spatially distinct lipid species.

Objective

To identify lipid groups and individual lipid species in proximal and distal parts of the human renal papilla, and map the regional distribution of lipid species with correlation to minerals.

Methods

After IRB approval, human papillae were obtained following nephrectomy for unrelated reasons. The specimens of whole renal papilla were fixed overnight in neutral buffered formalin, washed twice in phosphate-buffered saline, then dehydrated with ethanol solutions, followed by micro-CT scanning. The thin sections from specimen were stained using hematoxylin and eosin, Masson's trichrome, picrosirius red, alcian blue with nuclear fast red, and alkaline phosphatase for light microscopy. Imaging of unstained sections utilized matrix assisted laser desorption ionization time-of-flight mass spectrometry.

Anticipated Outcomes

Detailed maps of lipid classes and individual lipid species with corresponding distributions in human renal papillae are still in progress. The lipid signal intensity in proximal tubules and distal interstitial matrix is expected to be higher than lipid signal intensity of normal renal papillae in the same locations. The relative abundance of phospholipids, including phosphatidylserine (PS), phosphatidylcholine (PC), and phosphatidylethanolamine (PE) are expected to be higher in mineralized renal papilla.

Conclusion

This project allows for more detailed and accurate identification of lipid species and their locations within renal papillae, providing a plausible explanation for whether calcium phosphate structure could originate through different mechanisms.

Acknowledgements

Dr. Sunita Ho, Dr. Neelanjan Bose, Dr. Ling Chen, and Dr. Michelle Reyzer.

Keywords

Mineralization, lipid identification, renal papilla

Robin Yu

College of Marin

Funded by: National Institutes of Health

Mentor: Jennifer Price, MD PhD; Marion Peters, MD

The Application of Transient Elastography and Controlled Attenuation Parameter to Assess Liver Fibrosis and Steatosis in Patients with Chronic Liver Disease

My name is Robin Yu and I will be starting my junior year at San Francisco State University's School of Nursing. From a young age I was interested in medicine which drove me to enlist in the Navy as a Hospital Corpsman. My military career took me to Afghanistan's Sangin District where I faced many difficulties ranging from losing many Marines to being unable to aid locals due my limitation in knowledge and equipment. Eventually, these tribulations galvanized my interest into a passion to further pursue a career in medicine as a nurse. In the years following my battle brother's injuries, many had to undergo repeated surgeries due to recurring infections, improper organ function, and a host of other issues. This sparked an interest in clinical research which holds the answers to a better quality of life for everyone who has sustained traumatic injuries. CHORI has been a great blessing for allowing me to explore the intricacies of what it takes to expand the frontiers of knowledge. Special thanks to my mentors Dr. Price and Dr. Peters, as well as to the staff at UCSF and CHORI for everything.

Introduction

Traditional methods of staging liver disease and progression have been limited to invasive methods such as liver biopsy. However, the recent approval by the FDA of the Fibroscan has brought clinicians a new noninvasive option to measure liver stiffness using transient elastography (TE) and liver steatosis using controlled attenuation parameter (CAP). We aimed to determine the most common liver conditions Fibroscan was used for in clinical practice and their respective TE and CAP scores.

Hypothesis

Fibroscan will be mostly utilized in patients with Hepatitis B (HBV), Hepatitis C (HCV), and Non-alcoholic fatty liver disease (NAFLD), withTE/CAP scores ranging in severity, and most patients who undergo Fibroscan will not require liver biopsy.

Methods

TE/CAP data and clinical records from all patients who underwent a Fibroscan at UCSF's Liver Clinic from 01 October 2014 to 16 June 2017 were retrieved from the Fibroscan machine and electronic medical records. Statistical analysis performed were primarily descriptive with TE-measured median liver stiffness scores in kPa, and CAP-measured steatosis in dB/m.

Preliminary Results

Among the 1269 subjects who underwent Fibroscan, the majority (76.3%) had one of the three most common liver disease diagnoses (HBV, HCV, NAFLD; Table 1). There was a wide range of TE and CAP scores. Advanced fibrosis was most common in the HCV group (29.8%) and severe steatosis was most common in the NAFLD group (54.9%). A low number of patients also underwent liver biopsy (144).

TABLE 1

	HBV (367)	HCV (406)	NAFLD (195)	OTHER[1] (301)
MEDIAN TE	4.6 kPa	6.7 kPa	5.2 kPa	6.2 kPa
MEDIAN TE RANGE	2.3–37.4kPa	2.3–75 kPa	2.4–45 kPa	1.7–75 kPa
ADVANCED FIBROSIS[2]	26 (7.1%)	121 (29.8%)	37 (19%)	N/A
MEDIAN CAP	234 dB/m	232 dB/m	311 dB/m	238 dB/m
MEDIAN CAP RANGE	100–395 dB/m	100–501 dB/m	149–400 dB/m	100–400 dB/m
SEVERE STEATOSIS[3]	44 (12%)	50 (12.3%)	107 (54.9%)	52 (17.3%)
LIVER BIOPSIES	25 (6.8%)	23 (5.7%)	34 (17.4%)	62 (20.6%)

1 Abnormal liver enzymes (n=74), autoimmune hepatitis (n=28), cirrhosis (n=26), non-alcoholic steato hepatitis (n=45), primary biliary cirrhosis (n=33), primary sclerosing cholangitis (n=20), other conditions (n=75).

2 TE score range for advanced fibrosis (F3 or greater) by disease category: HCV >=9.5, HBV >=9.0, NAFLD >=8.0

3 CAP score greater than 300 dB/m indicates severe steatosis in all disease categories.

Preliminary Conclusion

The preliminary results indicate that Fibroscan has been widely used in clinical practice since its introduction, aiding in diagnosing and measuring disease progression. As hypothesized, the most common conditions it was used for are HBV, HCV, and NAFLD. Only 11.3% of patients had a biopsy performed within two years of a Fibroscan. Further investigation to determine factors that may influence TE/CAP scores, the utility of Fibroscan in patients with HIV infection or other medical conditions, and its impact on clinical decision making is warranted.

Acknowledgements

Special thanks to my mentors Dr. Price and Dr. Peters for their patience and guidance. Additionally, I would like to thank the staff at CHORI and UCSF for their support in this very special summer.

Keywords

Transient elastography, controlled attenuation parameter, steatosis, fibrosis.

Suyi Zhu

University of California, Davis

Funded by: Volunteer

Mentor: Barbara Laraia, PhD, MPH, RD

Past Food Security and BMI in the Women of the National Growth and Health Study at a First Glance

I am a fourth-year undergraduate student majoring in Neurology, Physiology, and Behavior at UC Davis. I chose this major because it would prepare me with the scientific background necessary for higher education in medicine and other health fields. During my undergraduate education at UC Davis, I have been involved in research lab that studies the molecular mechanisms of lipid-induced vascular diseases; I am also involved another health related internship. Through the CHORI program, I hope to experience a different type of research with the Nutrition Policy Institute at the Public Health Department in UC Berkeley. I think this internship will widen my respect and understanding for different facets of research methods and designs. The study that I am involved in is very intriguing to me because it looks at the role of stress on the transmission of obesity from mother to her offsprings. Not only will this research study reinforce the role of stress, which is compatible with my major at UC Davis, it will also introduce me to new public health research methods. Therefore, I hope to become a more well-rounded researcher after this experience.

Contributing Authors

Robin Frieber

Introduction

Food insecurity, the limited or uncertain availability of nutritionally adequate and safe foods, may be associated with disordered eating and a poor diet, potentially increasing risk for obesity and health problems. The objective of this project is to understand a possible linkage between past food insecurity and Body Mass Index (BMI) in a cohort of 200 women from the National Growth and Health Study.

Methods

Table 1 will consist of a description of the sample. Anthropometric data consisting of the women's height and weight were entered to be used to calculate BMI. The data about past/childhood food insecurity will be extracted from the National Growth and Health Study (NGHS) baseline questionnaire. Affirmative responses to past food insecurity will be used to compare BMI values using STATA programming.

Anticipated Outcomes

There will be sufficient number of women who reported affirmative responses to past food security to make a comparison with BMI. Overall, women from this NGHS cohort who reported affirmative responses to past food insecurity are expected to have higher BMI values.

Conclusion(s) (Suggested)

Women from this NGHS cohort who reported affirmative responses to past food insecurity are expected to have higher BMI values. They are more likely to consume more calorie dense and high fat diet to deal with the stress experienced in childhood due to food insecurity.

Acknowledgements

NGHS team members for data collection and conducting the study.

Keywords

BMI, past food insecurity, obesity, National Growth and Health Study (NGHS)

National Institutes of Health (NIH) Scholars

This group of undergraduate students was funded by the National Institutes of Health (NIH), Short Term Research Education Program to Increase Diversity in Health-Related Research. The students were selected from a competitive pool of undergraduates from all over the United States. Each NIH funded student developed their own hypothesis driven project, carried out this project during a 9-week one-on-one mentored program, presented a brief "elevator talk" about their work to their peers, participated in weekly educational enrichment activities and will be presenting the findings of the results from their project in today's symposium.

Pictured (Back Row: from Left to Right):
Ricardo Trujillo, Michael Fink, Robin Yu, Alishah Momin, Tyler Lunow-Luke, Ali San
(Front Row, Left to Right)
Jenny Juarez, Judy Kang, Maria Rodriquez, Adrian Valderrama, Maopeli Ali, Meghan Foe, Lilian Hernandez, Aditi Desai, Abigail Serrano, Brittney Deadwiler, Maribel Campos, Azar Dixit
Not pictured: Sarah Van Son, Anna White, Abu Sikder, Jia Yu

California Institute for Regenerative Medicine (CIRM) Scholars

This group of students was funded by the California Institute for Regenerative Medicine (CIRM)- Leveraging Investment in High School Training Summer Program to Accelerate Regenerative Medicine Knowledge: Light –A-SPARK. Their summer research project's focused primarily on stem / progenitor cell or translational research. In addition, they engaged in patient focused activities such as writing letters to patients who had experienced a bone marrow transplant and meeting with a patient who had received a bone marrow transplant, blogged about their research activities, and attended numerous additional education activities regarding stem and bone marrow transplant. They also volunteered their services to the BMT program here at UCSF Benioff Children's Hospital Oakland during a day long informational program about Bone Marrow Transplant to Families of Patients with Sickle Cell Disease. These students had the opportunity to present their results twice, at the CIRM-SPARK annual conference, and again today during the CHORI symposium.

Pictured (from Left to Right)
Sharad Mahajan, Amira Harara, Barbara Fairweather, Julia Nguyen, Emily Beckman, and Juan Valentin

Doris Duke Charitable Foundation (DDCF) Scholars

These students were funded by a grant from the Doris Duke Charitable Foundation, Clinical Research Continuum: High School to College Program. For the first time this year, both high school and returning CHORI DDCF Scholars who are now undergraduate students were funded under this program. All students are interested in pursuing careers in bioscience and/or health care. Each DDCF funded student developed their own hypothesis driven project with the assistance of their mentor, carried out this project over our 9-week program, created a detailed individual development plan (IDP), participated in weekly educational enrichment activities and is presenting the results of the findings from their project today.

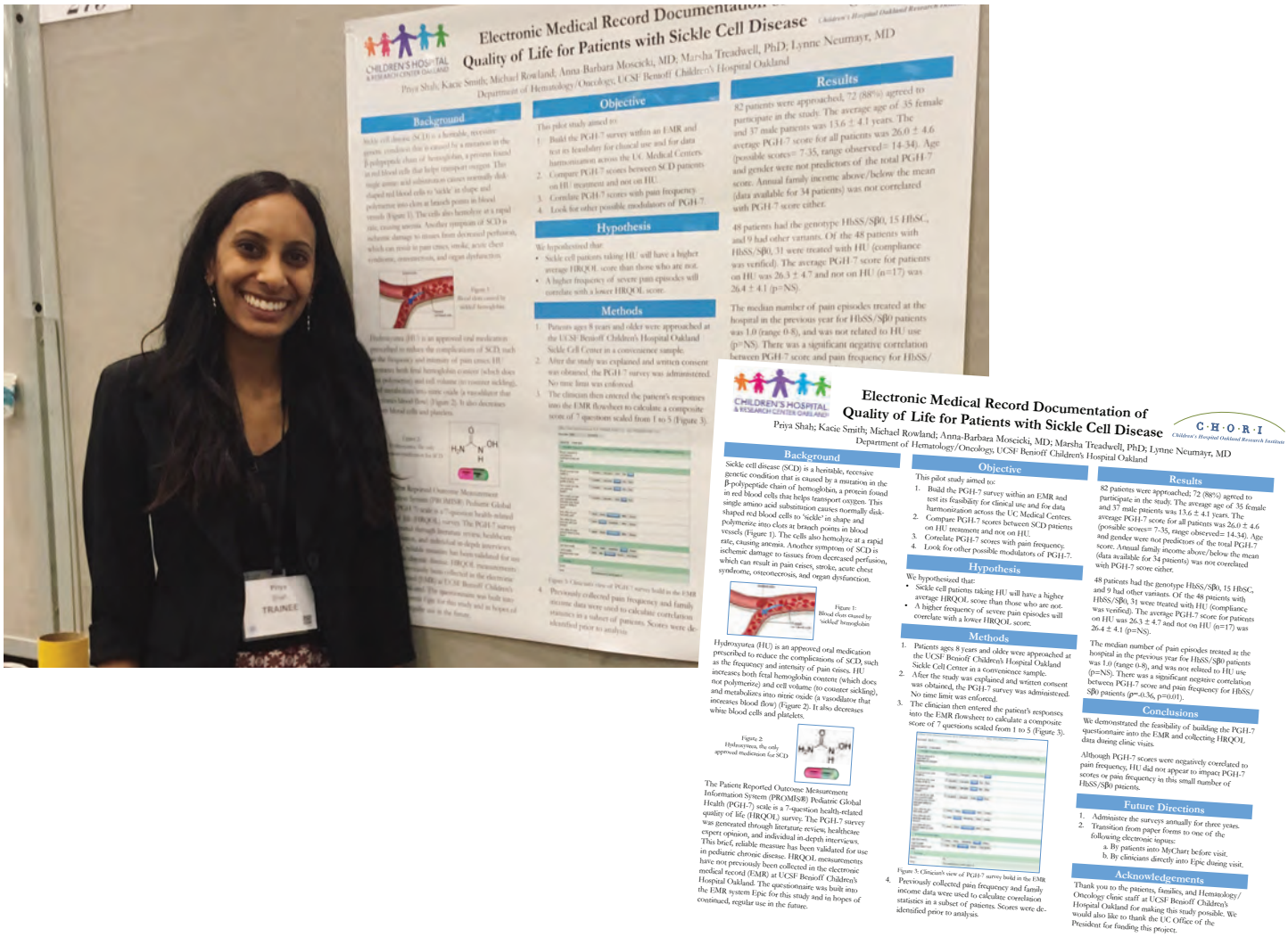
Pictured (from Left to Right):
Barry Brand, Fernando Delgado, Nuhamin Tassu, Jocelyn Diaz, Brianna Fredrick, Sebastian Hurtado, and Casey Smith
Not pictured: Christopher Alvarez

Elizabeth Nash Foundation Scholars

The objective of the Elizabeth Nash Foundation Cystic Fibrosis Summer Research Award is to provide short-term research training opportunities in the specific area of Cystic Fibrosis (CF) at the UCSF Benioff Children's Hospital Oakland. The program is open to high school seniors and undergraduate students. The goal is to identify students who have a strong interest in pursuing research in CF. The program provides the students with a research training experience to stimulate interest in biomedical and/or clinical research in a friendly and nurturing environment. This year the awardees were paired with Dr. Beate Illek, a scientist involved in CF research who provided direct mentorship for their projects. Similar to other CHORI programs, the NASH award is based on a structured curriculum, including participation in weekly seminars, culminating in a full day research symposium.

Pictured (from Left to Right):
Franny Kiles, Gopika Hari

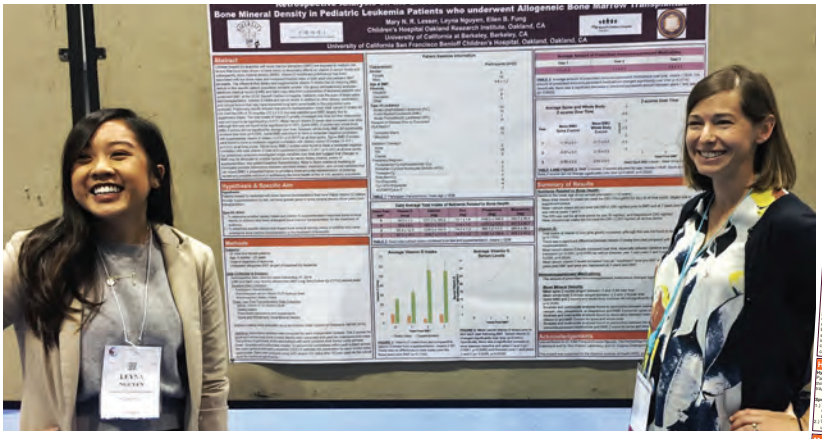
Students Presenting Elsewhere



Priya Shah, Summer Student 2016
Mentor: Lynne Neumayr, MD
Presented at the Pediatric Academic Societies Meeting, San Francisco, May 2017

The PAS Meeting was an awesome experience; there were SO many attendees! Unfortunately, I wasn't able to attend much of it outside of the poster exhibition (because my finals started the next day), but I did get to walk around and talk with other poster presenters. It was especially interesting to speak with people who were performing molecular research on the same medication used in my clinical research project. I loved meeting so many brilliant minds and learning about other research currently happening with sickle cell. This was part of what drove me to connect with Dr. Kuypers and spend some time in lab with him this summer. It was inspiring to see so many researchers and physicians committed to improving all aspects of children's health. Thanks again for all of your ongoing support; I have learned so much!

Students Presenting Elsewhere



Leyna Nguyen, Summer Student 2016
Mentor: Mary Lesser, PhD RD
Presented at the Experimental Biology Meetings, Chicago IL, April 2017

The research we presented on was titled, "Retrospective Analysis on the Effect of Vitamin D Intake and Supplementation on Bone Mineral Density in Pediatric Leukemia Patients who underwent Allogeneic Bone Marrow Transplantation." Children treated for leukemia with bone marrow transplant (BMT) are exposed to multiple risk factors that have been shown to have direct or secondary effects on vitamin D serum levels and subsequently, bone mineral density (BMD). Vitamin D insufficiency/deficiency has been associated with low bone mass and increased fracture rates in both adult and pediatric BMT recipients. The influence that dietary and supplemental vitamin D intake has on reducing BMD deficits in this specific patient population remains unclear. Our group retrospectively analyzed electronic medical record (EMR) and hard copy data from a population of leukemia survivors who underwent BMT at the UCSF Benioff Children's Hospital, Oakland, over the span of three years post transplantation. Vitamin D intake and serum levels in addition to other dietary, medication, and clinical factors that may have impacted long-term bone health in this population were analyzed.

We presented research as part of the American Society of Nutrition in the Diet and Cancer topic area at the Experimental Biology conference held in Chicago, Illinois this past Spring.

Experimental Biology is the annual meeting of six societies comprised of more than 14,000 scientists and 50 guest societies.

Primary focus areas include anatomy, biochemistry and molecular biology, investigative pathology, nutrition, pharmacology, and physiology. EB 2017 is open to everyone with interest in the latest research impacting life sciences. Attendees represent scientists from academic institutions, government agencies, non-profit organizations and industry.

This multidisciplinary, scientific meeting features plenary and award lectures, workshops, oral and posters presentations, on-site career services and exhibits spotlighting equipment, supplies and publications required for research labs and experimental study.

This Year's Mentors

Mentor	Department/Division	Location
Aimee Medeiros, PhD	Anthropology, History & Social Medicine	UCSF
Amber Jolly, PhD	Center for Immunology & Vaccine Development	CHORI
Ash Lal, MD	Hematology/Oncology	BCHO
Barbara Laraia, PhD MPH RD	School of Public Health	UCB
Beate Illek, PhD	Center for Critical Care Medicine	CHORI
Caroline Hastings, MD	Hematology/Oncology	BCHO
Carolyn Hoppe, MD	Hematology/Oncology	BCHO
Carter Lebares, MD	GI & Bariatric Surgery	UCSF
Christine McDonald, ScD	Center for Nutrition & Metabolism	CHORI
Chun Yang, PhD	Molecular & Cellular Engineering	UCB
Cindy Leung, ScD MPH	Center for Health & Community	UCSF
Dario Boffelli, PhD	Epigenetic inheritance	CHORI
David Killilea, PhD	Center for Nutrition & Metabolism	CHORI
Deborah Dean, MD MPH	Center for Immunology & Vaccine Development	CHORI
Ellen Fung, PhD RD	Center for Sickle Cell Disease/Thalassemia	CHORI/HEDCO
Elliott Vichinsky, MD	Hematology/Oncology	BCHO
Erv Epstein, MD	Center for Genetics	CHORI
Felipe Jain, MD	Psychiatry	UCSF
Grace Wang, PhD	Center for Genetics	CHORI
Greg Moe, PhD	Center for Immunology & Vaccine Development	CHORI
Janelle Noble, PhD	Center for Genetics	CHORI
Jennifer Michlitsch, MD	Hematology/Oncology	CHORI
Jennifer Price, MD	Hepatology	UCSF
Joanna Lee, PhD	Center for Cancer Research	CHORI
Julie Saba, MD PhD	Center for Cancer Research	CHORI
June Tester, MD MPH	Pediatrics, Childhood Obesity	BCHO
Karen Daley, MA	Primary Care / Asthma	CHORI
Kathy Schultz, MS	Center for Nutrition & Metabolism	CHORI
Katie Carlberg, MD	Emergency Medicine	BCHO
Kevin McCarten, MD	Emergency Medicine	BCHO
Kevin Tharp, PhD	Nutritional Science & Toxicology	UCB
Lisa Lavrisha, PhD	Adolescent medicine	BCHO
Lorrene Ritchie, PhD RD	Nutrition & Public Health	UCB, Nutrition Policy Institute
Lynne Neumayr, MD	Hematology/Oncology	BCHO
Marcela Weyhmiller, PhD	Iron Measurement Program	BCHO
Marion Peters, MD	Hepatology	UCSF
Marisa Medina, PhD	Cholesterol, Cardiovasular Disease	CHORI
Marsha Treadwell, PhD	Psychology	BCHO
Mary Jones, MD	Pediatrics, RETT Clinic	BCHO

This Year's Mentors

Mentor	Department/Division	Location
Mindy Benson, PNP	Primary Care / Asthma	BCHO
Nahal Lalefar, MD	Oncology/Bone Marrow Transplant	BCHO
Polina Ilieva	Anthropology, History & Social Medicine	UCSF
Rachel Kuperman, MD	Neurology	BCHO
Robert Yamashita, PhD	Hematology/Oncology	BCHO
Ron Krauss, MD	Atherosclerosis Research	CHORI
Ryo Higuchi-Sanabria, PhD	Molecular & Cell Biology: Dept of Aging Research	UCB
Sandy Calloway, PhD	Center for Genetics	CHORI
Sarah King, PhD	Center for Nutrition & Metabolism	CHORI
Sunita Ho	Dental School, Div of Biomaterials & Bioengineering	UCSF
Tanya Vayngortin, MD	Emergency Medicine	UCSF
Tariq Ahmad, MD	Endocrinology	BCHO
Vlad Senatorov, PhD	Integrative Biology & Neuroscience	UCB
Ward Hagar, MD	Hematology/Oncology	BCHO

Key to Locations

BCHO	UCSF Benioff Children's Hospital Oakland
CHORI	Children's Hospital Oakland Research Institute
HEDCO	Health Sciences Building
UCB	University of California, Berkeley
UCSF	University of California, San Francisco

Notes

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Children's Hospital Oakland Research Institute

36th Summer Research Symposium 2017

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