2013 CHORI SUMMER STUDENT RESEARCH SYMPOSIUM

CHILDREN'S HOSPITAL & RESEARCH CENTER OAKLAND

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Children's Hospital Oakland Research Institute

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2013 CHORI Summer Student Research Symposium

A Showcase for Young Minds in Research

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Children's Hospital Oakland Research Institute

August 10, 2013

We are pleased to invite you to the 2013 CHORI Summer Student Research Symposium! We are here to celebrate the spirit of scientific enquiry that has been initiated in young investigators and the future guardians of biomedical research. The CHORI Summer Research Program provides research education and training to high school, undergraduate and post-baccalaureate students with a broad range of backgrounds and experience. All these trainees have one common goal- they are considering careers in biomedical research and other health related fields. Today's symposium presentations constitute the conclusion of an eight-week long program that featured a rigorous research and education curriculum.

We invite you to learn about the various state-of-the-art research topics that the trainees were involved in, ranging from nutritional genomics, obesity and cardiovascular disease to diabetes, stem cells, and vaccine therapy, to name a few. Do feel free to mingle and chat with the scientists 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.

We take this opportunity to thank all CHORI, CHRCO and UC Berkeley mentors and supervisors who are the backbone of the program: we appreciate their time, effort and deep commitment to train the students. A special note of appreciation also goes out to Deborah Ellen and Phil Bollinger, all CHORI and CHRCO staff, the guest seminar speakers and other friends of the CHORI Summer Program for their effort and time, which made this program a huge success.

We acknowledge the support and funding provided by the National Institutes of Health (National Heart, Lung and Blood Institute) Short Term Research Education Program to Increase Diversity in Health Related Research, the Doris Duke Charitable Foundation Clinical Experience for High School Students, the California Institute for Regenerative Medicine Creativity Award, and the Elizabeth Nash Foundation.

The CHORI Summer Research Program has quadrupled in size since its inception about 30 years ago. Given the severe budget constraints that are slamming our research and education system, we are constantly maneuvering the program in an effort to uphold its excellence and value. Now is the time for you to consider supporting our program! Your philanthropic support will ensure continuation of this important scientific and educational experience for the trainees, as we remain committed to educating and fostering tomorrow's leaders.

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, M.D.
President, Chief Executive Officer and Principal Investigator
Children's Hospital & Research Center Oakland

Janet King, Ph.D.
Interim Senior Vice President, Research and Executive Director
Children's Hospital Oakland Research Institute

Vasanthy Narayanaswami, PhD
Associate Scientist,
Principal Investigator and Co-Director of Basic Research Program
Children's Hospital Oakland Research Institute

Barbara Staggers, MD, MPH, FAAP
Division Chief, Adolescent Medicine
Co-Director of Clinical Research Program
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Support for the 2013 CHORI Summer Student Program provided by:

The Short Term Research Education Program to Increase Diversity in Health Related Research
from the National Institutes of Health/National Heart, Lung and Blood Institute
#5 R25 HL096365
PI: Bertram Lubin, M.D. & Vasanthy Narayanaswami, Ph.D.

Doris Duke Charitable Foundation
Clinical Research Experiences for High School Students Program (CREHSS)
#2011114
PI: Vasanthy Narayanaswami, Ph.D. and Bertram Lubin, M.D.

California Institute for Regenerative Medicine (CIRM) Creativity Award
TC1-05946
PI: Vasanthy Narayanaswami, Ph.D.

NIH Grant 5R01AI046464-12
Novel vaccine strategies for prevention of N. meningitidis group B disease
PI: Dan Granoff, M.D.

CHORI Genetics Research Fund
PI: Edward Lammer, M.D.

American Heart Association
Award # 13UFEL17070149

DoEd, Title III part F, Hispanic Serving Institute Science Technology Engineering and Math (HSI STEM). The name of the project is Contra Costa College Link (CCC LINK)
PI: Setiati Sidharta, Ph.D. (#P031C110037-13)

Jennifer Leigh Wells Fellowship

Elizabeth Nash Foundation

Private Donor – Friends of Children's Hospital

Children's Hospital & Research Center Foundation

Children's Hospital Oakland Research Institute

Barbara Bass Bakar

2013 Program Directors

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Phillip Bollinger

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Marsha Treadwell, Ph.D.
Grace Wang, M.D.
David West, Ph.D.
Marcela Weyhmiller, Ph.D.

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2013 Weekly Discussions & Lectures

Monday, June 24, 2013 from 10:00AM to 4:00PM
Summer Student Research Program Orientation
Keynote Speaker: Charles J. Alexander, Ph.D.
Associate Vice Provost for Student Diversity, Director, Academic Advancement
Program University of California, Los Angeles (UCLA)
Title: *"How Leaky is the Health Sciences Pipeline"*

Wednesday, June 26, 2013 10:00AM
Common Equipment training:

- A demo of the new Common EQ online database
  Phillip Bollinger
- General Shared Room Philosophy
  Lorelle Parker
- Microscopy at CHORI - Horst Fischer
- Centrifuges - Jennifer Beckstead
- Tissue Culture Rooms
  David Killilea & Jennifer Beckstead
- Alpha Imager
  David Killilea & Phillip Bollinger

Thursday, June 27, 2013 12:00PM
Devan Block
CHORI/Ames Lab Former Summer Student
Title: "*CHORI Bar"*

Tuesday, July 9, 2013 4:00PM
Vasanthy Narayanaswami, Ph.D.
Basic Science Program, Co-Director
Associate Scientist, CHORI
Faculty, California State University, Long Beach
Title: *"Lipoproteins, Oxidative Stress and Cardiovascular Disease"*

Thursday, July 18, 2013 12:00PM
Patty W. Siri-Tarino, Ph.D.
Associate Staff Scientist and Program Director,
The Family Heart and Nutrition Center CHORI
Title*: "Shifting the Paradigm: How the Latest Research is Changing How We Think About Diet and Heart Disease"*

Thursday, July 25 12:00PM*
John Matsui, Ph.D.
Director, Biology Scholars Program,
Department of Integrative Biology
University of California, Berkeley
Title: *"Your Place in Science"*

Tuesday, July 30, 2013 4:00PM
Ellen B. Fung, Ph.D. R.D. CCD
Associate Research Scientist
Children's Hospital & Research Center Oakland
HEDCO Health Sciences Center
Title: *"Strategies for Optimizing Bone Health in Patients with Thalassemia"*

Thursday, August 1, 2013 12:00PM
Beate Illek, Ph.D.
Staff Scientist
CHORI
Title: "*Stem Cell Therapy for Cystic Fibrosis"*

Tuesday, August 6, 2013 4:00PM
Mark Shigenaga, Ph.D.
Assistant Scientist
CHORI
Title: "*Gut integrity: a determinant of health Metabolic consequences of diet and endocrine modulators of barrier function"*

Thursday, August 8, 2013 12:00PM
Phillip Bollinger, Senior Systems Analyst, CHORI
Title: Fear and Loathing of the Big Red X *"How to Correctly Assemble Your Microsoft PowerPoint Presentation Utilizing Sanctioned Procedures and Methodologies Within Accepted Microsoft Parameters"*

Tuesday, August 13, 2013 4:00PM
Janet King, Ph.D.
Senior Scientist and Interim Executive Director
CHORI
Title: *"Establishing a research program using the scientific method"*

Special CIRM Student Second Discipline:
"*Performance Arts"*

- Improvisational (Improv) sessions at CHORI: 6/27/13, 7/9/13
- 3-hour class offered by BATS Improv (http://improv.org/BATS-School-of-Improv/School-Home.aspx) on 7/30/13
- Improv performance, The Shelton Theater, San Francisco.
- Attended "Split Decision" a show by the BATS Improv
- Ushering at Cal Shakes Theater Productions: *"Lady Windermere"*

2013 CHORI Summer Student Research Program Curriculum

Orientation, June 24, 2013

There will be an all-day orientation for summer interns on Monday, June 24, 2013, from 10:00 am until 4:00 pm.
Continental Breakfast will be served at 9:30 a.m.
Lunch will be served.

Agenda to include:

- Introduction by Janet King, Ph.D.,Interim Executive Director, CHORI Senior Scientist
- Introduction and overview by Vasanthy Narayanaswami, Ph.D., Associate Scientist, CHORI, Faculty, California State University, Long Beach
- Keynote lecture:
  Charles J. Alexander, Ph.D.
  Associate Vice Provost for Student Diversity, Director, Academic Advancement
  "How Leaky is the Health Sciences Pipeline?"
- Explanation of curriculum: Vasanthy Narayanaswami, Ph.D
- Lunch
- IT Orientation: Phillip Bollinger
- Administrative Review: Deborah Ellen
- CHORI Tours

Safety Training, June 25, 2013
The mandatory Safety Training with CHORI Safety Officer, Miriam Fang will be held on Tuesday, June 25 from 9:30 am – 12:30 pm. The student will be required to complete this training BEFORE beginning their project.

Project: June 24, 2013 to August 23, 2013
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.

Written Research Proposal: July 12, 2013
Students must submit to the Program Coordinator a written Research Plan outlining their project. The Research Plan should be 250 words and include:
(a) Statement of hypothesis
(b) Specific aims
(c) Background
(d) Methods
(e) 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, and in the title of the project.

Weekly Lectures:
Current Topics in Health and Disease
Students are required to attend weekly lectures delivered by CHORI and CHRCO faculty members. The lectures will cover various scientific topics, including women's and minority's issues, career decisions, teen health issues and Responsible Conduct of Research.

Student Photo Day: July 16, 1:00 pm
All students must be present.

2013 CHORI Summer Student Symposium, August 23, 2013
A one-day symposium will be held on Friday, August 23, 2013 where all students are required to participate. The students will submit an abstract concisely summarizing their work, which will be considered for an oral or a poster session for the Symposium. Abstracts are due on August 5, 2013 by 4:00 pm. A committee comprised of the Director, Co-Directors and other leading members of the CHORI scientific community will review the abstracts for the Symposium. Students will work closely with their mentors in the preparation of abstracts and presentations. Family members, teachers, lab members and friends are welcome to attend.

The Symposium will be comprised of oral presentations (10 minutes each, with 5 minute discussion), and a poster session during which the presenters will be on-hand to explain their research project. A symposium book, which will include the Symposium program, personal statements, and the research proposals, will be presented to each student. A catered breakfast and lunch will be provided for all attendees on the Symposium day.

A certificate of participation in the CHORI Summer Student Research Program will be awarded to those who successfully complete the program.

Volunteer Recognition 2013

We would like to thank the many volunteers that took time out of their busy schedules to help this program succeed.

Volunteers:

CHORI:
Jennifer Beckstead
Tate Brazas
Karl Erhard
Horst Fischer
Tai Holland
David Killilea
Lorelle Parker
Elaine Pico
Kathy Schultz

Student Volunteers:
Alissa Chandler
Caroline Desler
Arjun Dhillon
Henry Duran
Vicki Lau
Rogelio Medina
Anu Menon
Rocio Ochoa
Jessica Ortiz
Charlotte Rosenfeld

A Special thanks to the following individuals for their help with the 2013 CHORI Summer Student Research Program:

Katherine (Tate) Brazas
Karen Catanese
Stephanie Garner
Debbie Dare

2013 CHORI Summer Student Research Program Group

Jasmine Aimua

Originally from Southern California, I'm an incoming senior at the University of California, Berkeley studying Biochemistry and Molecular Biology. Living in a world today in which medicine has helped cure sickness and keep humans alive longer have made me realize how important biomedical research is and I am thankful for the opportunity to participate in a lab that studies metabolic disease, which is a topic in which I am interested. Ever since I was young, I have taken a fascination with the human body and how it works, always flipping through the pages of my father's physiology book and learning about how the human body functions. Being a part of the CHORI program has been a major step in allowing me to be an integral part of this process and I am thankful to be given the opportunity to participate in biomedical research as an undergraduate at UC Berkeley.

Funded by: The Short Term Research Education Program to Increase Diversity in Health Related Research from the NIH/NHLBI

School: University of California, Berkeley

LAB PERSONNEL: Suheeta Roy

MENTOR: David West, Ph.D.

Title:
Effects of High Fat Diet on Mice Lacking Dusp1

Introduction:
Dual-specificity phosphatase 1 (Dusp1), also called MAPK phosphatase-1 (MKP-1) plays an important role in metabolic disease. MKP-1 is responsible for the dephosphorylation and inactivation of MAPKs in insulin-responsive tissue. MKP-1 knockout mice have been shown to be resistant to diet-induced obesity. We hypothesize that Dusp1 knockout mice will have phenotypic differences when compared to wild type mice when challenged with a high fat diet.

Objective:
We aim to evaluate the role of Dusp1 as a candidate gene for regulating percent body fat by using a knockout mouse phenotype.

Methods:
Mice are randomly assigned to either a high fat (45%) or a low fat (10%) diet for 11 weeks. They are weighed regularly during the feeding period and final weights will be recorded before sacrifice. Blood will be collected via terminal bleed using cardiac puncture, following an overnight fast. Liver, abdominal muscle and gonadal adipose tissue will be harvested and snap-frozen for further investigation. Plasma total cholesterol, triglycerides, glucose and free fatty acids will be measured by enzymatic assays. Liver triglycerides will be determined following saponified neutral extraction of lipids. Values will be expressed as mean ± SEM and comparisons between the groups of mice will be performed using Students t-test for unpaired samples. The level of significance will be determined at $P < 0.05$.

Expected Outcome:
We anticipate to be able to reproduce the phenotype seen by Wu et al (2006) in MKP-1 knockout mice. Differences in lipogenic and gluconeogenic gene expression in these mice are anticipated as well.

References:

1. Wu, JJ., Roth, RJ., Anderson, EJ., Hong, E-G., Lee, M-K., Choi, CS., Neufer, PD., Shulman, GI., Kim, JK., Bennett, AM. (2006) Cell Metabolism 4, 61-73.

2. Roth Flach, RJ., Bennett, AM. (2010) Expert Opin Ther Targets 14(12): 1323-1332.

Anna Akullian

My name is Anna Akullian and I am a recent graduate of UC Berkeley, where I studied psychology, focusing on cognitive development. I am fascinated by embryology and child development, and have been working on a project here at CHORI that focuses on identifying mutations in genes which may lead to congenital conotruncal heart defects. Participating in the CHORI summer program has instilled a new fire inside of me to learn more about genetics and biology. I am excited to take what I have learned here and continue to ask questions and learn more about health and child development. I am so thankful to have had the opportunity to work in Dr. Lammer's lab and be apart of a group that has both taught and inspired me so much.

Funded by: CHORI Genetics Research Fund
PI: Edward Lammer, M.D.

School: University of California Berkeley

Lab Personnel: Edward J. Lammer, Kazutoyo Osoegawa, Kathleen Schutlz, Nebil Mohammed, Christina Parodi, and Lydia Ruesch

Mentor: Edward Lammer. M.D.

Title:
Chromosomal Microdeletions Causing Heart Defects

Introduction:
The Lammer Lab has used array comparative genomic hybridization (array-CGH), a genome-wide screening technique, to detect submicroscopic chromosomal imbalances among children born with conotruncal heart defects, which comprise about 20% of congenital heart defects. Our summer investigations include DNA sequencing of genes that appear to be excellent candidate genes for conotruncal defects. We will use Next-Generation DNA sequencing methods to discover mutations among our large study population of infants with conotruncal heart defects.

Objective:
Our aim is to use Next-Generation DNA sequencing to identify mutations of the *TDGF1*, *SIX1* and *EYA1* genes among 389 California infants with conotruncal heart defects. The decision to focus on these genes was informed by previous research linking them to proper development of the embryonic heart conotruncus.

Methods:
We will design PCR primer sets to amplify each exon of *TDGF1*, *SIX1* and *EYA1*. Exon sequences will be defined based on the annotation provided by the UC-Santa Cruz Genome Browser. To enrich amplicons for sequencing on the GS FLX System, we will use the Access Array™ Integrated Fluidic Circuit (Fluidigm Corp.), which enables parallel amplification of sequencer-ready libraries from up to 48 samples at one time. We will use emulsion PCR for amplification and our amplicons will be sequenced with the GS Flex Titanium system. We will then identify polymorphisms and mutations within coding regions using SeqNext software.

Expected Outcome:
We anticipate that there will be novel mutations on *TDGF1*, *SIX1* and *EYA1* exons from our pool of infants with conotruncal heart defects.

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Haven Allard

When I was little, I would cover myself with band-aids. It wasn't until years later that I realized that I actually wanted to be a doctor. Having this opportunity to work in a clinical setting and meet patients at this stage in my education has cemented my desire to pursue a medical career. CHORI's combination of independence and mentoring has made me a more mature and confident scientist and student. As I asked my mentors question after question, I not only got intelligent responses, but my fascination with the inner workings of the human body grew. With three more years of undergraduate studies and medical school after that, I have a lot lessons ahead of me, but I will always remember the ones that I learned here at CHORI.
I'd like to thank Dr. Weyhmiller, Dr. Fung, Lisa and Leo for making this program a wonderful way to spend my summer.

Volunteer

School: Eckerd College

Lab Personnel: Marcela Weyhmiller, Ph.D.

Mentor: Ellen B. Fung, Ph.D. R.D.

Title:
Calamari, Jell-O and Ribs with a Side of Iron

Introduction:
Patients with hemoglobinopathies may become iron overloaded due to chronic transfusions or increased dietary iron absorption. The liver stores iron but when levels get too high, iron can enter bone marrow. It is unknown if high levels of iron in the marrow would interfere with the readings done by the Superconductive Quantum Interference Device (SQUID) due to the close proximity of the sensor to the marrow in the ribs. It is also unknown whether the density of the iron in the liver of highly iron-loaded patients would register in the Dual-Energy X-Ray Absorptiometry (DXA) as bone density.

Objective:
We aim to determine if the integrities of SQUID and DXA measurements are affected by high iron concentrations in specific tissues.

Methods:
Phantoms that model tissue and bone geometries will be constructed from ballistics gel, animal ribs and known concentrations of iron. Phantoms will be measured with SQUID and DXA to determine the effect of iron on measurement patterns. Using knowledge gained from the phantoms, patient data will be re-analyzed in search of similar patterns of iron in the ribs affecting the SQUID and iron in the liver affecting the DXA.

Expected Outcomes:
It is expected that patients with high liver-iron content will have a higher DXA Z-score for L1/L2 than L3/L4 because of the liver's position over L1/L2. It is also expected that ribs loaded with iron will increase the SQUID readings. The information collected from this study may lead to the development of techniques to account for iron in the ribs and liver when using the SQUID and DXA.

Ivan Arreola

My drive for science propels me to gain first-hand experiences in medicine. At a young age, I became fascinated by all that encompassed science. Attending an early college high school has allowed me to seek higher division science classes. However, taking so many science classes made it difficult to apply theoretical knowledge to the real world. As a result, I decided to apply to the CHORI Summer Research Program for the opportunity to expanded my knowledge and learn medicinal research. Throughout this summer, I have learned an immense amount of new and valuable information while solidifying my goal of pursuing a career in the medical field, with a long-term goal of practicing Emergency Medicine.

Funded by: The Doris Duke Charitable Foundation Clinical Research Experiences for High School Students Program (CREHSS)

School: Alameda Science and Technology Institute

Lab Personnel: Christine Hoehner-Cooper, Elliot Vichinsky, and Lynne Neumayr

Mentor: Ward Hagar, M.D.

Title:
Defining Mild Sickle Cell Disease

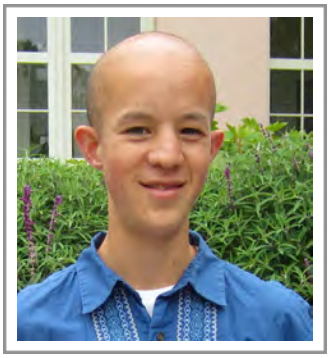
Introduction:
Sickle Cell Disease (SCD) typically causes debilitating pains, severe organ damage, and early death. However, there are some patients that do not experience many of these difficulties and appear to have a less severe form of SCD. Past studies suggest correlations between deviations of genotypes, presence α thalassemia, presentation of fetal hemoglobin and other factors that influence the severity of the disease [1, 2]. However, these do not explain the majority of mild cases [2].

Objective: Through this study we are aiming to clinically define Mild Sickle Cell Disease (MSD) by determining the proportion of sickle cell patients with MSD and identifying clinical markers and characteristics.

Methods:
This retrospective cohort study will use a novel scoring system to divide sickle cell patients by the severity of their disease. The scoring system uses already recorded clinical data to rate the severity of the disease on a Likert-like scale. Studied factors include hemoglobin electrophoresis, blood count with differential and reticulocyte count (CBC w/ diff), metabolic panel values, direct and indirect bilirubin, α thalassemia test, and lactate dehydrogenase (LDH) and the quality of life data scored by the Short Form- 36 (SF36).

Expected outcome:
To create a valid rating scale to classify patients with mild, moderate, and severe SCD.

Benjamin Barcklay



I am currently a senior at Berkeley High School and wanted to investigate more about what scientific career I might want to pursue in the future. I have learned so much at CHORI in the short time that I have been here. Interacting with the scientists, researchers, and fellow peers at CHORI has helped me broaden my views to include many more possibilities of science, and I hope to continue in the scientific field in the future.
I owe my life to Children's Hospital Oakland, and although not everyone here helped me directly, I would like to thank everyone at the hospital and research center for being a part of it all. Twice my life was saved here, and I am very grateful that I am able to spend time here and help find ways to make children's lives better and healthier.Funded by the Elizabeth Nash Foundation

Funded by: The Doris Duke Charitable Foundation Clinical Research Experiences for High School Students Program (CREHSS)

School: Berkeley High School

Mentor: Julie Lane and Janelle Noble, Ph.D.

Title:
Biomarkers and Genetic of Brain Injury Risk in DKA Pilot Study:
HLA sequencing of DQA1, DQB1, and DRB1

Introduction:
We are interested in why a percentage of Diabetic Ketoacidosis (DKA) patients suffer from cognitive impairment, and/or fatal cerebral edema. DKA is most often seen in children as the first evidence of Type1 Diabetes (T1D), but can also occur in established patients due to infection, illness, injury, surgery, or poor insulin control. DKA is the leading cause of morbidity and mortality in children with T1D, primarily due to cerebral edema which occurs in 0.3 to 1 percent of patients with DKA and has a high rate of morbidity. In addition, approximately 30% of patients will have some apparent cognitive impairment.

Objective:
Our goal, as part of the BIGBIRD Pilot Study, is to perform DNA sequence analysis of HLA Class II genes DRB1, DQA1, and DQB1. These genes are known to be associated with high risk for T1D.

Methods:
Thirty pediatric DKA patients have been enrolled from three sites in the BIGBIRD Pilot Study. We will extract DNA from each of the 30 samples. Next, we will amplify the selected HLA loci using PCR. We will sequence the DQA1, DQB1, and DRB1 genes using the Roche 454 DNA sequencing system.

Expected Outcome:
We expect that our Pilot Study sample genotypes will be consistent with alleles known to be associated with high risk for T1D. The HLA genotypes that we generate will be incorporated into the analyses of additional genetic markers that may be involved in risk for complications of DKA, including cognitive impairment and fatal cerebral edema.

Charmaine Chan

My name is Charmaine Chan and I will be a senior at Albany High School. This is my first research experience and I'm very grateful for this rare opportunity. This summer I hope to gain some direction in choosing my route for the future. In high school when I took AP Biology I realized that science was fun and interesting to me. We had a cat dissection and as soon as I laid hands on the cat I felt excited and couldn't stop probing. Now at CHORI, I am again in contact with science, and I realize how little I really know. However, this did not discourage me but, rather, has inspired me to seek more scientific knowledge. Thanks to my mentor, Dr. Robert Ryan, and everyone else in the Ryan lab, I've gained many skills. They've all been so friendly and patient with me, and I'm truly thankful for that.

Funded by: The California Institute for Regenerative Medicine (CIRM) Creativity Award

School: Albany High School

Lab Personnel: Betty Su, and Andrejz Witkowski

Mentor: Robert Ryan, Ph.D.

Title:
Effect of the "Wnt" Signaling Pathway on Apoptosis of Myeloid Progenitor Cells

Introduction:
Neutropenia is characterized by a deficiency of a specific type of white blood cell known as neutrophils. Individuals suffering from neutropenia lose their ability to fight infections. Neutrophils in blood arise from myeloid progenitor cells in bone marrow. I propose to use cultured HL60 myeloid progenitor cells as a model system to investigate Wnt mediated effects on progenitor cell fate. Wnt3a is a morphogen that plays a key role in regulating development, differentiation, and apoptosis. Wnt3a binds to a cell surface receptor termed Frizzled, initating a series of events that lead to stabilization beta-catenin, a regulator of gene transcription.

Objective:
My objective is to study the effect of Wnt signaling on neutrophil cell fate.

Methods:
Drosophila S2 cells will be used to generate recombinant murine Wnt3a, which will be isolated according to an established protocol. HL60 cells will be cultured under standard conditions. For experiments, an aliquot of these cells will be transferred to culture dishes and incubated in the presence or absence of Wnt3a. Following incubation, the cells will be washed and further incubated with a fluorescent tagged annexin V protein. The cell surface exposure of phosphatidylserine, characteristic of apoptotic cells, will be detected by flow cytometry.

Expected outcome:
We anticipate that incubation of HL60 cells with recombinant Wnt will alter their cell fate.

Alissa Chandler

As a student majoring in Human Biology at UC Santa Cruz, I have had a fair amount of exposure to science and lab classes. However, until the CHORI Summer Student Program, I had no idea how the process of designing and carrying out an experiment actually worked. This program has given me the opportunity to develop my critical thinking skills in a new environment, while getting unique hands on experience. As I am entering my Senior Year at UCSC, I have plans to start the application process for medical school. Before this program, I wanted to get a taste of research to appreciate the constant advancements in medicine. Now I see that research is something that can go hand in hand with practicing medicine, and I will consider this in the future. Between graduating college and applying to medical school there will be a lot of challenges and change in the next few years, but I will always remember the things I learned here and try to apply them to my life.

Volunteer

School: University of California, Santa Cruz

Lab Personnel: Alissa Chandler, Julia Moradian, and Matt Ono

Mentor: Frans Kuypers.Ph.D.

Title:
Validating Novel Flow Cytometry Imaging of Sickle Cells

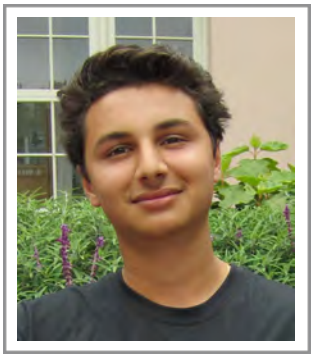
Introduction:
Sickle Cell Disease (SCD) affects individuals with a single point mutation in one subunit of their hemoglobin molecules. Normal hemoglobin consists of two alpha and two beta hemoglobin (Hb) chains and bind and deliver oxygen throughout the body. The mutated ß-globin in SCD, will lead to polymerization of Hb when it is exposed to low oxygen pressure. This polymerization causes the cells to change shape and increase in rigidity, leading to the blockage of blood vessels, vasculopathy, ischemia reperfusion injury, and acute events such as stroke.

Objective:
Our objective is to validate a new method to analyze large numbers of red blood cells (RBC's). We will deprive normal cells and sickle cells of oxygen. Using standard microscopy and ImageJ, a pixel-analysis program, we will analyze any changes in morphology. With ImageJ, the percent of sickled cells per sample will be defined, calculated, and data will be compared to analysis of the same samples with a novel imaging Flow Cytometry system. Following the time course of sickling will allow us to compare the kinetics of this process and evaluate antisickling treatments.

Methods:
Normal or sickle samples are deprived of oxygen for a varying amount of time in a tonometer at 37°C. Aliquots will be removed at specific times and fixed with deoxygenated paraformaldehyde and glutaraldehyde. Slides are prepared and 20 digital images are taken with 30-50 cells per image. Images are analyzed using ImageJ to calculate the circularity of each cell. This is used to calculate the percent of sickled cells. The timed data points will produce a graph that maps the kinetics of sickling. Data from image flow cytometry will be analyzed with a different program that calculates characteristics of thousands of cells at once.

Expected Outcomes:
With the data from ImageJ, we will be able to create a graph that will show the percent of sickled cells as a function of time. We expect this to be a sigmoidal curve representing the kinetics of sickling. If the data from ImageJ is comparable to data from image flow cytometry, flow cytometry can be validated as a way to analyze deoxygenation-induced morphology changes in RBC's. Once validated, the effects of anti-sickling compounds can be measured with this new method.

Zoey Chopra



Hey, I'm Zoey Chopra, a senior at The College Preparatory School. I applied to CHORI in doubt of my chances. Having received my acceptance letter, I was so enthused that I missed the deadline to affirm my participation. Fortunately, I still experienced, quite frankly, the opportunity of a lifetime. I have always been unsure about whether I am more interested in the sciences or the humanities, but have realized that the two fields are interlinked, and hope to pursue both tracks in life. I have also since been inspired to help promote our community's medical state of affairs.I would like to thank Dr. Borja, Ms. Lemke, Dr. Oda, Mr. Hammerson, and Ms. He for providing me with this opportunity. I would also like to acknowledge Ms. Ellen for replying to my incessant e-mails, and Ms. Shea, for her enlightening and entertaining improvisational classes. *Id Erat Maximum*!

Funded by: Private Donor – Friends of Children's Hospital

School: The College Preparatory School

Lab Personnel: Kalistyn H. Lemke

Mentor: Mark S. Borja, and Michael N. Oda, Ph.D.

Title:
Mutant Medley: The Generation of Protein Mutants for the Structural Analysis of Apolipoprotein A-I

Introduction:
We aim to understand better the structure of lipid-free apoA-I, the major protein component of HDL, known to protect from cardiovascular disease. Understanding apoA-I will provide us with a greater knowledge of its cardioprotective properties. The Oda Lab has determined the secondary structure of apoA-I using EPR, and using this data, has proposed a model of its tertiary structure. While evidence supports the Oda Lab's model, a detailed analysis is required to verify apoA-I's proposed tertiary structure. FRET allows us to find relative distances amongst regions of apoA-I, permitting us to test the proposed model.

Objective:
We aim to test the existing model of the tertiary structure for lipid-free apoA-I using FRET. Our project is to generate the apoA-I mutants necessary for FRET experiments.
These proteins will be labeled with fluorophores for FRET assays, through which we will investigate apoA-I's tertiary structure. In doing so, we hope to better understand the structure of lipid-free apoA-I.

Methods:
Our FRET protocol requires four mutant apoA-I proteins: Trp null, a donor (single tryptophan), an acceptor (AEDANS fluorophore), and a donor-acceptor pair (single tryptophan and AEDANS). Mutants will be generated by vector-based, primer-directed mutagenesis using PCR. We will transform these vectors into E. coli to express recombinant apoA-I. Proteins will be purified by affinity chromatography and assessed using PAGE.

Expected outcome:
We will generate a library of vectors and proteins that can be applied to our FRET assays. This will help towards acquiring a broader understanding of the tertiary structure of lipid-free apoA-I.

Caroline Desler

My name is Caroline Desler and I am entering my senior year at Bishop O'Dowd High School in Oakland. I have always been interested in pursuing a career involving children. In addition, this past year, I took an AP Biology course that renewed and furthered my interest in the human body and its many detailed processes. The opportunity to take part in CHORI's summer program couples my love for children with my interest in medicine, as I explore science and research at one of the nation's most acclaimed children's research facilities. I am grateful for the wonderful people I have met during this experience, particularly Dr. Saba, whose leadership inspires me, and my patient and supportive mentor, Dr. Ana Aguilar. I couldn't have asked for more nurturing, kind, generous, and knowledgeable instructors. I look forward to using this internship as a springboard for my future educational and career aspirations in research and medicine.

Funded by: The California Institute for Regenerative Medicine (CIRM) Creativity Award

School: Bishop O'Dowd High School

Mentor: Ana Aguilar, M.D. and Julie Saba, M.D.

Title:
Characterizing Sphingolipid Signaling In Glioblastoma Multiforme Stem Cells

Introduction:
The cancer stem cell (CSC) hypothesis suggests that a small, relatively chemotherapy- and radiation-resistant population of cancer cells that possesses self-renewal capability is responsible for the bulk of tumor growth and treatment failures. CSCs may, therefore, represent a cancer Achilles Heel, provided the requirements for their survival can be identified and targeted to kill CSCs. There is convincing evidence for CSCs in glioblastoma multiforme (GBM), a lethal brain tumor that affects both children and adults. Sphingolipids are endogenous signaling molecules that regulate tumor cell growth and carcinogenesis. We hypothesize that sphingolipid signaling plays a critical role in GBM-CSC biology.

Specific Aims:
1. Isolate GBM-CSCs from GBM tumors and cell lines.
2. Compare expression of sphingolipid-related genes/proteins in GBM-CSCs vs. non-CSCs.
3. Modulate expression of differentially-expressed sphingolipid-related genes/proteins and establish effects on GBM-CSC biology.

Approach:
Primary and transformed GBM cell lines or fresh tumor tissue are separated into GBM-CSC and non-CSC populations by labeling cells with fluorescently-tagged antibodies to CD133 followed by separation using a FACSAria cell sorter. Alternatively, cells are grown in two-dimensional cultures vs. conditions facilitating the formation of GBM-CSC neurospheres. Immunoblotting with Sox2, Nestin and Musashi will confirm CSC and non-CSC populations. Expression of sphingolipid-related genes/proteins are compared by immunoblotting and qRT-PCR. If time allows, differentially-expressed targets will be silenced and the effect on the number and size of clonally-derived neurospheres tested.

Anticipated Outcome:
We expect that growth-promoting sphingolipid signaling is enhanced in GBM-CSCs, and may represent a novel target for eliminating GBM-CSCs.

Arjun Dhillon

Arjun Alex Dhillon is an undergraduate fresh out of his first year at UC-Berkeley. Passionate about the healthcare system and social change he believes that projects should leave a sustainable positive impact. With a major in molecular cell biology in one hand and a minor in history in the other-he enjoys tackling problems from different perspectives and thinking outside the box. In addition to his participation in the CHORI program this summer, he is also involved at the UCSF Kim Lab where he studies malaria immunology. Outside of school he is an avid reader, closely follows world politics, is a self-professed Harry Potter lover, and claims to be an astounding cook of all things Indian. His current goals include becoming a pediatrician, being a leader in national healthcare policy, and ultimately working as a professor and doctor. He's incredibly grateful to his peers and mentors for all the big and small things he learns from them every day and looks forward to enjoying long lasting friendships.

School: University of California Berkeley

Mentor: Mindy Benson, Ph.D.

Project One:

Title:
An Improved Data Collection System for the Phat Beets Subsidized Produce Program
(CHORI Farmer's Market Voucher Tracking)

Introduction:
The current Phat Beets program aims to bring locally grown produce to our Children's Hospital patient population by promoting access using a voucher system. These vouchers, worth two dollars each, are distributed through four different affiliated clinics. The vouchers are then used at three different local farmer's markets. Unfortunately the tracking of these vouchers has been difficult. The status quo system ineffectively measures the efficacy of the Phat Beets voucher system and collects no data about our customers.

Objective:
My aim is to create a bar-code based system which, with a simple scan, can allow us to collect real time data about the number of vouchers used as well as when they were used. This data collection can easily be expanded to include basic questions such as the gender, age, or race or food item bought.

Method: I plan to use an Esponce based QR generator program which creates the "bar-code" to be read by any iOS or Android device with downloaded QR reader. I plan to link the QR code to a Google software based survey which can include any quick questions about the customer that the Phat Beets program sees fit to ask. I'll be managing both programs in order to compile the data in a meaningful format.

Expected Outcome: I expect that many users of the Phat Beet vouchers are buying at a farmer's market for the first time. If true, this will prove that the Phat Beet's vouchers are tapping into the population that needs them the most- those who are unaware of the healthy options available to them in their areas.

Project Two:

Title:
Using a Coupon System to Promote Local Produce Markets

Introduction:
The vast majority of the patients I work with in Primary Care come from disadvantaged ethnic minorities and low income neighborhoods. This includes the immediate surrounding area for the Children's Hospital Oakland Research Institute. Obesity is prevalent in these areas often due to dietary choices which are then linked to a number of other chronic illnesses. This chain effect of unhealthiness causes our health care system millions of dollars a year. The unfortunate dietary choices are often caused by a lack of knowledge and a lack of access.

Objective:
I aim to increase access to local produce markets by partnering with them to create fresh vegetable/fruit specific coupons. I then hope to distribute these coupons through two different avenues of the healthcare system: providers and the front desk.

Methods:
I have partnered with one local organic produce store in the area. We will begin by printing the 10% coupons the store owner and I decided on. Then I'll keep careful track of how many are distributed from each avenue mentioned, red coupons being provider originated and blue coupons being desk originated. Finally, I'll visit the store 3-4 weekdays every week for remainder of this 2013 summer in order to track just how many coupons are used.

Expected Outcome:
I expect coupons distributed through providers to be used more at a higher rate because of the personal environment of encouragement an appointment can create. Most importantly, the overarching goal is to give our patients access to healthy food resources while supporting their communities.

Parvati Dhurvas

From the time I was young, my parents instilled in me a sense of passion and determination to achieve my goals. At an early age, I experienced great familial loss, thus my initial experiences with illness and my dedication to helping others impacted my decision to enter the medical field. This summer I was involved in two projects with Dr. Tariq Ahmad, Division of Pediatric Endocrinology at Children's Hospital Oakland. The primary project I conducted with Dr. Ahmad aimed to investigate potential associations between demographic variables and atypical eating patterns in adolescents with type 1 or type 2 diabetes. In addition, I helped update and modify a database to reference type 2 diabetic patients for use in future studies involving lipid research. Through my wonderful experience of working with Dr. Ahmad, I gained invaluable knowledge regarding the world of clinical research and what life in a clinical setting is like.

Funded by: The Short Term Research Education Program to Increase Diversity in Health Related Research from the NIH/NHLBI

School: Boston University

Mentor: Tariq Ahmad, M.D.

Title:
Examining Atypical Eating Behaviors Among a Youth Population of Type 1 and Type 2 Diabetics

Introduction:
Atypical eating habits have been observed in adolescent females with type 1 diabetes. Depending on age and study, it has been shown ~15-30% of females admit to insulin restriction—a distinct form of disordered eating behavior (Markowitz et al., 2010). Recently, Joslin Diabetes Center researchers in Boston, Massachusetts, designed the Diabetes Eating Problem Survey- Revised (DEPS-R) as a method for screening disordered eating in pediatric type 1 diabetics. We propose to utilize the DEPS-R to investigate the prevalence of aberrant eating patterns among pediatric diabetics within Children's Hospital Oakland.

Objective:
We intend to statistically measure factors that may be associated with irregular eating patterns in a specific population of type 1/ type 2 diabetic youths, by using the DEPS-R. We aim to discover which factors may have stronger associations than others and whether clustering patterns exist.

Methods:
The DEPS-R will be administered in CHO and affiliated clinics to participants between ages 13 and 19 years with type1/ type 2 diabetes. The 16-item survey will be assessed using a 6- point Likert scale and scored by summation of the 16 items. Discrete variables will be analyzed to examine correlations between DEPS-R scores and evaluated factors, and clustering will be analyzed using zip codes.

Expected outcome:
We predict there will be significant correlations between aberrant eating behaviors and several factors examined among the type 1/ type 2 diabetic youths surveyed. It's anticipated that clustering patterns will be exhibited, thereby demonstrating parameters that may impact the prevalence of atypical eating behaviors.

Henry Duran

I am Henry Duran, am bilingual in Spanish, and I will begin a Pre-Health Post-Baccalaureate program at Mills College in Oakland, California, in the fall of 2013. This is the first time I have had an opportunity to participate in a science research program. My academic background in history and ethnic studies and my service to my communities as an after-school program coordinator and an Americorps, with Community HealthCorps East Bay, have greatly impacted my interests in medicine. Further, my personal background as a formerly obese adolescent, reaching a very healthy weight through lifestyle changes in my teens, and completing the 2013 San Francisco to Los Angeles AIDS Life/Cycle have also contributed to my strong commitment to combating the growing childhood obesity epidemic. However, I am confident the mentoring and stimulating research environment I will gain at CHORI will be especially valuable and positively contribute to my potential as an aspiring endocrinologist.

Funded by: Private Donor - Friends of Children's Hospital

School: Mills College

Lab Personnel: Nastaran Faghihnia, Sally Chiu, Ph.D. Stanley Hazen, June Tester, Lydia Tinajero-Deck and Ronald M. Krauss, M.D.

Mentor: Patty Siri-Tarino, Ph.D.

Title:
Relation of Dietary Choline, TMAO and Heart Disease Risk Factors in Obese Children and their Parents

Introduction:
Trimethylamine-N-oxide (TMAO), a gut-microflora-derived choline metabolite, has recently been shown to be a potential risk factor for cardiovascular disease (CVD). The association of dietary choline, an essential nutrient found in high amounts in eggs and beef liver, with atherosclerosis is less clear.

Objective:
We will assess the associations between 1) dietary intake of choline and plasma levels of TMAO and 2) plasma levels of choline and components of atherogenic dyslipidemia (increased triglycerides, and small LDL. and reduced HDL cholesterol) in families. Further, we will compare plasma levels of TMAO, dietary intake of choline, plasma levels of choline, and components of atherogenic dyslipidemia in obese children relative to their parents.

Methods:
Linear regression analysis will be used to evaluate dietary intake of choline, plasma levels of choline, plasma levels of TMAO and components of atherogenic dyslipidemia in generally healthy children (>7 years of age, n=40) and their parents (n=50). Multivariate regression analyses will be used to adjust for potential covariates including family history of CVD and lifestyle factors (e.g. smoking, alcohol consumption, and hormone-influencing medications). Analyses will be performed in obese children and adults in separate and combined groups.

Expected Outcome:
We expect that dietary levels of choline will be positively associated with plasma levels of TMAO in obese children and their parents. Further, we expect a positive association between plasma levels of choline with increased triglycerides, small LDL, and reduced HDL cholesterol. Children will likely have similar dietary and lipid profiles compared to their parents.

Andrea Fernandez

Before I begin an introduction to myself; I would like to give my sincerest thanks to my mentors Dr. Illek and Dr. Fischer, my lab colleagues, the CHORI summer program directors/ coordinators, seminar speakers and NHLBI/ NIH Foundations. Being a part of the CHORI summer program this year has been an incredibly valuable experience. I was born in Palo Alto, California to a Cuban father and Colombian mother. I grew up at the foothills of Mt. Diablo in Walnut Creek, and attended Bentley High School in Lafayette. After graduating high school, I moved across the country to Tampa, Florida for university. I am currently a junior at the University of South Florida, where I am majoring in biomedical sciences. The workings of the body have always fascinated me, and have served as an inspiration to study health sciences. Upon completing my undergraduate studies, I plan to pursue a career in medicine

Funded by: The Short Term Research Education Program to Increase Diversity in Health Related Research from the NIH/NHLBI

School: University of South Florida

LAB PERSONNEL: Anu Menon, Jasmin Griggs, and Yvette Zuo

MENTOR: Beate Illek, Ph.D. and Horst Fischer, Ph.D.

Title:
Confocal Analysis of DUOX1/2 and CFTR Expression in Clinical Samples of Cystic Fibrosis Nasal Poly Epithelium

Introduction:
Cystic Fibrosis (CF) is an inherited genetic disorder, affecting the Cystic Fibrosis Transmembrane Reductance gene (CFTR). Mutations in CFTR result in defective or nonfunctioning anion transport channels, and reduced function of airway defense mechanisms. The current airway defense mechanism being examined is the DUOX1/2 NADPH oxidase, HVCN1 proton channel and CFTR anion channel system. The interaction of DUOX1/2, HVCN1 and CFTR provides a functional unit to produce hypothiocyanate (OSCN-), an essential molecule in protecting mucosal membranes of the airways against bacterial infection. Mutations in CFTR can disrupt the homeostasis of this system. Novel compounds such as VX-809 have been shown to restore some CFTR expression in certain CFTR mutations; however, the effects of VX-809 on DUOX airway defense proteins are unknown.

Objective:
The goal of this project is to use immunocytochemistry and confocal microscopy to determine whether expression of CF epithelial membrane proteins DUOX1/2 and delF508/3905insT mutated CFTR are enhanced when treated with VX-809.

Methods:
Visualization of the effect of VX-809 on DUOX1/2 and CFTR will be achieved through immunocytochemistry and confocoal microscopy. DUOX1/2 and CFTR will be immunostained in clinical samples of untreated and VX-809 treated CF nasal polyp epithelium cell cultures. Expression of DUOX1/2 and CFTR proteins will be qualitatively observed using a confocal microscope.

Expected Outcome:
It is predicted that treatment of CF nasal polyp epithelium containing the delF508/3905insT mutation with VX-809 will increase CFTR and thus DUOX1/2 expression. In conducting this study, insight will be gained on the delF508/3905insT CFTR mutation and on airway defense mechanisms in general.

Dawa Gangshar

My name is Dawa Gangshar. I was born in Kathmandu, Nepal and came to the U.S. when I was five. Since then I have become deeply rooted to my Tibetan culture, history and our current political struggle. This year I will be a junior at UC Berkeley majoring in Integrative Biology. After graduation, I hope to travel in medical missions and then further my studies in medical school. Ultimately, I want to practice primary care, specifically in Pediatrics. One of my lifetime goals is to provide medical aid to Tibetan refugees in India and Nepal, as well as broaden their knowledge to prevent contagious diseases, such as TB, that are widespread in our diaspora. As a first-generation student and American, I hope to be a role model to my younger brother, nieces, nephews and other children, teaching them the importance of hard work, optimism and perseverance.

Funded by: The Short Term Research Education Program to Increase Diversity in Health Related Research from the NIH/NHLBI

School: Contra Costa College

Lab Personnel: Gary Kwan Leung Chan

Mentor: Giorgio Cavigiolio, Ph.D.

Title:
Contribution Of Methionine Oxidation To Amyloid Fibril Formation By Apolipoprotein A-I

Background:
Apolipoprotein A-I (apoA-I) contributes to cardiovascular health as it transports cholesterol in the body. ApoA-I dysfunction can thus lead to cardiovascular disease. One possible dysfunctional fate of apoA-I is protein aggregation and amyloid fibril formation; as suggested by high incidence of apoA-I amyloid deposits in atherosclerotic lesions. Recently it has been reported that upon oxidation of its three methionines, full length apoA-I can produce amyloid fibrils.

Hypothesis:
The three native methionines of apoA-I do not equally contribute to amyloid fibril formation upon oxidation.

Methods:
By creating three single methionine to leucine apoA-I variants (M86L, M112L, M148L), the contribution of single methionine oxidation to amyloid fibril formation will be tested. The proteins will be expressed in bacterial cells and purified. Oxidation will be performed in the presence of a high molar excess (1000:1) of H_2O_2 at 37 °C overnight. After dialysis to phosphate buffer (pH 6.0), the clear protein solutions will be incubated at 37 °C and visually inspected for aggregation (increase in cloudiness) at specific time points. Kinetics of amyloid fibril formation will be measured analytically by incubating the samples with Thioflavin T (ThT) and collecting the fluorescence spectrum of the dye at different time points. ThT fluorescence increases upon binding to β-structures that are commonly present in amyloid fibrils.

Expected outcomes:
Oxidation of specific methionine residues is essential for inducing amyloid fibril formation by apoA-I. The goal of this study is to gain perspective on the underlying mechanism of apoA-I amyloid fibril formation and deposition in atherosclerosis.

Nina Gnong

I was one of those annoying and impatient children that frequently asked how and why questions. But I was fortunate that my parents never pushed me to think a certain way about anything. Curiosity and freedom promoted me to become a jack of all trades. As a kid, I enjoyed spending most of my time observing animals in my backyard and imprinting patterns of leaves in a notebook. Thus, I came into college knowing that I wanted to major in biology. As I progressed with my studies, I could not decide what I want to do after college. By gaining hands-on experience in a research laboratory and guidance from an assistant scientist at the Children's Hospital Research Center Oakland, I hope to be able to decide if I want to pursue a career in biochemical research.

Funded by: The Short Term Research Education Program to Increase Diversity in Health Related Research from the NIH/NHLBI

School: University of California, Berkeley

Lab Personnel: Sarah Pfeil, Tamara Banda, Samuel Muiruri, Saidi Dahir, Ann Powers, Ginny Gildengorin, and Charles H King

Mentor: A Desiree LaBeaud, M.D

Title:
The Assessment of Risk Factors for Chikungunya Virus Infections in Sangailu, Kenya

Introduction:
Chikungunya virus (CHIKV) infection causes high fever and prolonged arthalgias that affects thousands of people worldwide. CHIKV continues to emerge and reemerge as demonstrated by the large outbreaks in Kenya and elsewhere in the world. Although CHIKV causes large outbreaks and long-term health problems, an ELISA (enzyme-linked immunosorbent assay) protocol that guarantees high sensitivity and specificity for CHIKV is still being formulated and is not commercially available.

Objective:
To optimize the sensitivity and specificity of an anti-CHIKV-IgG ELISA protocol and then to identify risk factors for CHIKV exposure in Kenya.

Methods:
1100 human blood samples from individuals collected in Sangailu, Kenya in 2011 will be screened for CHIKV exposure using our optimized anti-CHIKV IgG ELISA. Seropositivity will be linked to various factors such as occupation, gender, and age using bivariate and multivariate analysis.

Expected Outcome:
We expect adults to have a higher chance of exposure to CHIKV than children since adults have longer lifetime exposures to mosquito bites. We do not expect differences among genders or different occupations as the chikungunya is not a zoonotic disease. We also do not expect to find significant differences in exposure factors among villages because the villages are located in areas with similar landscape and climate.

Jasmine Griggs

I haven't dreamed since childhood about becoming a doctor. I'll be the first to admit that my career aspirations, and even my intended college major, change as frequently as the weather out there at Wellesley. Yet, there are a few things that always remain static: my obsession with the Oakland A's; my love of learning; and my belief that I have a duty to help people, instead of just helping myself.
Working in the airway defense lab through this program, I was able to learn from people who are similarly–minded, at least in two of these three aspects. I gained a better understanding of the complexities of cystic fibrosis and the research that goes into treating the disease, and thus helping people, than I could have ever obtained elsewhere. Thank you so much, Dr. Illek and Dr. Fischer. Working in your lab was a truly illuminating and incredible experience!

Volunteer

School: Wellesley College

Lab Personnel: Andrea Fernandez, Anu Menon, and Yvette Zou

Mentors: Beate Illek, Ph.D., and Horst Fischer, Ph.D.

Title:
A Novel Airway Defense Mechanism: Effect of CFTR Expression on Secretion of Hydrogen and Bicarbonate Ions

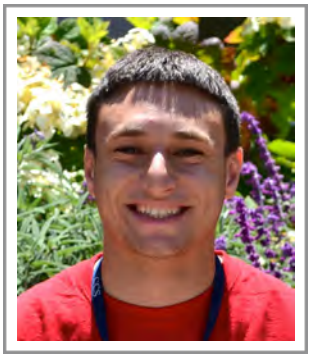
Introduction:
Cystic fibrosis is an autosomal recessive genetic disorder characterized by a diminished ability to fight off pathogens and resulting chronic lung infections. This disorder stems from a mutation in and defective expression of the cystic fibrosis transmembrane conductance regulator (CFTR). CFTR, a cAMP–activated, non–specific anion channel, allows for anions such as chloride and thiocyanate to passively flow down their concentration gradient. When lacking in either quantity or quality, CFTR results in the abnormal movement of these anions.

Objective:
We seek to determine whether CFTR expression similarly affects the distribution of bicarbonate (HCO_3^-) and hydrogen (H^+) ions, which may both have key roles in the cell's production of bactericidal hypothiocyanite ($OSCN^-$).

Methods:
Cells used for these assays will be cystic fibrosis bronchial epithelial cells either with or without correct CFTR expression. We will use the Ussing chamber assay and a pH electrode to measure the changes in pH, an indicator of charge distribution, that occur as either HCO_3^- or H^+ secretion into the mucosal compartment.

Expected outcome:
We anticipate that cells with normal CFTR will secrete HCO_3^- into the mucosal medium indicated by an alkalinization, whereas cells without normal CFTR will secrete less HCO_3^-. On the other hand, we predict that H^+ secretion, which will be indicated by an apical membrane that becomes more acidic, will occur similarly in both cell types.

Issam Hamdallah



My name is Issam Hamdallah and this is my second year in the CHORI Summer Student Program. Last year I studied Chlamydia in the Dean lab, and this year I am working to develop a transgenic model of epigenetic inheritance in Martin Lab. My involvement in CHORI has simulated my interest in the sciences and has inspired me to explore a career in research, or healthcare. Having been exposed to a vast array of scientific techniques and experiments, I am amazed by the seemingly impossible things that can be achieved in a lab. In the fall, I will be entering my Sophomore year at Kenyon College. At Kenyon, I will be playing varsity football and continuing my job as a research assistant in the Slonczewski lab. Until then, I will enjoy the rest of my summer coaching wrestling at my old high school and spending time with family and friends.

Funded by: The Short Term Research Education Program to Increase Diversity in Health Related Research from the NIH/NHLBI

School: Kenyon College

Mentor: Karl Erhard, and David I.K Martin, M.D.

Title:
Methylation Analysis of a Mouse Transgene that Undergoes Heritable Epigenetic Silencing

Introduction:
The mechanisms of epigenetic inheritance are not well understood. There could be no genetic change between two DNA sequences, but a gene could be either silent or active, and the expression, or lack of expression, is heritable. Hypermethylation of cytosine residues in promoter regions is typically associated with silent gene expression states. I aim to investigate the correlation between the methylation state of the promoter of the mouse Tg(Cp-EGFP)25Gaia (Cp-EGFP) transgene, which undergoes heritable epigenetic silencing, and its expression state.

Objective:
My objective is to conduct methylation analyses of the Cp-EGFP transgene promoter to determine if promoter hypermethylation is associated with the silent expression state. The results of these methylation analyses will aid in the development of this transgenic model of epigenetic inheritance.

Methods:
I will conduct bisulfite allelic sequencing of the transgene promoter, a sensitive assay for measuring the levels of cytosine methylation of a genomic locus. This method consists of sodium bisulfite treatment of DNA, which converts only unmethylated cytosine residues to uracil, PCR amplification of treated DNA and sequencing of cloned PCR amplicons to determine the methylation state of individual cytosines amplified from the treated DNA.

Expected Outcome:
We expect to see promoter hypermethylation of the Cp-EGFP transgene in mice carrying an epigenetically silent transgene as compared to mice carrying an active transgene.

Hiroe Hu

My name is Hiroe Hu and I graduated from Brown University this May. As a dual concentrator in Chemical Engineering and Independent Concentration in Contemplative Psychology, my undergraduate research focused on two very different areas that relate to human health: from using mathematical derivation and nanoscale manipulation to engineer a dual-function bio-imaging and drug-delivery device, to finding how the concept of 'self' plays a role in the meditative practices of mindfulness-based psychotherapies across cultures. My experience at CHORI in the Epstein lab has been radically different, yet infinitely rewarding. From running PCRs, taking mouse skin-biopsies, and staining tissues with immunohistochemistry, I gained an unprecedented level of appreciation for scientific and medical knowledge. I feel extremely privileged to take part in the research of Basal Cell Carcinoma, and therefore would like to thank Dr. Ervin Epstein, Dr. Grace Wang, and everyone else in our lab for this wonderful opportunity.

Volunteer

School: Brown University

Lab Personnel: Ervin Epstein, M.D.

Mentor: Grace Wang, M.D.

Title:
Determining the Major Pathway in Tumor Suppression Mechanism of BCC

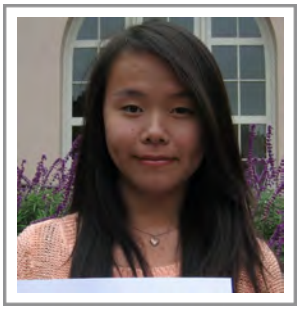
Introduction:
We aim to characterize the major signaling pathway in the molecular pathogenesis in Basal Cell Carcinoma (BCC): the most commonly diagnosed cancer among people of the European ancestry. We have found that p53, a tumor suppressor protein, has a significant role in the formation of BCCs in Ptch1+/- mice. p53 can be activated by two distinct signaling pathways: DNA Damage Repair (DDR), and Oncogene-induced stress (OIS). In our previous studies, we have found that abrogation of ARF, a tumor suppressor implicated in OIS pathway, accelerates BCC carcinogenesis in a manner similar to loss of p53, supporting a general view that ARF activates p53 in response to particular oncogenic signals. However, we also found that deletion of both ARF and p53 can further enhance BCC formation, suggesting some independent functions of ARF and p53.

Objective:
In this summer project, we aim to determine the association of ARF and p53 activation.

Methods:
We will use microscopic BCC containing skin biopsies collected from Ptch1+/- Arf-GFP/GFP and Ptchfl/fl K14CreER2 ArfGFP/GFP mice. We will examine these microscopic BCCs for the expression of GFP (driven by Arf promoter) and p53 using immunostaining followed by confocal microscopy analysis.

Expected Outcome:
There are four possible scenarios that we can expect. If we see GFP+ and p53-, meaning these microscopic BCCs induce ARF (probably by increased HH signaling), which fails to activate p53 (probably due to lack of functional ARF). This would support our hypothesis that p53 activation in tumor suppression is largely mediated by ARF. In contrast, if we see GFP+ and p53+, we will interpret that these microscopic BCCs induce ARF but p53 is still activated presumably via ARF-independent pathway. If we see GFP- and p53+, we will interpret that these microscopic BCCs fail in inducing ARF, and p53 is activated via ARF-independent pathway. If we see GFP- and p53-, we will interpret that these microscopic BCCs fail in inducing either ARF or p53.

Lily Huang



My name is Lily Huang and I am a rising senior at KIPP King Collegiate High School. As a senior anticipating college applications in the fall, I wanted to spend this summer exploring my interests. Even as a child, I had known that I wanted to work in the science or health field because I enjoy helping those in need. However, I have not decided on a specific career or major I would like to pursue. My interests range greatly from forensics to psychology. I applied to the CHORI program with hopes of narrowing down that tedious list. Although CHORI did not necessarily do that, it did indeed open my eyes to the vast spectrum of science and provide me with extraordinary hands-on lab experience. I would like to thank Dr. Don Reason, Dr. Jinying Sun, and Nancy Li for their guidance and patience this summer.

Funded by: The Doris Duke Charitable Foundation Clinical Research Experiences for High School Students Program (CREHSS)

School: KIPP King Collegiate High School

Lab Personnel: Jinying Sun

Mentor: Donald Reason, Ph.D.

Title:
Epitope Mapping of the HB-GEF-binding Toxin CRM_{197} Using a Mutated Yeast Display Library

Introduction:
Heparin-binding EGF-like growth factor (HB-EGF), a vital protein present on many cells in the human body and is involved in cellular function and replication. HB-EGF is over expressed in many cancers, however, and plays a significant role in cancerous cell replication. Diphtheria toxin (Dt) and its non-toxic derivative CRM_{197} also bind to HB-EGF, and when bound, the toxin is capable of inhibiting HB-EGF function. CRM_{197} therefore has potential for use as a therapeutic. Most people have been immunized against Dt, however, and the resulting antibodies might block CRM_{197} functionality. The receptor-binding domain of CRM_{197} (CrmR) also blocks HB-EGF function, but is also functionally hampered by preexisting antibodies.

Objective:
To identify the amino acids that comprise the CrmR antibody epitope and replace them with ones that eliminate antibody binding while maintaining HB-EGF binding.

Methods:
DNA from a randomly mutated CrmR DNA library is inserted into yeast cells. Antibodies are then allowed to bind the yeast cells, and antibody-negative cells selected by a cell-sorting flow cytometer. DNA isolated from sorted cells is sequenced and the mutated residues that led to the loss of antibody binding identified.

Expected Outcome:
We anticipate that the residues corresponding to the antibody's target residues (epitope) will be identified that eliminate antibody binding but still allow binding to HB-EGF. These amino acid replacements would have a major impact on the effectiveness of a cancer treatment based on CrmR.

Luke Karl

As a recent graduate of Contra Costa College, I'm transferring to UC Berkeley where I will major in Molecular and Cell Biology. I've always had a desire to understand the complexities of biology which has developed into a passion for healthcare. At CHORI I was given the autonomy to carry out my own research and learn from my mistakes. I want to thank my mentor Laura Hertel and my fellow lab members, Anthony Torres and Elvin Lauron for all their time and help. Dr. Hertel has been a true mentor: Supporting, critiquing, and guiding me, but never carrying me. Anthony and Elvin have spent countless hours teaching me and answering my endless and often abstruse questions. Thanks to all their selfless support and the staff who facilitate the summer program, my time at CHORI has given me a deeper understanding of medical science, the issues surrounding it, and the tools to succeed in my chosen field.

Funded by: DoEd, Title III part F, Hispanic Serving Institute Science Technology Engineering and Math (HSI STEM). The name of the project is Contra Costa College Link (CCC LINK)
PI: Setiati Sidharta, Ph.D.

School: University of California, Berkeley

Lab Personnel: Anthony Torres, and Elvin Lauron

Mentor: Laura Hertel, PhD

Title:
Detection Of A Putative Protein Encoded By Human Cytomegalovirus.

Introduction:
Human Cytomegalovirus (CMV) is a ubiquitous betaherpesvirus that can cause serious disease in immunocompromised individuals such as AIDS patients, organ transplant recipients, and fetuses. After primary infection, CMV remains latent in host hematopoietic cells for life, but how viral genomes are maintained in the nuclei of these cells remains largely unknown. To find new viral proteins possibly involved in this process, we used multiple intracellular localization prediction programs to identify novel viral open reading frames (ORF) potentially encoding nuclear proteins. One of these ORF that we named Teenie was selected for further analyses.

Objectives:
To determine if Teenie encodes a protein, if this protein is expressed in lytically and/or latently infected cells, and if it localizes to the nucleus.

Methods:
Rabbit polyclonal anti-Teenie antibodies will be tested for antigen recognition in immunofluorescence staining analyses (IFA) of cells transfected with a Teenie expression plasmid. Following successful antigen recognition, these antibodies will be used to assess if the Teenie protein is present in lytically or latently infected cells, using IFA and western blotting assays.

Expected outcome:
Based on the high antigenic and hydrophilic properties of the peptide used to inoculate rabbits, we predict that the anti-Teenie antibodies will recognize the Teenie protein when expressed in transfected cells, allowing us to subsequently determine if this putative protein is synthesized during lytic and/or latent infections, and if it localizes to the nucleus.

Nikitha Kosaraju

Throughout my life, I have always wondered how things work. I would ask my parents, teachers, and friends hundreds of questions about the things around me. They always nurtured my curiosity, but there was still so much to learn. My grandfather, along with my parents, inspired me to find the answers myself and have instilled in me a strong sense of helping others. I picture myself helping others by becoming a physician. Returning for my second year, I continue to work closely with my mentor, Dr. Hagar, to study the relationship between pregnancy, iron overload, and hypertransfused sickle cell patients. This project is both interesting and educational, providing us with more information about adult patients with sickle cell disease. I would like to thank Dr. Hagar, Christy Hoehner, Dr. Narayanaswami and CHORI for a rewarding summer full of learning and new experiences.

Funded by: The Doris Duke Charitable Foundation Clinical Research Experiences for High School Students Program (CREHSS)

School: Piedmont High School

Lab Personnel: Christine Hoehner, RN

Mentor: Ward Hagar, M.D.

Title:
The Effect of Pregnancy on Transfusional Iron Overload in Sickle Cell Patients

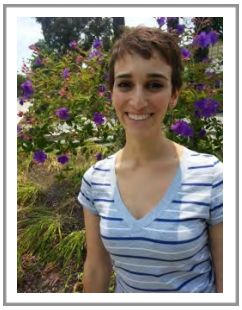
Introduction:
Sickle cell disease causes severe pains and bony disease. Only three treatments exist: bone marrow transplantation, hydroxyurea, and red cell transfusions. Red cell transfusions are increasingly used to treat symptomatic anemia and to suppress the production of sickle cells. An unavoidable effect from red cell transfusions is iron overload. Prior studies have shown that fifteen pregnant patients with sickle cell disease experienced decreased ferritin values as pregnancy progressed to 28 weeks and then the values rose gradually afterwards, corresponding with typical pregnancies. Compared to non-pregnant sickle cell patients, ten pregnant patients experienced significantly lower ferritin levels, which may be caused by increased iron demand by the fetus, but may also occur due to plasma dilution as in normal pregnancies. We aim to discover how much iron a pregnancy demands from its mother and if this demand helps to reduce the iron content within a previously iron overloaded patient.

Objective:
Our aim is to conduct a retrospective cohort study that will compare pre and post-birth iron levels to determine if total body iron stores will decrease post-birth in sickle cell patients.

Methods:
This study will collect clinical labs including serum ferritin, SQUID, serum iron, TIBC, and ALT values from electronic medical records. Afterwards, the data will be analyzed using STATA 12.1 software.

Expected outcome:
We hypothesize that total body iron stores will decrease during pregnancy in transfusional iron overloaded sickle cell patients. This study will give us a better understanding of the relationship between sickle cell disease, pregnancy, and iron.

Jessica Kyees



As a transfer student, I had the opportunity to explore a few different majors. The sciences were the most intriguing, as they were dynamic, challenging, and promised a fulfilling career. I grew up to be very inquisitive and somewhat of a perfectionist. I find that my scrupulous nature coupled by my perseverance and high self-expectations harmonize nicely with the world of research. Since being admitted to CSU Long Beach last year and joining Dr. Narayanaswami's lab, I have come to love doing research. There is certainly a thrill in investigating something that has not been studied before because sometimes you have to improvise your methods; these are the times that I learn the most about my field of study and it drives my intellectual ambitions. I will continue my education in graduate school and hope to someday improve lives and make huge advances in our scope of scientific knowledge.

Funded by: The Short Term Research Education Program to Increase Diversity in Health Related Research from the NIH/NHLBI

School: California State University, Long Beach

Lab Personnel: Yuan Yu Lee, and Tuyen Ngoc Tran

Mentors: Vasanthy Narayanaswami, Ph.D.

Title:
Mass Spectrometric Analysis Of Oxidatively Modified Apolipoprotein E

Introduction:
We aim to gain a better understanding of how oxidative stress affects apolipoprotein E (apoE), a lipoprotein that plays a key role in cholesterol homeostasis and the prevention of cardiovascular disease. Oxidative stress is mediated primarily by reactive oxygen species and their products of cellular oxidative damage such as acrolein and 4-hydroxy-nonenal (4-HNE). We propose that oxidative modification of apoE by acrolein and 4-HNE may alter the structure and conformation of apoE. This has implications in its ability to clear plasma triglycerides and cholesterol that eventually lead to a proatherogenic lipid profile, which is an established risk factor for heart disease.

Objective:
Our aims are to modify recombinant rat apoE with acrolein or 4-HNE and determine the effect of modification on the structure and conformation of apoE. In doing so, we expect to understand the molecular basis of the effects of oxidative stress on cholesterol transport.

Methods:
Following modification, we will assess the change in the isoelectric point, secondary structure by circular dichroism spectroscopy and oligomeric state of apoE by size-exclusion chromatography. In addition, we will employ Matrix Assisted Laser Desorption Ionization-Time of Flight/Time of Flight Mass Spectrometry (MALDI-TOF/TOF MS) to determine the specific modification site(s) on apoE.

Expected outcome:
We anticipate that acrolein and 4-HNE will modify protein side chains and thereby alter the tertiary fold of apoE. The overall outcome of the proposed study is to increase our understanding of the molecular mechanisms involved in oxidative stress and cardiovascular disease.

Vicki Lau

Before participating in the CHORI summer program, I had zero exposure to research in any setting. My preconceived notions about "research" painted a picture of what I expected my summer to consist of: a laboratory setting, endless amounts of pipetting, and conducting experiments to test my hypothesis. Instead, I was placed into clinical research where the focus is on analyzing existing data to identify trends, rather than running experiments. As an undergraduate attending Stanford University, I plan to major in a biological field and hopefully attend medical school. The time I spent shadowing my mentor, Dr. Pico, and analyzing patient data in an actual clinical setting was a very fulfilling, eye-opening experience that gave me a glimpse into pathways I could potentially take in the future. I am thankful for CHORI's commitment to increasing diversity in research for students like myself and especially Dr. Pico's strong mentorship and enthusiasm in creating an unforgettable summer of constant learning for me.

Funded by: The Short Term Research Education Program to Increase Diversity in Health Related Research from the NIH/NHLBI

School: Stanford University

Lab Personnel: Julianna Ponce, Coleen Sabatini, M.D., MPH, Nirav Pandya, M.D., and Cast Technicians: Dion Duncan, Willie Williams, George Harris, and Hector Cortez

Mentor: Elaine Pico, M.D.

Title:
The Effect of Waiting Time Between Botulinum Toxin Type A (BTX-A) Injections and Serial Casting in Patients with Cerebral Palsy

Background:
Cerebral palsy is a disorder due to abnormal development in the brain that causes a range of non-progressive conditions, including spasticity and increased tone which impair motor skills, and can be managed with serial casting and injections of BTX-A. Spasticity is a condition of the muscles characterized by involuntary tension and contraction. Muscle contractions are caused by nerves that send signals to the muscles at a site called the neuromuscular junction. When the signal reaches the junction, a neurotransmitter called acetylcholine is released from the nerves, causing the muscle to contract. When injected into the muscle, BTX-A binds to the neuromuscular junction, preventing presynaptic release of acetylcholine. Since the muscle is unable to receive the signal, it fails to contract in a process termed muscle denervation. The treated muscle is weakened for about three to four months until new, unblocked nerve sproutings appear. Serial casting is often prescribed after a set period following the BTX-A injections and is reapplied on a timely basis to gradually improve walking and range of motion in the affected joint.

Objective: Our aim is to identify how waiting times between BTX-A injections and casting correlate to contracture improvements in individuals with cerebral palsy and other conditions with spasticity of the lower extremities.

Method: We will analyze the change in gross motor functional scores (GMFCS) and degree of ankle dorsiflexion of study patients after the treatment period.

Expected Outcome: We anticipate that patients who receive delayed serial casting of about four weeks following BTX-A injections experience a greater improvement in their range of motion.

Jessie Mai

Growing up in Oakland, I watched in silence as the world placed the many flaws of my hometown under constant scrutiny. I thought there was nothing I could do but accept it as normal. College was what pushed me to leave my Oakland "bubble", where I became aware of the social injustices and systemic disparities that disproportionately affect low-income communities of color. And working in the King Lab at CHORI this summer has allowed me to witness firsthand the potential that research can have on improving the health of these communities, and has motivated me to seek further research in nutrition and public health. I finally discovered that my seemingly conflicting passions for social justice and hard science actually complement each other beautifully. I want to pursue a career in public health and medicine because I want to help level health disparities, raising the standard of "normal" so that future generations will not have to settle for anything less than they deserve.

Funded by: The Short Term Research Education Program to Increase Diversity in Health Related Research from the NIH/NHLBI

School: University of California, Berkeley

Lab Personnel: Adrian T. Moy, Sarah J. Burke, Tai C. Holland, Swapna V. Shenvi, Mark K. Shigenaga, and Barbara Sutherland

Mentors: David W. Killilea, Ph.D., and Janet C. King Ph.D.

Title:
Urinary Zinc as a Potential Biomarker for Zinc Status

Introduction:
More than one-third of the global population suffers from inadequate consumption of zinc, an essential micronutrient, making zinc deficiency a pressing public health concern. Low zinc intake can contribute to compromised immunity and metabolism, which in turn can result in elevated risks of infection, disease, and other morbidities. Evaluating zinc in the body is commonly done by measuring zinc levels in the blood plasma; however zinc levels in the plasma are strongly buffered against changes in dietary zinc, making it a weak indicator of zinc status. Thus, further research is warranted to identify markers that better reflect zinc levels in the body.

Objective:
This study focuses on urinary zinc as a potential biomarker for whole body zinc status. We want to know whether urinary zinc changes as a direct function of dietary zinc, and whether urinary zinc is a more sensitive indicator of zinc status when compared to plasma zinc.

Methods:
18 healthy, adult men were subjected to a 9-week depletion-repletion study, consisting of a 2-week low-zinc diet, a 4-week adequate-zinc diet, and a 3-week recovery with high zinc. Stable isotopes of zinc, ^{67}Zn and ^{70}Zn, were ingested with food or injected directly into the bloodstream, as a means to track dietary zinc absorption. Urine samples were collected at key dates between each dietary period, and zinc was extracted using column chromatography, then analyzed using Inductively Coupled Plasma-Mass Spectrometry (ICP-MS).

Expected outcome:
We expect that zinc levels in urine will correspond to fluctuations in zinc consumption. We also hope to find that changes in zinc absorption will be more sensitive to dietary zinc changes than plasma, making it a stronger indicator of zinc status. This biomarker can potentially be used to measure the efficacy of zinc supplementation in future studies.

Rogelio Medina

The prospect of ameliorating the effects of chronic diseases through medical practice and research is both exciting and personal to me. I have seen first-hand how the progression of diabetes and cancer has affected family members and know these and other conditions disproportionately affect socio-economically disadvantaged populations. I realize that my future as a physician-scientist will go far beyond treating the effects of these types of conditions. I intend to actively pursue understanding root causes of diseases and to contribute to the development of new treatments. This summer, I am working with Dr. Marsha Treadwell and her team to improve delivery of care for people affected by sickle cell disease. I have been able to witness how translational research advances the development of therapies. The mentorship I have received has allowed me to gain a better understanding of key research methodologies that will undoubtedly enhance my role as a physician-scientist.

Funded by: The Short Term Research Education Program to Increase Diversity in Health Related Research from the NIH/NHLBI

School: University of California, Berkeley

Lab Personnel: Fernando Barreda

Mentors: Marsha Treadwell, Ph.D.

Title:
Improving The Transition From Pediatric To Adult Care In Sickle Cell Disease: Assessing Transition Readiness

Introduction:
Transition from pediatric to adult care is a critical juncture for youth with sickle cell disease (SCD). Data is emerging that shows an increase in healthcare utilization (i.e. hospitalizations, emergency department visits) after the age of 18 years, and more alarming, a sharp increase in mortality in the young adult years. We hypothesize that structured programs focused on improving transition readiness can significantly enhance the health outcomes of youth with SCD transitioning out of pediatric care.

Objectives:
Our aims are: 1) to evaluate the properties of a tool to assess transition readiness in SCD and 2) to analyze factors such as mental health symptoms, social support, self-efficacy, knowledge about SCD and self-care as affecting transition readiness.

Methods:
We will evaluate the responses from a transition readiness assessment tool completed by 125 youth with SCD at two sites. We will review clinical records and survey data to identify factors that may complicate or enhance the transition process for a subset of youth still in pediatric care and for a subset who have moved into adult care.

Expected Outcomes:
We anticipate that factors that affect the ability of patients with SCD to lead an independent life, such as greater physical or mental health impairment, will complicate the transition into adult care. We expect that social support and greater self-efficacy will facilitate transition. Ultimately, we aim to improve understanding of factors associated with successful transition from pediatric to adult care in SCD, so that tailored programs to support transition can be created.

Nolan Meghrouni-Brown

My name is Nolan Meghrouni-Brown, and I'm a rising sophomore at the University of Chicago concentrating in Physics and Applied Mathematics. While I ultimately intend to pursue graduate study in condensed matter or plasma physics, I also have an abiding interest in biomedical research and engineering, largely thanks to my work in Dr. Granoff's lab. Both this summer and last, I have worked to extensively characterize antibodies against *Neisseria meningitidis*, a major cause of meningococcal disease. Besides giving me the opportunity to work with some of leading research scientists in the field of meningitis research, my work at CHORI has been a great introduction to the rigors of experimental work and data analysis -- valuable experience for students of any scientific discipline. I'd like to thank everyone in the Granoff Lab, particularly Peter Beernink, David Vu and Dan Granoff for their time, effort and patience; they have all been incredible mentors and valuable friends to me during my time at CHORI. I know it must be difficult to look after a relatively inexperienced student in addition to more important work and responsibilities, but they have done an incredible job – my experience here would not have been the same without them.

Funded by: NIH Grant 5R01AI046464-12
Novel vaccine strategies for prevention of N. meningitidis group B disease
PI: Dan Granoff, M.D.

School: University of Chicago

Lab Personnel: Leyu Liu, Peter Beernink, and Alexander Lucas

Mentors: Dan Granoff, M.D.

Title:
The Molecular Basis for Human Immunity to Meningococcal Factor-H Binding Protein

Introduction and Objective: Factor H binding protein (fHbp) is an important Neisserial antigen contained in a vaccine recently licensed in Europe for protection against serogroup B *Neisseria meningitidis.* While the antigen specificity and functional activities of mouse antibodies to fHbp have been extensively studied, little is known about the fine antigen specificity of the human anti-fHbp antibody repertoire, which is the objective of my study.

Methods:
A panel of recombinant anti-fHbp antibody fragments (Fabs) was prepared using PCR products from individual B cells from human subjects immunized with a vaccine containing recombinant fHbp. We selected 11 genetically diverse Fabs based on variable region gene sequence. The Fabs will be characterized by their breadth of reactivity with natural fHbp amino acid sequence variants by ELISA, their ability to inhibit the binding of fH to fHbp (which is important in eliciting complement-mediated bactericidal activity in human serum), by flow cytometry and the ability of site-specific single amino acid fHbp mutants to abrogate binding of the Fabs to fHbp. For certain antibodies, these data will be supplemented by screening the Fabs against an fHbp mutant library with 2-3 amino acid mutations per molecule to define the locations of the epitopes recognized by the fabs.

Expected Outcome:
The data will provide insights into the portion of the fHbp molecule that is immunogenic in humans. The fine antigenic specificity of the human antibody responses to fHbp will be correlated with antibody protective activity and help elucidate the basis of protection elicited by fHbp vaccine.

Isabeth Mendoza

I am a soon to be UC Berkeley Alumnae, majoring in American Studies focusing on the Health of Women of Color. I am a passionate pre-health student, interested in Maternity and Child Health and Immigrant Health. Through health and medicine I discovered the opportunity to affirm my community's value. I dream about my community's ability to live long healthy lives, to have access to opportunities that will advance their mental, emotional and physical health. I want to offer the chance of empowerment, agency and self-love. Through health and medicine I believe I can. I aim to pursue a Masters in Public Health and a dual MD/PhD degree. I intend to practice medicine, teach, start a student-mentoring program, perform research and open a practice for immigrant families. I aspire to be a familiar comforting face, to be a servant of my community and to make my family proud and their struggles worthwhile.

Funded by: The Short Term Research Education Program to Increase Diversity in Health Related Research from the NIH/NHLBI

School: University of California, Berkeley

Lab Personnel: Sarah J. Burke, Tai C. Holland, Swapna V. Shenvi, Mark K. Shigenaga, Barbara Sutherland

Mentors: David W. Killilea, and Janet C. King

Title:
Is Fingernail Zinc Content a Reflection of Zinc Status in the Body?

Introduction:
Zinc is an essential trace element that is required for proper growth, immune function and metabolism. Zinc deficiency has been linked to chronic infections, stunted growth, and delays in cognitive development. The recommended daily allowance (RDA) for zinc is 8mg/day for adult women and 11mg/day for adult men. Currently, one-third of the world population is at risk for zinc deficiency. In the U.S. there is a moderate level of zinc inadequacy that does not have the overt clinical symptoms linked to severe zinc deficiency. As a result, zinc inadequacy can persist for a long period of time without detection. Therefore, identifying a reliable measure of zinc status is an urgent public health issue.

Objective:
Traditionally, zinc status is measured using plasma zinc. However, the zinc in plasma is tightly regulated independent of dietary intake and can be affected by inflammation, changes in the immune system, and postprandial responses. A more sensitive biomarker of zinc status is needed. Previous studies have suggested that zinc levels in human fingernails can reflect changes in dietary zinc. An advantage to fingernail analysis is that collecting fingernail clippings is a quick and minimally invasive procedure that avoids the need for blood draws. Also, fingernail samples do not require any immediate processing and are stable at room temperature, making them ideal for use in fieldwork. Thus, our goal is to determine whether fingernail zinc is a sensitive biomarker of zinc status.

Methods:
In our present study we are analyzing human fingernail samples from healthy male participants (n=14) in an 11-week feeding trial with three phases: 2-week depletion at 4 mg zinc/day, a 4-week repletion at 8 mg zinc/day, and a 3-week recovery at 25 mg zinc/day. Fingernails were collected every two weeks from each participant for 24 weeks. The fingernail samples were thoroughly washed, acid digested, and analyzed for zinc content via Inductively Coupled Plasma (ICP) spectroscopy.

Results and Conclusion:
We expect the changes in zinc deposition in fingernails to reflect the changes in dietary zinc. We anticipate changes in fingernail zinc will positively correlate with other zinc biomarkers. If proven to be a viable biomarker, fingernail zinc analysis will be an invaluable tool for measuring zinc in future studies.

Anu Menon

Innovation lies at the heart of action and reaction, the interplay between the process of a thought and its application. As a medical student, my desire to participate in research stems from an inclination to explore that link that ties the content I imbibe from my textbooks with what I will experience in my future interactions with patients. I can't thank the Elizabeth Nash Foundation enough for sponsoring my opportunity to work at CHORI this summer. Their commitment to giving back and sparking awareness of Cystic Fibrosis has inspired in me a greater appreciation for research and its impact on the community. The chance to work in a lab alongside Dr. Fischer and Dr. Ilek and my wonderful lab partners has been such a rewarding experience. Their boundless curiosity and passion make for a lab environment that is both enriching and challenging as well as a joy to work in.

Funded by: the Elizabeth Nash Foundation

School: The Royal College of Surgeons in Ireland

Lab Personnel: Yvette Zou, Andrea Fernandez, and Jasmin Griggs

Mentor: Beate Illek, Ph.D. and Horst Fischer, Ph.D.

Title:
Correcting The Gap: The Effect Of A Novel Cystic Fibrosis Therapy On Ion Transport Across CF Airways

Introduction
Cystic Fibrosis (CF) is an autosomal recessive genetic disorder characterized by a mutation that results in a mis-folded ion channel protein, cystic fibrosis trans-membrane conductance Regulator (CFTR), which functions as an anion channel. Cystic Fibrosis is categorized by the identification of a vast number of mutations; in these sets of experiments, ΔF508/3905insT, a frame-shift mutation that results in the presence of a premature-stop codon and malfunctioning mRNA[3], will be the mutation of interest. The discovery of targeted therapies such as *Lumacaftor* (VX809), which enhances processing of the CFTR channel into its mature glycosylated form, has elicited the dawn of personalized medicine, and a renewed hope in the future of combatting this disease[2].

Objective
To test the hypothesis that the VX809 therapy (*Lumacaftor*) will correct for the CFTR defect, indicating an increase in apical membrane chloride ion conductance, which will be exhibited as an increase in cAMP-dependent chloride current.

Methods
CF nasal polys will be grown as differentiated airway epithelial cultures on permeable filter inserts to probe the efficacy of VX-809 on the DF508/3095insT mutation. To detect the passage of current across an epithelial cell, the Ussing Chamber Assay will be utilized. The Ussing Chamber serves to mimic the in-vivo environment of an epithelial cell membrane[4]. The tissue is short-circuited and transepithelial chloride current is recorded in response to the CFTR stimulators (forskolin, VX-770, genistein) and CFTR inhibitors (inh172, glibenclamide).

Expected Outcome
It is expected that the drug VX809 will stimulate the defunct CFTR channel, resulting in a detectable increase in the conductance of ions across the membrane.

Jordan Miller-Surratt

I have maintained a permanent residence in Oakland for my entire life, and during my formative years I've also spent a significant amount of time in other places- Andover, Massachusetts, and now Chicago, Illinois. Due to life experiences, I have developed a perspective in which I'm hyperaware of different communities, social circles and the challenges they face. I hope to pursue a career in the field of public health, as it deals with a majority of the issues that we face as a society. Public health is broad enough to allow me to focus on many aspects of health. My participation in this program is fueled by my interest in learning more about the determinants of physical health. This program has given me an opportunity to work in a laboratory, while exposing me to different facets of research and health. I'm grateful for the opportunity to explore my career interests.

Funded by: The Short Term Research Education Program to Increase Diversity in Health Related Research from the NIH/NHLBI

School: University of Chicago

Mentors: Gregory R. Moe, Ph.D.

Title:
Regulation Of Neisserial T And B Cell Stimulating Protein B Expression

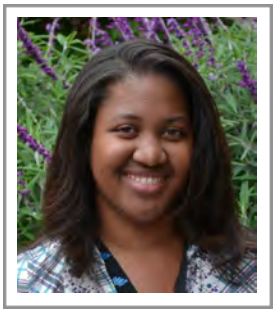
Introduction:
The reasons why some strains of *Neisseria meningitidis* (Nm) bacteria cause disease while others do not are unknown. Recently, our laboratory found that prophage DNA associated with pathogenic Nm strains contained a gene coding for an IgG-binding protein (Igbp) called TspB. Igbps are known to be important for serum survival by non-productively activating complement, and producing complexes that resist opsonophagocytosis by macrophages. Similarly for TspB, we showed that two or more functional *tspB* genes were necessary for Nm survival in human serum and that formation of Nm aggregates and biofilm containing TspB, IgG and DNA depended on TspB. Importantly, production of TspB depended on factors present only human serum.

Objective.
The goal of this project will be to determine the effect of human serum factors on the expression of TspB from each of three *tspB* genes in Nm.

Methods:
The size and identity of mRNA transcripts encoding TspB will be determined by Northern blot using biotin-labeled probes specific for each of three *tspB* genes. The relative expression of each *tspB* gene will be determined by quantitative real time PCR. mRNA will be prepared from bacteria grown Mueller-Hinton rich media, chemically defined media (CDM), and CDM supplemented with human serum Cohn fraction IV (CDM+CF4).

Expected outcome:
We expect: 1) to observe expression from at least two *tspB* genes, 2) that the TspB message will be one component of a polycistronic mRNA possibly including open reading frames from the entire prophage genome, and 3) that expression will depend on the presence of the human serum fraction.

Martinique Moncrieffe



My name is Martinique Moncrieffe and I am a senior at Wellesley College studying Neuroscience. My interest in neuroscience developed through my fascination with the interaction between the brain, body, and mind. This summer has been an honor and an unforgettable experience working at Children's Hospital Oakland Research Institute. Throughout my educational career, I have always wanted to pursue a career in the medical field. I have always had an interest in science, both inside and outside of the classroom. Figuring out how systems function and how they are structured continues to fascinate me. I have also been curious to know how manipulating one aspect of a process can lead to large changes in that process, for the better or for worse. This program has provided me with a short-term research training opportunity that has further stimulated my interest in pursuing a career in biomedical research in a nurturing environment.

Funded by: The Short Term Research Education Program to Increase Diversity in Health Related Research from the NIH/NHLBI

School: Wellesley College

Lab Personnel: Kalistyn H. Lemke

Mentors: Mark Borga, and Michael Oda, Ph.D.

Title:
What the FRET: Structural Anaylsis of Lipid-free Apolipoprotein A-I

Introduction:
Our aim is to gain a better understanding of the structure of lipid-free apolipoprotein A-I (apoA-I), the major protein component of HDL. ApoA-I is important in cholesterol metabolism, specifically reverse cholesterol transport through which it protects from cardiovascular disease. Understanding the structure of apoA-I is important for understanding the function of HDL. Several structural models of both lipid-free and lipid-bound apoA-I have been proposed based on information gathered from diverse techniques. The Oda Lab has presented the most complete and widely accepted secondary structural model of apoA-I to date, using EPR. A tertiary model of lipid-free apoA-I was proposed based on secondary structural information gathered from the EPR data. Verifying the tertiary structure is important toward refining the current model and understanding how apoA-I regulates HDL function.

Objective:
Our aim is to use FRET to verify the tertiary structural model of lipid-free apoA-I. This allows us to determine whether the EPR-derived secondary structural data correctly predicts apoA-I's lipid-free tertiary structure.

Methods:
We will be transforming plasmid vectors containing apoA-I into E. coli and purifying recombinant apoA-I using affinity chromatography. Following purification, the proteins will be labeled with AEDANS fluorophore and we will perform FRET assay to verify the model.

Expected outcome:
We anticipate that the model of lipid-free apoA-I is correct and that it will be verified by observed FRET signals. Overall, we expect to gain a better understanding of the structural features of lipid-free apoA-I, and increase our understanding of HDL function.

Julia Moradian

My interest in the science field has grown significantly over the past year, as I have just recently finished my freshman year at Tufts University in Medford, Massachusetts. Although I plan to double major in Biology and Spanish, my knowledge in the field of biology had never extended beyond the classroom before this summer. Having the opportunity to work closely in the Kuypers' Lab studying red blood cells as well as partake in the research community at CHORI has truly given me an alternate perspective of the medical field, as I now fully understand the integral role that research plays in medicine and healthcare. As I have always hoped to attend medical school, I strongly feel that my experience at CHORI will dramatically benefit my future and outlook in medicine.

Volunteer

School: Tufts Universisty

Lab Personnel: Alissa Chandler and Matt Ono

Mentors: Frans Kuypers, Ph.D., and Sandy Larkin

Title:
Validating Novel Flow Cytometry Imaging of Sickle Cells

Introduction:
Sickle Cell Disease (SCD) affects individuals with a single point mutation in one subunit of their hemoglobin molecules. Normal hemoglobin consists of two alpha and two beta hemoglobin (Hb) chains and bind and deliver oxygen throughout the body. The mutated ß-globin in SCD, will lead to polymerization of Hb when it is exposed to low oxygen pressure. This polymerization causes the cells to change shape and increase in rigidity, leading to the blockage of blood vessels, vasculopathy, ischemia reperfusion injury, and acute events such as stroke.

Objective:
Our objective is to validate a new method to analyze large numbers of red blood cells (RBC's). We will deprive normal cells and sickle cells of oxygen. Using standard microscopy and ImageJ, a pixel-analysis program, we will analyze any changes in morphology. With ImageJ, the percent of sickled cells per sample will be defined, calculated, and data will be compared to analysis of the same samples with a novel imaging Flow Cytometry system. Following the time course of sickling will allow us to compare the kinetics of this process and evaluate antisickling treatments.

Methods:
Normal or sickle samples are deprived of oxygen for a varying amount of time in a tonometer at 37°C. Aliquots will be removed at specific times and fixed with deoxygenated paraformaldehyde and glutaraldehyde. Slides are prepared and 20 digital images are taken with 30-50 cells per image. Images are analyzed using ImageJ to calculate the circularity of each cell. This is used to calculate the percent of sickled cells. The timed data points will produce a graph that maps the kinetics of sickling. Data from image flow cytometry will be analyzed with a different program that calculates characteristics of thousands of cells at once.

Expected Outcomes:
With the data from ImageJ, we will be able to create a graph that will show the percent of sickled cells as a function of time. We expect this to be a sigmoidal curve representing the kinetics of sickling. If the data from ImageJ is comparable to data from image flow cytometry, flow cytometry can be validated as a way to analyze deoxygenation-induced morphology changes in RBC's. Once validated, the effects of anti-sickling compounds can be measured with this new method.

Laila Mufty

My name is Laila Mufty and I am a senior at Holy Names High School. This summer I had the privilege of working with two incredible mentors and an amazing staff at the Children's Hospital Oakland Teen Clinic. After stepping into Children's Hospital Oakland seven years ago, I knew that I wanted to work in the medical field. It is people such as Dr. Staggers and Dr. Matthews that inspire me with their infinite passion for their job. My mentors not only took the time to answer all my endless questions, but they helped nurture my curiosity and offered me opportunities to expand my knowledge. I would like to thank the CHORI program, the Teen Clinic staff and my mentors for truly making this one of the best summers I have had thus far.

Funded by: Private Donor – Friends of Children's Hospital

School: Holy Names High School

Mentors: Jenifer Matthews, M.D., and Barbara Staggers, M.D.

Title:
Improving Identification of Adolescents and Young Adults who are at High Risk for Future Cardiovascular Disease

Introduction:
Children's Hospital Oakland Department of Adolescent Medicine provides service to a wide array of patients who among other obstacles, face the development of cardiovascular disease. According to the Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents published in 2011, children and adolescents between the ages of 9-11 and 17-21 should receive a lipid screening and adolescents between the ages of 12-16 should receive selected screening depending on specific risk factors.

Objective:
We will determine how well we are screening according to the guidelines as well as how many of those screened have abnormal values.

Methods:
We will identify 50 primary care patients who qualify for lipid screening according to the Expert Panel's guidelines and see if they have been screened or have a screening ordered at the end of their visit. To identify viable candidates, we will review medical charts and create a spreadsheet to keep track of all the qualified patients. If a patient between the ages of 12-16 has not previously received a screening, they will be asked to fill out a short questionnaire to determine whether they would be eligible for a screening based on their risk factors.

Expected outcome:
Because the guidelines were released in 2011 and are relatively new, we do not expect many patients to have received lipid screenings. Additionally, we expect that most kids screened will have abnormal values. We hope to improve our care by evaluating how well we are identifying kids at risk

Patricia Nguyen

My name is Patricia Nguyen, and I am enrolled at California State University, Long Beach. In the fall, I will be a third year majoring in Chemistry.

My parents originated from Vietnam. They were not able to obtain any education because they were trying to escape the war for a better life. As a result, I am a first generation student that had little guidance in education.

Entering CSULB as a freshman, I enrolled in a course that would help me find the right path to graduation. This class helped me discover a different side to science, which is research. As part of the course, I had to shadow a professor's lab, and the professor I chose was Dr. Vasanthy Narayanaswami. After spending half a semester shadowing her lab, I was lucky that Dr. Vas invited me to join her lab. I always enjoy going into lab because every day I am learning something new.

My future plan is to further my education and go on to graduate school with a focus in pharmaceutical science, and then I hope to find a career in the pharmaceutical industries.

Funded by: The Short Term Research Education Program to Increase Diversity in Health Related Research from the NIH/NHLBI

School: California State University, Long Beach

Lab Personnel: Roy Hernandez

Mentors: Vasanthy Narayanaswami, Ph.D.

Title:
Determination of the Lipid Binding Mechanism of Apolipoprotein E C-Terminal Domain

Introduction:
Apolipoprotein E (apoE) is one of the key residents of plasma lipoproteins and plays a critical role in maintaining cholesterol levels. It is folded as two domains: an N-terminal domain that bears high affinity binding to the lipoprotein receptor family of proteins, and a C-terminal domain that bears high-affinity lipid binding and apoE self-association sites. ApoE undergoes a large conformational change upon transitioning from lipid-free to lipoprotein-bound states; however, the structural details of this change and the lipid binding mechanism are not known.

Objective:
The purpose of this study is to employ spectroscopic and biochemical approaches to address the fundamental unfolding behavior of the C-terminal (CT) domain of apoE, which will aid in understanding the lipid binding mechanism.

Methods:
Isolated apoE CT domain will be labeled with fluorescent probes at specified sites to monitor the localized changes in structure upon chemical denaturant induced unfolding. The changes in the mobility of selected segments of the protein will be measured as changes in the mobility of the probe by fluorescence polarization. Further, we will assess the lipid-associated organization of apoE CT domain by cross-linking studies.

Expected outcome:
We anticipate that the loosely structured segments will unfold prior to the highly structured portions of apoE, and that the helices will be organized parallel to neighboring helices in the lipoprotein-bound state. Our studies will offer insight into the unfolding behavior of apoE and the lipid binding mechanism, which are essential to understand the molecular basis of the role of apoE in lipoprotein metabolism.

Rocio Ochoa

My name is Rocio Ochoa and I am an upcoming freshman at Agnes Scott College. This is my second year in the program and I am excited to be back working in the Ryan Lab. I grew up in the Lockwood neighborhood of Oakland with liquor stores on every corner and the notorious International Boulevard in my backyard. With most kids in my area not amounting to much, I was expected to become another statistic. But with the help of wonderful mentors along the way, I've been encouraged to spread my wings and pursue my dreams. I am thankful for the early exposure to research that CHORI has given me. This program has tested my confidence and readiness in math and science. I thank Dr.Robert Ryan and Betty Su for welcoming me into the lab and having me under their wing and CHORI for choosing me for this wonderful program.

Funded by: The California Institute for Regenerative Medicine (CIRM) Creativity Award

School: Agnes Scott College

Lab Personnel: Betty Su

Mentor: Robert O. Ryan, Ph.D.

Title:
Effect Of Organic Acids On Neutropenia In Barth Syndrome

Introduction: Barth Syndrome is a rare X-linked genetic disorder. Patients with Barth Syndrome have mutations in the *TAZ* gene that leads to neutropenia, hypocholesterolemia and urinary excretion of 3-methlyglutaconic acid (3MGC) and 3-methylglutaric acid (3MG). Neutropenia is characterized by a deficiency in specific white blood cells called neutrophils and a low neutrophil count often results in increased infections. We hypothesize that, in Barth Syndrome, organic acid buildup in myeloid progenitor cells inhibits cholesterol biosynthesis. Insufficient cholesterol in these cells affects their maturation and induces an apoptotic program, resulting in neutropenia.

Objective:
My objective is to determine if 3-MGC and/or 3MG inhibit the rate-limiting enzyme of cholesterol biosynthesis, 3-hydroxy-3-methylglutaryl CoA (HMG-CoA) reductase. In conjunction, the effect of simvastatin-mediated inhibition of cholesterol biosynthesis on apoptosis in myeloid progenitor cells will be determined.

Methods:
HMG-CoA reductase activity will be assayed in vitro to test if 3MGC or 3MG are inhibitory. Simvastatin will serve as a positive control. I will then incubate cultured HL60 cells with simvastatin to induce hypocholesterolemia and assay for apoptosis. Fluorescent labeled annexin V binding to cells will be measured by flow cytometry.

Expected outcome:
We anticipate that simvastatin treatment of HL60 progenitor cells will induce apoptosis. The HMG-CoA reductase assay will show 3MGC or 3MG organic acid present in Barth Syndrome patients may be a cause of neutropenia that is associated with this syndrome.

Matthew Ono

As a high school student in the small rural town of Bishop, California I have not had the hands on experience with, or exposure to, the world of laboratory science. This unique opportunity with Children's Hospital Oakland Research Institute has not only fed my appetite for experience but fostered a desire to pursue the sciences in college. Through my time here I have realized the true scope and progress of medicine in the United States and around the world. This has lead me to desire a career in the medical field so as to further the research and progress made by dedicated intellectuals at Children's Hospital Oakland and other research institutions. Working closely with the friendly and dedicated staff of Kuypers Lab I've had the privilege of acquiring priceless knowledge in both the realm of the red blood cell as well as lab science and experimental procedures. I can only thank the team of Frans Kuypers and CHORI as a whole for this wonderful opportunity.

Volunteer

School: Bishop Union High School

Lab Personnel: Alissa Chandler, and Julia Moradian

Mentors: Frans Kuypers, Ph.D., and Sandy Larkin

Title:
Validating Novel Flow Cytometry Imaging of Sickle Cells

Introduction:
Sickle Cell Disease (SCD) affects individuals with a single point mutation in one subunit of their hemoglobin molecules. Normal hemoglobin consists of two alpha and two beta hemoglobin (Hb) chains and bind and deliver oxygen throughout the body. The mutated ß-globin in SCD, will lead to polymerization of Hb when it is exposed to low oxygen pressure. This polymerization causes the cells to change shape and increase in rigidity, leading to the blockage of blood vessels, vasculopathy, ischemia reperfusion injury, and acute events such as stroke.

Objective:
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Methods:
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Jessie Ortiz

Growing up, my parents encouraged my passion for science by answering any question I asked to the best of their abilities, but sadly, this is where my search for knowledge usually ended. As a low income student from an inner city school who immigrated to the US, opportunities like CHORI were never really an option for me. Thankfully for the first time, as a rising senior in UC Berkeley I've been given the opportunity to expose myself to the world of professional research.
Thanks to CHORI and the Dean lab, I have been able to learn countless lessons this summer. They welcomed me and with great patience taught me the skills I needed to launch my research career. Their dedication has inspired me to keep going on my path towards medical school so that one day I like them, can take on someone like myself, and give them the necessary skills they need to embark on their journey towards their future.

Funded by: The Short Term Research Education Program to Increase Diversity in Health Related Research from the NIH/NHLBI

School: University of California, Berkeley

Mentors: Deborah Dean, M.D., and Loris Hwang , M.D.

Title:
Cytokine Response to Genital Chlamydia Trachomatis Infection in Young Women

Hypothesis:
Through multi-locus sequence typing (MLST) of *Chlamydia trachomatis* (CT), we hypothesize that different strains of *Chlamydia trachomatis* (CT) are associated with different cytokine profiles in the vagina.

Specific aims:
The project aims to prove that different in vivo cytokine profiles develop as a result of different CT strain types (STs).

Background:
CT is an intracellular pathogen; it infects the epithelial cells of the genital mucosa and is amongst the most common sexually transmitted infections reported in the US. CT infections can lead to tubal factor infertility, chronic pelvic pain, and ectopic pregnancy, all of which are sequellae of CT induced pelvic inflammatory disease (PID). Women who have CT and are asymptomatic are potentially at higher risk of infertility since they can't be diagnosed based in clinical symptoms, thus a better understanding of the in vivo cytokine response of the body to CT will help fight not only CT but infertility caused by PID as well.

Methods:
This project will use 29 cervical washes from women who tested positive for CT multiple times. MLST will help identify different CT strain, as well as recombinant stains and SNPS. Lastly, ompA genotyping will be used to compare the results of this study to studies which rely only on ompA genotyping and also, to provide historical context.

Expected Results:
Through MSLT identification, this study aims to find the connection between CT STs and different cytokine profiles; the relationship between the specific inflammatory responses caused by specific CT s STs would support the need for cost effective strain genotyping in clinical settings.

Julianna Ponce

My name is Julianna Ponce and I recently graduated from leadership Public School of Richmond. I will be attending Sonoma State University, in the fall and possibly majoring in nursing with a minor in Spanish. As you know my plans for the future have not been figured out. However, I'm inspired to be a nurse in the future because my ultimate goal is to give care to those in need. Throughout my life in high school English wasn't my best subject, on the other hand math and science are. At CHORI I have an opportunity to understand the meaning of science and research. This program has impacted my life in ways I never imagined. I will always be grateful for the lessons I've learned from my mentor Dr.Pico. I never imagined I would enjoy doing research.

Funded by: The Doris Duke Charitable Foundation Clinical Research Experiences for High School Students Program (CREHSS)

School: Sonoma State University

Lab Personnel: Vicki Lau

Mentor: Elaine L. Pico, M.D.

Title:
Verification Of Level Of Lesion And Its Effect On Modern Function In The CDC Spina Bifida, Register At CHORI Database

Introduction:
We aim to gain a better understanding about Spina Bifida and how the level of lesion can affect the spina bifida, a congenital defect of the spine in which part of the spinal cord and its meninges are exposed through a gap in the backbone. Spina bifida falls into three categories: spina bifida occulta, spina bifida cystica with meningocele, and spina bifida cystica with myelomeningocele. Lesion is any anomaly in the tissue of an organism, usually caused by disease or injures. We want to gain knowledge from information on what age the patient's back was closed and what surgery they had. Also the levels of lesion are weather if the patients can walk in different ways, yet there are different levels of walking. On the other hand, there are other symptoms to having spina bifida, which are bladder and bowel involvement.

Objective:
Our aim is to make sure the information from all the data in the sites are accurate and meets a common definition.

Methods:
Following the modification, we are going to reach the data of all the patients that were involved with the spina bifida evaluation. In addition, when getting the data we are going to learn the improvements of the spina bifida.

Expected outcome:
We anticipate in increasing the understanding in spina cored in lesion and its affect of mobility. Also, recording the data correctly.

Phillip Richards

My interest in science began when I was very young. In kindergarten my dad helped me enter into my first science fair where we tried to mummify fish together. My curiosity was piqued by the challenge of taking on a new project each year, and soon I had my heart set on becoming a scientist. I have learned that science is full of possibility and that no hypothesis is too far fetched to try. I now not only wonder why things work the way they do, but also how we can improve them. When I learned about CHORI, I knew that I wanted to get involved. As a high school student, I was very honored when Dr. Moe accepted me as a volunteer in his lab. I am very grateful for this opportunity to work even more closely with my mentor through the summer program. I have learned more in this lab than could be possibly taught in any classroom.

Funded by: The Jennifer Leigh Wells Fellowship

School: Campolindo High School

MENTOR: Gregory R. Moe, PhD.

Title:
Structural Studies Of Neisserial T And B Cell Stimulating Protein B

Introduction:
Pathogenic *Neisseria meningitidis* (Nm) bacteria are a major cause of life-threatening meningitis and sepsis in humans. Nm T and B cell stimulating protein B (TspB) was recently shown by our laboratory to be essential for Nm survival in human serum. The gene coding for TspB is contained in prophage DNA linked to Nm strains that cause invasive disease. TspB binds human IgG and DNA, The resulting TspB/IgG/DNA extracellular matrix non-productively consumes complement and promotes bacterial aggregation/ biofilm formation, which enhances resistance to antibody mediated bacteriolysis and opsonophagocytosis. A highly conserved region of TspB (TspB CR) was found to contain both IgG and DNA binding activities of TspB.

Objective:
The aim of this project will be to characterize the structure of TspB CR by x-ray crystallography to understand the mechanism of IgG and DNA binding and to develop vaccine antigens capable of eliciting antibodies that can block these activities

Methods:
We will express TspB CR derivatives and subdomains of the CR having IgG or DNA binding activities in E. coli and purify them by affinity and ion exchange chromatography. Initial crystallization conditions will be determined using the Hampton

Anticipated outcome:
Since TspB readily forms polymeric structures in solution without special precipitants, we expect to obtain crystals for TspB CR derivatives representing the range of sequence diversity as well as for subdomains that mediate the IgG and DNA binding activities.

Leonardo Rodriguez

Everything happens for a reason. I am a strong believer of this because if my younger brother was never diagnosed with autism I wouldn't have written a research report about it. Which meant I wouldn't have discovered neuroscience which is what I plan to dedicate my research towards. I still have quite a journey ahead of me as I just graduated high school and I am about to begin my college career at Wesleyan University this fall. The CHORI summer program is a crucial step in reaching my goal. I have been given the opportunity to explore a subject I haven't considered for me and it has been a great experience. Who would have thought that analyzing bones could be so interesting. Thanks to my mentor Ellen Fung I have gained knowledge in clinical research and reinforced the idea that a career in science is what I want to do.

Funded by: The Doris Duke Charitable Foundation Clinical Research Experiences for High School Students Program (CREHSS)

School: Wesleyan University

Mentor: Ellen Fung, Ph.D. RD

Title:
It's ALL Bones

Introduction:
Acute Lymphoblastic Leukemia (ALL) is a variation of cancer that affects the blood and bone marrow. It is the most common pediatric malignancy, with a peak incidence between 2 and 5 years of age and a survival rate of 80 to 90% ([1,2]). As many patients reach adulthood, they suffer multiple co-morbidities including low bone mass, bone pain and fractures. The goal of this project is to explore the many factors which may influence bone health in patients with a history of ALL.

Objectives:
This project has 3 specific aims: 1) to determine the prevalence of low bone mass in our clinical population of patients with a history of ALL 2) to assess parameters of bone strength by pQCT and 3) to explore possible demographic and clinical factors that influence bone mass and strength.

Methods:
Data will be collected primarily from 2 sources: the CHRCO Bone Density Clinical Database and a previous research study of 35 patients with ALL in which bone assessments were conducted one year apart. Information from the clinical database will be de-identified following extraction. Abstracted data will be merged into an excel file and related to the bone mass data by subject ID. All statistical analyses will be performed using Stata.

Expected outcome:
It is anticipated that patients who are diagnosed during puberty with low vitamin D and high intramuscular fat will have reduced bone strength and the lowest bone mass.

Citations:
[1] Inaba H, Greaves M, Mullighan CG. Acute lymphoblastic leukaemia. Lancet 2013;381:9881:1943-1955.
[2] Pui CH, Relling MV, Downing JR. Acute lymphoblastic leukaemia. NEJM. 2004;350:1535-1548.

Charlotte Rosenfeld

My name is Charlotte Rosenfield. I am a rising junior at Scripps College in Claremont, CA and majoring in Organismal Biology.
I have had a special connection with Children's Hospital in Oakland since I was young. In 2005, I was diagnosed with severe scoliosis, caused by a neurological birth defect. Dr. James Policy, a former Children's Hospital orthopedic surgeon, performed two resulting spinal fusion surgeries on me. He was an extremely inspirational person in my life, acting as the window into an influential and miraculous field of work that I completely admire. So when I was given the opportunity to volunteer at the Children's Hospital Oakland Research Institute, I was particularly excited. I deeply respect all of the researchers here at CHORI, not only as a biology student but also as a former patient.
The work that my mentor Peter Beernink and his lab do for meningococcal vaccination research is astounding. I admire and appreciate their dedication to their work and their willingness to take me under their wing these past nine weeks.

Funded by: The Short Term Research Education Program to Increase Diversity in Health Related Research from the NIH/NHLBI

School: Scripps College, Claremont, CA

Lab Personnel: Monica Konar and Rolando Pajon-Feyt

Mentor: Peter Beernink, Ph.D.

Title:
Meningococcal Vaccine Antigen Factor H Binding Protein Mutants Decrease Binding of Human Factor H and Differentially Affect Protein Stability

Introduction:
This project focuses on the meningococcal factor H binding protein (fHbp). This protein is an important component of a licensed vaccine against *Neisseria meningitidis*, a bacterial pathogen that is a leading cause of sepsis and meningitis in humans. The function of fHbp is to bind complement factor H (fH), which down-regulates complement activation and allows the bacteria to evade the immune system. Five amino acid residues make up a salt bridge network that likely stabilizes the structure of fHbp. These amino acids are present on a subset of fHbp sequence variants and may contribute significantly to fHbp binding, which is important to understand because other sequence variants lack these amino acids, but still bind fH strongly. By understanding the molecular details of fHbp, we can develop more effective vaccines against this lethal pathogen.

Objective:
We aim to understand the influence of the fHbp salt bridge network on fH binding, as well as its effect on stability.

Methods:
We will construct four single amino acid mutants by site-specific mutagenesis. We will express and purify the coded fHbps and test fH binding by ELISA and protein stability by scanning calorimetry.

Expected outcome:
From previous studies, we know that at least one residue in the network is important for fH binding to fHbp. The two amino acid residues that are connected, therefore, may also be vital to fH binding. Additionally, we expect some, or all, of the mutants to impact stability of the amino terminal domain of fHbp.

Lydia Ruesch

I have always been fascinated by patterns in the universe and the way in which entropy is countered by such a complicated and beautiful natural order. I also feel passionately about working with families to develop, early on, an understanding of and appreciation for the importance of a healthy mind and body. That is why, in 2010, after receiving my BFA in ceramics from Virginia Commonwealth University and then spending a few years in Seattle, I moved to Oakland and began volunteering at Children's Hospital. At the bedsides of the patients in the hospital's in-patient nursery, I fell in love with the healthcare environment and made the decision to start my journey toward becoming a pediatrician. I began at CHORI in 2012 and after completing my first year in the Mills College post-baccalaureate premedical program, I am back, working with Dr. Edward Lammer and his wonderful team of researchers. I would like to express my deep appreciation for the time and energy they have spent on the development of my knowledge and practice of genetic research. I am constantly blown away by their dedication to my growth and will be forever grateful.

Funded by: CHORI Genetics Research Fund
PI: Edward Lammer, M.D.

School: Mills College

Lab Personnel: Kazutoyo Osoegawa, Ph.D., Kathleen Schutlz, Nebil Mohammed, Christina Parodi, and Anna Akullian

Mentors: Edward Lammer, M.D.

Title:
Chromosomal Microdeletions Causing Heart Defects

Introduction:
The Lammer Lab has used array comparative genomic hybridization (array-CGH), a genome-wide screening technique, to detect submicroscopic chromosomal imbalances among children born with conotruncal heart defects, which comprise about 20% of congenital heart defects. Our summer investigations include DNA sequencing of genes that appear to be excellent candidate genes for conotruncal defects. We will use Next-Generation DNA sequencing methods to discover mutations among our large study population of infants with conotruncal heart defects.

Objective:
Our aim is to use Next-Generation DNA sequencing to identify mutations of the *TDGF1*, *SIX1* and *EYA1* genes among 389 California infants with conotruncal heart defects. The decision to focus on these genes was informed by previous research linking them to proper development of the embryonic heart conotruncus.

Methods:
We will design PCR primer sets to amplify each exon of *TDGF1*, *SIX1* and *EYA1*. Exon sequences will be defined based on the annotation provided by the UC-Santa Cruz Genome Browser. To enrich amplicons for sequencing on the GS FLX System, we will use the Access Array™ Integrated Fluidic Circuit (Fluidigm Corp.), which enables parallel amplification of sequencer-ready libraries from up to 48 samples at one time. We will use emulsion PCR for amplification and our amplicons will be sequenced with the GS Flex Titanium system. We will then identify polymorphisms and mutations within coding regions using SeqNext software**.**

Expected Outcome:
We anticipate that there will be novel mutations on *TDGF1*, *SIX1* and *EYA1* exons from our pool of infants with conotruncal heart defects.

Mayra Sainz

I am a rising sophomore at UC Merced pursuing a degree in Chemistry. The medical field has always sparked an interest in me; therefore, I decided to intern at CHORI and explore pediatric research. This summer I had the pleasure to work with my mentors, Mindy Benson and Christine Schudel. My time at CHORI has taught me about social issues our health care system is currently facing and the importance of preventative care. Interacting with staff members from Children's Hospital Oakland's Asthma Clinic and Primary Care Clinic has reinforced my desire to become a pediatrician. I have a sense of belonging when I am working and not even the morning traffic from an hour commute could keep me away. I hope in a few years I will be able to join the pediatricians at Children's Hospital Oakland and provide the same quality care to its patients.

Funded by: The Short Term Research Education Program to Increase Diversity in Health Related Research from the NIH/NHLBI

School: University of California, Merced

Mentors: Christine Schudel, and Mindy Benson, Ph.D.

Title:
The Relationship Between Health Care Employees' Race And Their Tendency To Address A Patient's Social Needs

Introduction:
Previous research shows that the majority of pediatricians agree that patients cannot have good health if their social needs are not being met. Patients' social needs include proper housing, suitable nutrition and assistance with transportation. Patient's social needs often go unsolved due to insufficient funds or lack of doctor-patient interaction time. One step health care professionals have taken to solve this problem is to educate physicians on social issues. One study showed that educating a group of primary care interns increased the amount of times these interns asked patients' about their social needs. However, social issues continue to plague our hospitals and clinics. In order to fully address patients' social need all angles of the situation need to be examined. Currently, there are no studies that explore the link, if any, between a provider's ethnicity and their willingness to address the social needs of their patients.

Objective:
The purpose of this study is to determine if among health care providers at CHRCO's Primary Care Clinic, there is a difference in reported willingness to ask patients about social determinants of health if the provider identifies as white or non-white.

Methods:
Health care providers at CHRCO will be asked to complete a short survey on their experiences addressing social determinants of health along with demographic information. Data from the survey will be entered in to analytic software and a statistical test will be run.

Expected outcome:
Providers that identify as non-white are more likely to report a willingness to ask their patients about social determinants of health.

Ranel Troy Santos

I am Ranel Troy Santos, a third year at UC Berkeley from San Jose, CA. The project I worked on this year focused on statins and their potential as a preventative drug for colorectal cancer. This project was very personal to me, as my grandmother passed away because of colon cancer. Because of the history, my family is very susceptible to colon cancer and that was my inspiration for working on this summer project.
I would like to thank CHORI and the summer program directors for the opportunity. I would also like to thank Dr. Medina, Dr. Krauss, and everyone in their labs for taking me in and fostering my growth as a scientist. Finally, I would especially like to thank Alexandra DiGiorgio, who personally worked with me every day on my project. She is an amazing teacher and is an inspiration I will remember throughout my career in science.

Funded by: The Short Term Research Education Program to Increase Diversity in Health Related Research from the NIH/NHLBI

School: University of California, Berkeley

Lab Personnel: Alexandra DiGiorgio, and Ron Krauss MD

Mentors: Marisa W. Medina, Ph.D.

Title:
Local Versus Systemic Effects of Statin on Colorectal Cancer

Introduction:
Statins have been reported to have chemopreventative properties against the development of colorectal cancer. *In vitro* statin exposure induces apoptosis of colorectal cancer cells at supraphysiological doses, suggesting the possibility of direct benefit of statins on CRC prevention. However, statins are also known to have anti-inflammatory properties, and chronic inflammation is an important factor in the development of colorectal cancer. Notably, disruption in the balance between pro-inflammatory and anti-inflammatory cytokines within the tumor microenvironment can promote unchecked cell growth. Thus, it is possible that statins may protect against CRC through both local effects on cells within the colon, as well as through systemic effects via their anti-inflammatory properties.

Objective:
To test if statin effects on immune cells can impact CRC viability and proliferation rates.

Methods:
We will first determine the concentration at which statins show an effect on the proliferation of multiple CRC cell lines (HCT116 and SW480) using the MTS assay. Then, we will assess the effect of co-culturing CRCs with B-cell and T-cells in the presence and absence of statins to for an interaction between statin and immune cell co-culturing. Finally, we will pre-treat CRCs and immune cells with statin before co-culturing to determine if statins effects are mediated by only one of the two cell types.

Expected Outcome:
We hypothesize that the immune cell co-culture will augment statin inhibition of CRC proliferation, with the greatest effects observed after statin pre-treatment of immune cells.

Manolis Sueuga

My interest in research began during first biology class. My teacher was engaging and passionate about the study of biology, and soon I became intrigued with the intricacies of life at a molecular level. Currently, I am on my way into my sophomore year of college at Stanford and although I am undecided on a major, I will continue studying molecular biology, and continuing to expand my field of knowledge in the natural sciences. Throughout my experience in CHORI, I have been able to interact with other majors and doctorate students in the laboratory who are highly knowledgeable in the research process, and learn important skills in performing bench research. I look forward to doing research in future years, and I am grateful to participate in such a stimulating summer program. I would like to thank Deborah Ellen, Christian Elabd, and Mike Conboy for supporting me in throughout the program.

Funded by: The Short Term Research Education Program to Increase Diversity in Health Related Research from the NIH/NHLBI

School: Stanford University

Lab Personnel: Mark Sun and Mark Conboy, Ph.D.

Mentor: Christian Elabd, Ph.D.

Title:
Analyzing the Effect of Hormones on Myotrauma and Muscular Regeneration

Introduction:
This study will help us understand how a peptidic hormone affects the process of muscle regeneration. After myotrauma, muscle exhibits great regeneration potential. Initially, satellite cells proliferate and surround the damaged myofiber then fusing with damaged myofibers and with each other to produce new myofibers. Unfortunately, this process diminishes with age due to decline in muscle stem cell function.

Objective:
We are investigating how this hormone affects muscular regeneration in both old and young mice, as well as in mice deficient for this hormone. We expect to better understand whether this peptidic hormone significantly affects muscular regeneration and is involved in diminished muscle regeneration with age.

Methods:
We will investigate the effect of this peptidic hormone through various in vivo experiments. We will identify proliferative muscle progenitor cells by using a BrdU incorporation assay and fluorescent immunostaining for both BrdU and the myogenic marker Desmin. We will also evaluate differentiation efficiency using the marker embryonic myosin heavy chain (MyHC–Neonatal), which identifies newly-formed muscle fibers in vivo or myotubes in vitro. We will be using RT-PCR and western blotting to investigate candidate molecules through which this hormone may affect muscle regeneration. Muscle regeneration assays will be performed using muscle sections stained with hematoxylin and eosin.

Expected Outcome:
We anticipate this hormone to improve the levels of muscular regeneration in aged mice and a decreased regeneration in mice lacking this hormone. This study will give us a better understanding of how this hormone and other candidate molecules affect muscular regeneration.

Mark Sun

Hello! My name is Mark Sun and I am going to be a freshman at UC Berkeley this coming fall. Growing up, I had always had a profound interest in the sciences, and this interest merely seemed to increase with every science class I took. I was introduced to CHORI by my parents, and was extremely excited to apply. When I learned of my acceptance into the program, I was ecstatic to be given such a promising opportunity to explore the world of biology. At CHORI/UC Berkeley, I was given the opportunity to learn much about what goes on in a lab and engage in important lab techniques. The weeks I spent at the Conboy lab working with knowledgeable undergraduates and post-doctorates at UC Berkeley were incredibly enriching and entertaining, and I hope to use what I have gained from this experience and continue lab work sometime in the future.

Funded by: The California Institute for Regenerative Medicine (CIRM) Creativity Award

School: University of California, Berkeley

Lab Personnel: Manolis Sueuga

Mentors: Wendy Cousin, Ph.D.

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Tashi Thukhotsong

My name is Tashi Thukhotsong and I am attending UC Santa Cruz majoring in Biochemistry. In 2009, I suffered from a spontaneous pneumothorax, also known as a collapsed lung, which led me to undergo multiple surgeries. This experience inspired me to pursue a career in the health field and taught me what patients go through emotionally. CHORI's summer program has given me the opportunity to meet daily with a practicing physician allowing me to gain experience and insight in medical practice and research. I have learned that, in addition to practical medical knowledge, a good doctor needs to be a flexible and nurturing professional who deals well with people of all personality types. I am also learning the importance of maintaining presence of mind during times of high stress. I would like to thank Dr. Karen Hardy, Kimberly Johnson and Alex Wulff for the opportunity to participate in clinical research.

Funded by: DoEd, Title III part F, Hispanic Serving Institute Science Technology Engineering and Math (HSI STEM). The name of the project is Contra Costa College Link (CCC LINK)
PI: Setiati Sidharta, Ph.D.

School: University of California, Santa Cruz

Lab Personnel: Kimberly Johnson

Mentor: Karen Hardy, M.D.

Title:
RC-Cornet's Impact On The Respiratory System

Introduction:
Oscillatory Positive Expiratory Pressure (OPEP) therapy is indicative for conditions such as asthma, atelectasis prevention and reversal, bronchiectasis, chronic obstructive pulmonary disease, and cystic fibrosis. Popular ACT devices open up airways and increase detachment of mucus from an airway wall. ACTs generally help move mucus from the smaller airways within the lungs to the central airways, allowing the patient to cough to clear the lungs. A new device, the RC-Cornet is FDA approved as another OPEP therapy. It is less expensive that the current device used at CHRCO and needs to be evaluated for comparative effect.

Objective:
To determine whether the RC-Cornet is associated with an immediate change in lung function and if repeated use for a short term trial will be associated with a change in lung function. We also wish to determine subject preference for this device.

Methods:
1. Subject identified by the doctor attending the pulmonary clinic
2. Form letter sent to subject signed by primary pulmonologist
3. Researchers call the subject to inform them of the study
4. Subject considers
5. Consent at clinic visit
6. Pre-spirometry
7. Use RC-Cornet
8. Post-spirometry
9. Subject is offered to use RC-Cornet for 1 week
10. Researchers call to get 1 week questionnaire at subspecialty clinic visit

Expected outcome:
The cost of the current PEP at CHRCO (theraPEP) is $44.24 while the cost of the RC-Cornet is $35. If the RC-Cornet is non-inferior, we can institute a change in ACT from the theraPEP to RC-Cornet. This pilot study assures safety with the new device.

Anna Wender

I have always been fascinated by the field of medicine, in particular in bone health and after taking a course in Epidemiology two summers ago I realized I wanted to work in the field of public health. The CDC's location, in the middle of Emory University's campus, lead me to enroll at the school. As a sophomore I am currently pursuing a Psychology major and a Global Health, Culture, and Society minor. I grew up in the East Bay and have enjoyed the change of scenery my first year at Emory provided, however, I was thrilled to spend my summer back home participating in the Children's Hospital Oakland Research Institute summer program. I am happy to be looking at bone health in patients with Rett Syndrome that are seen at CHORI. I would like to thank Ellen Fung, Elaine Pico for the time they spent guiding me through their research.

Volunteer

School: Emory University

Lab Personnel: Sarah Afzal, and Mary D. Jones, M.D., MPH

Mentors: Ellen Fung, Ph.D, R.D., and Elaine Pico, M.D., FAAP, FAAPM & R

Title:
Weight Bearing Coupled With Low Magnitude Mechanical Stimuli To Improve Low Bone Mass In Patients With Rett Syndrome

Introduction:
Vibration Platform Therapy (VPT) is thought to have the most robust effect on the skeleton before physical maturity. Previous studies have shown that VPT increases bone mineral density and improves bone quality and quantity.

Objective:
To test the effect of VPT on improving bone health in young patients with Rett syndrome.

Methods:
The study will consist of 20 minute daily sessions at home or school with the participant standing on the platform 5 days a week for 6 months of the 12 month study. The participant's bone density will be assessed at baseline, before intervention starts, and again at 6 months and 12 months. Fourteen subjects (3 to 21 years) with Rett syndrome will be studied.

Expected outcome:
We expect that the vibration therapy will improve bone mineral density Z-score, particularly at the distal femur, a weight bearing bone we believe to be particularly sensitive to VPT.

Lin Xi

Growing up, I was surrounded by books full of facts and figures that overwhelmed my infantile mind. I was frustrated and stubborn at first, but I grew patient because I knew that one day, with enough work, I might understand these tomes. These books were the biology, chemistry, and computational books that my father kept for reference, and the books that he would later give to me as I started my scientific career, here at CHORI.
When I first arrived at CHORI over a year ago, the torrential amount of information reminded me of that feeling of being overwhelmed. Throughout the year, as I became more involved with the research, I started to understand more and more of the subject matter. This understanding wasn't born out of rote memorization though. Research has fundamentally reshaped the way I think. In this, research has not only been an enriching experience, but an enlightening one.

Funded by: the American Heart Association Western Region Undergraduate Fellowship

School: University of California, Berkeley

Lab Personnel: Ronald Krauss M.D., Eugene Bolotin, Ph.D. , Chi-Yi Yu, Ph.D., , and Elizabeth Theusch, Ph.D.

Mentor: Marisa W. Medina, Ph.D.

Title:
Identification of MicroRNAs Associated with the LDLC Response to Statin Treatment

Introduction:
Statins, or 3-hydroxy-3-methylglutaryl-CoA reductase (HMGCR) inhibitors, are the largest class of drugs prescribed for the treatment and prevention of cardiovascular disease (CVD). Although statins have been demonstrated to reduce CVD risk, the magnitude of lipid lowering in response to statin treatment varies greatly among individuals. We aim to identify genetic influences on statin response using candidate gene and genome wide association studies (GWAS). Toward this goal, we have generated a repository of lymphoblastoid cell lines (LCLs) derived from participants of the Cholesterol and Pharmacogenetics (CAP) clinical trial, comprised of 944 individuals treated with statins.

Recently, a number of studies have identified a role for microRNAs in the regulation of cholesterol metabolism. Since many of the pathways targeted by these miRNAs intersect with those that mediate statin response, we hypothesize that miRNA expression level changes may modulate statin effects on plasma cholesterol.

Objective:
We aim to identify differences in expression levels of miRNAs after in vitro 2.0uM simvastatin versus sham incubation of 24 CAP LCLs and to identify statin-induced changes in miRNA expression levels that differ in LCLs from donors with either “high” or “low” LDL-cholesterol response to statin treatment.

Methods:
Following statin and sham exposures of the 944 LCLs of the CAP clinical trial, RNA-Seq libraries will be prepared and sent off for sequencing. After libraries are sequenced, edgeR will be used to identify differences in known miRNA expression levels between the statin and sham treated cells, as well as differences between high and low responders.

Expected Outcomes:
Through this project, we expect to identify a number of miRNA that may serve as predictors of statin response and can be used in further study.

Daishar Young

My name is Daishar Young and I am a recent college graduate of UC Berkeley, having received a B.A. in Medical and Cultural Anthropology. My studies emphasize the importance of social factors that contribute to the advancement of individuals in societies also while looking at the detrimental factors such as lack of healthcare resources. My interests include providing the necessary tools to help the underserved communities thrive by supplying those communities with the proper education (preventive medicine) and available and efficient healthcare. My next steps are to attend community college, complete my pre-requisites and apply to graduate school as a nurse practitioner. My hopes are to travel domestically and practice overseas in South East Asia or Africa. I also plan to eventually open my own clinic in underserved populations that need my services most. Lastly, I would like to thank the whole CHORI program. I would like to give a special thanks to Dr. Cassandra D. Calloway, Dr. Esteban Gomez, Hanna Kim , Dr. Lela Bachrach and Barbara Staggers for all their help.

Funded by: The Short Term Research Education Program to Increase Diversity in Health Related Research from the NIH/NHLBI

School: University of California, Berkeley

Mentors: Lela Bachrach, M.D., M.S., and Barbara Staggers, M.D.

Title:
Leveraging Technology to Enhance Asthma Control and Smoking Cessation
In Oakland Youth

Introduction:
The purpose of this project is to understand how technology could be leveraged to help teens reduce smoking and improve asthma control.

Objectives:
Assess how many teens have access to mobile technology that could be leveraged to improve their health. To pilot a smartphone app called QuitStart for smoking cessation and see how this may impact smoking behavior and asthma control.

Method:
Questionnaire administered in teen clinic by researcher (DY). This will be a convenience sample of patients registered in teen clinic during the study period. Our goal is to have at least fifty subjects. Phone follow-up in one week for those patients who agree to being contacted. Asthma control will be assessed with the asthma control test (ACT).

Expected Outcome:
Many patients appear to have access to smartphones. It will be interesting to see if there is interest in smoking cessation, if the app is appearing to them and if there will be any impact on their smoking behavior or asthma control.

Yvette Zou

This fall I will be entering my second year at Dartmouth College, where I plan to major in biomedical engineering. I feel extremely fortunate to have been able to participate in CHORI's summer research program, and I am so grateful to my incredible mentors Dr. Fischer and Dr. Illek; my inspiring colleagues and friends Anu, Andrea, and Jasmin; Ms. Deborah Ellen and everyone who organized this summer program; and especially Elizabeth Nash and the her family, who created the foundation that makes this wonderful opportunity available to students every summer. Elizabeth Nash, according to her biography, refused to let herself be limited by cystic fibrosis, and would strap oxygen tanks to her backpack to go skiing rather than give up one of her passions. I hope that in the future, I will have the opportunity to apply the same determination and passion towards medical research as Elizabeth felt toward life.

Funded by: the Elizabeth Nash Foundation

School: Dartmouth College

Lab Personnel: Andrea Fernandez, Jasmin Griggs, and Anu Menon

Mentors: Beate Illek, PhD and Horst Fischer, PhD

Title:
Impact of New Clinical Trial Drug on H^+ and HCO_3^- Secretions in CF Epithelial Cells

Introduction:
Cystic fibrosis (CF) is a genetic disorder caused by the mutation of a gene responsible for the production of the cystic fibrosis transmembrane conductance regulator (CFTR) protein that non-selectively transports anions across epithelial cells. CFTR is an integral part of a novel airway defense mechanism, which includes the proton channel HVCN1 and the membrane protein DUOX, whose overall purpose is to generate the bactericidal compound hypothiocyanate that prevents infection. Recently, the experimental drug VX-809 has been shown in clinical trials to improve the function of CFTR.

Objective:
We will determine whether the drug VX-809 will improve proton and bicarbonate release in CF cells with the del-F508/3905insT mutation.

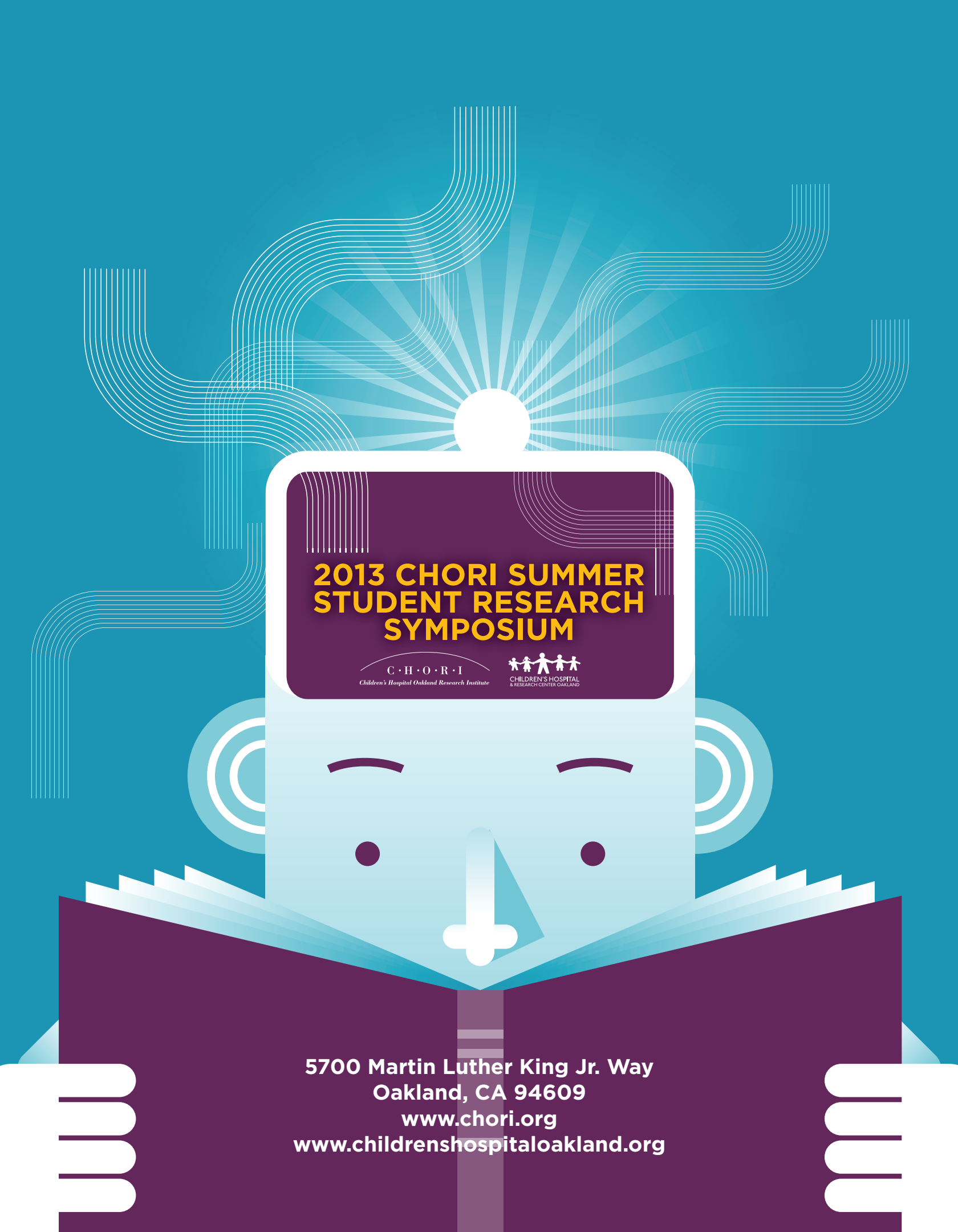
Methods:
To determine if VX-809-treated CF epithelial cells secrete bicarbonate at a higher rate than untreated control cells, we will measure the equilibrium pH reached by treated and untreated tissues from a clinical sample of CF nasal polyp cells with the del-F508/3905insT mutation. We will place the cells in an Ussing chamber in which the serosal chamber solution contains a high concentration of either bicarbonate or protons, and the mucosal chamber solution contains a low concentration. This will create a gradient that drives the ions through the channel proteins of the cells toward the mucosal solution, whose pH will be continuously measured, thereby allowing us to compare bicarbonate and proton secretion in VX-809 -treated and untreated cells.

Anticipated Outcome:
We expect that treatment with VX-809 will increase bicarbonate secretion, alkalinizing the ASL and resulting in a higher equilibrium pH.

2013 Student Photos

2013 CIRM Poster Day Photos

NOTES:



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