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Children's Hospital Oakland Research Institute

2014 CHORI SUMMER STUDENT RESEARCH SYMPOSIUM

A SHOWCASE FOR YOUNG MINDS IN RESEARCH

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Children's Hospital Oakland Research Institute

August 15, 2014

We are pleased to invite you to the 2014 CHORI Summer Student Research Symposium! Today we are here to celebrate both our wealth of diversity and the spirit of scientific enquiry that has been originated in these young investigators who are the future generation of biomedical research. The CHORI Summer Research Program provides short term education and training to high school, undergraduate and post-baccalaureate students with a broad range of backgrounds and experience. Despite their diverse backgrounds, all these trainees have one common goal, they are considering careers in biomedical research and other health care fields. Today's oral and poster presentations constitute the conclusion of a nine-week long program that has featured a rigorous mentored guided research project and education curriculum.

We invite you to learn about the various state-of-the-art research topics that the trainees were involved in, ranging from muscle reconstruction using stem cells, lipoprotein and apolipoprotein metabolism, epidemiology of rheumatoid arthritis, methodologies to study DNA damage, the host immune response and so much more. Please mingle and chat with the research scientists and physicians who served as mentors for the trainees. We feel truly privileged and honored to have the trainees in our organization and hope that their summer research experience offered a brief glimpse into the exciting world of biomedical research.

We take this opportunity to thank all of CHORI, UCSF Benioff Children's Hospital Oakland and UC Berkeley mentors and supervisors who are the backbone of the program. We appreciate their time, effort, and profound commitment to mentor the students. A very special note of appreciation also goes out to Deborah Ellen, Chandra Andrews-Wright, Phillip Bollinger, Beate Illek, Horst Fischer and all CHORI and CHRCO staff, guest seminar speakers and other friends of the CHORI Summer Program for their effort and time, which made this summer's program a huge success. We acknowledge the support and funding provided by the National Institutes of Health (National Heart Lung and Blood Institute), the Doris Duke Charitable Foundation Clinical Experience for High School Students, the California Institute for Regenerative Medicine Creativity Award, the Union Bank Foundation, the Elizabeth Nash Foundation and a number of Anonymous donors.

The CHORI Summer Research Program has quadrupled in size since it's inception over 35 years ago, yet each year, financial support for the program is one of our biggest challenges. Given the severe budget constraints facing our research and education systems, we are constantly revising 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 education 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, MD
President, Chief Executive Officer &
Principal Investigator
CHORI

Janet C. King, PhD
Interim Senior Vice President, Research &
Executive Director, CHORI

Vasanthy Narayanaswami, PhD
Associate Scientist
Principal Investigator & Co-Director
CHORI

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

Support for the 2014 CHORI Summer Student Research Program provided by:

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

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

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

Lammer Lab Education Fund (CHORI)

Elizabeth Nash Foundation

The Union Bank Foundation

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Children's Hospital Oakland Research Institute

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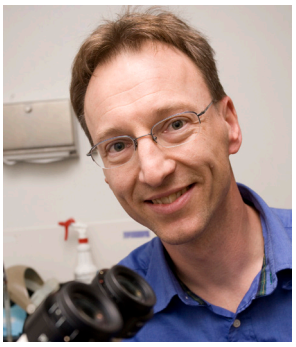

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Scientist at
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Deborah Ellen
Program Coordinator
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Phillip C Bollinger
Program Coordinator
Senior Systems Analyst at
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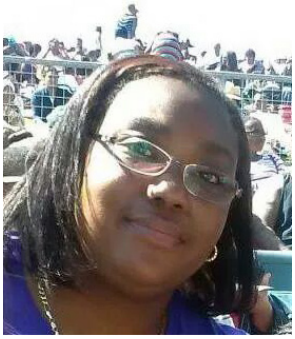

Chandra Andrews-Wright
Program Coordinator
Volunteer Coordinator at
Children's Hospital Oakland Research Institute

Mentors:

Anu Agrawal, MD
Mindy Benson, PNP
Mark Borja, PhD
Michael Conboy, PhD
Wendy Cousin, PhD
Deborah Dean, MD, MPH
Alexandra DiGiorgio, PhD
Karl Erhard, PhD
Horst Fischer, PhD
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Swapna Shenvi, PhD
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Wendy Su, MD
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Gordon Watson, PhD

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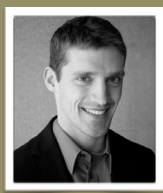
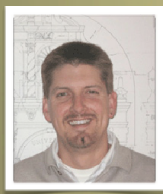
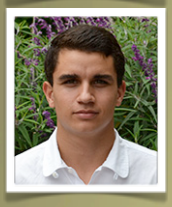
2014 CHORI SUMMER STUDENT LECTURE SERIES

Tuesdays 4pm CHORI Little Theater

	Kyle Kurpinski, Ph.D., UC Berkeley / UC San Francisco	June 24, 2014	“Translation: Creating new Medical Technologies is Not as Easy as it Looks”
	Robert Ryan, Ph.D., Senior Scientist CHORI	July 1, 2014	“Oil and water don't mix, opposites attract and why it matters”
	Dieter C. Gruenert, Ph.D., Prof Dept. of Octolaryngology, Head & Neck Surgery, Regen & Stem Cell Research, UCSF	July 8, 2014	“Correction of Cystic Fibrosis Mutations in Induced Pluripotent Stem Cells after Gene Targeting”
	Jyothi Marbin, MD Staff Physician UCSF Benioff Children's Hospital Oakland Department of Primary Care	July 15, 2014	“Asthma in Oakland - Clinical Care Meets Research”
	David Killilea, Ph.D., Staff Scientist, Nutrition and Metabolism Center, CHORI & Specialist, Department of Urology, UCSF	July 22, 2014	“A Role for Zinc in Urinary Stone Formation”
	Suzanne Rauzon, MPH, RD Director of Strategy, Atkins Center for Weight and Health, UC Berkeley	July 29, 2014	“Using the Concept of Population Dose to Identify Promising Community Level Nutrition and Physical Activity Intervention Strategies”
	Mark Shigenaga, Ph.D., Assistant Scientist, CHORI	August 5, 2014	"Poor diet, leaky gut, obesity and health risks: prevention mechanisms"

LECTURE SERIES

Thursdays 12pm CHORI Little Theater

 John Matsui, Ph.D., Director of UC Berkeley Biology Scholars Program	June 19, 2014	Ethical Issues & Conflict of Interest
 Haven Allard, Junior, Eckerd College Past Summer Student	June 26, 2014	Past Summer Program Experience
  Vasanthy Narayanaswami, Ph.D., Associate Scientist, CHORI; Associate Professor, CSULB and Ellen Fung, Ph.D., RD, Associate Scientist, CHORI	July 3, 2014	Peer Review Authorship Publications
 Beate Illek, Ph.D.	July 10, 2014	Student Meeting
  Horst Fischer, Ph.D., Scientist, CHORI and Beate Illek, Ph.D., Staff Scientist, CHORI	July 17, 2014	Collaborations Data Management
 Beate Illek, Ph.D.	July 24, 2014	Student Meeting
 Phillip Bollinger, Senior Systems Analyst CHORI IT	July 31, 2014	"PowerPoint/InDesign Preparation for Posters and Talks"

2014 CHORI SUMMER STUDENT RESEARCH PROGRAM CURRICULUM

Orientation: June 16, 2014
There will be an all-day orientation for summer interns on Monday, June 16, 2014, from 9:00 am until 4:00 pm. Continental Breakfast will be served at 8:30 a.m. Lunch will be served.

Agenda to include:
- Introduction and Welcome from Bertram Lubin, M.D., President & Chief Executive Officer, UCSF Benioff Children's Hospital Oakland
- Introduction by Janet King, Ph.D., Interim Vice President, Executive Director, CHORI
- Overview and program review by Ellen Fung, RD, Ph.D., Associate Scientist, CHORI, Co-Director CHORI Summer Program
- Explanation of curriculum by Vasanthy Narayanaswami, Ph.D., Associate Scientist, CHORI, Faculty, California State University, Long Beach, Co-Director CHORI Summer Program
- Keynote lecture by P.J. Utz, M.D., Professor of Medicine, Program Director, Medical Science Training Program, Stanford University
- IT presentation by Phillip Bollinger
- Administrative Review by Deborah Ellen
- Tour of CHORI and HEDCO buildings

Safety Training: June 17, 2014
The mandatory Safety Training with CHORI Safety Officer, Miriam Fang will be held on Tuesday, June 17th from 9:30 am to 12:30 pm. The students will be required to complete this training before beginning their project.

Research Project: June 16, 2014 to August 15, 2014
The students 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.

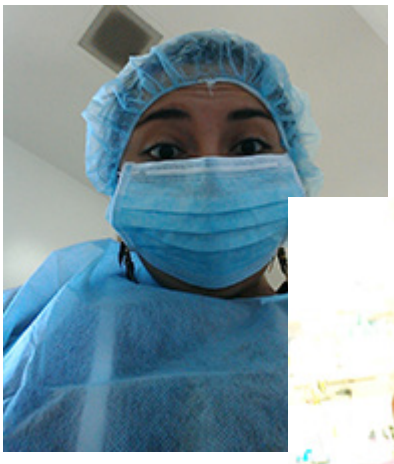
Written Research Plan: July 7, 2014
Students must submit to the Program Coordinator a written Research Plan outlining their project. The Research Plan should be 3 pages long and include:
(a) Statement of hypothesis
(b) Specific aims
(c) Background
(d) Methods
(e) Anticipated outcome of project
Students 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, mentor's name and the title of the project.

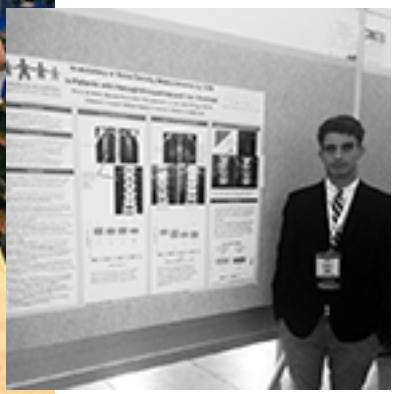
Weekly Lectures:
Current Topics in Health and Disease
Students are required to attend weekly lectures delivered by CHORI and CHRCO faculty members. The lectures will cover various scientific topics, including women's and minority's issues, career decisions, teen health issues and Responsible Conduct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

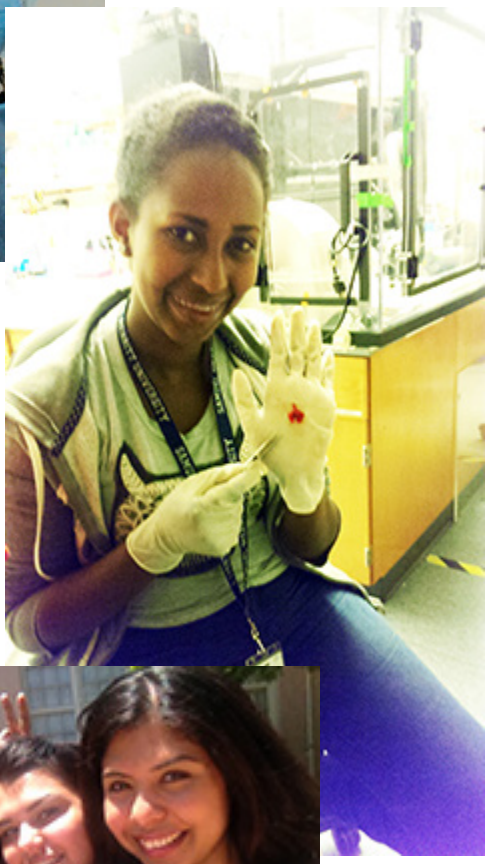
Student Photo Day: July 1, 2014
All students must be present.

Evaluations:
As part of the Summer Program, we ask that all students participate in an anonymous on-line survey at the beginning, midpoint and the end of the program. Links for these surveys will be sent out by the director. Completion will only take 5-10 minutes.

2014 CHORI Summer Student Symposium: August 15, 2014
A one-day symposium will be held on Friday, August 15, 2014 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 July 23, 2014 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 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.





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Oakland

Haven Allard

I am very fortunate to be a CHORI summer student for the second year in a row and able to finish the work that I started the summer before. This summer I am also thrilled to have the opportunity to learn more from my mentors and the lectures that are hosted at CHORI. I was also able to give back by speaking to the new interns about my research experience last summer and answer questions they may have about the program and process. Heading into my junior year I now have more scientific, academic and research confidence thanks to CHORI. It is great to be back! I'd like to thank Dr. Fung, Dr. Weyhmiller, Lisa and Nan for all their help.

Funded by: National Institutes of Health

School: Eckerd College

Mentors: Ellen Fung, Ph.D., Marcela Weyhmiller, PhD

Title:
Density Assessments by DXA in Patients with Iron Overload

Introduction:
When monitoring bone health in patients with hemoglobinapathies, it is unknown if iron in surrounding tissues can lead to inconsistences in the 2-dimensional assessment by Dual Energy X-ray Absorptiometry (DXA).

Objective:
The aim of this study was to determine if the accuracy of lumbar spine assessment by DXA is affected by high liver iron concentration in patients with Sickle Cell Disease (SCD), Thalassemia (Thal) or Bone Marrow Transplants (BMT).

Methods:
This study consisted of a retrospective chart review of DXA and Super Conducting Quantum Interference Device (SQUID) examination data collected by the CHRCO Bone Density Clinic and Iron Measurement Program between 2002 and 2014. Patients with a diagnosis of SCD, Thal or BMT, who had a DXA and SQUID measurement on the same day were divided into high, medium and low iron groups. Healthy controls were enrolled and assessed by SQUID and DXA prospectively to be compared with the patient populations. A lumbar spine scan of each subject was analyzed to compare the derived areal bone mineral density (aBMD) Z-scores of lumbar vertebrae that are covered by the liver (presumed L1 or L1/L2) with the Z-scores of the lumbar vertebrae not covered by the liver (L3/L4). All data were analyzed by STATA ver.9.2 and were considered significant with a $p<0.05$.

Results:
Data from 299 total visits abstracted from 138 subjects [31 SCD, 102 Thal, 5 BMT, age: 24 ± 12.8 years, mean ± SD], and 30 healthy controls (18 F) were analyzed. The patient group had an average LIC by SQUID of 2500 ± 1802 μg Fe/g wet tissue; while the healthy controls are anticipated to have an average LIC <500 μg Fe/g wet tissue. Initial analysis reveals that in patients with LIC > 5000 there is a significant difference between L1 and L3/L4, $p<0.001$. Results from healthy controls are pending.

Conclusions:
Initial results for this study suggest that there is a relationship between high liver iron content and lumbar spine aBMD Z-score inconsistencies evaluated by DXA.

Acknowledgements:

Frans Kuypers, Ph.D., Lisa Calvelli

Keywords:
SQUID, DXA, Bone Mineral Density, Liver Iron, Iron Overload, Hemoglobinapathies

Achivement:
My abstract was accepted by the American Society of Hematology to be published online in the November 15 supplemental volume of Blood.
I was also selected to provide a poster presentation at the 55th ASH Annual Meeting and Exposition in New Orleans, LA (Dec 7-10, 2013).
I then received a $500 ASH Abstract Achievement Award and ribbon.
Info regarding Abstract: Abstract ID # 64814: In-Accuracy Of Bone Density Measurements By DXA In Patients With Hemoglobinopathies and Iron Overload.

The authors were:
Haven M. Allard,
Marcela G. Weyhmiller, PhD
Ashutosh Lal, MD, and
Ellen B. Fung, PhD, RD, CCD

Here is the link to the publication: http://www.bloodjournal.org/content/122/21/966?sid=c7ac5881-bd9e-4e29-9ad0-a192d4dd8428&variant=abstract&sso-checked=1

It was a great experience and I was very honored for the recognition!

Nyle Almeida

I am Nyle Almeida, a senior at Washington High School in Fremont, CA. During sophomore year I worked on a semester long I-Search Project. This project entailed researching a career that I hoped to pursue. Through interviews and job shadowing I learned a great deal about the biomedical field. I was motivated to gain insight into the research field and learned about the internship opportunities available at CHORI.

During this summer program I have been able to gain a deeper understanding of research and the work ethic required to be successful in this field. I would like to thank my mentor, Dr. Moe, for his patience and willingness to guide me. Dr. Moe encouraged me to think critically and helped me understand the background knowledge. This experience has been very positive and I am confident that this will help me to pursue a career as a physician scientist.

Funded by: Volunteer

School: Washington High School

Mentor: Greg Moe, Ph.D., Sridevi Prasad

Title:
Inhibition of human melanoma SK-MEL28 cell adhesion and migration by anti-NeuPSA antibodies

Introduction:
Cell surface proteins that bind to components of the extracellular matrix such as collagen, fibronectin and laminin, have a critical role in cell adhesion and migration. Several of these cell surface proteins are modified with polysialic acid (PSA). Many human cancers overexpress PSA, which is associated with tumor cell metastasis and poor prognosis. Our laboratory has identified a derivative of PSA that contains de-N-acetylated residues. The derivative, called neuraminic acid-containing polysialic acid or NeuPSA, is highly overexpressed in many human cancers. Recently, we found that the morphology of human melanoma SK-MEL-28 cells was altered when they were incubated with anti-NeuPSA monoclonal antibodies (mAbs). The result suggests that anti-NeuPSA mAbs may affect the ability of cancer cells to adhere and migrate.

Objective:
The aim of this project was to measure the effect of anti-NeuPSA (SEAM 2 and SEAM 3) and anti-PSA (SEAM 12) antibodies on morphology, migration and adhesion of SK-MEL-28 cells.

Methods:
Cell adhesion to collagen, fibronectin, or laminin-coated microplates was determined in the absence or presence of mAbs using a Cell Titer-Glo luminescence assay. Cell morphology and expression of NeuPSA antigens were characterized using laser scanning confocal microscopy. A "wound healing" assay was used to measure the effect of mAbs on cell migration.

Results:
The cells were found to adhere to the three substrates, (fibronectin, laminin, and collagen). Treatment with SEAM 2 and 12 resulted in a significant increase in binding to laminin ($p<0.01$). The SEAM 2-reactive antigen was highly expressed on the surface and inside SK-MEL-28 cells, while SEAM 3 and 12 antigens were not expressed or expressed at low levels. Treatment with SEAM 2 caused cells to have decreased surface area with fewer and shorter lamellipodium. Also, SEAM 2-reactivity was co-localized with Type III ß-tubulin. All three mAbs appeared to inhibit the rate of cell migration.

Conclusions:
Antibodies to PSA/NeuPSA appeared to increase adhesive interactions with laminin decreasing the rate of cell membrane spreading on surfaces and movement of cells over surfaces. The result may have important implications for the use of anti-PSA/NeuPSA to inhibit cancer cell metastasis, which is associated with poor prognosis.

Dora Alvarez

My name is Dora Alvarez and I graduated from UC Berkeley in May 2014. I majored in Public Health and received a minor in Global Poverty & Practice. I grew up in Downey, California with my four siblings and parents. My interests include maternal and child health, global health, and under-served populations. I have had the opportunity to explore social research through two positions. The first was on a project that aimed to create a document for women that explained laws regarding maternity leave in California. By educating English- and Spanish-speaking women on the laws protecting leave, it was the hope that families in California would reap those benefits and thereby improve population health. This summer, I am helping with a variety of research projects based at the Children's Hospital Primary Care Clinic. One of these projects is aimed at integrating social needs into clinical practice. By addressing families' social needs, we hope to improve children's health.

Funded by: National Institutes of Health

School: University of California, Berkeley

Mentors: Mindy Benson, PNP, Christine Schudel, MPH, MSN

Title:
How Perception of Socioeconomic Status Affects Children's Health

Introduction:
Socioeconomic status (SES) is the most often used measure of a person's social standing, and is estimated by determining their educational level, income, and occupation. Studies show that people of low SES have a higher risk of chronic conditions. The way that SES expresses itself in biology is multi-faceted. Theories include the accumulation of factors such as exposure to environmental toxins, adverse health behaviors, chronic stress, high-risk jobs, and poor nutrition. It is critical to study and understand the effects of SES on health because research has shown that the connection starts in childhood. Currently, there are no studies that analyze the caregivers' perception of their SES and its effect on their children's health.

Objective:
To find whether children's health is correlated with their caregivers' perception of their social standing

Methods:
I will utilize Family Information and Navigation Desk (FIND) study data. FIND is a randomized control trial that aims to evaluate the intervention given to families to fill their unmet social needs. It is currently taking way in the primary care and emergency centers of Children's Hospital Oakland. I will use analysis of variance (ANOVA) to compare health status of the child to four different variables: the caregivers' income, the caregivers' highest educational attainment, the caregivers' perceived social standing in their community, and the caregivers' perceived social standing in the United States. Children's health status will be measured by primary care and emergency department visits over the study period.

Anticipated Outcomes:
We hypothesize that children's health will be just as correlated, if not more so, to their caregivers' perception of their social standing as to their actual income and educational level. However, we still expect to find positive associations between health status and yearly income as well as between health status and education.

Acknowledgments:
Thank you to Christine Schudel, MPH, MSN and Anais Amaya for their guidance on this project and to the FIND Health Navigators for collecting the data.

Chioma Amuzie

I've loved science my entire life. To think that I could be graced with a prestigious opportunity, such as research at CHORI, is still astonishing to me. My name is Chioma Amuzie and I'll be an incoming senior at Saint Joseph Notre Dame in Alameda, California this fall. Before spending my summer here at CHORI, I had no previous experience with knowledge application. It was, "Learn this" or, "Memorize this" or even "This will be your final grade." I could never appreciate the connection of what I was learning to its place in the real world. Then came along CHORI. I am eternally grateful for my summer spent here. I'd like to thank my mentors Karl Erhard, Ph.D. and David Martin, M.D. along with everyone else in the Martin lab, for making this experience unforgettable.

Funded by: California Institute for Regenerative Medicine

School: St. Joseph Notre Dame High School

Mentors: David Martin, M.D., Karl Erhard, Ph.D.

Title:
DNA Methylation Analysis of a Mouse Transgene in a Miwi2 Knockout Line

Introduction:
Epigenetics is the study of changes in heritable gene activity that are not a result of the alteration of DNA sequence. The Cp-EGFP transgene in mice is the model system I used in my project to study the mechanism of epigenetic inheritance. The Cp-EGFP transgene produces green fluorescent protein (GFP) in a subset of white blood cells. When transgenic mice with GFP+ cells - termed "expressers" - are mated, half of their transgenic progeny do not produce any GFP+ cells. These mice are termed "non-expressers." These two transgene expression states are not defined by DNA sequence differences. Silent transgenes are, on average, more methylated in their promoters than those that are expressing. The mechanism responsible for switching the expression of the transgene on and off and for targeting its promoter methylation is unknown. Another uncertainty is if DNA methylation is the only element affecting the silencing of the transgene. The MIWI2 protein represses transposon expression by producing small RNAs termed PIWI-associated RNAs (piRNAs), which target transposons for DNA methylation1.

Hypothesis:
I hypothesize that MIWI2 is recognizing the transgene as a transposon and is involved in its silencing.

Results:
The white blood cell enrichment from wild-type and MIWI2 knockout mice blood samples and cell lysis went as planned. Quantification of the phenol:chloroform-extracted DNA samples indicated that I had recovered sufficient DNA quantities from each blood sample to perform the Combined Bisulfite Restriction Analyses (COBRAs2). I carried out bisulfite conversions and successfully recovered the treated DNA samples from microtube columns. Gel electrophoresis analysis indicated that the PCR amplification of the bisulfite-treated DNA was successful. I then extracted the PCR amplicons from the gel and used them in restriction digest reactions to analyze the pattern of transgene promoter methylation. After running a gel, I could see that the amplicons were cut so digestion was successful.

Conclusion:
Results of the COBRAs will determine the pattern of methylation at the transgene promoter in wild-type and MIWI2 knockout mice. Another round of digestion and gel electrophoresis analysis is required to obtain conclusive results.

Keywords:
Epigenetics, gene expression, DNA methylation, MIWI2

References

1. DNA methylation of retrotransposon genes is regulated by Piwi family members MILI and MIWI2 in murine fetal testes. S. Kuramochi-Miyagawa et al. Genes Dev. April 1, 2008 22: 908-917.
2. COBRA: a sensitive and quantitative DNA methylation assay. Z. Xiong and P.W. Laird. Nucleic Acids Res June 15,1997 25(12): 2532-2534

Amarjit Bath

I am a senior at California State University, East Bay studying Health Science.
Being part of CHORI program has been a major stepping-stone in my life as this was my first basic science research experience. CHORI helped me nurture my curiosity and passion about medicine by exposing me to different facets of research. By working in the Dean Lab, I realized how powerful research is in medicine.
I would like to thank Dr. Treadwell, Dr. Fung and Dr. Dean for giving me this wonderful opportunity to work at CHORI and Trevor Rodriguez, MPH for taking the time to answer my endless questions and offering me the opportunity to acquire priceless knowledge on *Chlamydia Trachomatis*.

Funded by: Private Donor

School: California State University, East Bay

Mentor: Deborah Dean, M.D., MPH

Contributing Authors:
Deborah Dean, M.D., MPH and Trevor Rodriguez, MPH

Title:
Evaluate the host immune response to Chlamydia trachomatis infection of primary endocervical cells.

Introduction:
Chlamydia trachomatis is an intracellular Gram-negative pathogen, which infects various cells of the urogential mucosa. It is the most common bacterial cause of sexually transmitted diseases (STD) in the United States. According to the World Health Organization, over 110 million *C. trachomatis* infections occur every year. *C. trachomatis* infection can cause miscarriages, ectopic pregnancy, infertility, chronic pelvic pain and Pelvic Inflammatory Disease (PID). Women who have *C. trachomatis* infection are more likely to be asymptomatic and, therefore, unlikely to seek treatment, which is why there is an increased transmission and infection rate of *C. trachomatis*. As of today, there is no vaccine to prevent the transmission of *C. trachomatis*. Uncomplicated *Chlamydia trachomatis* infection can be treated by antibiotics (Azithromycin and Doxycycline) but antibiotic treatment may not resolve persistent *Chlamydia trachomatis* infection.

Hypothesis:
We hypothesize that *Chlamydia trachomatis* infection of endocervical cells produces a pro-inflammatory response. Then we will detect a cytokine profile that resembles characteristics of pro-inflammatory response.

Methods:
We will obtain and isolate discarded tissue from post hysterectomy procedures otherwise healthy pre-menopausal patients with no trace to patient name. Thus, the research does not constitute human subjects research. We will grow these tissues, primarily endocervical and endometrial cells in 24 well plates and wait until they were at 70% confluent. We will conduct immunocytochemical staining by fixing cells in methanol and adding primary antibody (Fibronectin, Cytokeratin 19, MOMP) that bind to target antigen and then adding secondary antibody (Cy 3 Alexa 488), which bind to primary antibody via constant region, to determine that we have epithelial cells for endocervical tissues. We will observe under fluorescent microscope. We will infect them with stock *C. trachomatis* (strain E) diluted with SPG and place the well on orbital shaker for two hours. We will collect the supernatant to measure the produced proteins and then fix and stain the cells to evaluate the level of infection by taking light and fluorescence microscopic pictures at 12, 24, 36 and 48 hour time intervals. We will use the Luminex assay to quantitatively measure the amount and distribution of pro-inflammatory cytokines and chemokines produced in response to *C. trachomatis* infection.

Anticipated Outcomes:
We aim to study the host/pathogen interactions in the pathogenesis of *C. trachomatis* STDs by looking at the local host immune responses to C*hlamydia trachomatis* infection by using primary endometrial and endocervical cells in our in vitro model.

Keywords:
Chlamydia Trachomatis, urogential mucosa, in vitro model, asymptomatic, endocervical and endometrial cells, immunocytochemical staining, primary antibody, secondary antibody, supernatant, pro-inflammatory response, cytokine and chemokines profile, fluorescence microscopic, Luminex assay.

Yohana Beyene

Beginning in the sixth to this day, I have been shadowing doctors in many different fields. I have seen over 30 surgeries pertaining to cardiology, ophthalmology neurology while learning about patient care and the politics of medicine. I am fortunate for this incredible opportunity that has allowed me to discover my future goals of doing research in the field ophthalmology in hopes of discovering a cure for blindness. However, after six years of watching physicians perform incredible tasks, I began to yearn for a more hands-on experience. Fortunately, I found CHORI, a program that is allowing me to do hands on experiments with stem cells. Most importantly, CHORI has allowed me to meet and interact with a diverse group of intellectuals who continue to inspire me to extend past my limitations and expectations. It is truly an incredible opportunity to work with people who have similar views and goals as myself and yet they come from such different backgrounds. CHORI is a program that stimulates intellectual thinking and fosters curiosity. Taking part in CHORI has gotten me a step closer to achieving my goals.

Funded by: California Institute for Regenerative Medicine

School: Oakland Tech High School

Mentors: Michael Conboy, Ph.D., Wendy Cousin, Ph.D.

Title:
Muscle regenerative properties of oxytocin in female mice

Introduction:
Previous studies give evidence that oxytocin (OT) is an age-specific circulating hormone that is necessary for muscle maintenance and regeneration. These studies show that inhibition of OT signalling in young animals reduces muscle regeneration, whereas systemic administration of OT signalling in young animals reduces muscle regeneration. This study was solely conducted on male mice. Thus, before OT could be used in clinical trials it would have to be tested to see if it has the same effects on female mice.

Objective:
Our aim is to compare muscle regeneration after injury of female mice KO for oxytocin and their Wild Type littermates and to determine if female OT KO mice develop premature sarcopenia.

Method:
My research involves mice who are knockout for OT along with their wild type littermates. Mice are injured using a cardiotoxin and allowed a period of time for their muscles to regenerate. The cardiotoxin was subcutaneously injected into the tibialis anterior (TA) and gastrocnemius (GA) of both legs. The left leg is injured five days before euthanasia, while the right leg is injured three days before euthanasia. These time points are specifically chosen to assess muscle cells proliferation (3 days) and muscle regeneration (5 days). Muscle is harvested and sectioned into fine sheets (10 micrometers thin) using a cryostat after the designated time for regeneration has ceased. To evaluate muscle regeneration, the 10 micrometers thick sections are then analyzed by quantifying the amount of myofibers with centrally located nuclei per millimeter square of muscle injury. To assess muscle stem cell activation/proliferation, sections will be immunostained for desmin (a myogenic marker) and BrdU (to monitor dividing cells).

Anticipated Outcome:
We anticipate the female WT to have a larger amount of newly formed muscle fibers in comparison to the OT KO mice. Moreover, we expect a larger amount of proliferating myogenic progenitors in the WT than the OT KO female mice. This study can lead to a universal treatment for muscle injuries at a quicker rate in those that are older, regardless of gender.

Skylar Tzu-Hsin Chuang

This is the age of science and technology. Every day, many new technologies and innovations are constantly emerging; nanotechnology, being one of such technologies, and its biomedical potential, has always fascinated me. Fortunately, this summer I have the opportunity to both synthesize and characterize one such particular type of bio-nanomaterial for my project. The research process has been truly rewarding: through bits and bits of data collection and analysis, not only have I learned the technical details in my fields, but also how to approach problems critically. I want to thank Dr. Narayanaswami for her patient guidance as well as this wonderful opportunity for me to explore my interests in both the fields of biochemistry and nanomaterials and combine them into something that may have plausible biomedical applications. The summer research program has definitely reaffirmed my decision to pursue a further education in science.

Funded by: National Institutes of Health

School: California State University, Long Beach

Mentor: Vasanthy Narayanaswami, Ph.D.

Contributing Author: Young-Seok Shon

Title:
The role of apoE-coated gold nanoparticles as a potential drug delivery system

Introduction:
Cancer is the second most common cause of death, responsible for nearly one in four deaths in the U.S. One way to treat cancer effectively is through a targeted drug delivery system exploiting the observation that tumor cells over-express the low density lipoprotein receptor (LDLr). Apolipoprotein E3 (apoE3) is a common plasma apolipoprotein that binds to LDLr with high affinity. We propose to generate apoE coated gold nanoparticles (ECGNP) as potential drug delivery vehicles for treating cancer. Gold nanoparticles are inorganic materials capable of inducing localized hyperthermia, thereby limiting tumor growth.

Objective:
Our objective is to synthesize ECGNP using 3, 10, and 17nm gold nanoparticles and to perform biophysical and biochemical characterization of the particles.

Methods:
ApoE3 was over-expressed in *E. coli* and purified by affinity chromatography. Gold nanoparticles (3, 10, and 17nm) were synthesized from colloidal gold and thiol ligands using established protocols. ApoE3 was conjugated to the gold nanoparticles through cycles of sonication and incubation, forming ECGNP. Ultraviolet-visible (UV-VIS) spectroscopy was used to confirm the presence of apoE3 on the gold nanoparticles. Size and diameter of ECGNP will be determined using transmission electron microscopy (TEM) by staining with uranyl acetate. Finally, the binding of ECGNP to the LDLr will be assessed by performing coimmunoprecipitation (Co-IP) assay.

Results & Expected Outcome:
ECGNP bearing 3, 10, and 17nm gold nanoparticles were successfully synthesized. ^{1}H-NMR confirmed the presence of the thiol ligands on the 3 and 10nm gold nanoparticles. Successful conjugation was confirmed by a red shift in the surface plasmon band in the UV-VIS spectra of ECGNP. We anticipate the TEM results will confirm the geometry and size of ECGNP. Further, we expect the ECGNP to bind to the LDLr in Co-IP assay.

Significance & Conclusion
Bioconjugation of nanoparticles is an emerging field of nanotechnology. Our approach will combine the power of LDLr binding of apoE3 with the heat-emitting property of gold nanoparticles to serve as nontraditional cancer therapy.

Keywords:
apoE, gold nanoparticles, cancer, drug delivery

Dulce Cruz

Hi my name is Dulce Cruz and I am going to be a senior at Oakland High School. My love for science grew in freshmen year when I started taking Biology. My perspective career is to become a veterinarian and major in biology. This is my first time having a research experience and I am thankful. The reason I chose to be in CHORI summer research program is because I wanted to get experience on how it felt like and by any chance see if by the end of this summer I would change my mind about my career. I got the chance to work with a wonderful mentor that works at the Children's Oakland Hospital Teen Clinic. I also got to work with some of the staff from the CHAMPS program. I would like to thank Barbara, Young and Michelle for their help and support throughout the program.

Funded by: Doris Duke Charitable Foundation

School: Oakland High School

Mentor: Barbara Staggers, M.D., MPH, FAAP

Title:
Teen Drug Abuse

Introduction:
Teens using and abusing drugs is becoming a big issue in health and producing consequences that harm others as well. The main drugs used and abused by teens is marijuana, electronic cigarettes, methamphetamine, bath salts, inhalants, prescription drugs, cocaine, spice, alcohol, ecstasy and tobacco. According to NIDA, the ones that used it the most is between 8th graders and 12th graders. The high school dropouts are really high which lowers the percentage of people to get careers in the future. The statistics say that the percent that manage to graduate and go to college from the Oakland Unified School District is 42.3 %. Some teens are not aware of the consequences of using drugs which makes them think it is safe to use them.

Objectives/Hypothesis:
The first specific aim is I want to conduct a survey for Oakland youth using a minimum sample size of 50 to see what type of drugs they use and how often. The second specific aim is to see if teenagers are aware of the effects of using drugs. The third aim is to see the reasons teenagers use drugs. I am guessing that if I survey teenagers, then approximately 40% of the students will admit to using drugs.

Methods:
The methods I plan to use for this project are making a series of surveys. The survey is going to be in paper and anonymously with approximately 10 or more questions. My target for this survey is going to be teens in the Oakland Public Library Teen Zone and Mills College Upward Bound summer students or Oakland Children's Hospital Teen Clinic. The survey targets teens between the ages 13-18 and my goal is to have at least 50 people to fill out the survey. Even though the target is for Oakland and I can include Richmond as well. The second method that I am doing is a literature research. I will compile data of the surveys and see if my hypothesis is true.

Results / Anticipated Outcome:
The outcome for this project is that I am going to learn why youth in Oakland use drugs, who uses drugs and the drugs they use. When I get my data, I think about putting all the information together to make a presentation to middle and high schoolers about drug abuse.

Siobanth Cruz

My name is Siobanth Cruz and I am enrolled in California State University, Long Beach, majoring in Biochemistry. I have always had an interest in science, both inside and outside of the classroom. Joining Dr. Narayanaswami's lab has given me the exposure to how professional research is conducted. Research has allowed me to hone my problem solving skills and continue my pursuit of knowledge. Research is filled with highs and lows and it is in times when things do not go according to plan when I learn the most about the field and drives me to keep going and succeed. My future plan is to go on to graduate school and hope to make a contribution that keeps advancing the scientific field.

Funded by: National Institutes of Health

School: California State University, Long Beach

Mentor: Vasanthy Narayanaswami, Ph.D.

Contributing Author: Sea H. Kim

Title:
Development of reconstituted HDL containing apoE for transport and delivery of luteolin, an anti-inflammatory agent

Introduction:
Inflammation plays a key role in cardiovascular disease and cancer. Our overall goal is to understand the role of luteolin, a flavonoid, as an anti-inflammatory and anti-oxidant agent and to effectively deliver luteolin to target cells. Flavonoids are found in a number of plants and fruits and bear strong antioxidant property, which was initially thought to be the main mechanism of which they reduced the risk of cardiovascular disease, diabetes and certain types of cancer. Luteolin has been shown to inhibit inflammatory cytokine release in macrophages and proinflammatory enzymes.

Hypothesis:
We hypothesize that apolipoprotein E3 (apoE3)-containing HDL will be an efficient transporter of luteolin in the plasma and across the cellular membrane via the low density lipoprotein receptor (LDLr).

Methods:
Reconstituted HDL (rHDL) was prepared by combining phospholipids and recombinant human apoE3 (1-191) in the absence or presence of luteolin followed by density gradient ultracentrifugation. Fluorescence spectroscopy was carried out to determine the presence of luteolin in rHDL. SDS-PAGE and Western blot analysis were performed to confirm the presence of apoE3 in the rHDL. Non-denaturing PAGE was carried out to assess the molecular mass and diameter of rHDL bearing luteolin. Co-immunoprecipitation analysis was performed to test the LDLr binding ability of rHDL containing luteolin.

Results:
Western blot analysis revealed a 24kDa band in rHDL preparations with or without luteolin indicative of the presence of apoE3 (1-191). Non-denaturing PAGE of rHDL shows the formation of large lipoprotein complexes (~700kDa, ~20 nm diameter). Fluorescence spectroscopic measurements of free luteolin display an emission maximum at 525 nm. In the presence of rHDL an additional blue shifted peak was observed at 486 nm indicative of a highly hydrophobic environment for luteolin such as that in the interior of rHDL. We anticipate that rHDL containing luteolin will retain the ability to bind the LDLr.

Conclusion:
We have successfully incorporated luteolin into rHDL containing apoE3. The significance of our findings is that rHDL may be an effective transporter of luteolin in the plasma and across cell membranes.

Keywords:
Reconstituted HDL, luteolin, anti-inflammatory

Karina Duarte

I am currently a rising senior at Saint Joseph Notre Dame High School in Alameda. Ever since I was a little kid I knew I had a passion for science whether it was helping my older sister with anatomy homework to watching the discovery channel with my dad. This passion that began years ago continued to flourish as time went on. This is what led me to applying to CHORI initially. I want this experience to further my knowledge in science and eventually guide me to making my career choice later on. In the short amount of time that I have been at CHORI I have been immersed into what life is like working in a lab. Everything is hands-on and I am enjoying every moment. I am so thankful to have this opportunity and being able to spend my summer at CHORI.

Funded by: California Institute for Regenerative Medicine

School: St. Joseph Notre Dame High School

Mentors: Michael Conboy, Ph.D., Wendy Cousin, Ph.D.

Title:
Muscle regenerative properties of oxytocin in female mice

Background:
A recent paper was published showing evidence that the hormone oxytocin (OT) plays a role in the regenerative properties of skeletal muscle in male mice. Yet before OT could be used in clinical trials it would have to be tested to see if it has the same affect on female mice as well. My research involves mice KO for oxytocin (OT KO mice) and their wild type littermates (WT) and comparing how well the muscle is able to regenerate itself. Mice are injured with cardiotoxin and time will be allotted to allow the muscle to regenerate. The left leg is injured five days before euthanasia, while the right leg is injured three days before euthanasia. These time points are specifically chosen to assess muscle cells proliferation (3 days) and muscle regeneration (5 days). The injured tibialis anterior (TA) and gastrocnemius (GA) muscles are harvested and sectioned using a cryostat. To evaluate muscle regeneration, the 10 micrometers thick sections are then analyzed by histology counting the amount of myofibers with centrally located nuclei per millimeter square of muscle injury.

Hypothesis:

Oxytocin is a necessary peptide for muscle maintenance and regeneration in female mice as it is in male mice.

Anticipated outcomes:
We anticipate the female WT to have a larger amount of newly formed muscle fibers in comparison to the OT KO mice. To assess muscle stem cell activation/proliferation, sections will be immunostained for desmin (a myogenic marker) and BrdU (to monitor dividing cells). We expect a larger amount of proliferating myogenic progenitors in the WT than the OT KO female mice. Since the population in people over the age of 60 is rapidly increasing it is crucial that we are able to improve as many aspects to the quality of their life as possible. This study can lead to a breakthrough in treating and possibly healing injuries at a quicker rate in those that are older, regardless of gender.

Kathryn Echavia

My name is Kathryn Echavia and I will be entering my senior year at Claremont McKenna College in the fall. As a Science and Management major, I focus on the dynamic interaction of biotechnology and economics, and aspire to become a physician. During the academic year I volunteer in the Neonatal Intensive Care Unit at Pomona Valley Hospital Medical Center, which has furthered my love for medicine and instilled in me the importance of patient care and advances in the biomedical field. The CHORI summer program has helped me explore the connection between biotechnology and patient care while providing firsthand laboratory experience and unprecedented involvement in cystic fibrosis research.
I would like to thank my mentors, Dr. Fischer and Dr. Illek, my lab teammates, Elleanor Pangilinan and Gopika Hari, as well as CHORI and the Elizabeth Nash Foundation for making this summer experience possible.

Funded by: The Elizabeth Nash Foundation

School: Claremont McKenna College

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

Title:
Treatment of Bacterial Infections in Cystic Fibrosis

Contributing Authors:
Horst Fischer, Ph.D., Beate Illek Ph.D.

Introduction:
Cystic fibrosis (CF) is one of the most common genetic diseases occurring in childhood affecting 70,000 people worldwide. Lung infection with a common bacterium called *Pseudomonas aeruginosa* is the major cause of disease and death in young adults with CF. By age 6-10 years, 40% of CF children are already infected. A mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene results in impaired anion transport for chloride and other anions such as, bicarbonate and iodide, leading to sticky mucus secretions that clog the respiratory system. The secretion of HCO_3^-, maintains airway surface liquid (ASL) at a near-neutral pH in healthy lungs, whereas defective HCO_3^- production lowers airway ASL pH that may affect its bactericidal properties. Our working hypothesis is that the reduced ASL pH affects the proper function of the lactoperoxidase (LPO) airway defense mechanism, which mediates the oxidation of iodide, producing bactericidal hypoiodite. Restoration of the proper function of the lactoperoxidase mechanism may delay the onset of bacterial infection in CF lungs.

Objective:
The present study will investigate the role of pH on bactericidal activity, the role of CFTR in iodide transport, and how fluctuations in ASL pH may mediate bacterial proliferation, in the hopes that pH alteration can restore the LPO defense mechanism impaired in CF lungs. Methods: Cystic fibrosis bronchial epithelial cell lines, as well as primary cells will be used as airway cell models for CF. The Ussing chamber assay will be used to measure iodide transport. Confocal microscopy will be used to assess bacterial growth of Pseudomonas aeruginosa at different pH levels. Outcomes: Transepithelial iodide transport was not stimulated by CFTR activators (forskolin, VX-770) in CF airway cells. Bacterial growth of Pseudomonas aeruginosa was affected by acidic ASL pH.

Acknowledgements:
Elizabeth Nash Foundation, CHORI

Keywords:
cystic fibrosis, iodide transport, bactericidal activity

Farhana Haque

Coming from a family without much scientific background, I made a quest to delve into the mysteries of science early on in life. What fascinated me the most was human anatomy and its emphasis on understanding the mechanisms that are integral to the functioning of the human body. Intrigued by this, I took in-class experiments very seriously knowing that the more dissections I participated in, the more competent I would be as a surgeon. Though being a surgeon is no longer my aspiration, I have since gained a sturdy scientific platform I wish to utilize in my future career. I am immensely grateful to CHORI for allowing me to pursue my goal of expanding and applying my knowledge to the real world. Furthermore, I would like to thank my mentors Dr. Mike Conboy and Dr. Wendy Cousin for giving me a summer full of fascinating investigations and experiences I will never forget!

Funded by: Volunteer

School: Milpitas High School

Mentor: Michael Conboy, Ph.D.

Title:
A Trigger to Muscle Cell Regeneration: Effect of Individual Fibroblast Growth Factors on Activation of Skeletal Muscle Cells

Contributing Authors:
Alefia Kothambawala, Mike Conboy Ph.D.

Introduction:
After muscle injury, parts of muscle fibers die off and are left with a functional void. Quiescent satellite cells, which are distributed along the muscle fiber, give rise to replacement myoblasts by exiting the G0 phase of the cell cycle and proliferating. Regenerated muscle is not from just the amount of satellite cells that are available, but from the amount of activation and proliferation a satellite cell undergoes. Therefore, to investigate what can trigger such abundant proliferation can lead to answers on what causes the most muscle cell regeneration and repair to tissue injury. Recent experiments have shown how fibroblast growth factors (FGFs) have been able to trigger satellite cells to eventually proliferate and replace damaged tissue.

Objectives:
We seek to study FGF-2 and FGF-19 to determine which has the better potential for satellite cell activation and, thus, have a bigger impact on muscle cell regeneration.

Methods:
Cells used for this assay will be satellite cells extracted from adult mice and cultured in the test FGFs without other growth factors. Bromodeoxyuridine (BrdU) will be added to label activated and proliferating cells. The satellite cells will be immunostained with two antibodies: anti-BrdU, anti-desmin to show if a cell is a myoblast, and Hoechst will indicate all nuclei (to confirm whether something is a cell). We will use a florescent microscope to analyze one hundred cells for each condition and determine which cells are myoblasts and are proliferating.

Anticipated Outcome:
We anticipate FGF-2 treatment will produce the most cells that are both myoblasts as well as proliferating. Furthermore, we predict that one hundred cells will be an adequate number to evaluate whether the quantitative data collected in this study is, indeed, statistically significant.

Keywords:
stem cells, sarcopenia, aging, muscular dystrophy

Gopika Hari

My name is Gopika Hari and I will be a rising senior at Cupertino High School. The CHORI summer program has given me a great firsthand glimpse into biomedical research and the laboratory environment. Having worked with a cystic fibrosis organization for 4 years and having interacted with several CF patients, it really meant a lot to contribute to the work currently being done. I'd like to thank Dr. Illek and Dr. Fischer for their mentorship and passion for CF research, as well as my amazing lab members Katie and Elleanor. I'd also like to thank the Elizabeth Nash Foundation for their continued support of research and student education. I've really started to understand that medical science is a collaborative effort, and I'm grateful that I had a chance to join a team so committed to fostering stronger and healthier lives.

Funded by: The Elizabeth Nash Foundation

School: Cupertino High School

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

Title:
Impact of the *Aspergillus fumigatus*-derived Gliotoxin on Airway Health

Contributing Authors:
Horst Fischer, Ph.D., Beate Illek Ph.D.

Introduction:
Cystic fibrosis is an autosomal recessive disorder affecting over 70,000 patients worldwide. Of the many organs affected, the lungs are especially damaged due to inflammation. Fungi such as *Aspergillus fumigatus*, which affects close to 50% of all CF patients at a given time, contribute significantly to progression of damage. Gliotoxin is a specific immunosuppressive mycotoxin produced by *A. fumigatus* – while it has been shown to induce apoptosis in leukocytes, its role in airway epithelia physiology is still under examination. Cyclodextrin, a cholesterol-depleting agent involved in lipid-raft disruption, has been recently shown protective effects during bacteria-mediated epithelial barrier breakdown and thus has potential for similar effects in the presence of fungus-derived products.

Objective:
To determine the impact of gliotoxin on transepithelial resistance, a measure of tight junction integrity, in CF and CFTR-corrected bronchial epithelial cell monolayers. Additionally, cyclodextrin will be tested as a possible protective compound in gliotoxin-mediated airway epithelial cell damage.

Methods:
CF and CFTR-corrected CF bronchial epithelial cell lines will be used. Ussing Assays an EVOM meter will be applied to measure time-dependent and concentration-dependent effects of gliotoxin. Furthermore, confocal microscopy will be used to visually assess the distribution of the tight junction protein zonula-occuldens (ZO-1) in response to gliotoxin.

Outcomes:
Addition of gliotoxin to the apical surface of airway epithelial cells decreased transepithelial resistance 17-fold in CFTR-corrected cells and 36-fold in CF cells (n=2), indicating that CF cells are experiencing more epithelial barrier breakdown than CFTR-corrected cells. It is expected that cyclodextrin may have some protective effects against tight junction breakdown.

Acknowledgments:
Elizabeth Nash Foundation, CHORI

Keywords:
Cystic Fibrosis, gliotoxin, transepithelial resistance

Catherine Hou

I will be a senior at Mission San Jose High School. I have always loved science and I know I want a career in medicine; however, I have been struggling to decide between becoming a physician or researcher. Working in the Red Blood Cell lab at CHORI, I have learned how medically relevant the research that Dr. Kuypers has led me to do is. It has been exciting, as it combines my two interests in the medical field into one. I am really thankful for my mentors Frans Kuypers and Sandra Larkin, for teaching me so much in such a short amount of time. They've encouraged me to ask questions and patiently lead me to find my own answers. I really enjoy being in such a supportive and nurturing environment! Being free to ask as many questions as I want has been liberating, and I enjoy research so much because of that freedom. I owe CHORI, my mentors, and my lab-mates all my gratitude for giving me such amazing experiences.

Funded by: Private Donor

School: Mission San Jose High School

Mentor: Frans Kuypers, Ph.D.

Title:
Comparing the Specific Activity of Secretory Phospholipase A_2 with Lipoprotein Metabolism and Cholesterol Levels in Sickle Cell Disease Patients

Introduction:
Sickle Cell Disease (SCD) is a genetic blood disorder characterized by sickle-shaped red blood cells (RBC). Hemoglobin polymerization, which causes the RBCs to sickle, reduces cell flexibility, causing issues in small vasculature like capillaries. SCD results from a point mutation in the hemoglobin gene and affects all organs in the patient. The normal RBC plasma membrane is renewed by the Lands pathway, which deacylates and reacylates the phospholipids to maintain membrane integrity. However, in SCD, mutated ß-hemoglobin results in a dysfunctional Lands pathway, causing the loss of RBC membrane integrity.

Objective:
We hypothesize that because of the Lands pathway and RBC membrane system, the lipoprotein system may be affected by the sickle hemoglobin. In SCD patients, the blood contains an elevated level of secretory phospholipase A_2 ($sPLA_2$). We hypothesize that both the lipoprotein system and the $sPLA_2$ levels are influenced by SCD, so we also hypothesize that there is a relationship between $sPLA_2$ levels and imbalanced lipoprotein metabolism. We will measure and compare the specific activity and concentration of $sPLA_2$. Then we will look for a correlation between $sPLA_2$ levels and altered lipid protein metabolism.

Anticipated Outcomes:
I expect a correlation between the level of plasma lipoprotein metabolism and $sPLA_2$ levels throughout the samples. It is believed that lipoproteins and RBC membranes are interrelated, that lipoproteins help regulate RBC protein activity in SCD. Logically, changes in lipoproteins would affect the membranes of the cells. Since LCAT and $sPLA_2$ both cleave the phospholipids, the lab suspects that they are related, which implies lipoprotein and RBC membrane alterations would affect both. A damaged RBC membrane leads to a dysfunctional Lands pathway, damaging the lipoprotein system. Therefore, if the level of plasma cholesterol LCAT activity and other components of lipoprotein metabolism is altered, $sPLA_2$ activity would too.

Acknowledgements:
I'd like to thank Frans Kuypers and Sandra Larkin for the time and patience they devoted to mentoring me. Thank you also to Gloria Tung and Eric Soupene for their assistance with equipment and wonderful advice. Finally, thank you to CHORI for giving me such an incredible and unique opportunity this summer.

Keywords:
Sickle Cell Disease, lipoprotein, sPLA2, Lands pathway

Sebastian Hurtado

My name is Sebastian Hurtado and I am a rising senior at Bishop O'Dowd High School in Oakland. My affinity for the sciences really came into fruition as I developed an interest in the study of the human body during school. Having an interest in medicine, specifically pediatrics and surgery, allows me to indulge in the complexity of the human body while having the opportunity to interact and serve real people. I am so grateful for the opportunity to participate at one of our nation's most acclaimed research/clinical facilities. I would like to thank the coordinators of CHORI who have put so much effort in giving high school students like me the chance to gain insight into the medical field and who have helped kindle our interests. I would also like to thank my mentor, Dr. Wendy Su, for the time and energy she has given to making my research memorable, as well as a past student and good friend, Caroline Desler, for informing me on this exceptional internship. I look forward to use my internship at CHORI as a foundation of experience for my career aspirations in improving global health for the children of the world. I will one day look back on CHORI as the spark that pushed me forward in my path towards medicine.

Funded by: Doris Duke Charitable Foundation

School: Bishop O'Dowd High School

Mentor: Wendy Su, M.D.

Title:
Pancreatic Neoplasms in Children: Review of Institutional Experience and Literature

Introduction:
Neoplasms, or abnormal cell growths of the pancreas are very rare maladies in the pediatric population. The four most common pancreatic tumors include: pancreatoblastomas; solid pseudopapillary tumors/ Frantz's tumors; pancreatic neuroendocrine neoplasms; and pancreatic ductal adenocarcinomas, all of which can be seen using ultrasonography, MRI, and CT scans. The presenting symptoms often arise from incidental findings in asymptomatic patients and include jaundice, weight loss, abdominal, and/or gastro-intestinal pain. The most common treatments include surgical resection, pancreaticoduodenectomy, and partial/distal pancreatectomy. Finally, the prognosis of children with pancreatic neoplasms is much better than the prognosis of adults; the majority of adults (80%) do not typically live past 6 months to 1 year after diagnosis (Cancer Research UK Statistics).

Objectives:
The management and outcome of pancreatic neoplasms are not well understood by the general medical community, so it is beneficial to give the public a better understanding of these rare neoplasms to improve primary care consultations and treatment. Specifically, we aim to hope to create an easily accessible database for primary care physicians to expand public understanding of the rare disease.

Methods:
We will review the institutional databases of Children's Hospital of Oakland's Electronic Medical Record, Meditech, and EPIC systems. Literature from medical journals on specific experiences in various countries will also be reviewed. We will then review diagnosis and treatment of pancreatic neoplasms from the national medical database Kid's Inpatient Database (KID) from the Healthcare Cost and Utilization Project. After conducting this retrospective analysis of the past 20 years and analyzing the results, we will create spreadsheets to synthesize collected data and represent statistical trends in an organized form, using descriptive statistics/tables. We also plan to examine pathology slides derived from pancreatic neoplasms under the microscope to better understand the histology of the disease.

Anticipated Outcomes:
Through our research, we hope to learn more about pancreatic neoplasms and gain a better understanding of the rare disease, examine the histology of the tumor types, identify typical outcomes from certain tumor types, and verify trends between tumor types and patients. Specifically, we believe there will be a verified correlation between females and SPTs and a consistent trend between patients of non-Caucasian races and SPTs. We also believe the majority (>75%) of patients found in databases will have survived without a reoccurrence of the disease, and that patients with SPTs will have had them situated on either the head or the body of the pancreas. We estimate that only around 10 patients from Children's Hospital of Oakland will have suffered from pancreatic neoplasms in the past 20 years.

Keywords:
pancreas, neoplasms, pancreatoblastoma, solid pseudopapillary tumor, pancreatic neuroendocrine neoplasms, pancreatic ductal adenocarcinoma, pediatrics

Judy Kang

As a lover of science, I wanted to expose myself to branches of biology other than medicine. To achieve this, I applied to the CHORI summer internship program. I am a rising senior at Dougherty Valley High School and the CHORI internship is my first work experience. Working as an intern requires that I apply knowledge learned from textbooks to more recent research topics. Experimenting in the lab and learning specifically about lipids, proteins, and stem cells has enlightened me and revealed that almost everything in science is connected, unrestrained by the different chapters portioned by textbooks. This program not only increased my curiosity for lab science, but it also made me realize the importance of organization since science is a self correcting endeavor. Nevertheless, I had an amazing time working here, and I am truly grateful for being under the tutelage of Drs. Ryan and Lalefar as well as my lab mates Jennifer, Aparna, and Nick. I appreciate the patience they have shown to me, which increased my love for science.

Funded by: California Institute for Regenerative Medicine

School: Dougherty Valley High School

Mentors: Robert Ryan, Ph.D., Nahal Lalefar, M.D.

Title:
Optimization of Hematopoietic Stem Cell Expansion Induced by the Wnt Morphogen

Introduction:
Hematopoietic stem cells (HSC) are a special type of stem cell that have the ability to differentiate into any type of blood cell. Administration of these cells could potentially replace damaged or destroyed HSC in a patient with leukemia, for example. HSC's, however, are difficult to culture in an external environment, and generally do not yield sufficient HSC's to perform a bone marrow transplant. Scientists have recently discovered a Wnt protein that induces stem cells to self-renew and proliferate. However, the Wnt protein is not soluble in aqueous solutions, causing it to degrade if it is not in a stable environment. Thus, scientists have been incorporating the Wnt protein onto detergent micelles. Recently, our lab has created nanodisks, a piece of phospholipid membrane with apolipoprotein A-1 (ApoA-1) bound around it for stability. We hypothesize that nanodisks can stabilize Wnt proteins in aqueous environments.

Statement of Hypothesis:
Wnt incorporation into nanodisk complexes will induce greater stem cell expansion in vitro than conventional Wnt detergent micelles.

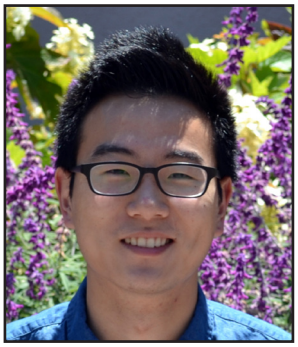
Methods:
To compare the abilities of Wnt nanodisks versus Wnt detergent micelles, samples of each will need to be acquired. The Wnt detergent micelles are already in the Ryan lab stocks, so only the Wnt nanodisks will need to be prepared. To generate the Wnt nanodisks, I will synthesize an ApoA-1 protein through bacterial transformation and protein purification, and then bind the ApoA-1 protein to lipid membranes in the presence and absence of Wnt. To test the two Wnt samples, HSC will be extracted from bone marrow of mice and incubated with Wnt on nanodisks and Wnt on detergent micelles. To compare the growth, I will perform a ß-catenin assay to measure the extent of the Wnt signaling pathway.

Anticipated Outcomes:
We anticipate that the Wnt nanodisk will yield a comparable level of stem cell proliferation as the Wnt detergent micelle. The nanodisk is hypothesized to provide a more favorable environment for the Wnt protein, which we hope will maximize its activity to regulate stem cell proliferation.

Acknowledgements:
Dr. Nahal Lalefar, Dr. Robert Ryan, Dr. Andrzej Witkowski, Jennifer Beckstead, Aparna Krishnamoorthy, Nick Ikon

Keywords:
Hematopoietic Stem Cells, Wnt Protein, Nanodisk, Wnt Detergent Micelle

Elijah Kim



Getting into the thick of an experience is the best way to learn about it. An epidemic arises, and within a year or so, the science and health community abates the disease. Cause and effect. Research is a kind of crossroad of cause and effect, where thought meets application. We may read about a disease in a textbook, and revel in its eradication on the news. But it is difficult to understand what processes really need to occur for biomedical advancements to take place.
Recently graduated from UC Berkeley, my career here at CHORI began as a freshman volunteer in the Ames lab. Working directly under my mentor, Dr. Shenvi, I have been able to explore that bridge between disease and solution. As a medical school applicant, my time at CHORI has truly been eye-opening to the contributions of research to the community.

Funded by: Volunteer

School: University of California, Berkeley

Mentors: Janet King, Ph.D., David Killilea, Ph.D., Swapna Shevi, Ph.D.

Other Contributing Members:
Jenny Nguyen, Judi Abegania, Alisa Goldrich, Darryl Chow

Title:
Use of Fpg-modified Comet Assay to determine extent of oxidized purines in DNA of men with inadequate dietary zinc

Introduction:
A study done by our group has shown that DNA damage varies with manipulation of dietary zinc levels. DNA damage was measured through single and double strand breaks by the Comet Assay, also known as Single Cell Gel Electrophoresis. DNA damage can theoretically be caused by both damage and repair. While the Comet Assay measures overall DNA breaks, in its current form, it lacks the ability to distinguish between causes of these breaks. However, it has been previously shown that zinc acts as an important regulator in the redox balance within cells (Oteiza 2012). Therefore, it is reasonable to hypothesize that some part of the observed DNA damage can be attributed to oxidation. In order to make the Comet Assay sensitive to detecting oxidized purines, certain enzymes can be added. The formamidopyrimidine glycosylase (Fpg) enzyme is added as a lesion-specific enzyme to produce breaks at the site of oxidized purines, the damage of interest. These breaks can then be detected by the Comet Assay.

Methods:
Cryopreserved whole blood samples are thawed, spun, and then diluted. The cells are mixed with agarose and put onto slides. The cells are lysed, and then washed with Fpg enzyme buffer. The slides are incubated with Fpg enzyme and subsequently electrophoresed.
The slides are dyed using SYBr Green and visualized under a fluorescent lamp microscope. Their images are analyzed using a comet analysis software. Each sample's subsequent comet tail DNA and Olive Tail Moments are exclusively scrutinized as a measure of DNA damage. Higher values correlate to higher levels of DNA damage.

Objective:
To use the Fpg-modified Comet Assay to assess the extent of oxidized purines in the white blood cell DNA of men at different levels of dietary zinc consumption.

Anticipated Outcome:
Based on the crucial role of zinc in redox regulation, we anticipate that zinc depletion will result in an increase of oxidized purines as detected by the Fpg-Comet Assay.

Alefia Kothambawala

My name is Alefia Kothambawala and I will be a rising senior at Milpitas High School. Throughout my life, I have had a fascination with science, always wanting to find out more about how the world works. I find it amazing how the human body comes together in parts to produce one harmonic machine. Different frames, shapes, and roles coalesce to form a beautifully functioning system. It is these numbers of combinations that I would like to decipher, for they help unveil new knowledge that many revolutionize the field of medicine and technology. After graduation, I plan to major in biomedical engineering, and then go to either medical or business school. I have always preferred to be engaged in hands-on research based work as opposed sedentary tasks, and I would like to thank Dr. Michael Conboy, Dr. Wendy Cousins, and CHORI for allowing me to do just that this summer.

Funded by: Volunteer

School: Milpitas High School

Mentor: Micheal Conboy, Ph.D.

Title:
Role of Individual Fibroblast Growth Factors in the Activation of Skeletal Muscle Cells

Introduction:
As tissues degenerate with age, they cannot regenerate as easily as in the past. Muscle stem cells (satellite cells) become unresponsive to injury and so must be triggered externally to proliferate, which we hypothesize can be done using fibroblast growth factors (FGFs). FGFs are key players in the processes of cell proliferation, cell differentiation, and morphogenetic events and are expressed widely in embryonic, fetal, and adult life.

Objective:
We seek to determine whether quiescent satellite cells will activate and proliferate from atypical FGF signaling (FGF-6 or FGF-19), thus propelling the cells out of the G0 phase of the cell cycle.

Methods:
Cells used for these assays will be adult mouse muscle satellite cells that have yet to proliferate. We will use an assay to determine which cells are proliferating by seeing if they take up bromodeoxyuridine (BrdU), a thymine analog. Two controls will be set up: a positive control (F10+ 20% serum+ BFGE), and a negative control (1% serum + basal medium), with FGF-2 and FGF-19 as experimental conditions. Also, the cells will be stained with desmin, a protein that forms the intermediate filaments of muscle cells, to confirm whether they are myogenic in origin.

Results:
The positive control had the greatest number of satellite cells that were actively proliferating (61%), while the negative control had the least amount (32%). In addition, the FGF-2 and FGF-19 conditions had 53% and 45% of cells that were proliferating respectively. Also, through statistical analysis, we determined that our results were statistically significant, with little chance variation occurring between samples.

Conclusion:
We conclude that FGF-2 and FGF-19 are potential activators of the muscle regeneration machinery, stimulating satellite cells from the G0 phase and causing them to proliferate.

Acknowledgements:
I would like to give my sincerest thanks to Dr. Michael Conboy for his instruction as well as the use of his lab. In addition, I would like to thank Dr. Wendy Cousin for her kind support and involvement despite her busy schedule. Lastly, I am grateful towards Prasana for serving as a guide through the details of the experimental procedure.

Keywords:
cell cycle, aging, sarcopenia

Mallika Lal

My name is Mallika Lal and I am a rising junior at UC Berkeley currently studying Molecular and Cell Biology, with an emphasis on cell and developmental biology. Prior exposure to the field of public health through research and coursework propelled my interest in the area and led me to work in the LaBeaud lab this summer. I have had the opportunity to not only learn new molecular techniques, but also to develop my confidence in all aspects of research, from scientific writing to data presentation. Learning about global health and the burden of disease in developing countries has been both interesting and eye opening. This summer has inspired me to continue learning about infectious disease and pursue this field in the future. I would like to thank Desiree LaBeaud, David Vu, Claire Heath, Patricia Zuno-Mitchell, and Monica Nayakwadi-Singer for mentoring me and making this summer such a rewarding experience.

Funded by: Volunteer

School: University of California, Berkeley

Mentor: Desiree LaBeaud, M.D.

Contributing Authors:
David Vu, M.D., Patricia-Zuno Mitchell

Title:
Age-related Acquisition of Natural Anti-pneumococcal Antibody in Kenya

Introduction:
Streptococcus pneumoniae (pneumococcus) is a Gram-positive bacterium that is a leading cause of pneumonia, meningitis, and sepsis worldwide, but the burden of disease is higher in developing countries where access to effective vaccines are limited. In Kenya, routine vaccination of infants with a pneumococcal polysaccharide-protein conjugate vaccine (PCV) began in 2011. Based on published data from studies in other countries, PCV vaccination is expected to be effective in reducing the incidence of pneumococcal disease in both vaccinated and unvaccinated individuals, likely due to reduced exposure of unvaccinated persons to strains with serotypes matching those contained in the vaccine. Our goal was to estimate exposure of residents of a single village in Kenya to different pneumococcal strains before initiation of routine immunization of infants by measuring serum anti-pneumococcal polysaccharide antibody as a surrogate for exposure.

Objective:
To characterize the natural acquisition of anti-pneumococcal antibody in serum samples from individuals of different ages from a single Kenyan village prior to initiation of routine pneumococcal vaccination of infants.

Methods:
Stored serum samples were available that had been collected between 2009 and 2010. For the present study, we chose a convenience sample based on residence of the subject in the same single village at the time of blood collection, availability of sufficient volumes of serum for our assays, and age with the goal to assay approximately 5 subjects per 5-year age group between 1 and 90 years (18 groups). Serum anti-pneumococcal antibody concentrations were measured using a novel sample-sparing multiplex assay that utilized fluorescent microspheres.

Expected outcome:
Based on previous epidemiologic studies, pneumococcal serotypes 19F, 6B, and 9V have caused more invasive disease in Kenya and therefore we anticipate measuring higher antibody levels against these particular serotypes. We expect most age groups will be exposed to pneumococci and that there may be no age-related differences in serum anti-pneumococcal antibody concentrations.

Keywords:
pneumococcus, pneumococcal polysaccharides

Destinee Lanns

My name is Destinee Lanns and I am a current student at SF State, where I study Biology concentrated in Physiology. Ever since I was young, I always had some interest in biology but after the birth of my younger sister Miracle, who has a life threatening disability; my love for science grew even stronger. I say proudly, Miracle plays a major role in my dreams and aspirations. Because of her and my passion for helping others, she has inspired me to be a gynecologist. I want to bring life into this world of opportunity, as well as coach mothers through their pregnancy. Having a sister like Miracle enhances my feelings about preserving life and all of its multiplicities. Being able to participate in the summer research intern program through CHORI is a blessing for me because it has given me an opportunity to broaden my knowledge in research, an area that I never explored before. I would like to thank CHORI and the Oda lab for providing me with a great learning experience that will help me in my future endeavors.

Funded by: Private Donor

School: San Francisco State University

Mentor: Michael Oda, Ph.D., Mark Borja, Ph.D.

Contributing Authors:
Mark Borja, Ph.D., Khosrow Adeli, Ph.D. (Hospital for Sick Children Toronto Canada) and Michael Oda, Ph.D.

Title:
The effect of diet-induced insulin resistance on HDL function in Syrian hamsters a model of diabetes

Introduction:
There is mounting evidence that HDL functional status is the strongest indicator of cardiovascular disease, wherein low HDL function is correlated with greater risk for cardiovascular disease. Insulin resistance and diabetes are major risk factors for cardiovascular disease. We have observed low HDL function in people with metabolic syndrome, a condition associated with insulin resistance and a precursor to diabetes. Hamsters are a good model for human insulin resistance and diabetes. Because insulin resistance can be induced fairly quickly by feeding them a high fructose diet and the resultant metabolic changes are very similar to those observed in humans, it is a highly convenient and significant model.
The Oda lab has developed a test that can determine HDL function directly in blood plasma. This test measures the exchange of lipid free Apolipoprotein A-I (apoA-I) on and off of HDL. ApoA-I is the major protein component of HDL and an important factor in HDL's function. The release of lipid-poor apoA-I from HDL is a rate-limiting step in reverse cholesterol transport, the process whereby HDL mobilizes cholesterol from tissues and returns it to the liver, kidneys and intestines for excretion. ApoA-I exchange is measured by adding lipid free spin-labeled apoA-I to a plasma sample and monitoring the degree of apoA-I association with HDL. The spin-label is a small molecule with an unpaired electron, whose mobility in solution can be detected using a technique called electron paramagnetic resonance spectroscopy (EPR). The mobility of the spin-label is representative of the lipid-free / lipid-bound state of HDL, so can provide a measure of how much apoA-I is bound to HDL by the intensity of its signal. By utilizing these tools, we investigated how HDL function is affected when insulin resistance is induced.

Objective:
We will measure HDL function in two groups of hamsters. One group was fed normal hamster chow and the other was fed a high fructose diet to induce insulin resistance. We examined the HDL function between the two groups.

Anticipated Outcomes:
We anticipated that the hamsters that were fed the high fructose diet will have lower HDL function and that the hamsters that were fed the normal chow diet will have a higher functioning HDL. This study will help us establish a baseline for the response of Syrian hamster HDL insulin resistance on HDL function.

Acknowledgements:
I would like to thank CHORI and the Oda lab for a great research opportunity.

Keywords:
HDL (high density lipoprotein), apoA-I (Apolipoprotein A-I), HDL function, hamsters and insulin resistance

Eduardo Lujan

As a child I sought explanations to questions far greater in detail than the simplistic answers I was given. By consequence, I would indulge in scientific books with the misguided hope of finding a scientist whose identity and experiences mirrored my reality. Having been raised in a working-class Hispanic family, I saw no correlation between my life and the various scientists I had come to admire.

Although disheartening, the aforementioned memory has motivated me and has allowed me to reach any endeavor I set for myself. Shortly after receiving a B.S. in Cell and Molecular Biology I was honored with the opportunity to take part in the CHORI program. My time at CHORI has been life changing; the values and people at CHORI have furthered my desire to pursue a PhD with the hope that one day I might be able to mentor and provide opportunities for other underrepresented individuals in the field of science.

Funded by: Private Donor

School: San Francisco State University

Mentors: Dan Granoff, M.D., Rolando Pajon, Ph.D.

Title:
Meningococcal native outer membrane vesicle vaccine with over-expressed Neisserial Surface Protein A

Contributing Authors:
Rolando Pajon,Ph.D., Dan M. Granoff, M.D.

Introduction:
There are no vaccines available in the U.S. against meningococcal serogroup B strains, which cause sepsis and meningitis and are responsible for ~35% of disease. The serogroup B capsule is an auto-antigen; therefore, research for a serogroup B vaccine has focused on non-capsular antigens. One promising candidate described more than 15 years ago by Brodeur and Martin, is Neisseria Surface Protein A (NspA), which is a highly conserved outer membrane protein (1). Serum anti-NspA antibodies from mice elicit complement-mediate serum bactericidal activity, which is the serologic hallmark of protection. However, for unknown reasons, in humans a recombinant NspA vaccine failed to elicit serum bactericidal antibodies (2). Recently, NspA has been shown to bind to complement Factor H (FH), in a human specific manner (3).

Hypothesis:
Binding of human FH to NspA impairs protective antibody responses. Protection can be increased by using a low FH binding mutant NspA, and by over-expressing the antigen in native outer membrane vesicles (NOMV), instead of using recombinant proteins.

Methods:
I cloned wildtype and mutant NspA (one amino acid substitution), which was then used to prepare prototype NOMV vaccines from *E.coli* expressing empty, wildtype or mutant NspA vectors. Proteins in the OMVs were visualized by SDS-PAGE, and NspA expression was measured by dot-blot using an anti-NspA mAb. Binding of human FH will be measured by ELISA and flow cytometry.

Results/Anticipated Outcomes:
The vaccines ultimately will be tested for immunogenicity in human FH transgenic mice. I anticipate that the NOMV vaccine with over-expressed mutant NspA, with decreased human FH binding, will elicit higher serum bactericidal antibody responses than the control NOMV vaccines expressing WT NspA that binds human FH, or lacking NspA.

Acknowledgements:
I'd thank Dr. Dan Granoff and Dr. Rolando Pajon for their support.

Keywords:
Neisseria Meningitidis, serogroup B, NspA, abrogated binding, increased immunogenicity.

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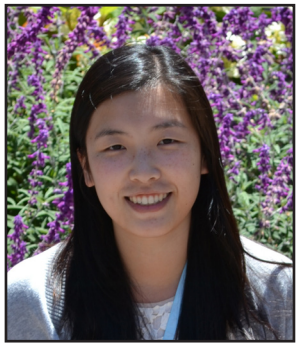
Nan Luo



Born in China, I moved to California when I was 10 years old. I'm currently an incoming senior at UC Berkeley, studying Integrative Biology. Due to family influence, I was introduced to the health field ever since I was a little kid, and I was guided in that general direction ever since. Upon entering school my interest in science also grew, and past research experience at CHORI really cemented my interest in biological science and prompted me to continue on the path to medicine. Since starting college, I have been able to explore my fascination with the human body more in depth, and deepen my understanding of human anatomy and physiology. I'm so grateful for this opportunity to come back to CHORI with more knowledge than before and to work with Dr. Ellen Fung, who has inspired me so much both in the past and the present.

Funded by: S. D. Bechtel, Jr. Foundation

School: University of California, Berkeley

Mentor: Ellen Fung, Ph.D.

Title:
Effect of Iron Chelators on Bone Health in Patients with Thalassemia

Introduction:
Thalassemia (Thal) is a genetic disorder of beta-globin chain synthesis, which leads to inadequate erythropoiesis. In its most severe form, patients with Thal require chronic blood transfusions in order to receive normal red blood cells. Patients who receive transfusion are prone to overload iron in their major organs. Because there's no natural way to excrete iron from the body apart from menstruation, those who receive transfusion therapy must depend on an exogenously administered iron chelator to remove iron from the body. The two most common iron chelators are deferasirox (DFX) and deferoxamine (DFO). Osteoporosis is prevalent in 60% of adult patients with Thal, and associated with iron overload and hypogonadism.

Objective:
To determine the impact of DFX and DFO on spine bone mineral density (BMD), and whether a reduction in spine BMD relates to an increase in vertebral abnormalities (VA) in patients receiving chelation therapy.

Methods:
This retrospective study analyzed clinical charts and dual energy X-ray absorptiometry (DXA) scans from patients with Thal who received care at CHRCO beginning in 2001 to present day. A longitudinal comparison of BMD and vertebral differences were made between patients who received DFX versus patients who either did not chelate or received DFO. Age, gender, liver iron concentration (LIC), time on chelation and hypogonadism were considered covariates in our analyses. All analyses were performed using STATA, 9.2.

Results:
Data from 94 patients with a total of 411 DXA examinations were abstracted, 48% Male, 94% ß Thalassemia. On average, patients had a spine BMD Z-score of -2.3 (range: 0.2,-5.5), and hip BMD Z-score of -1.4 (1.5, -4.1). Of the 411 examinations, 60% of the patients were prescribed DFO, 27% DFX, and 13% were not chelating. Preliminary multivariate regression analysis suggests spine BMD is predicted by younger age, increased LIC, increased yearly average units of transfused blood, and DFX use.

Future Analysis:
Data abstraction continues. Lateral spine scans will be analyzed for abnormalities and models developed to explore the effects of low BMD on VA. Though it appears deferasirox is related to higher BMD, future models must also control for time on chelation and hypogonadism.

Keywords:
Thalassemia, deferasirox, deferoxamine, bone mineral density, chelation

Acknowledgements:
Thank you to Dr. Ellen Fung for mentorship and assistance, and JR Bechtel Jr. Foundation for funding.

Isabella Maceda

My name is Isabella Maceda and, this summer, I was given the opportunity to work at CHORI with outstanding mentors. Since kindergarten, I have cherished the wonders and questions that accompany the subject of science, but my internship in the King Laboratory has allowed my love and awe of science to flourish in a way that would not be possible in a classroom. As a rising high school senior, I have begun to explore possible career and academic paths available to me. My experience, at CHORI, has greatly influenced me to seriously consider a job in the medical research field.

Funded by: Doris Duke Charitable Foundation

School: Holy Names High School

Mentors: Janet King, Ph.D., David Killilea, Ph.D., Elijah Kim, Swapna Shenvi, Ph.D., Tai Holland

Title:
Method to Analyze DNA Damage in Buccal Cells Using the Comet Assay

Introduction:
The Comet Assay is a method to measure DNA damage in individual cells. Typically, isolated leukocytes from whole blood are used in the Comet Assay. However, in this summer project, we propose to adapt this assay to cells isolated from cheek swabs (buccal cells). Unlike whole blood sampling, buccal cell procurement requires minimal training and is noninvasive, thus making buccal cells an attractive target for studying DNA damage. Buccal cells are composed of epithelial cells and leukocytes. Leukocytes are very amenable to the lysis and electrophoresis steps of the Comet Assay, which simplifies cell preparation procedures. The buccal epithelial cells, however, are extremely resistant to lysis and DNA unwinding. Thus, utilizing buccal cells in the Comet Assay requires a different cell preparation procedure with a more rigorous lysis step.

Objective:
We will develop a stronger and more effective lysis method to isolate and prepare buccal cells in a form suitable for the Comet Assay.

Methods:
In order to optimize a method for buccal cell preparation, we tested a series of lysis solutions ranging from mild to harsh and optimized cell pelleting and dilution procedures.

Results:
Our preliminary experiments indicate that we have developed an appropriate buccal cell preparation method. To validate our method, we will test multiple buccal cell samples to assess the method's reproducibility.

Conclusion
If successful, our adaptation of the Comet Assay for use with buccal swabs will provide a robust, non-invasive method to monitor DNA damage and provide a useful tool for researchers working in a field setting.

Acknowledgements:

Doris Duke Charitable Foundation
Metabolism and Nutritional Center, CHORI
Judi Abegania

Keywords:
Buccal cells, Comet Assay, Lysis, Leukocytes, DNA damage

Molly Murphy

I have known that I wanted to become a doctor and help others since I was old enough to talk. My persistence towards this goal has never wavered and therefore has leaded me to study Cellular and Molecular Biology at CSU Chico. I will be graduating next year and will continue my education further till my goal has been reached. This summer, I was lucky enough to work in the hematology lab under Frans Kuypers and Sandra Larkin, learning the mechanisms and significance of Sickle Cell Disease. I couldn't be more thankful for this opportunity to discover how genetics, cellular pathways, and the body's physiological processes are the basics for truly understanding all types of diseases or ailments. Without this knowledge and experience I couldn't be the best that I can be, and will forever be grateful for this opportunity.

Funded by: Volunteer

School: California State University, Chico

Mentor: Frans Kuypers, Ph.D.

Title:
Specific Activity of Secretory phospholipase A_2 compared with Cholesterol Levels and Lipoprotein Metabolism in Sickle Cell Disease Patients

Introduction:
The red cell plasma membrane contains a complex mixture of lipids and proteins. This organization is well maintained during its life and circulation. A process involving a deacylation/reacylation of phospholipids (commonly known as the Lands pathway) is continuously renewing the phospholipid molecular species in the plasma membrane to support the dynamic integrity of the red blood cell (RBC) membrane. Sickle Cell Disease (SCD) causes the loss of membrane integrity and proper RBC function that affects millions of individuals worldwide. SCD is caused by a single point mutation in the beta locus of the hemoglobin.

Objective:
We hypothesize that due to the abnormal functioning of RBCs in SCD patients, many other mechanisms including altered lipoprotein metabolism, increased secretory PLA_2 ($sPLA_2$) activity, and an imbalance in HDL metabolism occur as a result of the membrane and structure abnormalities. We will measure the specific activity of $sPLA_2$ in 80 plasma samples from sickle cell patients by measuring enzyme concentration and rate. The specific activity of $sPLA_2$ will be compared to the levels of cholesterol and other enzymes of lipoprotein metabolism found in the 80 samples.

Anticipated Outcomes:
I expect to see varying rates of $sPLA_2$ activity between the 80 blood samples due to the very nature that SCD affects each individual differently. We expect to see a correlation between the specific activity of $sPLA_2$ the pre-determined lipoprotein characteristics of our 80 samples. Given the sensitivity of $sPLA_2$ to membrane structure in general and cholesterol concentration specifically, it is reasonable to hypothesize that membrane cholesterol content might account, at least partially, for the difference in susceptibility of erythrocytes and lymphocytes to hydrolysis by the enzyme. I believe I will see a linear relationship between the rate of $sPLA_2$ and the level of lipoproteins reported. This is in part due to the altered functioning of the Lands Pathway due to the increased specific activity of $sPLA_2$ and low lipoprotein characteristics. All these factors can be traced back to the abnormal structure and functions of the RBC's seen in SCD patients.

Keywords:
Lands pathway; lipoproteins; secretory phospholipase A_2; sickle cell disease; red blood cells; lipids

Jasmine Nudanu

Originally from the Bay Area, I am currently a rising senior at Syracuse University in New York. Upon graduating, I plan to further my journey by attending medical school to become a physician. As a biology student, I have become particularly interested in basic, clinical and translational research in medicine. Seeing the impact of a variety of diseases on my family has shown me that good health is essential to quality of life. These experiences have made me increasingly passionate about the medical field and have strengthened my desire to become a physician. As a Ghanaian descendant, one of the major diseases affecting my family is sickle cell disease (SCD). Working with Dr. Treadwell and the hematology clinic has enabled me to concentrate on my particular interests by working directly with patients with SCD and allowing me to continually challenge myself as a student and clinician. This program has given me the confidence that I will need to fully embrace future challenges.

Funded by: Union Bank Foundation

School: Syracuse University

Mentor: Marsha Treadwell, Ph.D.

Title:
Barriers to Neurocognitive Testing in Children with Sickle

Introduction:
Children with sickle cell disease (SCD) are at risk for neuropsychological impairments and poor academic performance. (1) Children may suffer overt or silent stroke and exhibit deficits in memory, attention, perception, and communication. (2) Evaluation of neuropsychological function using neurocognitive testing (NCT) allows for the identification of cognitive challenges, even in children without overt neurological symptoms. It is essential to identify and address any barriers for families in accessing and utilizing NCT.

Objective:
To assess the barriers families might face in accessing neurocognitive testing (NCT).

Methods:
45 parents/caregivers of children with SCD will complete a survey describing barriers to accessing NCT.
We will use descriptive statistics to describe most frequently cited barriers and use cross-tabulations and chi-square analyses to determine if total number or specific barriers are associated with demographic or clinical variables, or with previous experiences with NCT.

Results:
To date, 23 parents/guardians (65% mothers, n = 15) of children with SCD completed the barriers to NCT questionnaire (∂ =.72, indicating good reliability). Patients had a mean age of 10.5 years (*SD* = 3.4), were 65% female (n = 15); 83% (n = 19) African American; and 70% (n=16) Hgb SS. Forty-three percent (n = 10) had stroke/ stroke risk/ school problems and 26% (n = 6) had previous NCT. The average number of barriers was 1.6 (*SD* = 1.5), with "not knowing enough about the testing" cited most often. There were no differences in barriers reported based on demographic or clinical variables. Parents whose children were already identified with neurocognitive challenges or previous NCT were more likely to cite "getting off work" and "emotional" barriers (chi square = 6.21, $p < 0.05$ for both).

Conclusion:
Caregivers of children with SCD need education about the potential for neurocognitive challenges with the disease, even for children not currently exhibiting school problems. For children already identified with neurocognitive challenges, parents need additional support to cope with emotional distress and logistical issues, such as getting time off work for the testing. Addressing these barriers is critical to assuring that strategies are implemented that assures that children with SCD remain successful in school.

Acknowledgements:
Participating children and families; Keith Quirolo, Christianne Ramdeen, Rogelio Medina, Erica Tringale, Lisa Hale, Valerie Syndor

Keywords:
sickle cell disease (SCD); quality of life (QoL); neurocognitive testing (NCT); school success

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Jackeline Ochoa

One of the primary reasons I was interested in joining the CHORI Program is because of my passion for health. When I was in ninth grade, my mother was diagnosed with Vasculitis, which played a huge role in the development of this passion. After my mom had been diagnosed, she was no longer able to work. This lack of income caused stress in our family and made me feel helpless. However, once I began to practice meditation and yoga, I was able to gain control over the health of my body and mind and completely eliminated this feeling of helplessness. Through this experience, I realized that I am most passionate about health and wellness, and that I would like to help other families who may be facing tough financial situations realize that the real wealth is what is within us: our knowledge, health, and our capacity to overcome hardships.

Funded by: Doris Duke Charitable Foundation

School: Holy Names High School

Mentors: Caroline Hastings, M.D., Anu Agrawal, M.D.

Title:
Changes in body mass index and risk of hypertension in patients treated for acute lymphoblastic leukemia

Contributing Authors:
Caroline A. Hastings, M.D., Anurag K. Agrawal, M.D.

Introduction:
Acute lymphoblastic leukemia (ALL) is the most common childhood malignancy and compromises 25% of all cancers in individuals younger than 20 years. Studies have shown that patients treated for ALL are prone to obesity and the development of hypertension with cranial radiotherapy and exposure to corticosteroids noted to be treatment-related risk factors. Contemporary studies have shown that patients with ALL have increased obesity, even with the absence of radiotherapy. Population specific factors such as ethnicity may play a role but have not been well-studied. Additionally, interventional studies to inhibit the development of obesity and hypertension are lacking in the pediatric oncology population.

Objective:
We aim to determine the prevalence of obesity and hypertension in our ALL population prior to the development of an interventional study to attempt to mitigate the development of these comorbid conditions during ALL maintenance therapy and after the completion of therapy.

Methods:
After institutional review board approval, patients with ALL treated at Children's Hospital and Research Center Oakland from May 1999-May 2014 who have completed treatment during this time period were included and de-identified prior to data collection. Background information recorded included ethnicity, age of patient at diagnosis, gender, diagnosis, treatment protocol, need/dose of craniospinal radiation therapy, and total exposure and type of corticosteroids utilized. Body mass index (BMI), systolic blood pressure and diastolic blood pressures were documented at the initiation of each treatment phase during therapy and at all documented physical exam time points after treatment completion. Trends in BMI as well as systolic and diastolic blood pressures over time will be analyzed and compared to age-based norms.

Anticipated outcomes:
We anticipate seeing a trend toward increased BMI as well as systolic and diastolic blood pressure in a subset of patients treated with ALL. We predict there may be ethnic factors related to this risk. By identifying patients at risk for overweight, obesity and hypertension during ALL therapy and after the completion of therapy we will secondarily be able to embark on an interventional study to attempt to alleviate this risk.

Keywords:
leukemia, lymphoid, pediatric obesity, hypertension

Danielle Odeh-Ajero

This fall I will be transferring to CSU East Bay as a third year nursing student. My mom being a clinical laboratory scientist was the first to expose me to science and from an early age I knew I wanted to work in the medical field. As I progressed through my education, I knew my passion was in health care but it was only until my time at Contra Costa College that I knew I wanted to be a nurse.

Since my time at CHORI I have met inspiring people and have been exposed to many learning opportunities. While I have had a lot of lab experience through my science classes, I had never done lab research. At first I was a little intimidated but was welcomed and encouraged. I would like to thank the Watson Lab, especially my mentor Gordon Watson, Dr. Sidharta and the Center for Science Excellence, everyone at CHORI for such a wonderful opportunity, and of course my mom for always being so supportive.

Funded by: Union Bank Foundation

School: Contra Costa College

Mentor: Gordon Watson, Ph.D.

Contributing Authors:
Siloni Pasta, Ph.D., Gordon Watson, Ph.D.

Title:
The Effect of Genetic Background on Phenotype in a Mouse Model for Smith-Lemli-Opitz Syndrome

Introduction:
Smith-Lemli-Opitz Syndrome (SLOS) is a congenital autosomal-recessive disorder caused by mutations in 7-dehydrocholesterol reductase (DHCR7) leading to cholesterol (C) deficiency and accumulation of its precursor 7-dehydrocholestrol (7-DHC). Cholesterol is an essential structural and functional component of cells and individuals with SLOS show delayed growth and development, and behavioral characteristics of autism. Mice have been genetically engineered to have DHCR7 mutations that mimic mutations found in SLOS patients. A T93M point mutation has been bred into two mice strains, B6 and FVB. In working with T93M/T93M mice, it appears that SLOS mice with the FVB genetic background may be less severely affected than those with the B6 background.

Objective:
This project adresses both the physiological severity (viability and growth rate) and biochemical differences (7DHC and cholesterol) between B6 and FVB mice with SLOS (T93M/T93M genotype).

Methods:
Viability was determined from breeding records. The weights of 4 week old and 10 week old T93M/T93M mice of FVB and B6 backgrounds were compared to corresponding normal mice weights. Cardiac blood and tissue from the liver, sciatic nerve, brain, and spinal cord, were harvested from T93M/T93M FVB and B6 mice of four weeks and 10 weeks of age. Sterols were extracted and run through GC/MS to quantify levels of 7DHC and cholesterol.

Results and Conclusion:
The viability of FVB mice is an 85% survival rate (from birth to weaning) as compared to 50% in B6 mice. We anticipate that the weight of 4 week old SLOS mice will be a smaller percentage of the weight of normal mice of the same age, while 10 week old mice will have a weight percentage close to normal as growth normalizes with age. We anticipate that the ratios of 7DHC/C will be larger in B6 mice than in FVB mice, which would attribute the increased viability of FVB mice to better cholesterol metabolism. So far results from liver samples of 10 week old B6 and FVB mice show an apparent difference in the ratio of 7DHC/C, but additional data analysis is still in progress.

Elleanor Pangilinan

My name is Elleanor Pangilinan and I will be entering my junior year at UC Davis this fall. After overcoming significant medical obstacles in my life, I have full appreciation for the efforts and impact of biomedical research. Through my internship here at CHORI, I have gained even more insight into the processes required to improve the quality of life for many and intend to apply this to a future career within the health sciences. I would like to thank my mentors, Dr. Illek and Dr. Fischer for allowing students like myself to assist in their contributions to cystic fibrosis research and my fellow interns, Gopika and Katie for all of their help. I would especially like to thank Dr. Setiati Sidharta from the Center for Science Excellence, Dr. Mayra Padilla and Dr. Chris Tarp for their constant support and guidance, and the many individuals who have shared their knowledge and passion of science to provide the next generation with direction and opportunities to support their educational goals.

Funded by: Union Bank Foundation

School: Contra Costa College

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

Title:
Impact of Pseudomonas aeruginosa on Airway Health

Contributing Authors:
Horst Fischer, Ph.D., Beate Illek, Ph.D.

Introduction:
Cystic fibrosis (CF) is an autosomal recessive genetic disorder with upwards of 1,000 new cases per year. CF results from a mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) protein and its loss of CFTR functioning inhibits proper movement of anions (such as Cl^- and bicarbonate) and water across epithelial cells, resulting in defective mucociliary clearance within the airways. The opportunistic bacterium Pseudomonas aeruginosa (PA) readily proliferates in 80% of CF airways and secretes quorum-sensing (QS) molecules that allow bacterial cell-to-cell communication resulting in biofilm formation. Of these QS molecules, *N*-(3-oxo-dodecanoyl)-*S*-homoserine lactone (3-oxo-C12), has been found to damage the function of the epithelial barrier and disrupts the organization of the tight junction protein, zonula occludens (ZO-1). Bacterial infections dramatically reduce lung function and life expectancy in CF patients, but improvements in treatment within the past 20 years have doubled the life expectancy of patients to 41 years of age. Treatment to completely eradicate PA presence in the airways has not been established. A recent report indicated a protective effect of cyclodextrin against 3-oxo-C12 induced epithelial damage in intestinal cells, though its effect in airway cells remains unknown.

Objective:
Determine the impact of 3-oxo-C12 on chloride ion transport and transepithelial resistance (TER) in CF vs. normal bronchial epithelial cell monolayers and test the effects of cyclodextrin for the protection of epithelial barrier breakdown.

Methods:
Ussing chambers and an Evom meter will be used in measuring TER (epithelial tightness) of CF- (CFBE41o-), CFTR-corrected cFBE41o-, and normal (16HBE14o-) cell lines; localization of ZO-1 will be visualized using confocal microscopy.

Outcomes:
CFBE41o- exposed to 3-oxo-C12 [50uM] exhibited a 2-fold decrease in TER values after 15 minutes. A long term experiment was conducted (n=1) with exposure at the same concentration of 3-oxo-C12 for up to ~3 hours in which CFBE41o- cells exhibited a 6-fold drop in TER. Cyclodextrin is expected to attenuate the decline in TER and help to preserve ZO-1 expression in the apical membrane pole during the presence of 3-oxo-C12.

Keywords:
C12-HSL, CFTR, Pseudomonas aeruginosa, quorum sensing, bacterial infection, epithelial resistance

Liliya Parkman

I have been interested in healthcare work since high school, when I worked as a medical assistant in the orthopedic surgery department of Kaiser Permanente. My job was fascinating, and it motivated me to pursue opportunities in medicine while at USC, where I have volunteered at the Orthopedic Institute for Children during the school year. As a volunteer, I was able to combine my enthusiasm for medicine with my love for helping children, fostered over many summers working as a camp counselor. This summer, I was looking for a similar experience, where I could also incorporate the scientific theories that I have studied at college over the last two years. I found exactly that in Dr. Lammer's laboratory, which focuses on researching the causes of conotruncal heart defects in babies. Our work includes analyzing blood samples with the goal of helping pediatricians to better anticipate and react to the risk of a child being born with a heart defect. My work this summer has made the science I have studied in school come to life, and I would like to thank everyone in the Lammer Lab for this wonderful experience.

Funded by: Lammer Lab Education Fund

School: University of Southern California

Mentor: Edward Lammer, M.D.

Contributing Authors:
Kathleen Schultz, Christina Parodi, Nebil Mohammed, Kazu Osoegawa, Ph.D.

Title:
Using Genotyping to Fine Map Candidate Loci on Chromosomes 8 and 12 in Infants with Conotruncal Heart Defects

Introduction:
Congenital heart defects comprise the most common birth defects, affecting about 4-8 per 1,000 births. Conotruncal heart defects constitute 20% of congenital heart defects. Tetralogy of Fallot (TOF) and dextro-transposition of the great arteries (d-TGA) represent about 75% of conotruncal heart defects. We plan to investigate chromosome region 12q24 and focus on the PTPN11 region because a recent genome-wide association study (GWAS) found a relationship between single nucleotide polymorphisms (SNPs) and risk for TOF on that locus. Furthermore, the PTPN11 gene is associated with Noonan's syndrome which makes it is a good candidate gene for isolated heart defects. Loci 8q21 was chosen because a male subject born with TOF showed a microduplication within the ZFHX4 gene.

Objective:
Fine map candidate loci at chromosome 8q21 and 12q24 among 391 California infants with conotruncal heart defects (425 controls) and identify genetic variants among candidate genes or regulatory regions within those four loci that show risk for conotruncal heart defects.

Methods:
We will use the case-control research method to conduct SNP genotyping on possible candidate genes in the target loci 8q21 and 12q24. SNPs will be selected if they have a minor allele frequency greater than 10%. We will then use the MultiPopTagSelect program to select TagSNPs that have substantial coverage across the candidate regions. We will use the matrix assisted laser desorption/ionization-Time of flight (MALDI-TOF) mass spec for the genotyping for association analysis after we design multiplexed genotyping assays for the Sequenom MALDI-TOF Mass Array System. Samples will then be distributed into batches of no DNA, cases, and controls. We will examine the associations between SNP genotypes/ haplotypes and risk for conotruncal heat defects in cases and control by calculating odds ratios.

Anticipated Outcomes:
We anticipate that the regions we focus on will show an increased risk (increased odds ratios) with conotrunal heart defects.

Keywords:
single nucleotide polymorphism, tetralogy of fallot, dextro-transposition of great arteries

Tanu Patel

I haven't always known that I want to pursue a career in science and medicine. Working in the LaBeaud lab at CHORI has been instrumental to my discovery process. This experience has opened my eyes to the great versatility of a career as a physician and scientist. I've seen that there exist opportunities to be investigative, to constantly expand your knowledge base, to act as an advocate at a global and personal level…. the list goes on. I've realized these attributes appeal to me immensely. I graduated from UC Berkeley this past May with a Bachelors of Science degree in Microbial Biology. In the near future, I plan to expand on my research experience before applying to medical school. I'm grateful to the SIMR organizers, and to all of the members of the LaBeaud lab for their mentorship, and for creating a very memorable summer.

Funded by: Volunteer

School: University of California, Berkeley

Mentor: Desiree LaBeaud, M.D.

Contributing Authors:
Claire Heath, Ph.D., Anika Sharma, Monica Nayakwadi-Singer, M.D.

Title:
Streptococcus pneumoniae serotype carriage study in Kenyan children

Introduction:
Streptococcus pneumoniae are encapsulated gram-positive bacteria that colonize the upper respiratory tract of humans, but can cause disease such as pneumonia, meningitis, and bacteremia. Annually, S. pneumoniae infects approximately 14.5 million children under the age of 5 world-wide. S. pneumoniae can be categorized into 91 serotypes which differ by capsular polysaccharide composition (Calix & Nahm, 2010). Most serotypes are immunologically distinct, and immune protection against one serotype does not necessarily protect against others, which is an important consideration in vaccine design. Serotype prevalence varies with age, location, and the implementation of vaccination campaigns, which can alter serotype prevalence in unnvaccinated individuals through a mechanism of "herd immunity." Data on serotype prevalence in Africa is relatively sparse. However, more than 98% of all deaths due to pneumoccocal disease occurs in developing countries, in particular those located in the African continent. Understanding the prevalence of pneumococcal serotypes in Africa will allow us to develop more effective vaccines and public health policies to address the morbidity and mortality caused by pneumococcal disease in this region.

Objective:
To investigate Streptococcus pneumoniae serotype prevalence among unvaccinated Kenyan children after initiation of routine conjugate vaccination of infants.
Methods: Bacteria from nasopharyngeal swab samples from unvaccinated Kenyan children ages 4 to 7 years were obtained in 2014 as part of a larger on-going study of vaccine immunogenicity. Swabs were stored in STGG media and shipped frozen to our lab. We cultured the samples onto blood agar plates and enriched for Streptococcal pneumoniae isolates that were optochin-sensitive. We used pools of serotype-specific primers that targeted the capsular locus which produced amplicons of different sizes which we visualized by electrophoresis.

Anticipated Outcomes:
We expect that routine infant vaccination with a 10-valent pneumococcal conjugate vaccine beginning in 2011 in Kenya will have affected the serotype carriage of S. pneumoniae in unvaccinated individuals. As such, we expect to see a shift towards serotypes not included on the PCV10 vaccine.

Keywords:
Streptococcus pneumoniae, serotype prevalence, PCR, Africa

Daisy Rangel

As a rising senior from Holy Names High School, I realize how important it is to explore my passions. One of my main passions has always been healthcare and the sciences. This passion primarily developed after my brother had a life-threatening case of pneumonia and I spent many weeks in the PICU getting to know the nurses. I really admire their emotional strength and everlasting compassion. I aspire to be just like these wonderful women.
The CHORI Summer Research Program provided students from under-represented groups, just like me, with an interest in the medical field a chance to get a glimpse at research. Whether I love research, or decided that it's not for me, I will take the tools that I learn while at the program and apply them to my life. It is truly an honor to have been chosen.

Funded by: Doris Duke Charitable Foundation

School: Holy Names High School

Mentor: Ward Hagar, M.D.

Title:
Association between liver and renal function in sickle cell

Introduction:
Sickle cell disease is a blood disorder that has sickled shape blood molecules which clog blood flow, inducing pain. Two of the most commonly damaged organs in sickle cell are the liver and the kidneys. The liver can become enlarged with red blood cells and damaged over time with clinically important decreases in synthetic functioning. The kidneys are filters and balance the amount of red blood cells in the body. The kidneys are particularly susceptible to damage from sickling. Persistent injury can cause a number of kidney disorders including infection and decreased function. Kidney failure is a major danger in older patients and accounts for 10 - 15% of deaths in sickle cell patients. Enlargement of the liver occurs in over half of sickle cell patients and acute liver disfunction occurs in up to 10% of hospitalized patients. Because sickle cell patients often need transfusions, they are at high risk for liver dysfunction from iron overload. In other conditions, the overall functioning of the liver has a direct effect on the function of the kidneys, such as in the hepatorenal syndrome. Whether a similar pathophysiology exists in sickle cell is unknown.

Methods:
Queries of Meditech, Epic, and the Adult Sickle Cell databases will be queried and combined to include all of the variables. Patients that have attended for the entire span of ten years will be included in the study.
Alanine aminotransferase and albumin will be used as serum markers to track liver function.
Glomerular filtration is a surrogate marker for kidney function. The Cockcroft-Gault and the MDRD equations are both clinically accepted methods to measure and calculate glomerular filtration rate (GFR).

Hypothesis:
Changes in liver function in adults with sickle cell disease will correlate with changes in renal function.

Anticipated Outcomes:
There will be correlation between the estimated glomerular filtration rate, albumin, and alanine aminotransferase in adults with sickle cell disease.

Keywords:
sickle cell, hepatorenal, estimated glomerular filtration rate, albumin, alanine aminotransferase, Cockcroft-Gault Equation, MDRD equation

Maritza Rodriguez

My name is Maritza Rodriguez, and this fall, I will be entering my third year at University of California, Santa Cruz as a human biology major. This is my second summer participating in the CHORI summer program working on clinical epidemiology projects. Two years ago, I worked on pediatric lupus and now, I am investigating whether gender affects treatment responses in rheumatoid arthritis. This experience with data analysis has broadened my view of what research is. I would like to thank my mentor, Damini Jawaheer, for allowing me to work with her again and for providing me with guidance and support throughout the program, and also Deborah Ellen, Ellen Fung, Chandra Andrews-Wright, Phillip Bollinger, and CHORI in general for allowing me to participate in the program.

Funded by: Union Bank Foundation

School: University of California, Santa Cruz

Mentor: Damini Jawaheer, Ph.D.

Title:
Do men and women with rheumatoid arthritis respond differently to treatment?

Introduction:
Rheumatoid arthritis (RA) is an incurable, autoimmune disease that afflicts one percent of the world's population. It is characterized by swelling, stiffness, and pain in joints, leading to joint deformation, disability, and poor quality of life. Although three times more women are affected by RA than men, current treatment regimens do not take gender into account. There are some reports, however, that gender may affect treatment response.

Objective:
To determine whether there is a significant difference in treatment response between men and women with RA.

Methods:
Patient data from the Treatment of Early Aggressive Rheumatoid Arthritis (TEAR) Trial were used for this study. Baseline disease characteristics between men and women were compared using t-tests, Mann-Whitney tests, and chi-squared tests. To determine if there was significant improvement in disease activity in men and in women, disease activity scores (DAS28) at baseline and at the end of the follow up (Week 102) were compared using t-tests. A multivariate longitudinal regression model (Generalized Estimating Equations, GEE) was used to assess whether treatment responses differed significantly by gender.

Results:
A total of 748 patients (541 women and 207 men) with RA were available from the TEAR trial. At baseline, all patients had moderate to severe disease activity (DAS28 > 3.2). Men and women had similar disease duration (median [interquartile range]: 1.0 [0.5-3.0] in women and 1.2 [0.5-3.3] in men). They also had similar mean disease activity (DAS28, mean ± SD: 5.9 ± 1.0 in women and 5.7 ± 1.1 in men). There were no significant gender differences in tender and swollen joint counts. During the 102 weeks of follow up, both men and women showed significant improvement in disease activity over time ($p<0.00005$). In the GEE model, gender was significantly associated with disease activity ($p=0.006$), and men showed a faster rate of improvement resulting in better responses throughout the follow up compared to women ($p=0.008$).

Conclusion:
In the TEAR dataset, gender significantly influenced treatment response, with men being able to achieve better responses than women.

Evelyn Sanchez

Hi, my name is Evelyn Sanchez and I will soon be senior at Mercy High School in San Francisco. Ever since I could remember, I had an immense interest in the medical field. I still remember watching shows like "Untold Stories of the E.R." at the age of 7 and not being grossed out. After my mother began experiencing medical issues, I grew even more interested in learning how doctors would care for her and how she could remain healthy. I have done my best to learn as much as I can about the careers in the medical field, however I had never been exposed to the research aspect of this field. I am very thankful for being given the opportunity to participate in CHORI's summer program. My experience in the Oda lab has taught me a lot about research and has been a lot of fun! I would like to thank my mentors Dr. Borja and Dr. Oda, as well as Ms. He for helping me with my project and always answering my never ending stream of question! I hope that this experience will aid me in determining what career in the medical field is right for me.

Funded By: Doris Duke Charitable Foundation

School: Mercy High School

Mentor: Michael Oda

Contributing Authors:
Mark Borja, Ph.D., Michael Oda, Ph.D.

Title:
The stability of HDL function in healthy subjects

Introduction:
HDL function (as measured by cell-based cholesterol efflux capacity) is a biomarker that is strongly associated with cardiovascular disease status. The Oda Lab has developed a test that measures a key function of HDL, that is, how well HDL moves cholesterol. We measure the exchange of apoA-I on and off HDL by adding lipid-free spin-labeled apoA-I to a human plasma sample. The release of lipid-poor apoA-I from HDL is a rate-limiting step in reverse cholesterol transport, the process whereby HDL mobilizes cholesterol from tissues and returns it to the liver, kidneys and intestines for excretion. The spin-label is a small molecule with an unpaired electron, whose mobility in solution can be detected using electron paramagnetic resonance spectroscopy (EPR). The mobility of the spin-label is representative of the lipid-free / lipid-bound state of HDL, so can provide a measure of how much apoA-I is bound to HDL by signal intensity signal intensity. Using this test, we have determined that HDL function is correlated with the degree of a subject's cardiovascular disease. However, we have not yet determined the stability of HDL-apoA-I exchange in healthy individuals.

Objective:
We monitored the rates of HDL-apoA-I exchange in five healthy patients who have maintained the same diet and exercise regime. Their blood has been drawn at monthly intervals over the course of six months. This provided us a series of samples that allowed us to determine the extent to which individuals can vary in their HDL function over a half-year period.

Anticipated Outcome:
We expect that healthy patients would have a stable level of HDL function if they maintain the same lifestyle and diet. However, if significant variability is observed, this study will provide the preliminary data necessary to justify further investigation into potential causes of HDL function changes.

Acknowledgements:
I would like to thank the Oda Lab, as well as CHORI for the amazing opportunity to work on this project.

Keywords:
HDL function, apoA-I

Sikai Song

As the oldest daughter of immigrant parents, I carry with me the aspirations of my family in our journey to achieve the "American Dream". My personal experiences growing up in a community with limited resources have shaped my passion for social justice and my desire to utilize scientific research as an avenue through which I can work towards addressing health disparities. Working at CHORI this summer has opened up a world of knowledge I would not have been able to otherwise experience. Without a doubt, this program has reinforced my desire to pursue public health, science, and medicine in the future. Who knew I would enjoy spending hours in the cell culture room plating an experiment?
To everyone who has made this program possible, to Dr. Medina and everyone in the Medina-Krauss Lab for providing such a supportive environment to help foster my intellectual growth, and to Alexandra DiGiorgio, who is not only a great mentor, but is also generally a wonderful human being- "thank you" doesn't seem enough.

Funded by: Private Donor

School: University of California, Berkeley

Mentors: Marisa W. Medina, Ph.D., Alexandra DiGiorgio, Ph.D.

Title:
Investigation of the Indirect Effects of Statins on Colorectal Cancer

Introduction:
Statins are the most widely prescribed class of drugs for lowering cholesterol levels and decreasing the incidence of cardiovascular disease. Furthermore, epidemiological and clinical studies have also found an association between reduced colorectal cancer (CRC) incidence and statin use. Although *in vitro* studies have demonstrated that statins can directly induce apoptosis of CRC cells at supraphysiological doses, statins are also known to have anti-inflammatory properties that may indirectly reduce CRC viability through the reduced expression of pro-inflammatory cytokines. Chronic inflammation is an important factor in the development of colorectal cancer and pro-inflammatory cytokines may orchestrate a tumor-supporting microenvironment. In this manner, statins are thought to exhibit anti-cancer effects through systemic effects due to their anti-inflammatory properties and potentially modulate the tumor microenvironment.

Objective:
To examine how statin effects on CRC cells in co-culture with immune cells can impact CRC viability and proliferation rates.

Methods:
Previous experiments have shown a reduction in CRC viability when CRC cells are grown in the presence of immune cells and statins. We will first confirm this phenomenon by co-culturing a CRC cell line (HCT116) with immortalized B-cells (LCLs) in the presence and absence of statins using the MTT assay. We will then determine if the decrease in CRC viability is due to an increase in apoptosis using the Apo-ONE Homogenous Caspase-3/7 Assay (Promega). Changes in cytokine production during co-culture with statin will also be assessed by measuring TGF-ß, a cytokine important in the progression of cancer. Finally, to determine if physical contact between the CRC cells and immune cells is necessary for a decrease in CRC viability, the above experiments will be repeated in a transwell system.

Anticipated Outcomes:
Based on preliminary data, we anticipate a reduction in CRC viability and an increase in apoptosis in CRC cell co-culture with immune cells and statins. We also expect to see a change in TGF-ß concentrations. We anticipate that these effects will occur in both normally plated cells and the transwell system.

Keywords:
statins, colorectal cancer, inflammation, cytokines

California Institute for Regenerative Medicine (CIRM)

Group Includes (left to right): Judy Kang, Yohana Beyene, Chioma Amuzie
Not pictured: Karina Duarte

This group of students was funded by CIRM, as part of their mission to train the next generation of California Stem Cell Scientists.
In addition to the CHORI summer program, these students also attended Improv classes in San Francisco on Tuesday evenings from 7-10 PM to spark their creativity.

They blogged about their research experience on social media outlets and also participated in an all day CIRM focused Symposium on August 4th, in San Francisco.

These high school students were extremely busy!

Doris Duke Charitable Foundation

Group Includes (left to right): Evelyn Sanchez, Daisy Rangel, Jaceline Ochoa, Dulce Cruz, Isabella Macedo. Not pictured: Sebastian Hurtado

These students were funded by the Doris Duke Charitable Foundations, which focuses on funding high school students interested in pursing future careers in the clinical health care field.

In addition to the CHORI Summer Program, these students also completed separate evaluations for their program and created a detailed individual development plan with the assistance of their mentor.

The IDP, serves as a 5-10 year career plan which can encourage the students as they continue to pursue their dreams.

Elizabeth Nash Foundation

Group Includes: Kathryn Echavia (right), Gopika Hari (left)

Katie and Gopika have a strong interest to find a cure for cystic fibrosis and learned how to perform biomedical research in the cystic fibrosis research laboratory at CHORI. They are the recipients of the Elizabeth Nash Foundation Cystic Fibrosis Summer Research Award with its mission to provide a short-term and hands-on research training opportunity in the field of cystic fibrosis.
In Addition to the CHORI summer program, these students also participated in an all day National Cystic Fibrosis Family Education Conference by the local Cystic Fibrosis Research Inc. in Palo Alto.


CHORI Summer Students invite you to a
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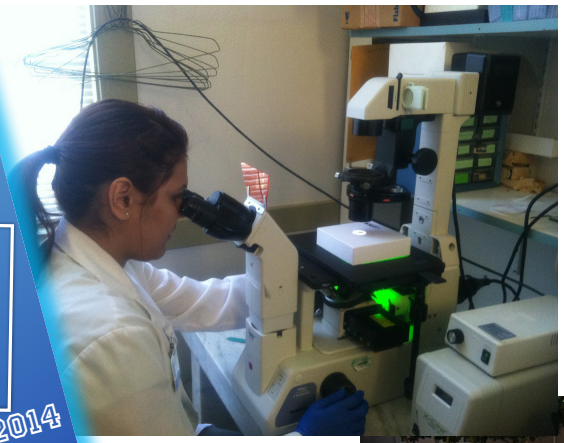


RESEARCH UPDATE

Children's Research Institute's Summer Student Program Increases Access and Diversity in Science Education

Children's Hospital Oakland Research Institute (CHORI) welcomed more than 30 high school and college students to the 2014 Summer Research Program that launched this summer on June 16. The program will culminate with an all-day Summer Student Research Symposium on August 15.

The program pairs students with one or two CHORI research investigators who serve as mentors, guiding students through the design and testing of their research. In addition, students participate in weekly seminars and research discussions. At the end of the nine-week program, students present their research findings to their peers and CHORI faculty, with a panel of scientists evaluating the research. Students may invite family members or friends to the symposium as well.

"The CHORI Summer Research Program is designed primarily for students who otherwise would not have access to such a high-quality program in scientific and clinical research," says CHORI Student Services & Visiting Scientist Coordinator Deborah Ellen, the principal program coordinator.

"Because the program is funded by a wide range of organizations and individuals, we can reach out to students from populations that are underrepresented in scientific research," she explains. "One of our main objectives is to increase the diversity of students going into research and medicine. For example, more than 70 percent of our students have been women, who traditionally have been underrepresented in science and medicine. Our high school program mostly targets students from the Bay Area, especially the East Bay. Our college undergraduate program also includes students from other parts of California, and our post-bachelor degree program has had students from as far away as New York."

Students are funded with stipends for their research work by CHORI and organizations such as the Doris Duke Charitable Foundation's Clinical Research Experiences for High School Students Initiative, the Elizabeth Nash Foundation's support for research in cystic fibrosis, the California Institute for Regenerative Medicine (stem cell research) and private donors. The program also has received funding in previous years from the National Institutes of Health (NIH).

"The Summer Research Program is one of the 'hidden jewels' of CHORI," says Senior Systems Analyst Phillip Bollinger, a program coordinator who also provides information technology (IT) support for students.

"It has been a pleasure and an honor to be a part of this program for the past 10 years," he says. "I originally wanted to be a teacher, and I love working with the students, helping them create Power Point and poster presentations for the symposium and evaluating their presentations in practice sessions. Many students have gone on to work in medicine and science labs both here at CHORI and elsewhere. It is great to see them succeed in their careers. I always love hearing back from them with updates on what they're doing, and I encourage them to come back and give presentations to current students in the program."

Every CHORI Summer Student Research Symposium concludes with presentations of students' laboratory and clinical research projects.

For more information, go to www.chori.org and click on "Summer Research Program"

CHORI Helps Young Woman Fulfill Her Dreams—And Her Father's

Anita Chanana, now age 20, went through a "traditional" grade school program—until she started taking night classes in math at Contra Costa College in San Pablo when she was only in 4th grade.

"My dad recognized my ability in math, and he thought the college classes would help me get ahead," she recalls. "He always said, 'You can lose everything you own, but you can't lose your education,' and he is the number one reason I have gotten to where I am today. He actually used to sit with me during my first few courses at community college because I was still pretty young and timid around adults."

Anita took community college classes in addition to her regular classes through middle school and high school at Vista High School in San Pablo. After completing her high school requirements at age 13, she became a full-time student at Contra Costa College. She was 16 when she transferred to the University of California at Berkeley, entering as a junior in August 2010.

That summer between colleges, Anita participated in the CHORI Summer Student Program, conducting laboratory and clinical research alongside Children's Hospital Oakland doctors and CHORI scientists.

RESEARCH UPDATE

CHORI student researcher Anita is heading to UCLA in the fall with a full scholarship

"I learned about the CHORI program at Contra Costa College's Center for Science Excellence and decided to apply," she says. "It was one of the best things I've ever done. I found my mentors at CHORI."

Anita's mentors at CHORI are Senior Scientist and dermatologist Ervin Epstein, MD, and Jean Tang, MD, PhD. Anita was assigned to their lab during the 2010 summer program to work on research into prevention and treatment of basal cell skin cancer, particularly in patients with basal cell nevus syndrome (BCNS), a rare genetic condition that causes hundreds to thousands of skin cancers. BCNS is not considered life-threatening, but it may require multiple surgeries to remove basal cell tumors. The researchers were conducting a trial of an oral medication, taken once daily, to reduce the need for surgical treatments. Patients in the study showed a dramatic reduction both in the growth of existing tumors and in the development of new tumors. (For information about this trial, visit www.childrenshospitaloakland.org/main/news/175.aspx)

Anita at CHORI; (below) Anita with her CHORI colleague XXX.

"It was my lab work at CHORI and the interactions with patients that definitely confirmed my reasons for wanting to be a doctor."

"My dad always said, 'You can lose everything you own, but you can't lose your education.'"
—Anita

The CHORI summer program allowed Anita to see the inner workings of medical research from a new perspective.

"While working on clinical trials for patients with BCNS, I learned the importance of comprehensive care," she says. "One of our patients had so many tumors on his face that he developed depression as a result of children being frightened by his appearance. The oral medication our patients receive often causes adverse effects such as hair loss, muscle cramps, weight loss and loss of the sense of taste. But this patient, like others in the trial, preferred to deal with the side effects of therapy because they were easier to bear than the impact of the disease. I embraced the level of compassion I felt during this difficult decision-making process and the remarkable trust that developed between the patient and researcher."

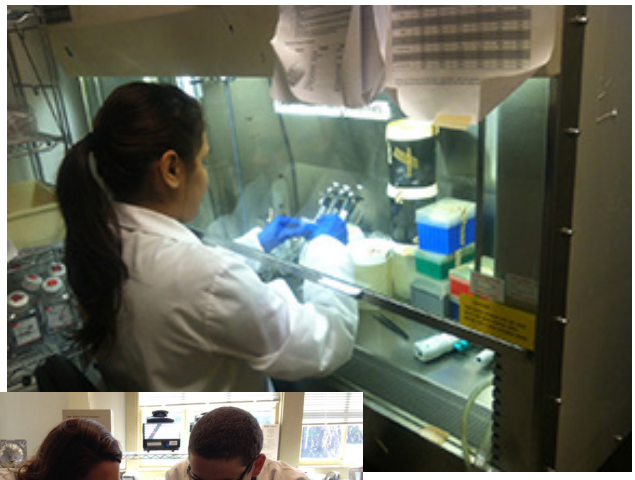
During her two years at UC Berkeley, Anita continued her CHORI research projects and completed a senior honors thesis, graduating with a bachelor's degree in 2012 at the age of 18. She then was hired as a full-time research assistant at CHORI to continue research on the basal cell skin cancer medication, to see if it is as effective and produces fewer side effects with less-frequent dosing. She now is looking forward to entering medical school this fall at Stanford, UCLA or UCSF.

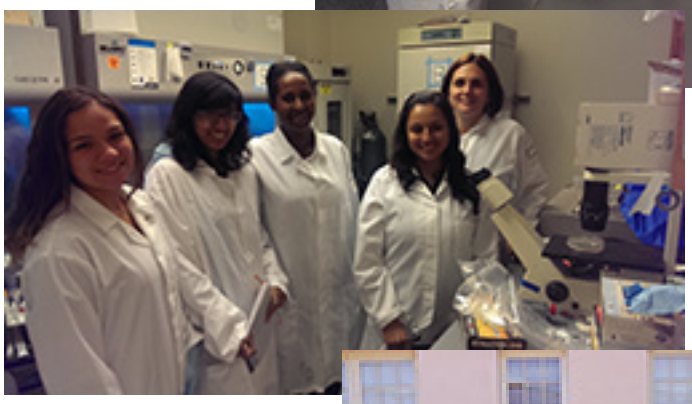
"Since I was in 1st grade, I knew I wanted to pursue a career in medicine," she says. "My mother was diagnosed with cancer that year. Fortunately, they caught it early and she has been cancer-free since then. Her illness and her concern impressed me, though, and the care her doctor provided made me want to be a doctor, too. My science courses in school—especially physiology—affirmed my desire. It was my lab work at CHORI and the interactions with patients, though, that definitely confirmed my reasons for wanting to be a doctor. I feel lucky to have been placed in this lab, with exposure to both lab work and clinical experience with patients."

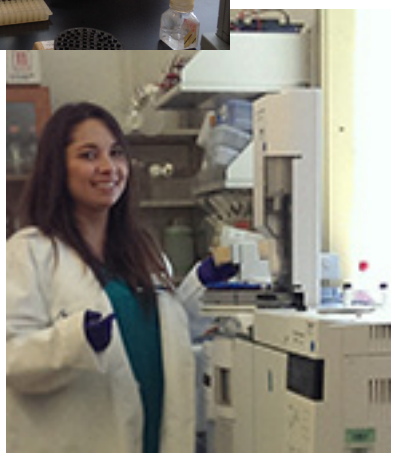
"Dr. Epstein and Dr. Tang have been major role models of what I aspire to be as a physician," she adds. "I have seen them balance research, family and mentorship with being amazing and compassionate physicians. Their minds are on another level when it comes to asking questions about important topics and in identifying approaches to answer those questions. Their bedside manner and interaction with patients is remarkable and inspirational. Assisting during patient visits showed me the incredible impact medicine and research can have on a patient's quality of life. If I can be half the clinician and researcher they are, I'll be doing well."

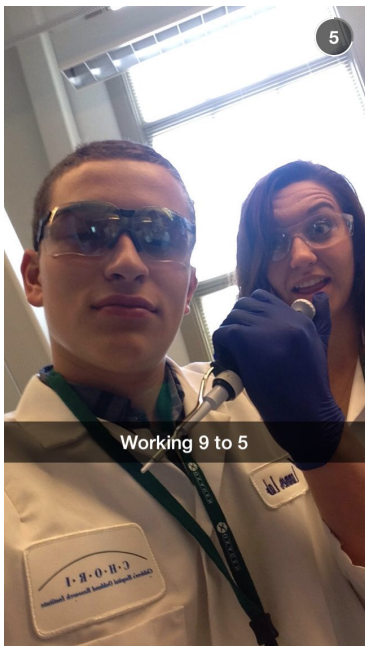
Unfortunately, Anita lost another source of inspiration in 2013 when her father died suddenly.

"My dad was the reason I had the drive to pursue great opportunities like the one at CHORI," she says. "His love and support also gave me the resilience to continue my medical school interviews during the most difficult period in my life after he passed away. He would have wanted me to complete our dreams."





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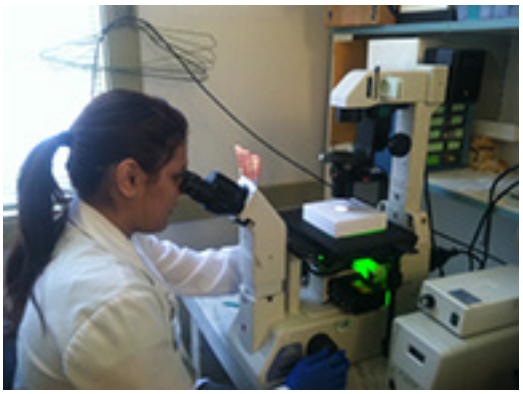

APS Physiology Research Award

Andrea Fernandez	Beate Illek Horst Fischer	Confocal Analysis of Airway Defense Proteins and CFTR Expression in Clinical Samples of Cystic Fibrosis Nasal Polyp and Bronchial Epithelial Cells

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Andrea Fernandez was one of the four students who worked in the Fischer Lab last summer in 2013. Andrea was funded by the NIH R25 Short-Term Research Education Program to Increase Diversity in Health Related Research.

Andrea presented her research project at the Undergraduate Research and Arts Colloquium at the University in South Florida and was recognized for her outstanding work. She received a prestigious Inaugural Award from the American Physiological Society for her summer research project related to airway defense and cystic fibrosis.

Notes

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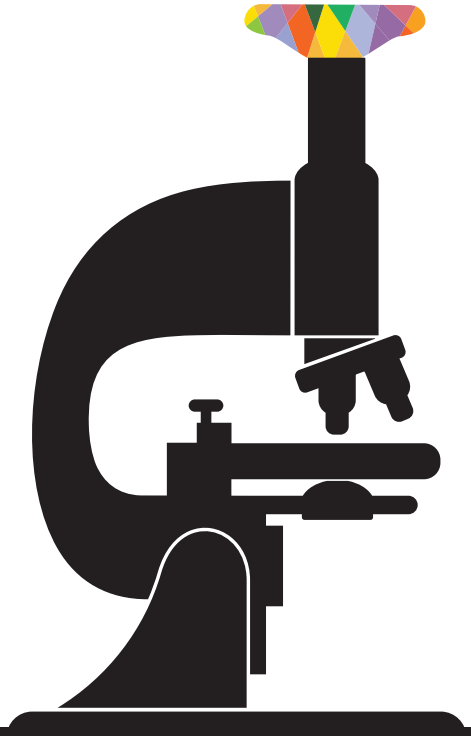
CHORI



2014 CHORI SUMMER STUDENT RESEARCH SYMPOSIUM

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