2011 CHORI SUMMER STUDENT SYMPOSIUM

A showcase for young minds in research

AUGUST 12, 2011

CHILDREN'S HOSPITAL
& RESEARCH CENTER OAKLAND

C · H · O · R · I
Children's Hospital Oakland Research Institute

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Children's Hospital Oakland Research Institute

August 12, 2011

This year we commemorate our 30th year of providing summer research opportunities for high school, college, post-graduate and pre-medical students. We are committed to educating and fostering tomorrow's leaders. The program provides research training to students who are considering research careers in biomedical science and other health related fields. Initiated in 1981 with a handful of trainees, the program has exploded in size and scope, with students currently participating in state-of-the-art research in topics ranging from stem cells to vaccine therapy, and nutritional genomics to obesity and diabetes. The program strives to provide research education, training and awareness on a range of topics in a mentored environment.

This summer we had an outstanding caliber of students from across the country, coming from a broad range of backgrounds and experience. About 40 were undergraduate or graduate students, and 10 high school students. They went through a rigorous research and education curriculum, which culminates in today's symposium presentations. As you read through the abstracts, listen to the talks or walk past their posters, we urge you to pause and discuss the research work with each participant. Our heartiest congratulations to every student for their performance. We wish them all the 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.

We would like to thank all the mentors and supervisors who dedicated time, effort, and deep commitment to train the next generation of young scientists and doctors. Without their participation, the students would not have a chance to experience the excitement of working in basic, translational, clinical or community-based research. We thank Dr. Vasanthy Narayanaswami, Principal Investigator and co-Director of Basic Research, and Dr. Barbara Staggers, co-Director of Clinical Research of the summer program, for their efforts and oversight. We deeply appreciate the roles played by Deborah Ellen and Phillip Bollinger, who did a phenomenal job in coordinating the program- they were the cornerstone of the program. We thank Dr. John Matsui, Biology Scholars Program Director, UC Berkeley, for his constant support of and involvement in the program. We also thank the guest speakers for taking time out of their busy schedules to discuss their research, career challenges and issues related to ethics and integrity in academia and research with the students.

We are grateful for the funding we received from the National Institutes of Health (National Heart, Lung and Blood Institute) Short Term Research Education Program to Increase Diversity in Health Related Research, the Elizabeth Nash Foundation, the American Heart Association, the Jolyce Hardesty fund, and the Children's Hospital Los Angeles / National Institutes of Health (National Heart, Lung and Blood Institute) Basic and Translational Research program.

Last but not the least, as the program continues to grow in size and scope, and given our budget constraints, we urge you to consider supporting our program. Despite realities of the present day economy, we remain committed to providing clinical and basic research-training experience to students. Your philanthropic support will ensure continuation of this unique scientific and educational experience for the students.

Congratulations to all participants and thanks to all members of the CHORI/CHRCO family for making the Summer Student Research Program a huge success.

Sincerely,

Bertram H. Lubin, MD
President, Chief Executive Officer and Principal Investigator
Children's Hospital & Research Center Oakland

Alex Lucas, PhD
Executive Director, Senior Vice President Research
Children's Hospital Oakland Research Institute

5700 Martin Luther King Jr. Way / Oakland, California 94609-1673
(510) 450.7600 FAX (510) 450.7910

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

The Short Term Research Education Program to Increase Diversity in Health Related Research from the National Institutes of Health (National Heart, Lung and Blood Institute) 5 R25 HL096365-03
&
UC Berkeley MARC Program: NIH T34GM092702 National Institute of General Medical Sciences

NIH Grant #5 R01AI070955-03 PI: Peter Beernink, PhD

NIH Grant #5 R37HL064159-12 PI: Robert Ryan, PhD

Jennifer Leigh Wells Fellowship

CHORI General Research Fund

Jordan Endowment Fund

Elizabeth Nash Foundation

Jolyce Hardesty Fund

American Heart Association

Children's Hospital Los Angeles (National Heart, Lung and Blood Institute, Basic and Translational Research Program) 1 U54 HL090511-03

Children's Hospital & Research Center Foundation

2011 Program Directors

Bertram H. Lubin, MD
President & Chief Executive Officer
Children's Hospital & Research Center Oakland

Barbara Staggers, MD
Director, Adolescent Medicine
Children's Hospital & Research Center Oakland

Vasanthy Narayanaswami, PhD
Associate Scientist at CHORI
Assistant Professor, Department of
Chemistry & Biochemistry,
California State University Long Beach

2011 Program Coordinators

Phillip Bollinger

Deborah Ellen

CHORI Summer Research Program

Children's Hospital Oakland Research Institute (CHORI) is proud to present the 2011 Summer Research Program, now in its 30th year.

Each year, the program offers a nine-week research training experience to stimulate interest in pursuing a career in biomedical, clinical and behavioral research in a friendly and nurturing environment.

The program pairs high school students, undergraduates, and medical and graduate students from diverse backgrounds with scientists and doctors who serve as their mentors. The students are guided through the process of completing a hypothesis-driven project, from design to final report. At the end of the internship, the students present their research at the Summer Student Research Symposium held at CHORI.

2011 CHORI SUMMER STUDENT SYMPOSIUM

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CHILDREN'S HOSPITAL & RESEARCH CENTER OAKLAND

C·H·O·R·I
Children's Hospital Oakland Research Institute

CHILDREN'S HOSPITAL OAKLAND RESEARCH INSTITUTE
2011 COMMEMORATION
30 years
Summer Research Program
Est. 1981
STUDENTS DISCOVERING THE POWER OF RESEARCH

SAVE THE DATE
AUGUST 12, 2011

8 A.M. - 5 P.M.

CHILDREN'S HOSPITAL OAKLAND RESEARCH INSTITUTE
5700 MARTIN LUTHER KING JR. WAY, OAKLAND

8 - 8:30 a.m. | Continental Breakfast
8:30 a.m. - 12:30 p.m. | Oral Presentations
12:30 - 1:30 p.m. | Lunch
1:30 - 3 p.m. | Poster Presentations
3 - 5 p.m. | Certificates and Refreshments

Directions: www.chori.org/directions.html

Support for the CHORI Summer Student Research Program is provided by: The Short Term Research Education Program to Increase Diversity in Health Related Research from the National Institutes of Health (National Heart, Lung and Blood Institute), 1 R25HL096365, and Elizabeth Nash Foundation, Children's Hospital Los Angeles (National Heart, Lung and Blood Institute, Basic and Translational Research Program) 1 U54 HL090511, and The Jolyce Hardesty Fund.

CHORI Summer Student Program

Common Equipment Overview and Training

June 17, 2011

Agenda

General Shared Room Philosophy
Lorelle Parker

Microscopy at CHORI
Horst Fischer

Attack of the Killer Centrifuges
Jennifer Beckstead

Guava
Lindsay Streirer Taylor

Use of Tissue Culture Rooms
David Killilea & Jennifer Beckstead

Alpha Imager
David Killilea & Phillip Bollinger

Autoclave - All
Common EQ Tour

Golden Rules for Research

1. Don't wear gloves in the hallway, even if they are clean. Remember that there are non-scientific staff working at CHORI. The site of gloves freak people out.
2. If you are carrying something around the halls that makes you want to wear gloves, it should probably be in a secondary container that you are not afraid to touch with bare hands.
3. Ethidium Bromide can cause cancer, do not touch a gel with your gloves and then touch anything else.
4. Leave an area just as clean or cleaner than before you used it.
5. Let someone know when reagents are running low so that they can be replenished.
6. ASK QUESTIONS WHEN YOU DON'T UNDERSTAND SOMETHING. Most everyone here would rather be asked the same question ten times than have you do something wrong.
7. If you are not comfortable doing something, tell someone and don't do it.
8. Ask before you borrow other people items, not everything in CHORI is common equipment.
9. Know who you can ask for help and where you can get answers if your query is not satisfied.
10. Pay attention to what you are doing. The little details are sometimes the difference between life and death (for experiments and you).
11. No open toe shoes, no shorts (this is an OSHA regulation, not a CHORI regulation). If you walk into a lab with this on, you are setting CHORI up for a finable offense.
12. Patience, Patience, Patience. Rushing causes oversight and mistakes.
13. Be nice to people. You may have to ask them for help one day.

Mentors

Bruce Ames, PhD
Peter Beernink, PhD
Mindy Benson, PNP
Dario Boffeli, PhD
Barbara Botelho, M.D
Cassandra Calloway, PhD
Ronald Cohen, MD
Deborah Dean, MD, MPH
Eva Delgato, MD
Stephanie Doniger, MD
Ervin Epstein, MD
Horst Fischer, PhD
Heidi Flori, MD
Ellen Fung, PhD
Feng Gao, PhD
Ward Hagar, MD
Karen Hardy, MD
Paul Harmatz, MD
Sumi Hoshiko, MPH, CDPH-EHIB
Beate Illek, PhD
Frans Kuypers, PhD
Ashutosh Lal, MD
Claudia Maier, PhD
Jyothi Marbin
Marisa Wong Medina, PhD
Rose Ellen Morrell, MD
Vasanthy Narayanaswami, PhD
Jacob Neufeld, MD, MSPH
Janelle Noble, Ph.D
Robert Ryan, PhD
Mark Shigenaga, PhD
Barbara Staggers, MD
Jodi Stookey, PhD
Chau Tai, MD
Sachiko Takayama, PhD
Lindsay Steirer Taylor, PhD
Marsha Treadwell, PhD
Gordon Watson, PhD
Lee Ying

Selection Committee

Chairperson
Vasanthy Narayanaswami, PhD
Assistant Scientist
Children's Hospital Oakland Research Institute
5700 Martin Luther King Jr. Way
Oakland, CA 94609
vnarayan@chori.org
Cell: 925-212-9354

Carolyn Kane, PhD
Director, Biology Fellows Program
Department of Molecular and Cell Biology
2075 Valley Life Sciences Building
University of California, Berkeley
Berkeley, CA 94720
510-642-4118
kanecm@berkeley.edu

Frans Kuypers, PhD
Senior Scientist
Children's Hospital Oakland Research Institute
5700 Martin Luther King Jr. Way
Oakland, CA 94609
510-450-7620
fkuypers@chori.org

John Matsui, PhD
Director, Biology Scholars Program
Department of Molecular and Cell Biology
2075 Valley Life Sciences Building
University of California, Berkeley
Berkeley, CA 94720
510-643-9768
matsui@berkeley.edu

Barbara Staggers, MD
Director and Division Chief, Adolescent Medicine
Children's Hospital & Research Center Oakland
747 52nd St.
Oakland, CA 94609
510-539-4541 pager
Private cell: 828-5391
bstaggers@mail.cho.org

Tomas Magana, MD
Co-Director, Faces for the Future
Children's Hospital & Research Center Oakland
747 52nd St.
Oakland, CA 94609
TMagana@mail.cho.org

2011 Weekly Discussions/Lectures

Friday, June 9,
9:30 a.m. to 4 p.m.
Orientation and Introduction
by Alex Lucas, PhD, Executive Director, CHORI

Introduction by Bert Lubin, MD, President & CEO, CHRCO; and Vasanthy Narayanaswami, PhD, CHORI Scientist, Basic Science Program Co-Director

Friday, June 10,
9:30 a.m. to 12:30 p.m.
Keynote speaker: John Matsui, PhD, Director, Biology Scholars Program, Department of Integrative Biology, University of California, Berkeley
"Your Place in Science"

Monday, June 13, 9:30 a.m.
Make up Orientation
Deborah Ellen and Phillip Bollinger

Tuesday, June 14
1:30 to 5 p.m.
Make up Safety Orientation
Miriam Fang

Friday, June 17, 10 a.m.
Special Training: Guava, Centrifuge, Tissue Culture and Autoclave Equipment (required)

Tuesday, June 21, 4 p.m.
Patrick Walter, PhD,
Staff Scientist, CHORI;
Adjunct Assistant Professor, Department of Biology, University of Victoria
"Transfusional Iron Overload and Thalassemia"

Tuesday, June 28, 4 p.m.
Phillip Bollinger
Fear & Loathing of the Big Red X
"How to Correctly Assemble Your Microsoft PowerPoint Presentation Utilizing Sanctioned Procedures, and Methodologies Within Accepted Microsoft Parameters"

Wednesday June 29, Noon
Frans Kuypers, PhD,
Senior Scientist, CHORI
"Membrane Biology and Hemoglobinopathies"

Tuesday, July 5, 4 p.m.
Griselda Velasquez, Former CHORI Summer Student, Program Advisor for the Biology Scholars Program at the University of California, Berkeley

Wednesday July 6, Noon
David Killilea, PhD,
Associate Staff Scientist, CHORI
"Consequences of Micronutrient Deficiencies"

Tuesday, July 12, 4 p.m.
Deborah Dean, MD, MPH,
Senior Scientist, CHORI
"Recombination In Chlamydia And Implications For Emergence Of Virulent Strains In Human Populations"

Wednesday, July 13, Noon
Carolyn Kane, PhD,
Director, Biology Fellows Program, University of California, Berkeley
"Women in Science"

Tuesday, July 19, 4 p.m.
Fernando Vitteri, MD, ScD,
Scientist, CHORI
"Importance Of Iron In The Reproductive Process: Not Too Little And Not Too Much"

Wednesday, July 20, Noon
Lunch in the Courtyard

Tuesday, July 26, 4 p.m.
Vasanthy Narayanaswami, PhD, Basic Science Program Co-Director; CHORI Scientist; Faculty at California State Univ., Long Beach
"Apolipoprotein E: A Tale of Two Diseases"

Wednesday, July 27, Noon
Barbara Staggers, MD,
Clinical Program Co-Director, Director Adolescent Medicine; Executive Director, External Affairs and Community, Relations, CHRCO
"Life"

Wednesday, July 27, 4 p.m.
Ben Hanes, CHORI IT
"Poster/InDesign Training"

Tuesday, August 2, 4 p.m.
Bert Lubin, MD, President & Chief Executive Officer, CHRCO
"Film"

Tuesday, August 9, 2 p.m.
Phillip Bollinger, CHORI IT
"Oral Presentation Practice"

Friday, August 12,
8 a.m. to 5 p.m.
Summer Student Final Symposium

2011 CHORI Summer Research Program Curriculum

ORIENTATION, JUNE 9, 2011
There will be an all-day orientation for summer interns on Thursday, June 9, 2011, from 10:00 a.m. until 4:00 p.m. Continental Breakfast will be served at 9:30 a.m. Lunch will also be served.

Agenda to include:

- Introduction by Alex Lucas, PhD, Executive Director, CHORI
- Introduction and by Vasanthy Narayanaswami, PhD, Scientist CHORI, Basic Science Program Co-Director
- Keynote lecture: John Matsui, PhD, ***"Your Place in Science"***
  Director, Biology Scholars Program, Department of Integrative Biology, University of California, Berkeley
- IT Orientation: Phillip Bollinger
- Explanation of curriculum: Vasanthy Narayanaswami, PhD
- Administrative Review: Deborah Ellen
- CHORI tour

SAFETY TRAINING, JUNE 10, 2011
The mandatory Safety Training with CHORI Safety Officer, Miriam Fang will be held on Friday, June 10 from 9:30 am to 12:30 pm. The student will be required to complete this training BEFORE beginning their project.

Make up Orientation
Monday, June 13, 2011 9:30 a.m.
Deborah Ellen and Phillip Bollinger
Badging: TBD

Make up Safety Orientation
Tuesday, June 14, 2011
1:30 to 5:00 p.m
Miriam Fang

RESEARCH PROJECT: JUNE 13, 2011 TO AUGUST 12, 2011
The student will conduct research with assigned mentor. The details of project and research plan are left entirely to the individual mentor and each summer intern will follow the procedures, and schedule, laid out by their respective labs.

SUBMIT WRITTEN RESEARCH PLAN: JUNE 24, 2011

Students must submit to the Program Coordinator a written Research Plan outlining their project. The Research Plan should be 3-4 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, and teen health issues. Please see Schedule for dates and times.

2011 CHORI SUMMER STUDENT SYMPOSIUM, AUGUST 12, 2011

A one-day symposium will be held on August 12, 2011 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 24, 2011 by 5:00 p.m. 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. Details of the Symposium and the scientific sessions will be available by August 1, 2011.

The Symposium will be comprised of about 12 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. An abstract book, which will include the Symposium program, personal statements, and the research project abstracts, will be presented to each student. A catered breakfast and lunch will be provided for all attendees on the Symposium day.

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

SUMMARY OF IMPORTANT DATES:

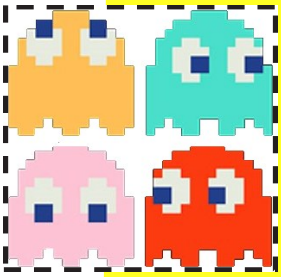
June 9, 2011	Orientation: 10 a.m. to 4 p.m.
June 10, 2011	Safety Training: 9:30 a.m. to 12:30 p.m.
June 13, 2011	Make up Orientation: 9:30 a.m. to 11 a.m.
June 14, 2011	Make up Safety Training: 1:30 to 5 p.m.
June 24, 2011	Written Research Plan due
July 1, 2011	Personal Statement for Program Guide due by 5 p.m.
July 24, 2011	Abstract for Program Guide due by 5:00 p.m.
August 12, 2011	Summer Student Research Symposium

2011 CHORI Summer Research Program BBQ

CHORI Summer Students '11 Present:

80s BBQ Bash

WHEN? Friday, July 22nd from 12-2 pm!



WHO?

All Summer Students, mentors and CHORI staff

WHAT?

SummerFest BBQ #2
A flashback to the 1980's full of good food, music and fun!

WHERE?

CHORI Main Courtyard

Feel free to bring food

If you have any questions or concerns feel free to email:
mbustill@wellesley.edu or samanehb11@gmail.com

Volunteer Recognition 2011

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

VOLUNTEERS:

CHORI:
Jennifer Beckstead
Tate Brazas
Karen Catanese
Sally Chiu
Horst Fischer
Ben Hanes
David Killilea
Katrina King
Mirella Machuca
Lorelle Parker
Brigid Roy
Hector Sandoval
Kathy Schultz
Lindsay Streirer Taylor

Student Volunteers:
Marleny Acosta
Devan Block
Karen Burtt
Janice Dalida
Rigoberto DelToro
Crystal Ghosh
Adriana Gonzalez
Lauren Meiss
Bissy Tekie

Symposium Schedule – Friday, August 12, 2011

8:00 – 8:30	**Check-in and Continental Breakfast** at the CHORI Library
8:30 – 8:45	Welcome by CHORI Executive Director, Senior Vice President of Research **Alex Lucas, PhD** **Vasanthy Narayanaswami, PhD**, Basic Science Program Co-Director Scientist at CHORI, Faculty at California State Univ, Long Beach **Barbara Staggers, MD**, Clinical Co-Director, Director, Adolescent Medicine, Executive Director, External Affairs and Community Relations
8:45 – 12:30	Oral Presentations in the CHORI Library

	PRESENTATIONS - SESSION 1	**PAGE**
Chairs:	**Sally Chiu, PhD**, Assistant Staff Scientist Children's Hospital Oakland Research Institute and **Lauren Meiss**, Senior, Arizona State University	
8:45 – 9:00	**Samaneh Bolourchi**, Sophomore, University of California, Berkeley Mentors: Barbara Staggers, MD, Jyothi Marbin Title: **Improvement in Asthma Care for Adolescents at Children's Hospital Teen Clinic**	32
9:00 – 9:15	**Anita Chanana,** Junior, University of California, Berkeley Mentor: Ervin Epstein, MD Title: **Pre-Clinical Study of 5% Itraconazole Cream in Mice for the Chemotherapy and/or Chemoprevention of Basal Cell Carcinomas**	40
9:15 – 9:30	**Rigoberto Del Toro**, Senior, University of California, Berkeley Mentor: **Jodi Stookey, PhD** Title: **Free Fruits and Vegetable Study**	44
9:30 – 9:45	**Roy Hernandez**, Post-Baccalaureate, University of California, Long Beach Mentors: Vasanthy Narayanaswami, PhD, Claudia Maier, PhD Title: **Hydrogen/Deuterium Exchange and Mass spectral Analysis of the High Affinity Lipoprotein Binding Domain of Apolipoprotein E3**	56
9:45 – 10:00	**Jacquelyn Knapp**, Post-Baccalaureate, San Francisco State University Mentor: Janelle Noble, PhD Title: **A Comparative Study of Three High-Resolution Genotyping Technologies: Linear Arrays, Suspension Arrays, and 454 Sequence Based Typing**	68
10:00 – 10:15	**Zian Liu**, Senior, Albany High School Mentor: Ashutosh Lal, MD Title: **The Effects of Iron on Mitochondrial Respiratory Complexes**	74
10:15 – 10:30	Break	

	PRESENTATIONS - SESSION 2	PAGE
Chairs:	**Jennifer Beckstead**, Senior Research Associate, Children's Hospital Oakland Research Institute and **Bisrat Tekie**, Junior, Sarah Lawrence	
10:30 – 10:45	**Rajan Manmohan**, Post-Baccalaureate, Mills College Mentor: Bindu Kanathezhath, MD Title: **Determining changes in thiol redox profile of the T cell effector phenotypes associated with alloreactivity**	78
10:45 – 11:00	**Lauren Meiss**, Senior, Arizona State University Mentors: Beate Illek, PhD, Horst Fischer, PhD Title: **Role of CFTR and p53 during Pseudomonas Aeruginosa Homoserine Lactone Induced Apoptosis and Epithelial Barrier Breakdown**	80
	Maria Bustillo, Junior, Wellesley College Mentors: Beate Illek, PhD, Horst Fischer, PhD Title: **Novel ways to improve the success of CFTR gene therapy: role of hyperthermia**	36
11:00 – 11:15	**Dawit Melak**, Post-Baccalaureate, University of California, Berkeley Mentor: Cassandra Calloway, PhD Title: **Examining the Correlation of PGC-1α with Mitochondrial DNA Content in mice fed a High Fat Diet (HFD)**	82
11:15 – 11:30	**Napala Pratini**, Junior, St Mary's College of California Mentor: Jacob Neufeld, MD, MSPH Title: **Administration of Hydroxy-Propyl-Beta-Cyclodextrin (HPBCD) using the Medtronic SynchroMed II Programmable Drug infusion system for the treatment of Niemann Pick Type C Disease (NPCD)**	92
11:30 – 11:45	**Katie Reget**, Junior, Osseo Senior High, Osseo, Minnesota Mentor: Ellen Fung, PhD, RD, CCD Title: **Pain and Bone Mineral Deficits in Thalassemia: Is there a Link?**	96
11:45 – 12:30	**Rathana Yim**, Junior, University of California, Berkeley Mentors: Ronald Cohen, MD, Sumi Hoshiko, MPH, CDPH-EHIB Title: **Abdominal and Craniocerebral Pediatric Computed Tomography (CT) Exposures in California**	108
12:30 – 1:30	Lunch in the Library Courtyards	
1:30 – 3:00	Poster Session in the Senior Center Courtyard	
1:30 – 2:15	Even Posters presenting	
2:15 – 3:00	Odd Posters presenting	
3:00 – 5:00	Certificate Presentation and Reception in the CHORI Library	

Notes

2011 Students

MARLENY ACOSTA

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

Long Island University Master's Program
Brooklyn, NY

Mentor: Deborah Dean, MD, MPH

Currently, I am working on a master's degree in medical microbiology at Long Island University in Brooklyn, NY. I graduated recently from Fordham University with a bachelor's degree in natural science. As I was leaving high school behind and entering college, I realized that what I wanted most is to become a physician. I have had the opportunity to work and volunteer in health clinics and hospitals in NY, which exposed me to the many disparities in the health care system. Witnessing the critical need for a physician's training in my community and the impact of a compassionate physician for countless families further encouraged me to consider a career as a medical doctor.

As a Dominican American woman from Washington Heights, NY, I strongly believe that I can offer a great service to my community and many others as a physician. As a physician, I am committed to reinvesting in my community in a similar capacity in educating younger professionals and investing in preventative educational programs to improve the delivery of health care information and treatment.

In order to attain this goal, I realized that I lacked a major component in my education. What I lacked was a research background and because of the CHORI summer program I was able to change that. I had the opportunity to be mentored by Dr. Dean, whom is working with Chlamydia, one of the leading causes of sexually transmitted diseases. I would also like to express my gratitude towards Deborah Ellen, whom took me under her wings this summer. No words can express how thankful I am for everything she has done for me. I felt terror at the thought of coming to a new place yet she made me feel at home. I would also like to extend my thank you to Phillip Bollinger for all the work he put into making this program a success. I feel blessed to have been accepted into this fascinating program that through education is helping shape many young people into future professionals. My goal is to sharpen my skills to learn, integrate, and apply advance concepts that will strengthen my academic profile and prospects for medical school. Thanks to the CHORI summer program I am more confident about reaching that goal.

Super-infection of HEp2 Cells by multiple strains of *Chlamydia trachomatis* and effect on organism recombination

Hypothesis: Infection of HEp2 cells with one strain of *C. trachomatis* facilitates subsequent infection with the same or another strain; independent inclusions fuse to form one inclusion where the population of progeny EBs is comprised of recombinant and non-recombinant EBs from the two infecting strains.

Introduction: *Chlamydia trachomatis (Ct)* is the leading bacterial cause of sexually transmitted diseases (STD) in the world today[1]. *Ct* is an obligate intracellular bacterial parasite, well known for its distinctive intracellular development cycle. The infectious elementary body (EB) fuses with the host cell. Transformation of the EB into the metabolically active reticulate bodies (RB) occurs. The reticulate bodies undergo binary fission within an intracellular phagosome or inclusion, which develops within a few hours after infection. The phagosome manages to avoid fusion with host cell lysosomes (not understood how). Within the inclusion, reticulate bodies retransform into mature EBs. Finally, the inclusion ruptures or extrudes the inclusion and the new EBs are released and are ready to infect other host cells. To study this prokaryote, cell lines such as HeLa cells and HEp2 cells are widely used to test *Chlamydia* pathogenesis. HEp2 cells specifically are an immortalized cell line derived from tumor cells. In a study done by Ridderhof and Barnes, they reported in vitro infection by multiple serovars of *C. trachomatis.* They found that co-infection of a single cell by two strains of *C. trachomatis* resulted in the fusion of the inclusions, which could bring chlamydial organisms into close contact and would potentially allow for genetic exchange of the organisms leading to diversity[2].

Objective: The purpose of this study is to determine whether different non-virulent (E, F) strains can infect the same host cell (i.e. super-infection) and provide future information regarding possible mechanisms of phagosomal membrane fusion and opportunities for genetic exchange.

Methods: The HEp2 cells have to be split first into wells of a 24 well plate. The next step is preparing serial dilutions for infection to determine titers of the strains pre and post EB dye staining. Antibody staining is then done to confirm correct labeling of the EBs. Finally, the super-infection is done in a 24 well plate by first infecting with serovar E and after a four hour incubation period, infecting with serovar F. Results can be seen using light and confocal microscopy.

Results: Pending

Conclusion: Research on super-infection was done many years ago. HeLa cells were infected by two strains of the organism (E and F). In the current study, I am testing sequential infection with various strains, both virulent and non-virulent, to determine any differences in super-infection, inclusion formation and inclusion fusion. Though results are pending, I anticipate that as in the previous study, I will find that prior infection of HEp2 cells can facilitate super-infection by another strain. In addition, using confocal microscopy, it will be possible to observe two or more strains within a single inclusion and whether these two have recombined during formation of the EB. This will give us more insight into the opportunity for genetic exchange.

References:
1. Centers for Disease Control and Prevention. <http://www.cdc.gov/std/chlamydia/>
2. John C. Ridderhof and Robert C. Barnes. Fusion of Inclusions following Super-infection of HeLa Cells by Two Serovars of Chlamydia trachomatis. (pg. 3189)

ANAIS AMAYA

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

University of California, Berkeley, Junior

Mentor: Mindy Benson, MSN, PNP

I had never been interested in doing research until I met a great friend whose son Abel was diagnosed with autism. Abel has been involved in several studies looking at autism. He has taken his part to help researchers fully understand his condition and one day finding a treatment for it. I had always pictured research as a very long and boring process inside a lab. I never fully understood the different aspects to it and the impact it can have on an individual outside the lab.

Working in the Primary Clinic at Children's Hospital Oakland has been an amazing experience. Doing clinical research has given me a better perception of how exiting research can be. I feel very fortunate to have the opportunity to work with great people who are masters at what they do. I will walk away from this experience as a new person and with great respect for all those who spend their lives searching for ways to better the lives of others. I would like to thank Mindy Benson MSN PNP, Robert Mok LVN and the entire Asthma Team for all the patience and support they have showed me since day one.

Effectiveness of Preventative In-Home Based Programs in Decreasing the Number of Emergency Department (ED) Visits for Asthma Related Symptoms

Introduction: Asthma is the leading diagnosis for patients seen in the Emergency Department (ED) at Children's Hospital and Research Center Oakland (CHRCO). Three years ago CHRCO staff began a pilot of The (ATTACK) Asthma Tools and Training Advancing Community Knowledge clinic. The ATTACK Clinic was designed to reduce repeat ED visits for asthma by scheduling pts who were in the ED for asthma with a follow-up appointment within a week of their ED visit. The attack clinic provides a follow-up medical assessment, intensive asthma education, and referral to home based asthma case management from the Asthma Start program. The Asthma Start Program works with patients with asthma in Alameda County under the age of 18. This program serves to educate the patient as well as the family on reducing the number of asthma attacks by reinforcing education to parents and families and helping to identify asthma triggers in the home and solutions to reduce these triggers. The program consists of 2-3 home visits in an average of 3-6 months.

Objective: The main objective of this project is to demonstrate the effectiveness of ATTACK Clinic and The Asthma Start Program in reducing the number of further Emergency Department visits for asthma symptoms. As a result, the development of more programs that are geared towards educating the community about asthma to prevent Emergency Department visits could spread to more counties in the area.

Methods: Data from the shared drive collected between 2008 and 2009 for patients seen at the ATTACK clinic will be analyzed. The patients seen between this timeline will be divided into two groups: the ones who agreed to participate in the Asthma Start Program (treatment group) and those who declined or could not be reached to participate in the Asthma Start Program (control group) after being referred to it by the providers from the ATTACK Clinic. The number of times each individual returned to the CHRCO ED for asthma symptoms within one year after being referred to the Asthma Start Program will be recorded. The data collected from the two groups will be compared and analyzed for any differences.

Results: No significant difference was found in the total number of ED visits between the two groups (T-test, $p=0.7460$, $df= 148$, $t= 0.3245$). The average of patients that returned to ED after accepting The Asthma Start Program was 42% compared to 49% that did not accept to participate in the program.

Conclusion: Even though the P value showed no significant difference in the number of ED visits, there was a decrease in the number of patients who returned to the ED. More data should be collected and analyzed to get more significant numbers.

ARIEL APPLBAUM

Funded by Children's Hospital Los Angeles (National Heart, Lung and Blood Institute, Basic and Translational Research Program)

Jewish Community High School, Junior

Mentor: Marisa Wong Medina, PhD

Throughout my schooling the greatest constant has been my enjoyment of the sciences. Beginning with my kindergarten experience of shaking both milk and cream to test which of the two makes butter, to middle school efforts at measuring the acidity in the bay area water, or building my first rollercoaster to test the concepts of momentum and resistance, to finally being in a real lab dissecting animals and doing actual chemical experiments in high school – experiential science has been my most rewarding and engaging area of study. Yet there was always an element of incompleteness in my studies and that is -- how can this study be meaningfully used in the real world? Thanks to CHORI I am on way to understanding the answer to this question, making my study and thirst for knowledge and understanding of science all the greater.

At CHORI, I have been given the opportunity to work in a lab studying how the body regulates cholesterol and the possible impact that genetics could have on the efficacy of statin in the treatment of cholesterol. Although a strange sentiment, cholesterol has played a large role in both my life and the life of my family. My late grandfather suffered from both strokes and heart disease. My father drastically changed his lifestyle and became a vegetarian because of his high cholesterol levels. Personally, I have been placed in the "high risk" category because of my elevated cholesterol levels. Having the opportunity to understand cholesterol better has been not only informative but epiphytotic. Although I have been categorized as high risk, I have never taken the fact to heart (excuse my pun). I have always brushed aside the potential deleterious effects and the fact that I had the power to do something about it. Now with both greater knowledge of the body and the negative effect that high cholesterol can have, I am working to lower it.

Working with Marisa Wong Medina (in the Medina Lab) has been a great honor and a privilege. While I fully expected to be awed by her knowledge and skill and that of others in the lab, I had not expected to be treated with such patience and willingness to explain and teach. The relaxed atmospheres, brilliance, drive for scientific discovery and advancement and love of the work have been inspirational for me.

Thanks CHORI for advancing my knowledge, enhancing my drive to work in the scientific arena, and providing me with such a rare opportunity to view and participate first hand in cutting edge scientific research and advancement.

Does SUGP1 affect cholesterol through alternative splicing?

Introduction: Cardiovascular disease (CVD) accounts for 42% of all deaths in the US, killing around 1,000,000 Americans annually. One of the most well established risk factors for CVD is elevated plasma low density lipoprotein (LDL) cholesterol. Single nucleotide polymorphisms (SNPs) in *HMG-CoA reductase (HMGCR)*, the gene that encodes the rate limiting step of cholesterol biosynthesis, and the *low density lipoprotein receptor (LDLR)*, the gene responsible for uptake of LDL-cholesterol from the plasma, have been associated with variation in plasma LDL-cholesterol. Both of these SNPs regulate alternative splicing of either *HMGCR* or *LDLR*, suggesting that alternative splicing may be an important process that influences variation in plasma cholesterol levels. Recently, a SNP within SUGP1 (also known as: SURP and G patch domain containing 1 or SF4), a known splicing factor, was reported to be not only associated with variation in LDL-cholesterol, but also variation in expression of the *SUGP1* transcript itself, suggesting that this particular splicing factor may play a role in the maintenance of intracellular cholesterol homeostasis. Thus, we hypothesized that SUGP1 may be associated with variation in plasma cholesterol by acting as a regulator of alternative splicing of genes involved in cholesterol biosynthesis and uptake.

Objective: 1. Test if SUGP1 transcript levels are altered in response changes in intracellular cholesterol content. 2. Determine if *SUGP1* influences alternative splicing of genes involved in the cholesterol biosynthesis *(HMGCR)* and uptake *(LDLR)*.

Methods: To determine if *SUGP1* transcript levels changed in response to intracellular cholesterol content, HepG2 cell lines were grown in 6-well plates, and treated in quadruplicate with sham buffer or 2.0μM simvastatin + 10% lipoprotein deficient serum (n=5). After 24 hours, 50μg/ml LDL-cholesterol was added to one set of samples, 1 μg/ml 25-hydroxycholesterol was added to the second set, the third set was left untreated, and the fourth set was harvested. All remaining samples were collected after additional 24hr incubation. To ascertain the effect of *SUGP1* knock-down on alternative splicing, HepG2 were also transfected for 48hr with either an siRNA that targets *SUGP1, GAPDH,* or a non-targeting control (n=3). RNA was isolated, cDNA synthesized and gene expression measured by quantitative real-time PCR.

Results: We did not detect changes in *SUGP1* transcript levels after either 24hr or 48hr of extreme sterol depletion, or after addition of either LDL-cholesterol or 25-hydroxycholesterol. After 48hr transfection with the *SUGP1* specific siRNA, *SUGP1* transcript levels were reduced 73.48 ± 0.07 %, however, we failed to detect a difference in alternative splicing of either *HMGCR* or *LDLR* compared to cells treated with either the *GAPDH* or NTC siRNAs.

Conclusion: Although these preliminary results suggest that the relationship between *SUGP1* and plasma cholesterol is not mediated through changes in either *HMGCR* or *LDLR* alternative splicing, they do not discount the possibility that *SUGP1* may regulate alternative splicing of other genes involved in cholesterol metabolism.

JASMINE BAFAIZ

Funded by Children's Hospital Los Angeles (National Heart, Lung and Blood Institute, Basic and Translational Research Program)

Dublin High School, Junior

Mentor: Frans Kuypers, PhD

My name is Jasmine Bafaiz and I will be a senior at Dublin High School. Ever since I was a child, I have always wanted to become a doctor, precisely a hematologist. I want to become a doctor because it is one of the few careers that contain all of the things I desire in a career. I love to help people, and I want a job that also makes a difference in the community. I hope to get into a great university where I can work hard to become the doctor I know I can become.

This summer, I have the opportunity to work alongside Frans Kuypers, Bindu Kanathezhath, Sandra Larkin, and Marcel Fens at Children's Hospital Oakland Research Institute (CHORI). I appreciate the help I have been receiving from my mentors; you have all been so patient with me, thank you. I would also like to thank my family for supporting me in whatever I decide to do and for always being there for me.

My time so far at CHORI has given me the chance to thoroughly explore the medical field. Through the weekly seminars and my interactions with both pre-med students and medical professionals, I am certain that I want to become a hematologist, so I can help children who have sickle cell disease or thalassemia. I have learned a lot during my time at CHORI, and I look forward to using my experiences in the near future.

Nitrite Reduction to Nitric Oxide by Red Blood Cells

Hypothesis: Normal red blood cells (RBC) will have a different nitrite (NO2) reduction capacity compared to the blood of hemoglobinopathy patients due to the different oxygen affinities.

Background: Hemoglobin (Hb) is the oxygen-carrying protein in RBC. The most common types of normal Hb are: Hb F (fetal Hb) and Hb A (adult Hb). Hb F, which has a higher oxygen affinity than Hb A, is normally replaced by Hb A shortly before birth. However, some diseases, such as severe forms of thalassemia, may cause Hb A levels to be low and Hb F levels to be high. One of the most common types of abnormal Hb is Hb S, which has a lower oxygen affinity than Hb A. This type of Hb is present in sickle cell disease (SCD) patients who experience episodes of vaso-occlusive crisis (VOC), which lead to decreased blood flow and decreased oxygen availability to the tissues. VOC is counteracted by the formation of nitric oxide (NO), resulting in vaso-dilation and increased blood flow. Some current treatments for these patients are aimed at increasing their levels of NO.

Objective: We aim to evaluate the ability of RBC to reduce NO2 to NO.

Methods: Normal control blood samples were drawn from lab donors after informed consent. Four discarded patient samples (1 Thalassemia, 3 SCD) were obtained from Children's Hospital Oakland (CHO) with Institution Review Board approval. Blood cell composition was measured by Advia 120 Analysis (Bayer; Tarrytown, NY), Hb modification by Spectroscopy (Varian; Walnut Creek, CA), and oxygen affinity by Hemox Analyzer (TCS Corp.; Huntingdon, PA). RBC NO2 reducing capacity was determined by a novel setup including a tonometer (Instrumentation Laboratory Lexington, KY) and a Nitric Oxide Analyzer (GE Analytical; Boulder, CO). All blood samples were deoxygenated in the presence of non-limiting amounts of NO2. Hb F values were obtained from CHO.

Results: There was no significant difference in NO production between one patient with thalassemia and one normal control. The amount of NO produced in 30 minutes was 16.5 ± 4.6 mmole NO/mole Hb in three SCD patients (Hb S + Hb F) compared to 9.9 mmole NO/ mole Hb in a normal control (Hb A). The amount of Hb F in the SCD patients was 0.9 ± 0.5 g/dL. The reduction of NO2 by RBC also caused a shift in the Hb spectrum.

Conclusion: The higher NO production seen in SCD RBC compared to normal RBC suggests that a shift towards a higher oxygen affinity leads to increased reduction of NO2 to NO under deoxygenation. This higher production of NO increases the signal to the surrounding smooth muscle to relax, thus resulting in vaso-dilation. As a result, NO2 could be used as a potential treatment for VOC in the future. In order to solidify this conclusion, more samples were needed together with oxygen affinity measurements at p50.

DEVAN BLOCK

Funded by the CHORI General Fund

University of California, Berkeley, B.A. Public Health

Mentor: Bruce Ames, PhD

In 2009, I received my A.A. in Liberal Arts from Santa Barbara City College. At the time, I knew I wanted to continue my education, but I was unsure about which subject to focus on. A friend had mentioned that he had enjoyed Public Health. I wasn't really sure what Public Health was but after discovering that it encompassed the sciences with an emphasis of the human aspect of biology, I knew it was the right major for me. After just a few classes I knew I had found something I was passionate about. I recently graduated from UC Berkeley with a B.A. in Public Health. Public Health encompasses a wide variety of viewpoints in the health field such as policymaking, management, research, clinical work, data analysis, caregivers, and much more. Even though these subfields are very different, they all focus on prevention and helping people and my participation with the development of CHORI, a nutrition bar for children has been a fantastic opportunity to do just that. Even more specifically, the Ames lab that is interested in using nutrition to help prevent diseases later on in life.

Just as I felt uncertain before I choose Public Health undergraduate major, I feel unsure about what career I would like to pursue. However, I know that whatever I do choose, it will involve the health sciences and some method of prevention or treatment of diseases. Working in the Ames Lab has been an important part of my college experience. I have learned so much working in a research lab. It is not just the knowledge I've learned while working here, but it is also the whole experience and all the amazing people that work here that makes my time here invaluable. I will keep the experiences from CHORI with me and use it further my knowledge and experiences in the future.

Addition of a synthetic soluble fiber hydroxypropyl methylcellulose (HPMC) to nutrient-dense fruit-based supplement reduces risk factors linked to metabolic syndrome in healthy adults in a 2-month pilot trial

Introduction: We have previously shown in a short-term 2 month intervention trial that consumption of a nutrient-dense high fiber fruit-based bar (CHORIBar) favorably changes cardiovascular risk factors, but not biomarkers linked to sub-chronic inflammation and/or metabolic syndrome in healthy individuals. The synthetic, viscous, non-fermentable (non-metabolic) soluble fiber hydroxypropyl methylcellulose (HPMC) has been demonstrated to decrease low density lipoprotein-cholesterol (LDL-C), a cardiovascular risk factor as well as biomarkers of insulin resistance in pre-diabetic individuals. *We hypothesize that twice-daily consumption of the CHORIBar for two months with HPMC as the soluble fiber source will improve biomarkers related to cardiovascular disease and metabolic syndrome.*

Objective: The main objective of this study was to determine if twice daily consumption of the CHORIBar for 8 weeks would lower LDL-C and fasting insulin and enhance high density lipoprotein-C (HDL-C) levels in healthy individuals.

Methods: Sixteen healthy subjects participated in an eight week trial of twice daily intake of the CHORIBar with HPMC as the soluble fiber source. Anthropometric and biochemical markers measured included body mass index, waist circumference, blood pressure, lipid panel, fasting glucose, insulin, C-reactive protein and homocysteine. Quantitative changes in different biomarkers from baseline to 2 and 8 weeks were assessed using paired t-tests. Statistical significance was assessed at the 0.05 level.

Results: Plasma LDL-C significantly declined after a 2 week consumption of the CHORIBar with HPMC. The biochemical markers that showed a favorable shift after 8 weeks included HDL-C increase and fasting insulin decrease in addition to the LDL-C decrease.

Conclusion: Consumption of the CHORIBar with HPMC significantly lowered fasting insulin and LDL-C. In contrast, previous interventions with the CHORIBar containing a fiber other than HPMC did not alter these biomarkers. This suggests that the addition of HPMC to this nutritional supplement may provide additional metabolic benefits beyond that provided by the CHORIBar itself.

SAMANEH BOLOURCHI

Volunteer

University of California, Berkeley, Sophomore

Mentor: Barbara Staggers, MD, and Jyothi Marbin

The expression, "curiosity killed the cat", never applied in my family. As a child, my parents always encouraged me to ask questions and provoke discussions, constantly trying to motivate me to learn more and more everyday. On our annual trips to Lake Tahoe and Yosemite, I was always fascinated by the wildlife, giant trees and enormous mountains. I loved to examine things up close, questioning how they were made and contemplating the purpose of their existence. It was from that age that I knew I had a passion for science that only seemed to grow as I grew. Since then, not much has changed: my inquisitiveness about the world and our environment continues to push me towards broadening my knowledge about the things that surround me. This fall, I will be beginning my second year at Cal pursuing a Bachelors of Science in Molecular Environmental Biology and a minor in Ethnic Studies.

In addition, my parents always stressed the importance of giving back to the community in my life, and at the Teen Clinic, Dr. Staggers personified that goal. Despite her extremely busy schedule, she always made the time to visit and talk to her patients, and I have so much respect for her for that. She demonstrated her dedication to the Clinic, the employees, and especially the patients to me on so many occasions. She has shown me her constant commitment to making this community a better place and helping the underprivileged to attain the health services and respect that every person deserves. I cannot forget to thank Dr. Jyothi Marbin for her indispensable guidance, genuine kindness and dedication to mentoring me despite her busy schedule. Without her help, I would never have been able to carry out this project and complete it thoroughly; she is truly a remarkable doctor and inspiring mentor.

Through this internship at CHORI, I have strengthened my enthusiasm for science and learned so much through hands on lab work, lectures, and from the doctors around me. In the Teen Clinic, I have gained invaluable knowledge and experience that I would never have achieved in a large classroom. From this experience I was able to build connections that I would never have been given the opportunity to make before. I am extremely grateful to the faculty at CHORI and to my mentors, Dr. Staggers and Dr. Marbin, for providing this opportunity to explore clinical research and further reassuring my pursuit of a career in medicine.

Improvement in Asthma Care for Adolescents at Children's Hospital Teen Clinic

Introduction: Asthma prevalence continues to increase worldwide in adolescents, yet studies clearly indicate that a majority of patients are not able to manage their symptoms. Because the patients at the CHO Teen Clinic are usually high-risk teens who are experiencing more pressing problems, their asthma management is not high on their list of priorities. Furthermore, as published in many previous studies and journals, compliance is a major struggle in regards to the treatment of asthmatic teens. Many are in denial of being asthmatic or of the severity of the illness; others underreport symptoms, desert necessary medication regimens (usually because of carelessness, laziness, or forgetfulness), or simply have so much going on in their life that managing their asthma is not a major concern. These teens are in a developmental phase where it is critical for them to learn to broker their healthcare.

Objective: The aim of my research project with both Dr. Marbin and Dr. Staggers is to better understand asthma in this high-risk urban population by tracking the ACT forms.

Methods: The Asthma Control test is a both nationally and globally implemented five question health survey used to measure asthma control in individuals 12 years and older. Based on a range from 0 to 25 points, an ACT score below 19 usually indicates that a patient's asthma is not being controlled properly and intervention must be considered. At the Teen Clinic we have included several questions to the ACT form inquiring about current use and access to medications as well as smoking habits to better understand factors that could impact the patients asthma. This implementation of the revised ACT form allows for the quality of asthma care to be improved.

Results: ACT forms will continue to be collected through until the end of the summer, therefore, the results are not finalized. Currently, 99 surveys have been collected indicating that at least 36% of patients were in need of medication, 23% in need of a spacer, and an overall 41% of patients claiming an ACT score below 19. The data showed that 48% of the patients surveyed claimed that their asthma had kept them from getting work done at work, school or home at least a little of the time. Also, 61% of patients claimed to have experienced shortness of breath at least 1-2/ week in the past four weeks. Furthermore, 56% of surveyed asthmatic adolescents indicated that their asthma symptoms woke them up at night or in the morning at least once or twice in the past month. In addition, 45% indicated that they had used their rescue asthma inhaler at least once a week in the past four weeks. In a self-assessment, 21% on patients stated that their asthma was either somewhat, poorly, or not controlled in the past four weeks. Moreover, this survey showed that 73.7% of self-claimed asthmatic smokers at the Teen Clinic indicated that they would like help to quit. Lastly, in one group of surveys, 42 out of 47 patients indicated that asthma was not their reason for their visit to the clinic. From this series of patients 38% still demonstrated an ACT score below 19.

Conclusion: The use of the ACT form allows the clinic to follow asthma patients' health and help improve asthma management in the busy lives of this urban adolescent population. This survey creates a system where asthma management is easily tracked and medication/asthma related health needs are addressed efficiently for asthmatic adolescent patients that are visiting the clinic.

KAREN BURTT

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

Diablo Valley College, Sophomore

Mentor: Chau Tai, MD

After spending the summer 2010 at Children's Hospital and Research Center Oakland (CHRCO), I could not imagine spending this summer elsewhere. CHRCO is unique in the rarity of the patients it attracts; it is not unusual for me to see what most would consider once-in-a-lifetime surgeries once a week. I look forward to going to the hospital every morning; each day is a new adventure, from removing IMF and examining CT scans in clinic to pinning fractured bones and performing tendon transfers in the OR. Regardless of where I am, or what I am doing, Dr. Tai never ceases to be an engaging mentor and inspiring role model. Whether she is teaching me how to spot edema on an X-ray or explaining her decision-making process in surgery, her commitment to educating me has had a profound impact on my development as a student. I would like to thank Dr. Tai for being supportive when I needed encouragement, insightful when I needed a mentor, and enthusiastic when I needed a friend.

I wish the summer would never end. Paradoxically, I look forward to discovering the molecular and anatomical basis of the pathologies I have seen at Children's Hospital when I begin studying bioengineering at UC Berkeley in the fall.

Proposed Clinical Pathway for Treatment of Upper Extremity Dysfunction in Children with Cerebral Palsy at CHRCO

Introduction: Cerebral palsy (CP) is a progressive impairment characterized by increased muscular spasticity resulting from a lesion on the brain. Upper extremity involvement is characterized by poor joint and muscle control, weakness, and altered stereognosis. Posturing of the upper extremity typically includes shoulder adduction and internal rotation, elbow flexion, forearm pronation, wrist and finger flexion, and thumb-in-palm deformity. The typical contractures of elbow, thumb, wrist, and fingers impair execution of many activities of daily living.

Currently, there is disparity within the medical community regarding treatment of this impairment. Factors such as age (Green WT, 1962; Malizos KN, 2010; Ozkan T, 2009; Patterson JM, 2010), intelligence quotient of the patients (Green WT, 1962; Tachdjian MO, 1997), type of operations, and type of deformity result in inconsistent recommendations among physicians. Additionally, the volition of the patient and family strongly impacts the functional outcome of any procedure, adding another complicating factor to a condition that requires diligent rehabilitation in order to optimize outcome.

Objective: The purpose of this study is to determine the degree to which patient factors affect surgical outcome, in order to establish a clinical decision pathway at CHRCO that helps guide upper extremity reconstruction in selected patients that may improve their function and independence.

Methods: A literature review was conducted on surgical outcomes of major centers in the US that treat upper extremity dysfunction in cerebral palsy. Data on stereognosis, volition, age, type of CP, intelligence quotient, type of surgery, and their preoperatively and post-operative conditions were collected as available. Due to the different measurement scales used by different centers, statistical analysis was not feasible.

Results: All children with cerebral palsy are surgical candidates, regardless of the presence of stereognosis or cognitive ability. Purely athetotic patients should not undergo soft-tissue procedures, but mild athetosis should not prevent such surgical interventions. Intervention should begin at an early age; the age of intervention should not be dependent on ability of the child to cooperate with therapy, since alternate modalities such as neuromuscular electrical stimulation, constraint-induced movement therapy, and botulinum toxin-A have all shown benefit. Decision for surgery is guided by response to above interventions, and tailored to augment or make permanent the benefits achievable with temporary measure. Surgical intervention can also rebalance the extremity unachievable by other means, and earlier intervention in childhood may be better than waiting for skeletal maturity that allows development of more severe contractures.

MARIA BUSTILLO

Funded by the Elizabeth Nash Foundation

Wellesley College, Junior

Mentor: Beate Illek, PhD, and Horst Fischer, PhD

A rising junior at Wellesley College majoring in biology, I am thrilled to be returning to CHORI for a second summer of research in the Fischer-Illek Lung Biology and Pathology Laboratory. As a baby, my cousin was diagnosed with cystic fibrosis, and her courageous struggle with cystic fibrosis is a constant inspiration to me. I appreciate the opportunity to do research at CHORI on a disease that affects so many families across the country. While last summer's research introduced me to basic science research in the field of lung biology, I left with many questions unanswered. Hopefully, this summer's research will provide us with some answers to those questions and will take us one step closer to fully understanding and successfully treating this disease.

After college, I hope to continue with research in a more transitional manner as an MD/PhD. I credit CHORI's summer program with sparking the "research bug" and am excited for where it will take me. I owe many thanks to the scientists (both students and staff) of the Fischer-Illek laboratory for the camaraderie, support, and wealth of knowledge they have provided me this summer. I am particularly grateful to Dr. Illek and Dr. Fischer for their continuous guidance and encouragement through this great adventure.

Novel ways to improve the success of CFTR gene therapy: role of hyperthermia

Introduction: Gene therapy is a promising method of treatment for monogenetic diseases such as cystic fibrosis (CF) that do not yet have sufficient treatment options. CF is characterized by a mutation in the gene for the cystic fibrosis transmembrane conductance regulator (CFTR), a membrane chloride ion channel protein. Clinically, CF is characterized by thick mucus build up, preventing optimal lung function and allowing for the prevalence of bacterial infections. It is estimated that as little as a 6-10% correction of normal CFTR function is enough to support normal tissue function. Clinical gene therapy trials in the U.S. and the U.K. have been moderately successful, but are currently limited by the epigenetic silencing and limited uptake of the CFTR gene, as well as the eventual loss of CFTR gene expression. We hypothesize that prevention of epigenetic silencing enhances the efficiency of CF gene therapy treatment. We further hypothesize that BHT exerts an inhibitory mechanism of action on DNA methylation of the CMV promoter in the pCEP4-CFTR expression plasmid.

Objective: To elucidate the mechanism of action of brief hyperthermic treatment (BHT) as an enhancer of CFTR transgene expression in CF airway epithelial cells.

Methods: CF bronchial epithelial cells (CFBE41o-) stably transfected with a 6.2 kb cDNA construct (containing the open reading frame of CFTR plus 3' and 5' untranslated regions, 6.2N) or a 4.7 kb CFTR construct (open reading frame, 4.7N) were grown as confluent monolayers on Snapwell cell culture inserts. Cells undergoing brief hyperthermic treatment (BHT) were treated at 41-43°C for one hour, followed by a period of recovery (0-48 hours) in a 37°C incubator. To compare BHT effects to epigenetic modifications by DNA methyltransferase inhibitors (DNMTi), cell monolayers were treated with 5-aza-2'-deoxycytidine (5-aza-dC) or RG-108 for 2-72 hours. Following treatment, cell culture inserts were mounted in Ussing chambers for a functional assay of CFTR activity and subsequently stained for CFTR expression. Four different CFTR antibodies (450, 570, 596, 660 kindly provided by CFF Therapeutics) were tested using confocal microscopy. Methylation studies were performed on nuclear extracts after treatment with BHT and 5-aza-dC using a kit from Epigentek.

Results: Compared to untreated CFBE41o- monolayers, both 4.7N and 6.2N constructs responded to BHT treatment: 4.7N expressing CFBE41o- monolayers demonstrated a 3-fold increase in cAMP-dependent CFTR Cl currents (stimulated by forskolin and genistein) and 6.2N expressing CFBE41o- monolayers responded with a 4-fold increase. Additionally, the treated 6.2N clone demonstrated 4-fold higher transepithelial chloride currents than did the treated 4.7N clone. Similar results were seen after treatment with DNMTis (5-Aza-dG: 3.3-fold; RG-108: 2.3-fold increase), and effects were not additive to BHT. Using confocal microscopy, we determined a ~3-fold increase in the number of CFTR-positive cells between untreated and BHT-treated 6.2N CFBE41o- monolayers and an increase in the intensity of CFTR expression at the apical cell membrane.

Conclusions: BHT's similar functional profile to DNMTi , and non-additive effects when treatments were combined, suggest a common underlying mechanism of action involving demethylation of sites that had been methylated by DNA methyltransferases and were responsible for gene silencing of CFTR. Confocal imaging data support the hypothesis that both BHT and DNMTi enhance CFTR transgene expression as well as trafficking of CFTR to the apical membrane when compared with untreated cell monolayers. We conclude that BHT may provide a novel treatment modality to improve the success of gene therapy in CF.

DANIEL COHEN

Funded by Children's Hospital Los Angeles (National Heart, Lung and Blood Institute, Basic and Translational Research Program)

College Preparatory School, Senior

Mentor: Paul Harmatz, MD

My name is Daniel Cohen and this year I will be a senior at the College Preparatory School. I did this program last summer with Dr. Jacob Neufeld and it really jumpstarted my interest in the medical field. A year later and a year more mature, I am trying to expand my knowledge of medicine even further. I am very grateful for the great opportunities that the CHORI Summer Student Research Program has given me these two years and I am certain now that I be able to peruse a career in the biological sciences.

This summer I am working with Marcella Weyhmiller and I will be investigating the discrepancies between written and computer-based medical records of patients with iron overload (hemochromatosis). This is a little bit of an unusual project but I decided to take it because it is a change of pace and because I realized that this project could have large ramifications. If we discover that the computer records are inaccurate to a large enough degree it could make a big difference in how much medicine or blood these patients receive. These results could potentially save lives and this is the real reason behind my choice of project this year. I would also like to thank Dr. Paul Harmatz for agreeing to take me on and Marcella Weyhmiller for showing me the ropes and helping me along the way.

Investigating the Challenges in Keeping Accurate Medical Records in Patients with Transfusional Iron Overload

Introduction: Patients with severe thalassemia or sickle cell anemia sometimes are treated with regular blood transfusions because the bone marrow cannot produce normal or healthy red blood cells. These patients need the erythrocytes in the healthy blood to restore normal blood function. Unfortunately, the regular transfusions can cause another problem. Each unit of blood contains approximately 250 mg of iron (either floating in the blood plasma or bound to hemoglobin) and the body does not have a way to metabolize iron in any significant amount except for the sloughing off of the intestinal lining so free floating iron slowly accumulates in the blood of patients who receive regular transfusions. The liver tries to filter out the excess iron and eventually it can build up in the major organ systems and overload them, causing numerous physiological problems. If untreated, iron overload can cause cardiac failure, liver cell death and endocrine dysfunction. This project looked at the transfusion volumes of patients with iron overload. This is an important piece of data because the volume of blood that a patient receives plays a part in helping both researchers and doctors understand that patient's level of iron overload.

Objective: The main objective of this project is to determine the extent of the error between the digital and the written medical records. I performed a data analysis and then tried to determine if the deviation between the digital medical record and the written record is significant. Furthermore, I estimated the patient's average annual transfusion volume with a simple model.

Methods: First, I performed a chart review to extract the transfusion volumes from the blood bank records and compared them with the existing Meditech digital records. Then, I calculated the differences between the written and digital entries and did a comparison of the data from four different patients. I then performed a data comparison using three sets of data derived from the medical records. The first set of data is the average transfusion volume for a patient in one year based off of the written records, the second is another average transfusion volume based off of the Meditech record and the third is the average transfusion volume per year based off of a simple model created using the patient's age at the onset of chronic transfusion.

Results: Data is still being analyzed and collected. The results will be presented at the symposium on the completed poster.

Conclusions: A conclusion will be drawn once the data has been fully collected and analyzed.

ANITA CHANANA

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

University of California, Berkeley, Junior

Mentor: Ervin Epstein, MD

My name is Anita Chanana, and I am currently a senior at UC Berkeley majoring is Molecular Toxicology.

I have worked for Children's Hospital Oakland Research Institute (CHORI) for a little over a year now. During my time here, I have achieved a greater understanding of what is involved in medical research and the importance of research. The Epstein lab performs a lot of translational research; therefore, I have witnessed medicine going from the lab bench to the patient's bedside. One of the main things our lab studies is the development of new treatments and preventive measures for Basal Cell Carcinomas (BCCs) in order to reduce surgical removal of the tumors. Having witnessed the impact a drug can have on a patient's quality of life has been amazing, and having taken part in it makes this experience even more powerful. I have seen patients with Basal Cell Nevus Syndrome (BCNS), a rare heritable disorder that causes patients to be more susceptible to developing BCCs, go from having hundreds of BCCs to a much lesser burden. I appreciate what our lab contributes to the medical field and my time at CHORI has further solidified my goal to enter the field of medicine.

I would like to thank everyone in the Epstein lab for dedicating their time to teaching me during my time at CHORI, especially my mentors, Dr. Jean Tang and Dr. Ervin Epstein. Having attended patient visits with both Dr. Tang and Dr. Epstein, I have seen their commitment to their patients and their true care for their well-being. They have not only taught me how to perform good research, but also how to be an excellent doctor. They have provided me with a model for someone I aspire to be. I would also like to give many thanks to my co-mentor, Alex Lee, for teaching me various lab techniques this summer. Last, but not least, I am grateful for my parents, without their everlasting love and support I wouldn't be where I am today.

Pre-Clinical Study of 5% Itraconazole Cream in Mice for the Chemotherapy and/or Chemoprevention of Basal Cell Carcinomas

Introduction: Itraconazole is a commonly used drug to treat fungal infections that has been recently identified using small molecule screens as inhibitors of the Hedgehog signaling pathway that drives basal cell carcinoma carcinogenesis.[1] Basal cell carcinoma (BCC) is considered the most common human cancer. The occurrence of BCCs affects almost 1 million Americans a year. This number has substantially increased over the past 40 years.[2] Basal Cell Nevus Syndrome (BCNS) is a rare autosomal inherited disorder, which causes patients to have an increased susceptibility to developing BCCs. The common administration of itraconazole is oral; however, patients with BCNS will be unlikely to take oral itraconazole throughout their entire lifetime due to the associated adverse effects of the drug. Therefore, the goal of this study was to repurpose itraconazole cream to treat and/or prevent BCCs with less adverse effects to the patients that will require the drug. Five different cream formulations were studied.

Objective: To determine whether itraconazole creams are able to reduce a biomarker of BCCs (Gli1) and tumor size compared to systemic oral itraconazole. We hypothesize that blood levels of itraconazole cream will be less than that of oral administration. Additionally, we will determine whether any of the five cream formulations can reduce tumor growth in 30 days.

Methods: The study used passage I, II, and III, NOD/SCID allograft mice that received BCC tumors from Ptch1+/-K14-Cre p53fl/fl mice.

To determine the systemic effect, 70 mg/kg of itraconazole and control drug were administered orally to mice daily. Passage II mice were used and the average starting tumor size for each test group were between 7-8 mm. To determine the topical effect, five different itraconazole formulations 5% in various excipients (lecithin, cyclodextrin, etc.) were administered to passage I and III mice, twice daily, to mouse tumors with an average size of 6-7mm.

Gli1 levels, BCC tumor size, and pharmacokinetic (PK) levels of the drug were measured to determine the systemic and oral effects of Itraconazole. Gli1 levels were determined via qPCR analysis. We measured itraconazole and hydroxylated itraconazole (the major break-down product) in tumor, plasma and liver samples from treated and control mice.

Results: When plotting the relative growth rate of Passage I, II, and III control tumors from both oral and topical studies, passage III tumors had the largest growth rate and Passage I had the smallest growth rate. BCC allografts treated with control cream increased by 3.3 to 5.6 mm in size over 14 days (Passage I, N=13 and Passage III, N=14). In contrast, tumors treated with itraconazole cream increased by 1.9 mm in length and passage III tumors by 4.3mm in length. QPCR analysis exhibited different values of Gli1 expression for the different cream formulations. The values were as follows: formulation #1 (N=9), #2 (N=5), #3 (N=2), #4 (N=2), and #5 (N=3) showed 99%, 59%, 5%, 116%, and 27% Gli1 expression, respectively. LC-MS data showed that there was not a concentrated amount of itraconazole in the blood.

Conclusions: Oral itraconazole decreased BCC tumor size and Gli1 expression, but had high systemic blood levels. Topical itraconazole cream also decreased BCC tumors and Gli1 on average. Specifically, formulation #3 and #5 were better. Topical itraconazole creams caused low plasma levels compared to oral drug. The majority of drug was concentrated in the epidermis with some levels present in tumor.

References:
1. Beachy, Philip, Tang, Jean, Epstein, Ervin. "Itraconazole, a Commonly Used Antifungal that Inhibits Hedgehog Pathway Activity and Cancer Growth." Cancer Cell. 17, 388-399 (2010).
2. Tang, Jean, So, Po-Lin, Epstein, Ervin. "Novel Hedgehog pathway targets basal cell carcinoma." Toxicology and Applied Pharmacology. 224, 257-264 (2007).

JANICE DALIDA

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

Contra Costa College, Sophomore

Mentor: Karen Hardy, MD

This Fall I will embark on my last year at Contra Costa College (CCC) before I leave to continue my studies in Cell Biology. As a high school graduate, I came from a community that lacked the resources to provide a proper education in science and math. I had always been interested in issues of public health and the dynamics of disease, but was reluctant to admit my interest in becoming a doctor for fear of rejection. After a few successful semesters at CCC, it was recommended that I join a program called the Center for Science Excellence (CSE), which works to increase the number of students from financially and academically disadvantaged backgrounds in areas of science, technology, engineering, and mathematics; through CSE, I discovered the CHORI Summer Research Program.

As I become more confident in my capabilities as a scientist and my ability to do well by others, I revisit my desire to serve the community through working in the hospital and at the lab bench. This summer, I was able to exercise that desire, as well as gain a few enlightening experiences. I learned how to build a survey and obtain IRB approval, spent some time observing in the Neonatal Intensive Care Unit (NICU), and shadowed a few of the doctors at the Cystic Fibrosis (CF) Clinic. It was heartening for me to learn about CF and meet all of the lovely children. Being in the hospital has given me a more realistic view of the difficulties and rewards that come with being a doctor; I hope to have many more experiences, which help me to gain as much insight.

I would like to give a special thanks to my mentor, Dr. Karen Hardy, for being patient and flexible while guiding me through this summer despite her hectic schedule. Thank you to everyone in the Pulmonolgy Department for the friendliness with which I was received. Many thanks should go out to the respiratory therapists and NICU staff of California Pacific Medical Center and Children's Hospital Research Center Oakland who were happy to give their input and allow me in their workspaces, especially Barbara Haley. I would also like to thank my mentors from CSE for encouraging me and helping me to pursue this opportunity.

'Rainout' in Heated Humidified High-Flow Nasal Cannulae (HFNC)

Introduction: A Heated Humidified High-Flow Nasal Cannulae (HFNC) is a system used by Neonatal Intensive Care Units (NICU) in the respiratory assistance of premature infants. A nasal cannulae consists of a clear tube that delivers oxygen and airflow to a set of prongs which are inserted into the infant's nares. The gas being delivered to the infant is heated and humidified in order to keep the mucus within the nose from drying and thickening. High-flow refers to the system's ability to deliver 1-10L of gas per minute. For premature infants, the airsacs within the lungs may collapse when they exhale. When inhalation occurs, the sacs must be forced completely open again; this creates more work for the child, as well as causes respiratory distress. High-Flow Nasal Cannula therapy helps the infant to conserve their energy while assisting them to breathe on their own by allowing positive pressure to be delivered to the lungs through an increase in airflow.

In order for the gas to be warmed and humidified, it must pass over a chamber containing heated water. Upon exiting the chamber, the gas travels through a tube with a heated wire circuit. Often times, despite the use of said circuit to maintain heat and humidity, the gas cools and condensate forms inside of the tube. The condensate formed is known as "rainout", and is a common problem faced by NICU's. If too much rainout finds its way out through the prongs and into the infant's nares, their oxygen supply will be blocked. A continuation of droplets over a period of time may increase the infant's susceptibility to infection.

Objective: The purpose of this project is to define the scope of the problem posed by rainout in the NICU, gain an understanding of what amount of rainout is to be expected on a regular basis, and to discover protocols for use in the nursery that may prevent any unnecessary increase in the expected amount of rainout.

Methods: Data was collected through a survey for Respiratory Therapists (RT); the surveys will be used as a tool to gauge the current situation of HFNC staff education and to analyze observations made in the nursery. In a room temperature setting, the average rainout collection was measured at different prescribed airflows; a similar experiment will be run with brief interruptions in the temperature of the environment.

Results: Thus far, we are in the process of analyzing the data from rainout collection, as well as collecting surveys for analysis.

Conclusions: Using the results obtained from the experiments run on the HFNC, we will have formed a better gauge for the expected amount of rainout to be observed in the nursery. If we are successful with our survey, we hope to use the observations of the RT's to continue to research variables within the nursery that may affect the formation of rainout, as well as continue to make improvements in the protocol for HFNC use in the NICU.

RIGOBERTO DEL TORO

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

University of California, Berkeley, Senior

Mentor: Jodi Stookey, PhD

Through a program called the Biology Scholars Program (BSP): an academic program that offers services to underrepresented and low-income minorities studying the biomedical sciences at the University of California, Berkeley, I have learned that it is not ONLY about knowing how to solve a problem, but knowing the concept and reason behind solving problems. This insight gave me the foundation I needed to be successful in my coursework in the biomedical sciences and has helped me acknowledge health disparities affecting our communities.

My experiences in BSP have been very diverse and each has contributed to my growth and appreciation for others. These experiences have strengthened my understanding of medicine, while my interests in medicine stemmed from clinical research and outpatient experiences. Since becoming a volunteer at the Children's Hospital of Oakland Research Institute (CHORI) in November 2009, I had the privilege of not only working with Dr. Jodi Stookey but with patients, a Registered Nurse, and a Research Assistant. I was able to appreciate the different factors needed to provide the greatest quality of nutritional care, such as nutritional history, patient-doctor relationship, and personal and cultural sensitivity. I translated the concerns of Spanish-speaking patients, and my presence as a Latino helped the patients feel comfortable and confident in their nutritional care. I am now a Summer 2010 CHORI intern working at the Pediatric Clinical Research Center (PCRC) with Dr. Stookey spending most of my time and energy analyzing data and carrying out a professional research study project. My work involves evaluating overweight 9- 12 year old children in the Water Study with the hope of identifying different factors that may be associated with beverages and fat oxidation.

I want to continue working in helping disadvantaged communities excel. My involvement in Dr. Stookey's research project reflects my passion in making a difference in the world by helping others. Participating in the CHORI 2010 Summer Program has given me a stronger foundation in my ultimate goal to become a Physician that will help me find ways of helping people in need of health access. I would like to thank Dr. Jodi Stookey and the CHORI Program for giving me this invaluable and exciting opportunity.

Free Fruits and Vegetables Study

Introduction: Reversing childhood obesity is a national priority. Strategies to end childhood obesity are particularly needed for lower income children, and young children, to reduce health disparities and prevent tracking of overweight from infancy through adolescence into adulthood. Tailoring a food assistance program to the needs of overweight participants holds great potential to address the food environment on a national scale, and reverse childhood obesity, because half of the foods provided by existing programs (e.g. WIC approved foods) are high glycemic foods that depress fat oxidation and limit weight loss. A food assistance program that provides low glycemic of fruit and vegetables to overweight participants might better leverage the power of 'free' food for dietary change, and quickly shift large numbers of lower income children towards normal weight. Unlike higher income individuals who do not have the time, resources, inclination, or transportation to shop and cook from scratch, low income individuals with the same constraints have a much more limited range of healthy food options. A program that addresses the income disparity in access to ready-to-eat salads, soups, bean/vegetable entrees, and fruit may facilitate compliance with clinician dietary change recommendations.

Objective: The primary goal of this project was to find out if a food assistance program is made available that provides **ready-to-eat** fruit and vegetables **for free,** in amounts consistent with the value of other foods offered by WIC or school meals, then it would facilitate dietary change for low income, overweight individuals counseled to increase fruit and vegetable intake for weight loss.

Methods: Clinicians at Healthy Hearts at Children's Hospital Oakland and La Clinica de la Raza in Fruitvale will identify overweight patients that might benefit from increased fruit and vegetable intake and a program to provide free fruit and vegetables. The clinician will give the patients (potential participant) consent materials that describe the pilot program. By signing the consent forms, individuals will indicate willingness to help design a free fruit and vegetable program, including willingness to participate in three phone surveys, within approximately two weeks about factors that influence what people eat day-to-day. Individuals who are interested in receiving free fruit and vegetables will be randomly selected to get a Safeway home delivery. Including delivery fees, the order will cost $50. Each participant will receive only one delivery. Every participant will be surveyed at least once before and at least once after the food delivery. Half of the participants will be randomly selected to be surveyed twice after the food delivery. The other half of the participants will be surveyed twice before they receive the food delivery. This design will allow us to determine if the food delivery is associated with a change in fruit and vegetable intake (i.e. compared to no change in the group that has not yet received the delivery). At the end, study staff will ask the participating clinicians to report how many overweight children/pregnant/postpartum women they identified during the study window and how many needed support from a food assistance program.

Expected Results: We expect patients and clinicians' to have a strong interest in the free fruit and vegetables food assistance pilot study which may significantly increase the fruit and vegetable intake of low income, overweight individuals.

Conclusions: Further analysis is needed in order to make any conclusions.

GABRIELLE DIAZ

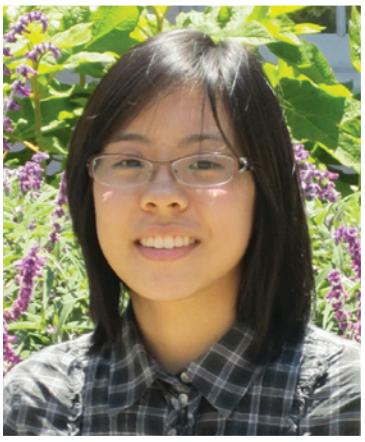
Funded by the Short Term Research Education Program to Increase Diversity in Health Related Research from the NIH/NHLBI

Saint Mary's College of California, B.S. Biochemistry

Mentor: Eva Delgado, MD, and Sara Leibovich, MD

I am a recent graduate from Saint Mary's College of California, where I earned my bachelor's degree in Biochemistry. Science and the pursuit of knowledge have always been my drive. It's captivating to transcend our understanding of basic concepts and mechanisms into real life applications such as medicine and research, all to enhance our way of living. Growing up, I had this innate desire to help people, but I didn't really know how—only recently did I understand how to do so. Last year, I participated in the Remote Area Medical and it was a revelation to see doctors work together in a non-traditional setting and serve countless of people who had no means to healthcare. It was at this moment that I realized I did not want to pursue a career in the health field solely for the love of science. Rather, I want to be in this field because I want to become a health activist and a resource to people.

This summer, I have been working on a clinical study to assess ways in which medical education can be improved. I have learned that patients need more than a prescription to be set on their way. In addition to medical regimens and treatments, guidance and education are essential to improve health awareness and lifestyles. Being a part of the summer program has allowed me to come to terms with the challenges facing the medical field, such as accessibility and adherence for treatments. Throughout it all, the CHORI program has granted me with more motivation to face these challenges as I strive towards my goals.



A Descriptive Analysis of Asthma Knowledge and Access to Care

Abstract: A survey has been developed to assess sources of pediatric asthma knowledge that parents receive and to determine any association with risks for non-adherence. The survey highlights, among other things, six different sources of education. For this cross-sectional study, we will conduct a descriptive analysis of where asthma is learned about as reported by parents. The main outcome would be to establish a mean number and the frequency of which parents use each source. In the process of recruitment, parents will also be directly asked which sources were most helpful to them. This study is inclusive to parents/guardians of pediatric asthma patients presented to the asthma clinic and emergency department for asthma care at Children's Hospital Oakland. The hypothesis for the study is that parents presented to an asthma specialty clinic will report to have more resources for asthma education and thus more access to care than those presented to the emergency department. In comparing recruitment between these two settings, the parents recruited from the asthma clinic will more frequently cite that the clinic is most helpful.

JAMIE K. FUNG

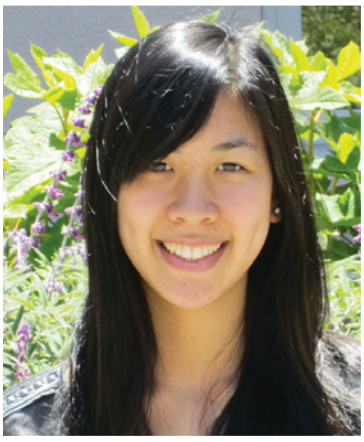
Volunteer

Mentor: Cassandra Calloway, PhD

I have always been a person of many interests, and so it was not until I had molded two prominent desires of mine into one convicting passion that I realized I wanted to become a doctor. Growing up in a hard-working family, I always knew of the sacrifices that my parents made for my brothers and me. Seeing how diligently they worked just so that my brothers and I could have a better life stimulated a desire in me to care for other people. It was this simple desire that would later develop into a lifestyle. The mentality of taking care of people and neglecting the cost stems from the compelling example set by my parents' actions. Thus, with this ideal engraved into my character from the outset, the desire to purposefully take on the role of providing care to those who need it emerged.

My sense of sacrificial care for other people can be seen as so general that I could apply it in any field- not just the medical field. However, seeing the powerful ability for medicine to change people's lives for the better really hooked me in. When I was still in middle school, my mom discovered that tumors had developed in her uterus. This news instilled a fear within me that drove me to create crazy possibilities of life without my mom. Fortunately soon after, the doctors assured us that these uterine fibroids were benign. All that was required was a simple, noninvasive procedure called Magnetic Resonance-guided Focused Ultrasound. After hearing about this procedure, I was not only relieved but also very amazed. Ten years ago, uterine fibroids may have required much riskier procedures, increasing the chance for other complications. But thankfully, technology within medicine has developed immensely to achieve so much to improve people's lives. Because of this knowledge, my fear subsided.
After experiencing the comfort of medicine, I knew I wanted to be a part of providing care for people at the time of their greatest need. Thus, coupled with my passion to help people, my fascination with what has been done and what can be accomplished in the influential field of medicine is driving me to become a part of this fight.

Ultimately, none of this would be possible without all the research poured into improving people's lives. I'm so thankful that I have this opportunity to do research at a facility like CHORI with so many resources and supportive people like Dr. Calloway. Research is the backbone of medicine, and I am truly grateful to be able to learn so much and to be a part of it.



Frequency of Somatic Heteroplasmic Mutations in Mitochondrial DNA from Single Hairs of Twins

Introduction: In the field of forensics, mitochondrial DNA (mtDNA) proves to be very useful in areas where nuclear DNA fails. When only a very small or degraded amount of sample is available, as is often the case in forensics, the high copy number of mtDNA allows for adequate collection of data for analysis. However, mtDNA mutations and the presence of heteroplasmy in an individual can lead to ambiguity in identifying people. Heteroplasmy is the existence of more than one mtDNA sequence within an individual, tissue, cell, or mitochondrion. Previous studies from Dr. Calloway's lab have shown a difference in the level of heteroplasmy between tissues within an individual and twin pair. Germline point mutations were observed in buccal and hair samples but not in blood samples from twins. Additionally, somatic mutations resulting in heteroplasmy were observed in hairs from these heteroplasmic twins but not in their buccal or blood samples. We propose to extend this study to analyze hairs from normal individuals to determine the overall frequency of somatic heteroplasmic mutations in the general population.

Objective: The goal of this project is to screen single hairs from 19 twin pairs for heteroplasmy using a multiplex PCR and the mtHV+ HaploArray. The hair mitochondrial haplotypes will then be compared to previously gathered buccal and blood data to determine the somatic mutation rates.

Methods: Hair, blood, and buccal samples from 19 twin pairs were collected for a previous study. mtDNA from hairs from each individual in these twin pairs were extracted using the Qiagen QIAampTM DNA Micro Kit for this study. Hair-derived DNA was then amplified using an established multiplex PCR (5-plex and 10-plex system). Finally, the amplified products were typed using the mtHV+ HaploArray, which targets 61 polymorphic sites distributed throughout the mitochondrial genome. This technique results in the hybridization of amplified DNA to 104 sequence-specific oligonucleotide probes that are attached to a nylon membrane. The hybridization product is then detected colorimetrically, revealing the sample's mtDNA haplotype. Samples are determined to be heteroplasmic if two probes are observed within a region. Somatic point heteroplasmy will be determined by comparing the hair mtDNA haplotypes to the buccal and blood haplotypes.

Results: We expect to find that the somatic mutation rate in the hairs will be higher than the somatic mutation rates in blood and buccals. Further investigation is needed to determine results.

Conclusions: Conclusions will be made when results are obtained.

EIA GARDNER

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

Agnes Scott College, Junior

Mentor: Stephanie Doniger, MD

I am Eia Gardner, a junior at Agnes Scott College in Atlanta Georgia, majoring in Biology with a focus in Public Health. This summer has been both a privilege and an honor participating in the Children's Hospital of Oakland Research Institute. The weekly lectures and seminars have grasps my attention and increased my knowledge on various subjects such as Sickle Cell and Molecular Diseases along with life skills like knowing how make presentations. Being in a learning environment with the rest of the students all with different educational backgrounds was another good way to meet new long term friends and learn from each other.

The highlight of my summer was working in the clinical setting along with conducting research with my mentors Dr. Stephanie Doniger and Dr. Nell Latronica. I could not thank these two women enough for giving up their time around such busy schedules working in the Emergency Department at Children's Hospital. They each guided me through the process of creating a research plan, writing a protocol, getting it approved by the IRB and conducting the research in a rapid environment. They gave me skills such as using the ultrasound, reading X-Rays, understanding medical terminology, creating a data sheet, surveys, flyers and being an independent worker.

I have always been indecisive as far as a career. I always knew I wanted to go into the medical field, I just didn't know exactly what. Participating in CHORI has helped me decide. I have became more and more interested in Pediatric Nurse Practitioners, they have a wide range of opportunities in the medical field. As a Practitioner I feel as though I could combine my interest in clinical work with my interest in public health and welfare working with the community. With out the amazing team at CHORI, I would have never been able to make that decision. I thank all of CHORI's marvelous staff, especially Deborah Ellen because of her committed work and contact that she has with each student. I thank my mentors Dr Doniger and Dr Nell for their patience working with me daily and teaching me. I thank Students Rising Above (Lauren Brener and Susan Troung), the program that gave me the information about CHORI and helped me along the way, and lastly my family for their support through out the summer, my amazing grandmother and God for placing the opportunity in my life.

Emergency Department Bedside Ultrasound Diagnosis of Constipation in Children

Introduction: Constipation is extremely common in children with an estimated prevalence as high as 28%. The National Institutes of Health defines constipation as the passage of hard, dry stool that is difficult or painful to eliminate, less than three times per week.

Specific Aims: We aim to demonstrate that the transverse rectal diameter can be quickly, easily, and accurately measured by bedside ultrasound in the pediatric emergency department to diagnose constipation. Bedside ultrasound may serve as an alternative to plain radiograph, which are not reliably associated with constipation, exposes patients to radiation and may lengthen emergency department stays.

Methods: Our experimental study design is an observational prospective descriptive pilot study. Patients age 4-18 presenting to the emergency department with a chief complaint of constipation or abdominal pain were provided a validated questionnaire—Questionnaire on Pediatric Gastrointestinal Symptoms-Rome III (QPGS RIII)— to determine whether patient meets established clinical criteria for a diagnosis of functional constipation. A measurement of the transverse rectal diameter was made by ultrasound noting the bladder volume, as this can alter measurements.

Results: Two patients who met criteria for constipation by the QPGS RIII had measured transverse rectal diameters of 3.85 cm and 4.0 cm. A third patient who did not meet criteria for constipation by the validated questionnaire had a transverse rectal diameter of 1.46 cm. The age of the patients ranged from 6-16 years old. Conclusion: These preliminary results indicate that obtaining a measurement of transverse rectal diameter via bedside ultrasound may accurately diagnose constipation and serve as an alternative to abdominal radiographs to confirm a clinical diagnosis of constipation.

CRYSTAL GHOSH

Volunteer

University of California, Berkeley

Mentor: Gordon Watson, PhD

While reading the New York Times Bestseller The Elephant and the Dragon: The Rise of India and China and What It Means for All of Us, *I came across a passage I found interesting. It read, "... Philips has outfitted a van that travels to rural areas where doctors are rare. The van carries doctors as well as diagnostic equipment like X-ray and MRI machines for those who need care.... sick rural residents who might not otherwise make it to a doctor can get diagnosis and care without leaving their villages." This piece of information made me realize the truly transformative power that both science and technology have on the lives of others. It engendered in me a desire to delve into the world of medicine and research.*

The opportunity to volunteer in Dr. Watson's lab at CHORI has not only deepened my love for scientific research, but also it has enabled me to start thinking and working like a scientist- with creativity, innovation, and persistence. However, I never could have had this insightful experience without the guidance of my mentor Lee Ying, Dr. Watson, and countless others who have helped me throughout.

In the future, I hope to combine my interests in Molecular and Cell Biology and Global Poverty Practice, both of which I plan on majoring in at UC Berkeley, in an effort to make a positive and significant impact on the lives of the impoverished afflicted with disease.

Inflammatory Response in the Mouse Model of Smith-Lemli-Opitz Syndrome

Introduction: Smith-Lemli-Opitz syndrome (SLOS) is an inherited disorder characterized by inadequate cholesterol synthesis. It is caused by defects in the enzyme 7-dehydrocholesterol reductase (DHCR7), which converts 7-dehydrocholesterol (7DHC) to cholesterol (C). Because the last step in the cholesterol metabolic pathway does not occur, excess amounts of 7DHC accumulate and cholesterol is deficient. One outcome of cholesterol deficiency is the abnormal myelination of neurons, which leads to decreased nerve conduction in human patients. Decreased nerve conduction may affect the inflammatory response of SLOS patients.

Objective: The purpose of this project is to determine whether SLOS mice will have a reduced inflammatory response compared to that of wild-type mice, because of the lowered activity of the vagus nerve, which plays a role in mediating an inflammatory response.

Methods: Mice will be tagged with an ear tag for identification purposes and a sample of their tail tissue obtained at the time of weaning so that they can be genotyped. Blood will then be collected through the retro-orbital bleeding of mice that have been anesthetized with isoflurane. Sterols will be extracted from the blood serum and analysis of the ratio of 7DHC to C will be performed using mass spectrometry. Mice with SLOS are expected to have a higher ratio of 7DHC to C compared to wild-type mice. After distinguishing between the SLOS mutant and wild-type mice, ten male mice from each experimental group will be weighed and their paw volumes measured with a plethymometer, a device that measured fluid displacement volume. The mice will then be anesthetized with isoflurane. A syringe containing 1% solution of lambda carrageenan, a mucopolysaccharide extract used to induce inflammation, in 0.9% saline will be injected subcutaneously into the underside region of the left hind paw, whereas a 0.9% saline solution will be injected into the underside region of the right hind paw. Mice will then be injected will buprenorphine, a pain reliever, and returned to their cage, which will be placed upon a heating pad. The mice will then be monitored until they are fully recovered from the anesthetic. Paw volumes will be measured at regular time intervals. The volumes of both paws before and after the injection will be used in order to determine the percent increase in paw volume. The percent increase in paw volume in SLOS mice will be compated to that of wild-type mice in order to determine whether SLOS mice have a reduced inflammatory response.

Results: So far, we have identified which mice are SLOS mutants and which are wild-type using PCR. We are in the process of analyzing the ratio of 7DHC to C using mass spectrometry. Soon, we hope to inject the mice with carrageenan and measure the initial and final paw volumes in order to compare the percent increase in paw volume in both experimental groups.

Conclusions: If we see a marked difference in the inflammatory response of the wild-type and SLOS mutant experimental groups, more specifically, if the difference between initial and final paw volumes of the SLOS mice is much lower than that of the wild-type mice, we can conclude that SLOS mice have a reduced inflammatory response. If a significant difference between the two groups is not observed, then the inflammatory response test cannot be used as a physiological marker in the future. However, if the SLOS mice do indeed have a reduced inflammatory response, we can use the inflammatory response test in order to determine the effectiveness of gene therapy in treating this disorder, the ultimate goal of this lab.

ADRIANA GONZALEZ

Funded by Childrens Hospital Los Angeles (National Heart, Lung and Blood Institute, Basic and Translational Research Program)

Holy Names High School, Junior

Mentor: Ward Hagar, MD

Hola! My name is Adriana Gonzalez and in the fall I will return to Holy Names High School as a Senior. I have been a part the ACHIEVE scholarship program for the last three years. I found out about this wonderful opportunity after Mrs. Bakar, the founder of the Achieve program , met with Dr. Bertram Lubin MD. Mrs. Bakar believed that I had the potential of what it took in being accepted into the CHORI Summer Student Program. I knew that it would be a challenge, but I knew that I could do it because as long as you try hard for something you really want to accomplish, everything can be done. Just like Cesar Chavez said "Si se puede!" As a child I really wanted to be a teacher and then a lawyer, but as I got older I decided I wanted to become a pediatrician because I am passionate about helping kids. I feel great when I help others because I love to see a smile on their face.

I would like to thank Dr. Ward Hagar, my mentor, for teaching me so much this summer and Dr. Bertram Lubin for allowing me to have this wonderful experience. I also want to thank Christy Hoehner for always being there to help me and for always having things for me to do. Thanks to CHORI, I now have an advantage and experience in the medical field.

Liver Iron, Vitamin D, and Bone Mineralization in Sickle Cell Disease

Introduction: Bone disease is an understudied and poorly understood complication of sickle cell disease. Poor bone mineralization, avascular necrosis, and microfractures are common consequences of this condition that impact quality of life. Devastating collapse of the hip joints occur in patients as young as 9 years of age. Such patients must choose between total hip replacement surgeries or life in a wheel chair.

Red cell transfusions are increasingly used in sickle cell disease. Patients with sickle cell disease often receive red cell transfusions once a month. The iron loading from regular transfusions is not adequately addressed. New approaches to iron chelation are decreasing body iron burden, but siderosis is still a common problem. The complications of iron loading include small joint disease, along with liver disease, diabetes, endocrine dysfunction, and heart abnormalities. It is not clear if iron loading affects bone health more generally.

Vitamin D deficiency is common in sickle cell disease. The effects of this deficiency specifically in Sickle Cell Disease are not well studied. Interestingly, a key iron homeostatic protein, hepcidin, is regulated by Bone Morphogenic Proteins. Additionally, expansion of bone marrow to support the dramatically increased erythropoiesis is hypothesized to play a role in long bone pain and avascular necrosis of the femoral and humeral heads. Whether these factors play a role in bone mineralization more generally is currently unknown. DXA scans estimate the degree of bony mineralization. How iron loading, vitamin D, and bone mineralization interact has not been investigated.

Objective: This pilot study will examine whether associations between iron overload, vitamin D levels, and bone health exist in persons with Sickle Cell Disease.

Methods: The Adult Sickle Cell Program has 372 patients. We looked at patients who had data for Vitamin D levels, SQUID measurements, and DXA Scans. An ACCESS database was created to record the relevant information needed. SQUID (Superconducting Quantum Inference Device) values used to quantitate liver iron was a surrogate marker for volume of red cell transfusion. Vitamin D levels were collected from clinical data with the pre-replacement value being used where appropriate, and matched to the date of the DXA scan. Hip bone mineralization and hip Z-scores by DXA scans represented bone health. Age, smoking status, calcium intake, and gender were abstracted from the medical record. After a univariate analysis of the most relevant markers and possible associated factors, linear regression models were constructed to explore the effects of iron on bone health in sickle cell disease. The dataset was analyzed by STATA 11.2 software.

Results: Data for DXA scans, SQUID, and vitamin D values were available for 48 adults with sickle cell disease. Their demographic characteristics are presented in the Table. Not surprisingly, vitamin D levels correlated with hip z-scores. Surprisingly the higher the vitamin D level, the lower the bone density. Furthermore, the higher the liver iron concentrations were, the lower were the vitamin D levels. Multiple regressions showed significant associations with vitamin D and iron with hip bone mineral density, but not hip Z-scores. In models including only hip bone mineralization, vitamin D levels, and liver iron, the vitamin D and liver iron levels both significantly explained 28% of the variation in the serum vitamin D levels. When models also included age, smoking, gender, and calcium intake, only Vitamin D and female gender continued to be associated with low hip bone mineralization.

Limitations: Cross-sectional studies have inherent limitations of patient selection, no time component, and possible unrecognized confounding variables. No clear biologic model is available to guide possible statistical analysis.

Conclusions: This preliminary study suggests that further study of the effects of transfusional iron overload on hip bone health in sickle cell disease and its mediation by vitamin D is warranted.

ROY HERNANDEZ

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

California State University, Long Beach, Post-Baccalaureate

Mentor: Vasanthy Narayanaswami, PhD

My interest in the inner workings of cell biology has changed my outlook on the world. With so many unanswered questions in biochemistry that need to be explored, my curiosity has driven me forward. I knew that I would dedicate myself to pursue a path of science. I come from a first generation working class background; most of my family has been relegated to service of manual labor work. Despite their strong work ethic, education to them has not always been a priority. I had a very different path in mind. Over the years, during my college career my interest in biochemistry has been developing and has concentrated on protein biochemistry and cell biology. With many interesting topics in biochemistry today and the unfilled gaps in science, my education thus far will not suffice for what I truly want to become. Thus the most logical path for me is the research setting where I can truly show my desire for enhancing the knowledge that exists today.

My mentor Dr. Nawayanaswami and I have been working on the molecular structural differences of apolipoprotein E3 and aplioprotein E4 using hydrogen-deuterium exchange coupled with mass spectrometry. ApoE4 is an isorform of the protein which displays an increase development of atherosclerosis and Alzheimer's. Apolipoproteins play a huge role in maintaining proper levels of cholesterol, lipid, and fatty acid contents in human blood. ApoE3 deficient mice are perfect models for atherosclerosis, stressing the importance of functional apoE3. Being part of this summer research at CHORI has given me the wonderful experience to work with fellow researchers that love and enjoy their work. I would love to thank all the people that worked hard to put this together because without them, this wonderful research opportunity would not be possible.

Hydrogen/Deuterium Exchange and Mass spectral Analysis of the High Affinity Lipoprotein Binding Domain of Apolipoprotein E3

Introduction: The focus of this research revolves around gaining insight into the conformational behavior of human apolipoprotein E3 (apoE3). ApoE3 is an anti-atherogenic protein that plays a critical role in cholesterol homeostasis in plasma and central nervous system. It is composed of a 22-kDa N-terminal (NT) domain and a 13-kDa C-terminal (CT) domain that are linked by a loop. The NT domain serves as the ligand for interaction with cell surface localized low density lipoprotein receptors (LDLr), while the CT domain bears high affinity lipid-binding sites, apoE self association sites and cellular cholesterol efflux capability, especially from atherosclerotic lesions. High resolution structural information for the NT domain reveals a helix bundle comprised of 4 long amphipathic helices; that for the CT domain is not known.

Objective: The objective of this study is to learn new information about the structural aspects of apoE CT domain in an effort to understand the structure-function of this domain. Earlier computer-based sequence algorithms and biophysical studies revealed that apoE CT domain is composed of amphipathic α-helices that play a critical role in maintaining subunit interactions in the protein in lipid-free state. We propose to employ a combination of hydrogen/deuterium exchange (HDX) and mass spectrometry to obtain further information regarding amide-backbone structural dynamics, solvent accessibility, and helical contours of apoE CT domain.

Methods: ApoE CT domain (residues 201-299) bearing a hexa-His tag at the N-terminal end was over expressed in E. coli cells and purified by affinity chromatography. The purified protein was dialyzed against 10mM sodium phosphate buffer containing 150 mM NaCl (phosphate-buffered saline, PBS) at pH 7.0 and stored at -80^0 C. SDS-PAGE analysis revealed that the purified protein was ~ 95% pure. HDX was performed by incubating apoE CT domain with deuterated 10mM PBS pD 7.0 This was followed by ultra performance liquid chromatography (UPLC) and on-line pepsin digestion for mass measurements.

Results: HDX reactions with apoE CT domain were performed for varying lengths of time and the reaction quenched at specific time points between 30 s and 14 h by adding aliquots to an acidic solution at pH 2.5 and flash frozen for minimum back exchange. The quenched samples were analyzed in a Quantitative Time of Flight High Definition Mass Spectrometer (Q-TOF HDMS) and monitored apoE CT peptide peptic digest mass fragments. Our preliminary results show time-dependent deuterium incorporation in the peptic fragments and local specific mass increase.

Conclusions: We expect that the amide hydrogens of the peptide backbone involved in H-bonding interactions to form an α-helix will exchange at much lower rates and thus undergo slow HDX. In contrast, segments that are unstructured or in loop regions will undergo exchange at measurable rates to detect HDX. We will generate a HDX protection map to define the helical segments of lipid-free apoE CT domain. This will give more clues into the overall folding conformation and structural insight of the apoE CT in the lipid-free state.

VANESSA HERRERA

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

Contra Costa College, Sophomore

Mentors: Rose Ellen Morrell, MD, and Barbara Botelho, MD

I am Vanessa Herrera, a full time student at Contra Costa College, my local community college, and I hope to transfer to the University of California Berkeley. Apart from my scholastics, I volunteer at a local hospital and because of Children's Hospital Oakland Research Institute (CHORI) I have the opportunity to participate in research and to my preference I am mentored in a clinical setting by two esteemed specialists in their field of Pediatric Nephrology. The lovely, welcoming, and intelligent mentors I refer to are the renowned Dr. Barbara Botelho and Dr. Rose Ellen Morrell. Guided by my mentors, I am undertaking research intending to unveil the commonly dismissed frequency of hypercalciuria in the obese youth population. Based on our findings it can be recommend or not recommend that screening for hypercalciuria should be part of the initial evaluation of an obese child. I am honored to have this mentoring and Hypercalciuria in Overweight Patients research opportunity made possible by the partnership of both the benevolent CHORI Summer Research Program and my mentors. Today, I find myself in a clinical setting I see myself working in, in the future to come, contributing to my own Richmond community as a physician.

Hypercalciuria in Overweight Patients

Introduction: Renal calculi (calcium stone) frequency is increasing in the obese youth population. Therefore, screening for hypercalciuria needs to become part of the preliminary screening treatment for the youth with an emphasis on the obese youth population.

The prevalence of kidney stones has increased in children. It is believed that the prevalence of kidney stones is due to dietary habits primarily the increased levels of dietary salt intake that in turn induce elevated urine calcium secretion. Hypercalciuria is a disease under which an individual excretes elevated levels of calcium in their urine. Among other solutes, high calcium concentrations in the urine can aggregate and form stones. Excessive calcium excretion can induce stone formation and osteoporosis. Hypercalciuria has the potential to lower one's quality of life. Awareness and prevention are the best arms in combating the frequency of hypercalciuria. From these necessities for awareness the Hypercalciuria in Overweight Patients research project is rooted and has emerged to unveil the dismissed frequency of hypercalciuria in the obese youth population.

Objective: Based on the data analyzed from cumulative administered tests, of the targeted >85 percentile of obese children between the ages of 5-21 years (two above normal spot urine test calcium/creatinine ratios, three day diet, and twenty-four hour urine analysis), it can be recommend or not recommend that screening for hypercalciuria should be part of the initial evaluation of an obese child.

Methods: In a clinical setting the following techniques were utilized and the aggregated data was analyzed:

Subjects between the ages of 5-21 years with a body mass index (BMI) >85 obesity percentile were administrated a first spot urine test analyzing the calcium/ creatinine ratio; subjects with a >0.2 calcium/ creatinine ratio were administered a second calcium/ creatinine ratio spot urine test to confirm the above normal calcium excretion in the urine; subjects with a >0.2 calcium/ creatinine ratio considered to have hypercalciuria were administered a three day diet and 24 hour urine collection analysis.

Control: Historical Population

Results: Thus far, out of seventeen of the projected fifty subjects, one subject had a >0.2 calcium/ creatinine ratio. Results are still pending.

Conclusions: Based on our findings we can recommend or not recommend that screening for hypercalciuria should be part of the initial evaluation of an obese child. Study still in progress.

KATHERINE JONES

Funded by the CHORI General Fund

University of California, Berkeley, Post-Baccalaureate

Mentor: Mark K. Shigenaga, PhD

My name is Katherine Jones and I recently graduated from the University of California Berkeley this past spring. I majored in Molecular Cell Biology with and emphasis in Immunology and infectious Disease, and minored in Ethnic Studies. I have been an intern at CHORI for 2 years in the Shigenaga lab, but this is my first time participating in the summer research program. I am particularly interested in the field of internal medicine and previously interned at the Crohn's and Colitis Foundation of America (CCFA) located in San Francisco. The work I did with patients at CCFA made me realize I wanted to pursue a career in medicine. Currently I am taking two years off and hoping to pursue EMT work before applying to medical school. I believe that patients should be given the knowledge they need to make proactive healthcare decisions –which is why I enjoy the work I am doing so much. The research focus in the Shigeneaga lab emphasizes accessible healthcare –focusing on diet and nutrition as a means of treatment. CHORI is a wonderful learning environment and I am glad I have this opportunity to explore this area of research and looking forward to seeing the outcomes of this summer.

Does Lactate Improve Gut Barrier Integrity?

Introduction: Chronic inflammation requires long term immune activation that can be corrosive to tissues. Evidence from our lab and others suggest that much of this inflammation may arise from bacterial antigens, such as LPS penetrating a vulnerable gut barrier. A strong gut immune system is designed to limit systemic dissemination of gut-derived endotoxin and represents a crucial component of the gut barrier. Lactate may promote gut immune function and barrier integrity by improving bioenergetic capacity and responsiveness, enabling better proliferative response to antigenic stimulation possibly through mitochondrial biogenesis and/or increased efficiency in calcium handling. There are two major endogenous sources of lactate exercising muscles and health promoting lactic acid bacteria (i.e. lactobacillus or bifidobacteria). Exogenous lactate can be provided to the gut by consuming lactate rich fermented foods, such as yogurt and kim chee. Lactate at the proper concentration may increase energy output and improve cellular function. We predict that such improvements may lead to a more robust immune response and stronger gut barrier. This results in better containment of a perceived microbial threat and a corresponding reduction in the systemic exposures to gut-derived endotoxin that is known to drive chronic inflammation and increase disease risk.

Objective: To assess if lactate improves T-lymphocyte proliferation under conditions of chronic stimulation, and then to identify if lactate is acting through the up-regulation of mitochondria.

Methods: We isolated human peripheral blood mononuclear cells (PBMCs) by density gradient centrifugation. These cells were pretreated with lactate for different durations and then assessed the proliferative response to mitogen using CFSE staining and flow cytometry.

Results: Lactate is capable of activating the T-lymphocyte population in PBMCs, causing increased proliferation when administered at 30mM concentrations over 30 and 60 minute exposures, with an approximate doubling in proliferation from baseline, no lactate to 30mM, 60 min exposure lactate; results are based on the CFSE PBMC manually gated lymphocyte population. In addition, lactate is able to maintain this proliferative trend when challenged with the mitogen ConA over 72 hours (as shown by FACS). These lactate induced proliferative responses are observed when cells are pretreated and then washed, however if cells are allowed to sit in 30mM concentrations for prolonged periods of time lactate shows cytotoxic effects (seen at 4 and 6 hour time points).

Conclusions: We anticipate that provision of lactate will increase the bioenergetic capacity and energy output of exposed cells, resulting in improved responsiveness and stress resistance. In T-lymphocyte populations, improved responsiveness may yield increased rates of cell proliferation upon exposure to mitogenic antigens. In addition, in intact mice, lactate may improve the physical integrity of the gut and render this barrier more resistant to the stress of a high fat diet. By exerting such effects, intestinal permeability induced by dietary fat challenge may be blunted. Evidence in support of these benefits will encourage follow-up studies to evaluate the utility of lactate in promoting gut health and improving insulin resistance in human subjects.

JAMES KARNEZIS

Funded by NIH Grant #5R37HL064159-12

St. Mary's College of California, Junior

Mentor: Robert Ryan, PhD

It is hard to think back to how my journey at CHORI all began. I had stumbled upon the research institute as a possible place to reach out into the community. My adventure at CHORI all began as a mini internship for the month of January, but has transformed into a full summers worth of excitement and new friends. Joining the Ryan Lab was like entering a family full of individuals with the same aspirations as my own. This coming year, I will be Junior at Saint Marys College of California the reason for why my new home is in the Bay Area. I am currently pursuing a degree in Biochemistry with hopes to extend my education into the medical field. There is no better way to immerse oneself in a medical career dream than through research.

Growing up in a Greek household has really helped place me where I am today. The Greek culture is centered around hospitality and reaching out into the community. I have grown up always wanting more and researching at CHORI has been the perfect way to satisfy that craving. Working in the laboratory has given me a new appreciation for scientists. There is a whole other world that lies behind a doctor's office that needs to be given credit.

Working for Dr. Ryan and Jennifer Beckstead has been a gratifying and unbelievable experience. Alongside Jennifer Beckstead I am studying a mutant protein that may play a role in reducing coronary artery disease. I have learned more than I could have ever imagined and owe them my highest regards. I would also like to thank everyone in the Ryan Lab for helping and making this a very memorable experience.

Apolipoprotein A-I (ApoA-I) Milano

Introduction: Lipoproteins are complexes of protein and lipid used to transport triglycerides and cholesterol throughout the body. A key protein used in the regulation of cholesterol and lipid metabolism is Apolipoprotein A-I. ApoA-I (1-243) is also the major protein component of HDL, which helps in transporting cholesterol to the liver to be broken down into bile acids. A naturally occurring mutant form, ApoA-I Milano was identified in a family in Milano, Italy. Studies have shown that carriers of this mutant protein have low HDL levels and high triglyceride levels, but still have a very low prevalence of atherosclerosis and increased life span compared to non-carriers. This variant has the same basic composition as ApoA-I, but there is a mutation at the 173 residue in the amino acid sequence. The arginine to cysteine mutation may play a role in the increased atheroprotective effects. Thus, structural analysis around ApoA-I Milano is needed to understand the importance of this mutation.

Objective: To reconstruct a functional ApoA-I Milano variant using expressed protein ligation in order to create a model that can be used to help characterize the structure of the protein.

Methods: Studies have shown that a truncated ApoA-I Milano (1-192) without its C-terminal domain can be used in place of the complete protein to study its composition. A recombinant protein technique will first be used to express ApoA-1 Milano using an E. coli vector grown in minimal media conditions. The protein will then be purified using a Hi-Trap chelating column and lyophilized prior to cleavage. The mutation in the protein occurs at the 173 residue, which is where CNBr digest will hydrolyze the peptide at the C-terminus of methionine to obtain the desired peptide fragments. The glutamine at position 172 before the mutated cysteine group has been converted into a methionine, so that CNBr cleavage will occur at this point. The peptide containing the cysteine group (173-192) will be ligated together with the n-terminal region of a MESNA tagged ApoA-I (1-172).

Results: An ApoA-I Milano variant can be successfully cleaved using CNBr digest. The accumulated peptides (173-192) after cleavage can be combined and isolated from the remainder of the protein using a Hi-Trap chelating column. The peptide can hopefully be ligated with MESNA tagged ApoA-I (1-172) to reform a functional protein variant.

Conclusions: Expressed protein ligation can be a useful technique to help identify the structure of a given region on a protein. By successfully reforming this ApoA-I variant knowledge can be gained about how the structure of the protein may relate to its increased function. The hope is to repeat this procedure with an isotopically labeled peptide, so the results can be characterized on a NMR spectrum.

KIMPREET KAUR

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

University of California, Berkeley, Junior

Mentor: Marsha Treadwell, PhD

Hello! My name is Kimpreet Kaur and I am an Integrative Biology major attending the University of California, Berkeley. I will be a senior this fall, which makes me overcome with joy as I will be one year closer to applying to medical school and one year closer to making my childhood, teenage, and adult ambition into a reality. This may sound cliché, here's another story about a girl with a childhood dream of becoming a doctor. But from coursework to fieldwork, I have had some amazing opportunities to dive deeper into the field of medicine and I only have a greater desire to know more. This year I was fortunate enough to find a very kind Emergency Department (ED) doctor who took me under his wing and allowed me to be part of his outreach program to assess patient satisfaction. The ED is great exposure for me because I get to see everything from a small cut on the arm to gun shot wounds, as well as assisting the doctor during certain procedures. I hope I have been an asset to the program because the program has definitely benefited me by helping me appreciate on so many levels what it means to be a physician.

My hunger for clinical exposure has been nurtured this summer in the Hematology/ Oncology department. I could not have asked for a better educator, intellectual, and person as my mentor. I truly appreciate Dr. Marsha Treadwell for exposing me to public health issues within my community that I would have been oblivious to otherwise. I am gaining knowledge about the disparities that exist within our community and I am becoming better able to appreciate the different factors that are essential to providing the greatest quality of care for people with chronic illnesses. I would like to thank the Sickle Cell Team for welcoming me and allowing me to contribute to their overall project. I would especially like to thank Fernando Barreda, the project coordinator for the Northern California Network of Care for Sickle Cell Disease. I am grateful and thankful to the wonderful people at CHORI for this summer internship experience.

Introduction: Individuals with sickle cell disease (SCD) face a number of barriers as they attempt to access timely and appropriate health care. We previously reported that adult and pediatric patients with SCD differed significantly on some barriers reported, with adults citing more insurance, provider and individual barriers. Patients' emotional status, including worry, frustration and anger, were also reported barriers to accessing health care. However, there has been limited research formally assessing mental health symptoms as potential barriers to accessing health care.

Objective: 1. To describe mental health symptoms, quality of life and reported barriers to accessing healthcare; 2. To investigate the relation between mental health symptoms, quality of life and reported barriers to accessing healthcare. We hypothesized that mental health symptoms would be associated with number of reported barriers, for adults with SCD compared with children. We also hypothesized that quality of life would be inversely related to the number of reported barriers, for both adults and children.

Methods: Individuals with SCD were enrolled in the Northern California Network of Care for Sickle Cell Disease program evaluation. Adults, and parents of children, completed a checklist of barriers to accessing healthcare for SCD; screening measures of depression *(Patient Health Questionnaire-9 or Children's Depression Inventory)* and anxiety *(Generalized Anxiety Disorder- 7 or Multidimensional Anxiety Scale for Children-10)* and categorized with no, mild, moderate or severe symptoms. They also completed quality of life measures *(SF 36v2® or PedsQL®),* with scores ranging from 0 to 100, with higher scores indicating better quality of life.

Results: Participants were 35 children (M age 9.5, 1- 17 years) and their parents and 77 adults (M age 31.2, 18 - 68 years). 53% were female; 71% were diagnosed with SCD-SS. Adult and pediatric patients did not statistically differ in number of barriers reported, but adults reported worse quality of life (QoL) in both physical and mental health domains (Table 1). A large percentage of adults reported mild to severe depression and anxiety compared with less than 25% of children. For the sample as a whole, the number of barriers was significantly correlated with age (r = .21, p<.05), depression (rho = .45, p<.001) and anxiety (rho = .41, p<.001). The number of barriers was significantly negatively correlated with quality of life in the physical (r = -.41, p<.001) and mental health (r = -.46, p<.05) domains.

Table 1. Summary of Measures	Adults	Children
#Barriers Reported - M(SD)	9.2(10.1)	6.3(8.2)
QoL Physical - M(SD)	53.0(23.7)	65.6(21.4)*
QoL Mental Health - M(SD)	49.4(23.2)	66.0(17.9)**
Mild to Severe Depression (%)	61	15**
Mild to Severe Anxiety (%)	44	23*
*p<.05 **p<.01		

Conclusions: Adults with SCD reported impaired quality of life and a high prevalence of mental health symptoms, often moderate to severe, compared with children in our sample. Contrary to our expectations, mental health symptoms were associated with barriers to accessing healthcare for both adults and children. As expected, as barriers increased, quality of life decreased. There is an urgent need to address barriers to health care for patients with SCD and to improve mental health services available to adults in particular.

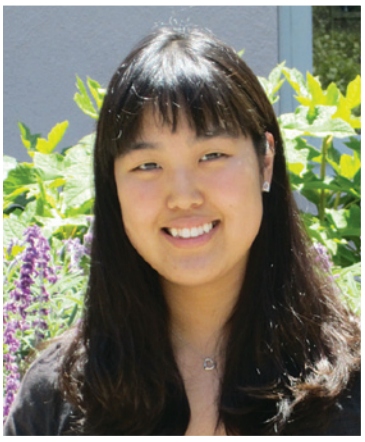
HANNA KIM

Volunteer

Mentor: Cassandra Calloway, PhD

I believe the purpose of one's everyday life is to learn: no matter what one's religious background may be, where one is from, or how old, they are constantly learning and work to contribute to the society they belong to. No matter where I am, or what I am doing, I believe I am constantly learning. Whether I am taking notes in chemical biology class at the University of California, Berkeley, teaching an inmate how to add fractions at San Quentin State Prison, holding an infant patient at Children's Hospital in Oakland, or having a late night talk with my roommate with a tub of ice cream and a box of Kleenex, there's one thing I am constantly doing: learning. I am very grateful for this wonderful opportunity to be able to participate in CHORI Summer Student Program, and I believe this program will be a great experience that will teach me so many invaluable lessons. As a Molecular and Cellular Biology major and premedical student, I am thrilled to be exploring a research project that links molecular scale of study (involving mitochondrial DNA) to a larger health issue (iron deficiency), as I find it relevant to my current study and career interest, yet it is a new knowledge that I am gaining.

I want to take this chance to thank Cassandra Calloway, PhD, and Saloni Pasta, PhD for guiding me through this program with such patience and support, being true mentors, teachers.



The Effects of Iron Deficiency and Repletion on Mitochondrial DNA Copy Number/Mutation in Rats

Introduction: Iron deficiency is the most common nutritional deficiency worldwide affecting approximately two billion people and an estimated nine million people in the United States alone[1]. Iron deficiency is a significant public health concern impacting mostly women and children, and it is therefore associated with an increased risk of poor pregnancy outcomes and impaired cognitive development in young children. Iron deficiency ranges from depleted iron stores without functional or health impairment to iron deficiency with anemia, which affects the functioning of several organ systems.[2]

Defects in the regulation of mitochondrial DNA (mtDNA) copy number and mtDNA damage/mutation are associated with various metabolic diseases. Results from a previous study indicated that iron deficiency results in mtDNA damage[3]. Other studies have also shown that nutritional deficiencies such as folate[4] can lead to mtDNA mutation, namely the 'common' 4834bp deletion in rats. Increased frequency of the common deletion was also observed in alcoholics, and the deletion frequency was reportedly reversible after two weeks of alcohol abstinence. The common deletion results in loss of a 4834bp or 4977bp region flanked by a set of direct 16 bp or 13 bp repeats in rats and humans, respectively. This deletion is the most common mtDNA mutation studied and can serve as a mtDNA mutation/damage biomarker. Exploring the possibility of mtDNA copy number and the common deletion as biomarkers of iron deficiency and the reversibility of the effect of iron deficiency on mtDNA would be useful for understanding the health concern that is so common around the globe.

Objective: The overall objective of our project is to determine if iron deficiency induces a change in mtDNA copy number and leads to mtDNA damage. We will determine the relative amount of mtDNA to nuclear DNA (nDNA) by using a qPCR Taqman assay. We also seek to conclude whether iron deficiency results in mtDNA damage by targeting the common mtDNA deletion. Furthermore, the project aims to determine if any observable mtDNA damage induced by iron deficiency is reversible upon iron replenishment.

Methods: For the project, a total of 16 weanling male F344 rats were studied. The rats were divided into the following four groups to study the effects of iron deficiency and replenishment: iron depletion (4 rats), iron depletion controls (4 rats), iron repletion (4 rats,), and iron repletion control (4 rats). Eight animals (iron depletion and iron repletion rats) were fed an iron-deficient diet for 34 days. The iron-deficient group and their controls were then sacrificed to collect blood and liver tissues. After the depletion phase, iron was reintroduced in the diet for an additional 34 days for the iron repletion animals. These animals were then sacrificed along with their iron normal controls and blood and liver tissues were collected. Total genomic DNA was extracted from the liver tissues using the Qiagen Mini Tissue Extraction kit (Valencia, CA) and from blood using Qiagen Blood Extraction kit (Valencia, CA).

Relative copy numbers of mtDNA to nDNA will be measured using a Taqman real-time qPCR assay in the blood and liver tissues. We will also determine the relative amount of mtDNA deletion using a second Taqman real-time qPCR assay targeting the mtDNA deletion and mtDNA D-Loop (total mtDNA). We are currently in the process of optimizing the deletion qPCR assay and testing the primers for this system. Once the qPCR assay is optimized, then we will determine the level of mtDNA damage assessed by quantifying the relative amount of mtDNA deletion.

Results: Since previous studies have shown that iron and other micronutrient deficiencies have led to an increase in level of mtDNA damage, we anticipate an increase in the frequency of the common deletion under conditions of iron deficiency compared to that of the control group. We also expect to observe a reversal or decrease in the mtDNA common deletion frequency in iron replenished animals relative to that of the iron depleted animals. We may also expect to see a change in mtDNA copy number in iron deficient rats.

Conclusions: We are in the process of optimizing the deletion qPCR assay. Further experiments and analysis with the optimized assay are needed in order to make any conclusion.

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JACQUELYN KNAPP

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

San Francisco State Universtiy, Post-Baccalaureate

Mentor: Janelle Noble, PhD

There have been many events in my life that have brought me to CHORI. Starting with a two-year stint in Peace Corps, I was assigned to be an Information Technology Educator in a small rice-farming village in Guyana, South America. As a high school teacher in a developing country, day in and day out, I was faced with many obstacles. Teaching data security in a village where donkey carts traveled the road, and only one of my students had a computer, demanded creative pedagogy.

This demanding job forced me to learn many things about myself, including my inclination to put myself in uncomfortable situations, my placid approach and resourcefulness to these situations, and the fulfillment that often came as a result. Additionally, I unearthed a passion for health-related matters, as I coordinated HIV/AIDS behavior-change workshops and assumed the role as school nurse with a newly-acquired first aid certificate from the Red Cross Guyana.

After returning from the Peace Corps, I found myself in a cushy office job working in the corporate snow globe, again. But I longed for the feeling of being indispensable. I joined a pre-health, post-baccalaureate program at San Francisco State and began volunteering at Children's Hospital Oakland, helping kids with their homework bedside. I really enjoyed being in a clinical setting but wanted a holistic view of the medical field before I embarked on my immediate goal of going to medical school.

For the past year and a half, I have had the opportunity to work in Dr. Janelle Noble's lab, assisting in a clinical research study that aims to help physicians more quickly and accurately distinguish type 2 diabetes from type 1 in underserved -- particularly African American and Hispanic American -- pediatric populations. It is from this experience, I have come to appreciate the importance of research in these communities. I am grateful for the invaluable knowledge I have gleaned from both mentors and colleagues I have worked with over the past year and this summer. And as an aspiring physician, I hope to continue research efforts that improve the medical treatment of the socioeconomically disadvantaged; an appreciation engendered by the amazing people (and their efforts) in the Noble Lab.

A Comparative Study of Three High-Resolution Genotyping Technologies: Linear Arrays, Suspension Arrays, and 454 Sequence Based Typing

Introduction: Sequence-based typing (SBT) using the 454 next-generation sequencing platform is replacing linear arrays used for sequence specific oligonucleotide (SSO) HLA genotyping, both because the 454 SBT results provide higher resolution and linear array reagents are no longer readily available. Although the genotyping cost is comparable when the 454 SBT system is used at capacity, a high-resolution alternative is needed for HLA genotyping of small numbers of samples and as a backup system to the 454. A comparative study was performed to determine if suspension array assays using SSO microsphere beads, such as the Luminex 100/200, produce comparable results to the linear arrays and, thus, represent a suitable replacement for linear array technology.

Objective: To determine if Luminex suspension array genotyping is a suitable replacement for linear array assays, when comparing throughput, resolution, amount of required template, cost, time, availability of reagents, and ease of data analysis. Additionally, to determine how these two technologies compare to 454 SBT.

Methods: Eleven DNA samples from the Network for Pancreatic Organ Donors with Diabetes (nPOD) were amplified and HLA genotyped at eight loci (HLA-A, HLA-B, HLA-C, DRB1, DQA1, DQB1, DPA1, DPB1) using SSO linear arrays. A subset of the template samples (3 out of 11) were amplified and HLA genotyped at the same loci using OneLambda LABType SSO reagents and the Luminex 100/200. Additionally, the same three samples were HLA genotyped for DRB loci by SBT on the 454. The results were compared across all three technologies.

Results: In the three samples tested, suspension arrays displayed higher resolution than linear arrays at both the DQA1 and DPB1 loci. Other calls were identical between the methods. 454 SBT results for the DRB1 locus gave the same result as both SSO technologies and, in addition, produced data for other DRB loci including DRB3, DRB4, and DRB5. A detailed cost, time, and throughput analysis will be presented.

Conclusions: Preliminary data shows suspension arrays have a higher resolution than linear arrays. Although 454 SBT gives the highest resolution of any of the three technologies tested, the need for 454 SBT resolution must be weighed against the cost if performing an assay on a small number of samples. Specialized software for all three technologies requires an experienced user to make final allele pair calls. Suspension array assays appear to be less expensive than linear arrays on a per sample per assay basis. Overall, suspension arrays may be a cost-effective alternative to linear arrays and the 454 (if run not done at capacity or equipment malfunctioning).

JOSHUA LEE

Funded by the Jennifer Leigh Wells Fellowship

University of California, Berkeley

Mentor: Lindsay Streirer Taylor, PhD

My journey towards becoming a doctor is one that I would actually consider not extremely unique. Unlike some of my peers' stories, it is one that would probably not bring someone to tears upon hearing it. I grew up in a place of privilege, with all of my physical needs met. I had a loving family that supported everything I wanted to do. Growing up, I had always wanted to be an engineer. So then, why did I want to be a doctor?

To put it briefly, it was not until the start of my second year of college where I began to understand the dichotomy between my place of privilege and the greater needs of people around me. I had begun actively participating in a student-run nonprofit start-up called The Hep B Project, which aimed to reduce the Hepatitis B prevalence among API populations in Alameda County. At the same time, I had been realizing the ways in which the God I believed in empowered me to seek the healing of the community around me.

I joined the Moe Lab at CHORI around April this past year originally because I simply wanted to gain research experience, but it has turned out to be more than that. I thank my mentor Lindsay Steirer Taylor, Mike Cheng, Maike Muller, and our PI Greg Moe, for creating an exciting and supportive atmosphere in the workplace.

Effect of PolyST gene knock down on NeuPSA expression in melanoma cells

Introduction: Polysialic acid (PSA) is a homopolymeric sugar molecule that plays an important role in fetal development and is involved in maintaining plasticity of some adult tissues. Additionally, PSA is produced as a capsular polysaccharide by some pathogenic bacteria and can be expressed at high levels in some malignant tumors. Our laboratory found that a derivative of PSA, known as de-N-acetylated PSA (NeuPSA), is expressed in human tissues, but at significantly higher degree in tumors compared to the corresponding normal tissues. PSA is a polyanion that has a repulsive anti-adhesive effect on cells whereas NeuPSA is zwitterionic, and promotes adhesion. Two polysialyltransferases (PolySTs), PST (also known as ST8Sia4) and STX (also known as ST8Sia2), are the enzymes that synthesize PSA. We have shown that knocking down one of the PolySTs, PST, results in decreased NeuPSA expression. We have also shown a strong correlation between the levels of PST and STX mRNA and NeuPSA expression in human tissues.

Objective: The goal of this project will be to characterize stable clonal cell lines with knocked-down expression of the PolySTs PST and STX as a means to understand the role of PSA/NeuPSA in cancer cell biology.

Methods: Knock-down cell lines were produced in SK-MEL-28 human melanoma cells using vector-based interfering RNA. After genome integration, the vector produces miRNA that targets PST or STX mRNA sequences for cleavage by RISC. We transfected SK-MEL-28 cells with one of four vector constructs, two targeting each gene, called pcDNA 6.2-GW/+ EmGFP – PolyST, where PolyST represents STX1, STX2, PST1, and PST2. For each construct, multiple clonal cells lines were established and screened. First, we confirmed vector integration by screening the cells for EmGFP expression through fluorescence microscopy. Second, we confirmed correct integration of the vector sequence using conventional PCR and sequenced the PCR product. Then, using real-time quantitative PCR (qPCR), the samples were screened for decreased expression of the respective PolySTs.

Results: Using fluorescence microscopy we determined that cells transfected with constructs STX2 or PST1 expressed EmGFP. PCR and sequencing confirmed that DNA from all four vector constructs integrated into the genomic DNA. qPCR determined there was decreased STX and PST gene expression in all clonal cell lines.

Conclusions: We have successfully generated and identified stable clonal cell lines containing each of the four vector constructs targeting STX or PST mRNA. Interestingly however, qPCR showed reduced expression of both STX and PST regardless of whether the vector construct integrated into the genome targeted STX or PST.

FLORENCE LIU

Funded by Children's Hospital Los Angeles (National Heart, Lung and Blood Institute, Basic and Translational Research Program)

Albany High School, Junior

Mentor: Feng Gao, PhD

My name is Florence Liu and I will be entering my senior year this Fall at Albany High School.

Recently, I realized that happiness is achieved by pursuing one's passion. Finding my passion has been difficult, and I can't say I have it completely figured out. However, my love for science will always be a basis for what career I will pursue in the future. Coming from a family of scientists, science has always been a part of my life growing up. However, it wasn't until taking AP biology last year that the subject came alive personally. Science has always been a topic I was decent at, but the classes I took didn't particularly interest me. AP biology felt entirely different from all of my previous science classes. Whether we were learning about molecular mechanisms or ecology, the material interested and made sense to me. I realized there were so many unanswered questions, and the more I learned it seemed the less I knew. These mysteries in science, the unanswered details, were what sparked my interest.

I wanted more hands-on experience, something that would put me on the path to pursuing a career in scientific research. When I heard about the CHORI Summer Program, I knew it was what I was looking for. Although I have gotten a glimpse into the world of scientific research, I still have much more to learn and experience.

I want to thank Dr. Feng Gao for patiently guiding me throughout the summer as well as being an amazing mentor, and Dr. Krauss along with this Summer Program for allowing me to pursue my interest in science with this opportunity.

Functional study of coding synonymous SNPs in the LDLR gene

Introduction: Low Density Lipoprotein Receptor (LDLR) plays a central role in cholesterol homeostasis by the uptake of LDL-cholesterol. Mutations in the LDLR gene can cause familial hypercholesterolemia and risk of Cardiovascular disease.Three coding synonymous single nucleotide polymorphisms (SNPs), rs2228671 (Cys249 TGC->TGT), rs5930(Arg471 AGG->AGA) and rs688 (Asn591ACC->ACT) have been shown significantly associated with LDL cholesterol levels. rs2226871 is located in the ligand binding domain of LDLR while both rs5930 and rs688 are located in the beta-propeller region. These three SNPs have been shown not to be in link dislinkage disequilibrium (LD) (r2<0.5). LDLR transcript containing rs2228671, rs5930, and/or rs688 are predicted to have decreased translation efficiency due to lower free energy and altered function and form in the ligand binding domain or (EGF)-beta propeller domain. Consequently, we hypothesize these three SNPs may increases level of accumulation of LDLR in the lysosome and/or endosome resulting in reduction of LDL uptake.

Objective: To investigate if these three coding synonymous SNPs rs2228671, rs5930, and/or rs688 reduce LDLR activity.

Methods: pCMV-LDLR-FLAG plasmid containing either wild type or mutant LDLR with SNPs rs2228671, rs5930 and rs688 were transfected to HepG2 cells. 25-Hydroxycholesterol was added into the medium to suppress the endogenous LDLR synthesis. We then incubated the transfected HepG2 cells with DiI-LDL to assess the effects of rs2228671, rs5930 and rs688 on LDLR activity. Levels of DiI-LDL uptake were quantified by Victor Fluorescence Plate Reader and normalized by fluorescence intensity measured for Hoechst DNA. DiI-LDL uptake was also observed by confocal microscopy on a Zeiss LSM 710 confocal inverted microscope. All results were compared to cells transfected with an empty plasmid pCMVas a negative control. Two-way interactions among these SNPs were analyzed using JMP version 8.0 software. Two-tailed paired Student t-tests were used to determine the difference of Di-LDL uptake between SNPs.

Results: SNP-SNP interaction analysis indicated there is no interaction observed among these three SNPs. As a result, these three SNPs are not associated with each other. Therefore, DiI-LDL uptake split by these SNPs genotype were assessed individually. Remarkably, both rs2228671(T/C -16.0% difference p<0.0001) and rs688(C/T -5.2% difference p=0.0487) are shown to have statistically significant reduction of DiI-LDL uptake in HepG2 cells individually, while rs5930 has been found to show no significant difference on uptake of Di-LDL (p=0.075). The experiments are underway to quantify SNPs effects on distribution of LDLR protein in HepG2 cells.

Conclusions: Our results suggest that common coding SNPs within LDLR (rs2228671 and rs688) may play a functional role in lipid metabolism. Hence, future work should shed light on the functional relevance of these coding synonymous SNPs within LDLR in regulating cardiovascular disease risk.

ZIAN LIU

Funded by Children's Hospital Los Angeles (National Heart, Lung and Blood Institute, Basic and Translational Research Program)

Albany High School, Senior

Mentor: Ash Lal, MD

This fall, I will return to Albany High School as a senior, President of the Chemistry Club and the Game Designing Club, and record holder for owning the most number of ties. In addition, I will return with a new perspective on science.

The son of two doctors, nephew of an engineer in China's NASA, and grandson of a math teacher and a chemistry instructor, I grew up deeply surrounded in science. As a result, I took an early interest in how the world functions.

After moving to the United States from my native China, my questions intensified as I became accustomed to short but extremely confusing terms such as "PCR", "blot" and "ELISA" from listening to my parents' dinner table conversations. I discovered after AP Chemistry the power of equilibrium and after AP Biology, the importance of homeostasis. This summer, I was privileged to have had the chance to work with Dr. Ash Lal, studying the mitochondria, an organelle essential to cellular respiration. I am beyond grateful for an experience that allowed me to use my skills both in Biology and Chemistry to develop and complete experiments that determined what too much iron, a nutrient very essential to cellular function, can do to the mitochondria. But this project taught me even more – it taught me the importance of translational research. It taught me to connect class to research and research to everyday practice. Science should always have useful applications for the people.

When I first heard about this program, I dreaded the possibility of working in the same place as my parents. Now, I feel lucky that I chose to accept this opportunity. Mom and dad: thank you for sparking my interest in science. Shing, Nancy, Amy, Juneyoung, Veronica, Daniel(s), et al: thanks for putting up with my daily rants on the incredibility of Western Blot, Flow Cytometry, and ELISA. To my teachers: thank you for teaching me everything I know. Lastly, I cannot thank enough Dr. Lal and the entire Ames Laboratory for opening up their work to me and allowing me to learn. Thank you for showing me the vastness of science and how it can always connect to everyday use. Thank you for making these two months perhaps the most meaningful summer of my entire high school career.

The Effects of Iron on Mitochondrial Respiratory Complexes

Hypothesis: Mitochondrial genome is more susceptible to the deleterious effects of oxidative stress owing to greater exposure to free radicals and less efficient repair mechanisms. Thus, we propose that an overexposure to iron in cultured cells will alter the quantity of proteins encoded by the mitochondrial DNA (mtDNA).

Specific Aim: This project aims to determine the effects of increased environmental iron (emulating conditions similar to that of iron overload) on Jurkat cells through measuring the ratio of the quantity of mitochondrial respiratory complexes I and IV (partly encoded by the mtDNA) to the amount of alpha-ketoglutarate dehydrogenase (OGDH, encoded by nuclear DNA, or nDNA).

Background: Mitochondria are organelles in eukaryotic cells that perform the essential steps of cellular respiration. Unlike other organelles, mitochondria contain their own DNA and thus "encode" some of their own proteins. In patients with Sickle Cell Anemia, DNA mutations cause the formation of sickle red cells. The sickle red cell, unlike the common red cell, often forms reactive oxygen species, which often damage cells and increase the rate of hemolysis. Sickle cell patients also often need blood transfusions. Both contribute to an increased concentration of iron within the bloodstream, causing iron overload. Iron is essential for the normal function of cells and their mitochondria, but an excess of iron damages the mitochondria. Iron catalyzes the formation of free radicals (hydroxyl radical), a very reactive species capable of binding to practically any component of the cell, including the relatively unprotected mtDNA. Such iron-induced DNA damage can affect protein production and mitochondrial function. This project aims to examine iron's effects on the mitochondria of Jurkat cells (a line of immortalized human T-cells).

Methods: We prepared three different batches of cells, one of which served as the control. The other two batches were cultured in buffers containing 250 μM and 1000 μM of ferric ammonium citrate, respectively. After allowing the cells to absorb the excess ferric ions within the solution, we performed a "crude mitochondrial prep" on the cells: we harvested the cells by centrifugation and broke the cell membranes using a homogenizer; mitochondria were isolated using differential centrifugation and protein was extracted using extraction buffer. A BCA assay was performed on the protein to determine concentration, followed by a sandwich ELISA to determine the relative concentrations of mitochondrial-encoded proteins Complex I and IV and nuclear-encoded protein OGDH. The concentrations of Complex I and IV in iron-enriched cells are standardized by the concentrations of OGDH, and then compared to the concentrations of Complexes I and IV in control cells. The change in concentration reflects the mitochondrial DNA damage resulting from iron overload.

Results and Conclusion: A crude mitochondrial prep performed on three Jurkat samples – control, 250 μM iron exposure, and 100 μM iron exposure – with roughly equal volumes and cell concentrations showed that the iron-exposed cells have a much lower concentration of mitochondrial protein. We expect that an ELISA would show that the iron-exposed cell would contain a smaller amount of mitochondrial-encoded protein Complexes I and IV, and a relatively unchanged concentration of OGDH. We would infer from such results that mitochondrial DNA encoding the two complexes examined is no longer expressed at the normal rate, likely due to damage caused by iron overload. Therefore, overexposure to iron would appear to be extremely damaging to mitochondrial respiration. If these methods are validated, we will use blood samples from patients with sickle cell disease in the future to measure changes in mitochondrial proteins in leukocytes.

TANEA LUNSFORD

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

Columbia University, Sophomore

Mentor: Barbara Staggers, MD

My name is Tanea Lunsford and I am a junior at Columbia University studying anthropology and human rights. Although I am studying topics in humanities I have a great interest in medicine and public/global health. After witnessing the increasing number of devastating (and often preventable) diseases related to unsafe sex habits and practices among the youth in my own community I was inspired to research the correlation of unsafe sex habits with lack of education, lack of accessibility, cost barriers, and a number of other barriers to safe sex practices and condom use in Oakland this summer during the CHORI Summer Program.

This summer I have had many outstanding opportunities presented to me that I could not have anticipated upon my acceptance to the program. This is my second consecutive year in the program and it was amazing to see the progress that has been made in the teen clinic, where I had the privilege of working again this summer. I have had the opportunity to see patients in the teen clinic alongside phenomenal doctors such as Dr. Barbara Staggers and Dr. Jenifer Matthews who continue to awaken interest and admiration for the field of medicine, which I was having doubts about over the school year.

The CHORI Summer Program has given me the opportunity to be inspired and get hands-on experience in the place of textbooks and assignments. This summer has helped reaffirm my passion, interest, and confidence in my choice to pursue a career in the medical field, whether it is as a medical anthropologist, a doctor, or researching in the global health field. This summer I have had the chance to do what I have always wanted to do and it gives me hope that this career will one day be a reality for me.

Barriers to Condom Use for Sexually Active Females in Alameda County

Introduction: Although the rates of teens diagnosed with STIs has decreased over the years, the numbers are still jarring, specifically for Alameda county, where there is the highest incidence of Chlamydia and Gonorrhea diagnosis in females ages 15-24 in the entire state. Chlamydia and Gonorrhea infections can increase the chances of becoming infected or transmitting HIV in both males and females. These infections can be prevented largely by condom use, however, the larger questions of access, education, and a host of other barriers may be standing in the way of safe sex habits for a large number of females in Alameda County. Some information gathered by Youth Health and Wellness in Alameda County offer statistics as to how large of a barrier is created by the absence of education, "Among teens who had ever had sexual intercourse, 5% of females and 13% of males had received no formal education on either topic." Similar barriers to safe sex include awareness of the risks and dangers that can ensue from lack of safe sex practices, access to condoms, affordability of condoms, and the lack of knowledge about how to use contraceptives as a preventative measure against STIs and pregnancy.

Objective: The objective of this study is to assess the barriers to condom use and safe sex practices among sexually active females in Alameda County. By identifying these barriers and targeting them for re-evaluation and better service (i.e. subsidizing condoms so that all teens can afford them if cost is a large barrier to condom use) this project works to increase the knowledge and improve the behaviors associated with safe sex habits for sexually active females in Alameda County.

Methods: I surveyed 50 female sexually active patients from the Oakland Children's Hospital Teen Clinic while they waited to be seen by their physicians. I created a nine question anonymous survey that asked patients to rank the barriers to condom use and discuss why they did and did not use condoms. The survey asked when the patients' first sexual intercourse was, the number of partners they had in the past six months and their percentage of condom use over the last six months (0% meaning never, 100% meaning with every sexual intercourse). These questions were asked to gauge sentiment towards safe sex practices, identify barriers to condom use, and to inquire if these habits might improve given the removal/improved service of the identified barriers. Only sexually active females were surveyed for a number of reasons, some of the reasons include the statistics of females diagnosed with STIs in Alameda County, the lower percentage of females educated in sexual education/health, and to gauge improvement and sentiment based on percentages of females who had been pregnant in the past. The survey also asks if the patient would be interested in attending a workshop to learn more about safe sex habits and sexual health to discuss any questions they might have at a later date as a means to offer follow-up education to eliminate the barrier of education for those who choose to participate.

Results: The fifty surveys yielded a number of interesting results including a large pool of patients that had been pregnant in the past, a small number of patients reporting 100% condom use (about the same number of patients who reported 0% condom use), and more than half of the patients said that they did not use condoms at times because they trusted their partner. The main barrier identified was lack of knowledge of the risks and dangers of not using condoms, which justified the necessity for a follow-up educational seminar. The next most popular identified barrier was access to condoms, which would call for a increase in condoms for teens who are sexually active and thinking about becoming sexually active in places they frequent.

Conclusions: The identification of barriers to safe sex habits and condom use demand an increase of peer and/or community based sex education to raise awareness of the serious risks of not using condoms and education on not only how to use contraceptives, but why it is important to do so. The anticipated outcome of this research project was that safe sex methods of contraception would be made affordable and accessible for all sexually active teens. In addition, the project aims to improve safe sex behaviors of teens in Alameda County via education and improvement of informed habits and choices of sexually active teens.

RAJAN MANMOHAN

Funded by The Jordan Endowment Fund

Mills College, Post-Baccalalureate

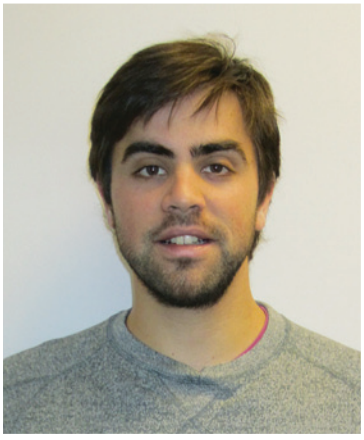
Mentor: Bindu Kanathezhath, MD

I currently study at the premed post bac program at Mills College here in Oakland. I studied business as an undergraduate at Carnegie Mellon, and soon realized that it was not for me. Biology and medicine were always of interest to me, but remained on the periphery of my life as I pursued a career in finance. When I realized that I lacked a genuine passion for the business world, I began to delve into the medical field, tentatively at first, but with more and more tenacity as I discovered how much I loved it. Science and medicine are so appealing to me because the level of knowledge and understanding is constantly being built upon and new discoveries are always being made, which results in a continually evolving field. Further, the level of compassion that goes into medicine and caring for other people, either in a clinical setting or through scientific investigation and discovery, makes it a field/career worth going in to. My fascination with biological sciences continues to grow the more I learn and experience, and I hope to go to medical school in the near future.

My mentor, Dr. Bindu Kanathezhath, MD, is an inspiration to me. She splits time between Children's Hospital as a bone marrow transplant clinician and CHORI as a basic researcher working with T cells and graft-versus-host disease, a major problem affecting bone marrow transplant patients. By intertwining her clinical specialty in bone marrow transplantation with her research on ways to improve the process and reduce graft-versus-host disease, Dr. Kanathezhath impacts her field daily and offers a special insight that affects translational research.

I plan to continue research with Dr. Kanathezhath as long as I am in the area so that I can continue to enjoy this incredibly fulfilling experience.

Getting involved in research is highly educational and focused and the research we are doing has the potential to transform the bone marrow transplantation protocol, improving the lives of patients with a number of different hematological disorders.



Determining changes in thiol redox profile of the T cell effector phenotypes associated with alloreactivity

Introduction: Graft versus host disease (GVHD) is a major cause of morbidity and mortality in bone marrow transplant recipients. GVHD results when donor T lymphocytes (T cells), recognize epitopes in host antigen presenting cells (APCs) and mount an immune response consisting of lymphocyte proliferation and cytotoxicity4. Symptoms of GVHD include abdominal pain, jaundice, weight and hair loss, hepatitis, and disorders of the liver, lung, and GI tract. Incidence of GVHD ranges from 30-40% for related donor/recipients and from 60-80% for unrelated donor/recipients with current HLA matching criteria for human transplantation2. Research shows metabolic processes in lymphocyte alloreactive T cells generate reactive oxygen species (ROS) in high concentrations. Oxidation of bound sulfhydryl (thiol) groups by high concentrations of ROS is known to result in cell and tissue damage and increased incidence of GVHD. Although eliminating GVHD entirely is not possible, current research is focused on reducing GVHD while enabling engraftment of hematopoietic stem cells in curing hematological disorders such as sickle cell disease, thalassemia, and leukemia. The full potential of bone marrow transplantation to cure hematological disorders will not be reached until incidence of GVHD is minimized.

Objective: This study aims to identify differential levels of thiol expression in T lymphocytes under different conditions simulating immune response and GVHD.

Methods: To simulate bone marrow transplantation, allogeneic cultures containing irradiated whole splenocytes of FVB/NJ mice and isolated T cells from C57BL/6 mice were analyzed using flow cytometry at four timepoints (2, 3, 7, 9 days following harvest) to determine thiol profiles. Results were compared against a syngeneic control culture containing irradiated whole spelnocytes and isolated T cells from C57BL/6 mice. Simultaneously, separate cultures containing isolated T cells from C57BL/6 mice with PMA and Calcium Ionomycin stimulants were analyzed using flow cytometry at the same four timepoints. PMA and Calcium Ionomycin act to stimulate immune response in T lymphocytes, thus allowing further comparison of thiol profiles in a different immuno-response culture.

Results: In the stimulated and unstimulated cultures, exofacial thiol content decreased over time, while at any given timepoint, exofacial thiol content was higher in the stimulated culture. In the stimulated and unstimulated cultures, intracellular thiol content increased over time, while at any given timepoint, intracellular thiol content was higher in the unstimulated culture. These results are consistent with our hypothesis. In the allogeneic and syngeneic cultures, results were not as conclusive. Exofacial thiol content decreased over time for syngeneic and allogeneic cultures, while at any given timepoint exofacial thiol content was higher for the syngeneic culture. Intracellular thiol content increased over time for syngeneic culture and decreased for allogeneic culture. Intracellular thiol content at any given time was higher in the syngeneic culture.

Conclusions: Results for the allogeneic culture were inconclusive and not consistent with our hypothesis. Further study will be done to determine thiol content of subset populations within the T lymphocyte population. Results in the stimulation experiment showed that exofacial thiol content increases with stimulation over time, while intracellular thiol content decreases. This was consistent with our hypothesis that T lymphocytes display exofacial thiol as part of signaling in the immuno-response pathways, with the displayed thiol content coming from intracellular sources.

LAUREN MEISS

Funded by the Elizabeth Nash Foundation

Arizona State University, Senior

Mentors: Beate Illek, PhD, and Horst Fischer, PhD

Because I was diagnosed with cystic fibrosis (CF) when I was 3 months old, I have always been all too familiar with the clinical side of the disease: the daily treatments, medications, frequent testing and hospital visits. However, it was not until my first summer in the CF lab at CHORI that I understood the basic defect that occurs on a cellular level and is manifested in the daily medical struggles. This insight has completely changed my perspective of my disease and treatment, and for that I thank Dr. Illek and Dr. Fischer. Their passion for research in this particular field is contagious, and their vast knowledge serves as an endless supply of all of the information I have been craving to learn about my disease. I would like to thank them both for their guidance and willingness to share their knowledge.

I am studying biomedical engineering at Arizona State University. I plan to continue on in translational research by earning an MD/PhD dual degree after first taking a year off of school to conduct research in another country, most likely Sweden or New Zealand.

Role of CFTR and p53 during *Pseudomonas Aeruginosa* Homoserine Lactone Induced Apoptosis and Epithelial Barrier Breakdown

Introduction: In the United States, approximately 1 in every 3000 Caucasian newborns has cystic fibrosis (CF), making it one of the most common fatal genetic disorders among the Caucasian population. The basic defect in CF is hindered transportation of electrolytes across epithelial cell membranes due to mutations in the gene encoding the cystic fibrosis transmembrane conductance regulator (CFTR). A recent study suggests that CFTR trafficking is essential for epithelial tightness, an effect independent of its anion channel function. Chronic lung infection with *Pseudomonas aeruginosa,* a gram negative, opportunistic bacterium, leads to progressive loss of lung function and results in the death of >80% of patients with this autosomal recessive disease. Once colonized in CF patients, the bacteria secrete quorum sensing molecules, including N-(3-oxo-dodecanoyl)-S-homoserine lactone (C_{12}-HSL), to act as signaling molecules which regulate their own gene expression. C_{12}-HSL is present in significant amounts in biofilms, the phenotype of *Pseudomonas aeruginosa* in CF patients. It has been estimated that concentrations of C_{12}-HSL in CF sputum are in the nM range, but may reach >100 μM in regions adjacent to biofilms. Preliminary data has shown that C_{12}-HSL may act in parallel with protein 53 (p53) to activate the apoptotic pathway in human bronchial epithelial cells. P53 is a protein that regulates the cell cycle and, thus, functions as a tumor suppressor. It is known to activate protective mechanisms such as cell cycle arrest and apoptosis.

Objective: To determine the role of CFTR expression on C_{12}-HSL induced epithelial barrier breakdown and ascertain the role of p53 during C_{12}-HSL induced apoptotic events, and to characterize the mechanism for epithelial changes induced by C_{12}-HSL.

Methods: Bronchial epithelial CF cells with and without genetically corrected CFTR function (CFBE41o-wtCFTR and CFBE41o-parent) and intestinal cells with altered p53 gene expression (HCT116 p53 +/+, +/-, and -/-) grown to confluency on Snapwell inserts. The Ussing chamber assay is used to monitor chloride ion currents (ICl) and transepithelial resistance (R_t). When testing the effect of the signaling molecule, monolayers are exposed to C_{12}-HSL (50μM) in presence of a Cl gradient to characterize the breakdown of paracellular barriers. Following the Ussing assay, monolayers are fixed with methanol, stained with a monochromal, mouse anti-human ZO-1 antibody and an anti-mouse Alexa 488 secondary antibody. Cells are also treated with a Hoechst nucleotide dye to stain nuclei. Slides are excited with laser light (405 and 488 nm) and emission collected at ~450 and ~530 nm. Confocal images are analyzed by a 3D reconstruction of acquired image planes.

Results: Efforts to investigate the role of p53 in apoptotic events showed that the cell line HCT116 has no ZO-1 staining between cell contacts and therefore is not suitable for electrophysiological studies with Ussing assays. Confocal imaging shows the breakdown of tight junction integrity in CFBE41o-wtCFTR cells following 1 hour exposure to C_{12}-HSL. Within 10 minutes of exposure to C_{12}-HSL, R_t of CFBE41o-parent cells dropped by 800 Ω cm^2, while R_t of cells expressing CFTR (CFBE41o-wtCFTR) was reduced by 175 Ω cm^2, suggesting that CFTR trafficking is essential for epithelial tightness. The exposure of CFBE41o-parent cells to C_{12}-HSL led to a transient response of I_{Cl}. The addition of bumetanide, a blocker of the NaK_2Cl cotransporter responsible for the uptake of chloride had no effect on chloride currents, suggesting that the C_{12}-HSL increased currents are due to increased paracellular currents.

Conclusions: The exposure of epithelial cells to the *Pseudomonas aeruginosa* homoserine lactone C_{12}-HSL causes the breakdown of barrier integrity, leading to an increased number of apoptotic cells that build up in the biofilm and thicken the mucus within CF airways.

DAWIT MELAK

Funded by the Short Term Research Education Program to Increase Diversity in Health Related Research from the NIH/NHLBI University of California, Berkeley

University of California, Berkeley, B.A. Molecular and Cell Biology/Physiology

Mentor: Cassandra Calloway, PhD

First of all, I want to give my greatest appreciation to CHORI Summer Program for funding me and my PI, Cassandra Calloway, for providing me the opportunity to work with her outstanding lab teams to work on mitochondrial DNA. One interesting fact about me is that I was born and raised in a small town in Ethiopia. I immigrated to the United States my sophomore year of high school. I went to International Studies Academy High School in San Francisco. Then, I got accepted to the University of California, Berkeley for my undergraduate. I recently graduated from Cal with a bachelor's in Molecular and Cell Biology/Physiology.

Why did I choose science as my goal to pursue? Growing up in a small town in Ethiopia, I strongly enjoyed learning any type of science. However, when I was about 7 years old, I lost my father from a disease that could have been treated if healthcare was easily accessible in the town. Since then, I have always wanted to be a doctor to one day help people like my father who lack access to quality of healthcare. Even though I never envisioned myself as a researcher, I have always wanted to be a doctor and help others who cannot afford a quality healthcare. All this changed when I shadowed Dr. Electron Kebebew at UCSF, who has devoted his entire career on both aspects of science: research and clinical trials. My visit with Dr. Kebebew encouraged me to apply to a two year UCSF UC LEADS Research Program in the spring of 2008 to have an experience in scientific research. Fortunately, I was accepted to the program and for the first time, I experienced how wonderful it is to work closely with principal investigators who were experts in the field I applied for. UC LEADS taught me how research works and also taught me how to think critically. For the first time I began envisioning myself working in clinical research while simultaneously practicing medicine in my future career.

I was very excited when I received acceptance to the CHORI Summer Research Program for this summer. Since I have started the program, I have been challenged to read various protocols and literatures on my own, which I think will be an integral part of my future career in medicine. I have learned how to conduct several different experiments that I did not know when I came to this program such as real-time qPCR and DNA extraction from tissue. I am confident that these skills I have gained from CHORI will help me excel in medical schools and beyond.

Examining the Correlation of PGC-1α with Mitochondrial DNA Content in mice fed a High Fat Diet (HFD)

Introduction: Cardiovascular diseases such as heart attack and type II diabetes are closely associated with the consumption of a high fat diet (HFD). Mitochondrial DNA (mtDNA) copy number plays a key role in the pathophysiology of metabolic syndrome-related phenotypes. It has been determined that the transcriptional co-activator, Peroxisome Proliferator Activated Receptor Gamma Coactivator-1α (PGC-1α), plays a major role in regulation of mitochondrial biogenesis. Previously, Dr. Mark Shigenaga's lab has determined that PGC-1α expression is significantly reduced in the liver and adipose tissues of mice fed a HFD.

Objective: For our project we hypothesized that HFD may affect expression of genes involved in mitochondrial function and biogenesis, resulting in a change in mitochondrial DNA content, which may have an effect on metabolic activity. Under this premise, we want to evaluate if the liver mtDNA copy number correlates with the observed change in levels of PGC-1α.

Methods: Prior to the study, 15 C57BL/6 male mice strain were fed either standard chow diet (n=8) or a HFD (45% kcal fat without fiber) (n=7) for 20 weeks. These mice were then sacrificed and all tissues were stored frozen until needed. Total genomic DNA was extracted from 25mg frozen mouse liver tissue using the QIAMP DNA Mini Kit protocol for this study. The relative amount of mtDNA was determined using a quantitative PCR SYBR green assay targeting mtDNA (cox2 or cytochrome b) and the nuclear genome (beta-globin).

Results: Our preliminary results indicate no significant change to a very modest increase in mtDNA content in the livers of mice fed a HFD compared to the control animals. Although we expected to see a decrease in mtDNA copy number in mice fed a HFD correlating with a decrease in PGC-1α levels in liver, our results were consistent with studies by Adhihetty et al. They found that the lack of PGC-1α in a knock-out mouse model had no effect on mtDNA content in the liver, but resulted in a decrease in mtDNA content in muscle and some adipose tissues.

Conclusions: Based on our preliminary findings, we are expanding the analysis of our study to include additional tissues and markers. We now plan to monitor the expression levels of the mitochondrial transcriptional factor A (TFAM) in livers of mice fed a HFD due to its direct association with mitochondrial replication and transcription. We also propose to monitor the mtDNA copy number and expression levels of TFAM and PGC-1α in the muscle and adipose tissue of mice fed a HFD and control animals. We will then determine if there is a correlation with TFAM levels (mtDNA replication) and mtDNA copy number or PGC-1α levels (mitochondrial biogenesis).

Reference:
Peter J. Adhihetty, Giulia Uguccioni, Lotte Leick, Juan Hidalgo, Henriette Pilegaard, and David A. Hood. "The role of PGC-1α on mitochondrial function and apoptotic susceptibility in muscle." Am J Physiol Cell Physiol July 2009 297:C217-C225; published ahead of print May 13, 2009, doi:10.1152/ajpcell.00070.2009

JOYCE NGUYEN

Funded by NIH Grant #R01AI070955-03

Brown University, Sophomore

Mentor: Peter Beernink, PhD

Having participated in the CHORI summer research program for two summers and now for a third, I have gained invaluable experience that have shaped me as a person entering the field of health sciences. As an impressionable high school student, I undertook clinical research under the direction of Dr. Lydia Tinajero, a pediatrician at the Oakland Children's Hospital. From interacting with her patients and reading up on acanthosis nigricans, I discovered that my passion lies in medicine. With that seed planted in my head, I entered Brown University's Program in Liberal Medical Education. After a year, I returned to CHORI – this time to work in the Granoff lab where I got to dabble in immunology. After being intrigued by the countless ELISAs (enzyme-linked immunoabsorbent assays) I carried out and mutant proteins I made, I chose to take a Principles of Immunology course this past fall back at Brown. Working at CHORI is unique in that it is based in an inner city where all employees, volunteers, and patients of the Oakland Children's Hospital cannot deny the social injustice and economic disparity prevalent throughout Oakland. My summers here have forced me to reevaluate the position of the doctor in patients' lives and the larger community. On campus, I volunteer with Health Leads, a non-profit organization that utilizes energetic college students to help bridge the gap between the doctor's office and a patient's living conditions at home. Due in part to my experience with Health Leads and in Oakland, I declared Community Health as my concentration this past year. Now, this summer I am back in the Granoff lab exploring new approaches to finding improved vaccines for meningococcal disease. As examples show, my cycle of learning and exploration begins at CHORI, continues elsewhere, and returns to Oakland – whether it manifests itself in my volunteer or academic work.

I would like to thank Dr. Dan Granoff and Dr. Peter Beernink for asking me to come back this summer and the rest of the Granoff lab for sharing their knowledge and expertise with me for the past two summers. Not only are the scientists here looking for a vaccine to prevent disease, they are also studying the epidemiology of meningitis to improve patient mortality. In that way, the work done at this lab truly is life-saving work.

A Random Approach to Identify Meningococcal Factor H Binding Protein Mutants with Improved Vaccine Immunogenicity

Factor H binding protein (fHbp) is currently in clinical development as a vaccine for prevention of meningococcal disease caused by group B strains. The antigen is an attractive vaccine target because it binds to the complement inhibitor, human factor H (fH), and enables the organism to evade the immune system. Since binding of fH to fHbp decreases the protective antibody responses to fHbp, the objective of our studies is to identify fHbp mutants with little or no fH binding. To enable cell sorting of an fHbp mutant library in *E. coli*, we investigated several strategies to express fHbp on the cell surface. Using two of these strategies, we confirmed surface expression by binding of an anti-fHbp monoclonal antibody, designated JAR 5, to *E. coli* by flow cytometry. To create an fHbp mutant library, we performed error-prone PCR mutagenesis and determined that there were two to three nucleotide substitutions per fHbp gene by DNA sequencing. This error rate corresponded to an average of one amino acid substitution per fHbp molecule. Our forthcoming studies will be to transform the mutant library into *E. coli* and to identify clones that bind to the control antibody but do not bind fH by single cell sorting. Such clones will be further investigated for conformational integrity of the protein and immunogenicity in wild type and human fH transgenic mice. These studies have the potential to identify novel fHbp antigens that elicit higher protective antibody responses than fHbp antigens currently in clinical development.

ADRIENNE NICHOLAS

Volunteer

Mentor: Janelle Noble, PhD

The medical profession is often considered one of the most difficult vocations, as the human bodies we work with contain such a high degree of complexity that it is often only too easy to make a sometimes, fatal mistake. It is therefore not unexpected that many careers in medicine require some of the longest educational trainings, involving completion of a Bachelor's, two to four year in graduate school, and even in some cases, numerous years of internship. But the question arises, what to do with the time in between? What outside experiences can we accumulate to aid us in our comprehension of our chosen field of work, and motivate us past the years of school and bottomless pit of student loans?

I found my answer in the Children's Hospital Oakland Research Institute. Studying the molecular mechanisms behind major diseases such a type I diabetes has expanded exponentially my knowledge not only of the autoimmune disease but genetics in general, and the wide array of techniques and machines being used and developed to explore them further in depth. Pathology is such an interesting field as the diseases we examine interact in unique ways with the different people they embody. Genetics has paved the road for the possibility of personalized medicine with the development of gene-specific drugs. Understanding why certain races are particularly vulnerable or susceptible to various illnesses due to their genetic makeup has been a captivating experience, and given me a hold new outlook on the term diversity.

I would like to thank in particular Julie Lane, Julie Roessig, and Janelle Noble for their support and patience in welcoming me to their group. In addition I would like to thank my fellow student intern Jacqueline Knapp, whose has made many a day in the lab echo with laughs. Finally I am indebted to both my mother and father, both of whom compassion and generosity I hope someday to live up to.

HLA Sequencing of Diabetic Patients from Children's Hospital Research Center Oakland

Introduction: The human leukocyte antigen (HLA) genes are located within the major histocompatibility complex, and play a key role in the body's immune response. HLA molecules notify the immune system when pathogens enter the body by encoding antigen-presenting transmembrane proteins. HLA genes have been determined to account for about 50% of genetic susceptibility to Diabetes Mellitus Type 1 (T1DM), however, HLA genes are highly polymorphic, making it difficult to determine specific allele combinations that increase susceptibility. So far studies have shown that the presence of haplotypes containing the alleles DRB1*03:01 and DRB4*04:xx, found in class II of the histocompatibility complex, dramatically raise the risk of T1DM. As HLA alleles and haplotypes differ across ethnic groups, these discrepancies represent one possible reason for differences in disease prevalence.

Objective: To sequence the HLA-DRB loci region in the DNA of diabetic African American, Hispanic and Caucasian patients, as well as their first degree relatives as controls, to determine differences and similarities in alleles and haplotypes between ethnic groups.

Methods: DNA from blood samples taken from diabetic African American, Hispanic and Caucasian patients as well as relatives as controls at CHO was extracted by use of the QIAamp blood kit, and respective DNA concentrations were measured using PicoGreen® dsDNA Quantitation Reagent. DNA concentrations were subsequently normalized to equal concentration and amplified using the polymerase chain reaction (PCR) with 454 locus specific primers targeting the HLA-DRB locus. An amplicon library was then created from purified and normalized PCR products. Amplicons were hybridized to 454 capture beads, amplified via emulsion PCR (emPCR) and sequenced using the 454 GS Junior, which utilizes chemoiluminescent sequencing chemistry. Finally determined DNA allele and haplotypes were added to other genetic data from previous studies of different ethnic groups.

Results: Pending.

Conclusions: Pending.

MATTHEW OGBUEHI

Funded by the MARC program UC Berkeley: NIH T34GM092702 National Institute of General Medical Sciences

University of California, Berkeley, Junior

Mentor: Stephanie Doniger, MD

Research in the life sciences fascinates me for the pure fact that it is a philosophical endeavor; trying to understand what makes life possible and how we can manipulate and change our biology and thus continue our evolution as a species. My primary research interests include understanding and manipulating the biology of organisms for human interest at the molecular level. Of particular interest is the field of aging research and tissue regeneration. I wish to do graduate work in the field of molecular biology or bioengineering or related fields where creativity and insightfulness are valued as a means to arriving at the proper conclusions.

My decision to become a researcher developed slowly overtime, from striving to get a lab position my freshman year to being mostly a lab tech at a phylogenetics lab my sophomore year and finally working on my first research project in an aging research lab my junior year. Each transition throughout the years has developed my interest in research further. Working in the hospital with Dr. Doniger and Dr. Latronica has helped me to put a human context to the relevance of bench-side research and motivates me to continue to pursue a research career where my contributions to the field, be it discoveries or inventions, may help to have a wide-spread effect on human health and well-being.

I would like to thank the people at CHORI who made this program possible, my mentors and my advisors, and all my loved ones who inspire me to continue pursuing research in the field of molecular biology.

Emergency Department Bedside Ultrasound Diagnosis of Constipation in Children

Introduction: Constipation is extremely common in children with an estimated prevalence as high as 28%. The National Institutes of Health defines constipation as the passage of hard, dry stool that is difficult or painful to eliminate, less than three times per week.

Objectives: We aim to demonstrate that the transverse rectal diameter can be quickly, easily, and accurately measured by bedside ultrasound in the pediatric emergency department to diagnose constipation. Bedside ultrasound may serve as an alternative to plain radiograph, which are not reliably associated with constipation, exposes patients to radiation and may lengthen emergency department stays.

Methods: Our experimental study design is an observational prospective descriptive pilot study. Patients age 4-18 presenting to the emergency department with a chief complaint of constipation or abdominal pain were provided a validated questionnaire—Questionnaire on Pediatric Gastrointestinal Symptoms-Rome III (QPGS RIII)— to determine whether patient meets established clinical criteria for a diagnosis of functional constipation. A measurement of the transverse rectal diameter was made by ultrasound noting the bladder volume, as this can alter measurements.

Results: Two patients who met criteria for constipation by the QPGS RIII had measured transverse rectal diameters of 3.85 cm and 4.0 cm. A third patient who did not meet criteria for constipation by the validated questionnaire had a transverse rectal diameter of 1.46 cm. The age of the patients ranged from 6-16 years old.

Conclusions: These preliminary results indicate that obtaining a measurement of transverse rectal diameter via bedside ultrasound may accurately diagnose constipation and serve as an alternative to abdominal radiographs to confirm a clinical diagnosis of constipation.

JENNIFER PINAL

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

University of California, Berkeley, Senior

Mentor: Ellen Fung, PhD, CCD, RD

I am a fifth year at the University of California, Berkeley majoring in Integrative Biology and I am from Pomona, Ca. Last summer I had the pleasure of working with researchers at UCSF on a study analyzing women's preferences on genetic testing. This summer I am examining the effect of calcium supplementation on bone changes during pregnancy. My research examines possible dietary changes in pregnant, low-income women by analyzing dairy consumption and overall food intake versus that of low-income post-partum or lactating women. Another objective is to examine factors associated with dietary changes such as education level and sources of nutritional information.

Doing research with Dr. Fung has escalated my interest in doing clinical research in the future by working with patients and applying what I have learned at Cal to a medical-related setting. My experiences with clinical research thus far and doing health-related community work has ignited my passion to give back to my community through medicine in the field of reproductive health and to be an example for students of different ethnic backgrounds, economic backgrounds, and student-parents like myself to pursue academia and other fields that benefit their communities. On a personal level, I have twin boys, Adrian and Julian, and the most supportive and caring husband, Robert. In my spare time, I enjoy spending time with my family and learning how to cook by trying new recipes.

Thank you CHORI for giving me this amazing opportunity to learn from a talented and passionate research team like Dr. Fung's.

Low-Income Pregnant Women and Dietary Modifications: Are Women More Likely to Make Changes to their Diet at this Stage in Life?

Introduction: Pregnant women have much to gain from optimizing their health and nutritional status. Researchers have been interested in the nutritional status of pregnant women, particularly in dairy consumption. This cross-sectional study investigated whether pregnant women made better dietary choices compared to post-partum or lactating women. Additionally, the relationships between dietary change and socioeconomic and cultural influences were studied.

Objectives: (1) Compare overall dietary intake of pregnant versus post-partum or lactating women through the use of a semi-quantitative Food-Frequency Questionnaire (FFQ). (2) Compare dairy intake of pregnant women versus post-partum or lactating women through the use of a dairy focused food record. (3) Examine the associations of dietary intake (e.g. dairy, whole grain foods) with measurable influences (ethnicity and language preference).

Methods: Data was collected from the baseline assessments of a previously completed study that examined the dietary impact of the addition of yogurt to WIC food provisions. Women in the WIC study completed both a FFQ as well as a dairy-focused 3-day food record on food preferences. Data was also collected on subject demographics which included ethnicity, age, and education level, and analyzed using SAS with a $p<0.05$ considered significant.

Results: 509 women enrolled in the WIC study of which 456 completed the study protocol; 61% were pregnant (PG, n=305), 28% lactating (LC, n=139), and 11% post-partum (PP, n=54). The mean age was 26 ± 6 yrs and 78% of subjects were Hispanic. PP consumed twice the amount of salad (0.8 servs/d) as PG and LC women ($p=0.01$). Vegetable juice consumption was also significantly higher in PP women ($p=0.04$). 16% of PG women reported that yogurt cost was too high ($p= 0.02$) compared to 11% of PP women. Average dairy consumption in PG, LC, and PP was 4 servings per day and only 9% reported lactose intolerance.

Conclusions: In this study of low-income women, differences were not observed in the dietary choices of pregnant versus lactating women. Unexpectedly, post-partum non-lactating women consumed more salad and vegetable juice than pregnant women possibly due to the lower-caloric content and their weight consciousness. The data stems from a population of high-dairy consumers which may account for our inability to observe differences in dairy consumption among groups. There were no significant associations between dietary changes and ethnicity or language preference. A limitation of this study is that data was taken from a baseline questionnaire which reflects dietary habits at one time. A longitudinal examination would be more informative to investigate dietary changes within individuals from pre-conception through post-partum.

NAPALA PRATINI

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

St. Mary's College of California, Junior

Mentor: Jacob Neufeld, MD

Almost three years ago, I sat in my very first general chemistry class, the "weeder" class for pre-meds and most science majors, at Saint Mary's College and thought, "I'll never be able to do this!" I didn't take chemistry in high school, and I was almost positive that my teacher was speaking a different language (chemistry-ese?). I floated through my first couple of weeks, attempting to study here and there, until the first test brought me closer to reality. Having grown accustomed to adapting the motto "never back down" when it came to school, however, I cracked down and became very familiar with the library and tutoring center. Much to my surprise, I actually acquired a real affinity for this and my subsequent science classes. I knew all along that I wanted to apply to medical school, but I had no idea that I would also develop a love for the sciences. This led me to an independent study project followed by summer research program in enzyme research at Saint Mary's last year. When I found out that I had been accepted to the CHORI student summer research program and would be working with Dr. Neufeld in the rehabilitation department, I was thrilled to have even more experience in different areas.

Some of my peers know exactly what field of medicine they will go into. I, on the other hand, am completely opposite. I have shadowed doctors in general osteopathy, oncology, radiology, and dermatology in hospitals, private practices, and community clinics in the past, in attempt to see a little bit of everything. This summer, however, has been eye opening to a much greater degree than any of these past experiences. Working with Dr. Neufeld and the other rehab doctors, as well as getting to know the residents, therapists, and nurses, and seeing their daily interactions with patients, has given me a very valuable perspective on how hospitals and how medicine in general works. In addition, the opportunity to help Dr. Neufeld with his medical journal has offered insight into the scientific article publication process that I would never have gained from the outside.

"Are you sure you want to do that?" is by far the most common response I've received when I tell someone my plans to attend medical school. Before this summer, I always responded timidly, not really knowing what was being asked. After my short time here, however, my answered is a definite yes. I truly feel that I have benefited from this program and the many opportunities it has provided me; I now have even further determination to become a doctor and to help those less fortunate than myself.

Administration of Hydroxy-Propyl-Beta-Cyclodextrin (HPBCD) using the Medtronic SynchroMed II Programmable Drug infusion system for the treatment of Niemann Pick Type C Disease (NPCD)

Introduction: NPCD is an inherited, fatal, autosomal recessive neurodegenerative disorder that is caused by mutations in the genes NPC1 and NPC2. The disease usually appears in infancy or early childhood with onset of hepatosplenomegaly (swelling of the liver and spleen), progressive ataxia (inability to control muscle movements), and vertical supranuclear ophthalmoplegia (inability to move the eyes vertically). Life expectancy for children with early-onset disease is very low (less than 5 years) due to rapid disease progression. The Food and Drug Administration (FDA) has not yet approved any of the drugs proposed for treatment of NPC disease. In July of 2010, Dr. Hastings at Children's Hospital & Research Center Oakland (CHRCO) submitted an Orphan Drug Application for the use of HPBCD in treating the disease based on promising neurological data found in animals treated with HPBCD (Lui, Vite, Abi-Mosleh). HPBCD has very low toxicity and is approved for use in food and household products in Asian and European countries (Roquette). The proposed instrumentation for drug delivery is a Medtronic SynchroMed II Programmable Drug Infusion System. This device, which consists of a pump and catheter, is implanted under the skin in the thoracic or lumbar region. A non-invasive programmer is used to set the pump's infusion parameters, and the catheter delivers medication directly to the intrathecal space. The pump implantation and subsequent drug infusion is proposed for a set of twin patients with NPCD at CHRCO.

Objectives: To obtain FDA and Institutional Review Board (IRB) approval for use of a Medtronic SynchroMed II Programmable Drug Infusion System for administration of HPBCD for patients with NPCD by composing a written report of all potential complications of the Medtronic pump.

Methods: A comprehensive literature review was performed on PubMed, Google Scholar, and other indexes, using various combinations of the following terms; children, baclofen, pump, complications, and catheter. Language and age range qualifiers were used to narrow search results in order to identify applicable articles. The articles obtained were read and a summary was written of the relevant complications. The written results were included in the case study by Dr. Hastings and submitted for review by the Institutional Review Board and for approval by the FDA.

Results: The proposal will be submitted to the IRB for approval. Catheter related complications, pump related complications, and infection, were the three most commonly occurring complications. Complications rates were variable between studies. Catheter complications, including kinking, disconnection, breakage, migration outside the thecal sac, and microfracture, occurred in 3.7-56% of patients, depending on the study. Pump complications including battery depletion, pump hypermobility, pump failure, malfunction, and catheter access port defect, were seen in 1.25-28% of patients. Infection was usually caused by Staphylococcus aureus, and was seen in anywhere from 3-39% of patients. Various surgical complications and recommendations were noted in the summary for review by the surgeon performing the implantation. Less common complications ranged from neck hyperextension to pump misinjection: these were all reported. Pump explantation was performed in 4-44% of patients, usually due to infection but less frequently upon patient or family request or severe cerebrospinal fluid (CSF) leakage.

Conclusions: Pending FDA and IRB approval, the patients participating in this study will have Medtronic pumps implanted and drug infusion and disease progression will be monitored. Complication rates associated with use of this pump have been reported and include both infection and drug delivery system complications. We expect that the drug delivery system of the pump with HPBCD will be successful, but the significant mechanical complications reported in the past mean that close follow-up, monitoring, and evaluation of the patients must be performed.

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ANGELICA PRITCHARD

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

Santa Rosa Junior College, Post-Baccalaureate

Mentor: Barbara Staggers, MD

Three years ago, I stepped into the CHORI building, unsure of what to expect. There was a small group, around three or four of us that day, who had arrived early and anxiously waited in the foyer. I was attentive to the hustle and bustle of the front door, wondering who I may be working with and what was in store for the future. Since that time, I have had a variety of experiences in both the clinical and laboratory setting at Children's Hospital, which have been extremely influential on my goals and dreams. Looking back, I am so very grateful that I chose to apply to the student research program that first summer. Not only have I gained insight and knowledge regarding a wide range of topics and techniques, I have also had the opportunity to give my time and energy for a great cause, the well-being of others.

My journey towards the science and eventually medical field began with my mother's diagnosis with cancer, eight years ago. Something changed that first day, when I began to invest in my mother's health and well-being. I believe a spark was produced. Since then, my mother has faced a variety of treatments, complications and challenges, but I have stayed by her side, offering my support and learning a great wealth of knowledge. Through these additional experiences with my mother, as well as personal pursuits in the hospital, scholastic and laboratory settings, my small initial spark has been kindled into a vibrant flame. It is by the light of this flame, that I have discovered my true passion, a life of service in the medical field.

The value of education is a principle I learned and understood from a young age, due to my families circumstances. Thankfully I had the opportunity to attend college, Saint Mary's College of California, following high school, becoming the first in my family to be a college graduate. In 2010, I earned a degree in Biochemistry. I loved the rigor and challenge that the science courses offered, especially those which related to the human body and mechanics. After Saint Mary's, I have taken courses at a local Junior College with the objective of obtaining a handful of healthcare certifications and AA's in both Spanish and Physiology. However, it is my dearest hope that within this next year, my education will also progress, through the admission into and initiation of medical school.

While I have been at Children's Hospital, there have been a variety of physicians, scientists and staff, which have had a significant impact on my education and life. I want to express my sincere appreciation and gratitude for all of your support and kindness through the years. Thank you for teaching, believing in and for inspiring me. I can definitely state that my life has been touched and truly blessed because of my association with you! Thank you!

Development of an Injury Prevention Center

Introduction: Amongst children and adolescents today, accidents are by far, the leading cause of death. Most of these accidents are comprised from vehicle crashes. However, drug and substance overdoses as well as other poisonings can be included in this description. Other major causes of death for children and adolescents amongst the age range of 5-24 are homicides, cancer and suicides. Most of these causes of mortality amongst youth and young adults are preventable. *However, despite organized programs, these rates and statistics still remain high.*

Objectives: An Injury Prevention Center is striving to be established amongst Children's Hospital Oakland in coordination with other academic, medical and state institutional centers and programs. This center will allow research to be conducted and transformed into saving those lives most at risk from Child Maltreatment, Motor Vehicle Injuries, Drug and Substance Overdoses, Poisonings, as well as Youth Violence. As such, it will be actively working towards reducing the mortality rate of both children and adolescents from unintentional injuries as well as homicides.

Methods: The Injury Prevention Center will be organized with four different structural components, an Administrative Core, Outreach Core, Training and Education Core and finally a Research Core as a part of the overarching design and goal of reducing mortality amidst children and young adults. The Administrative Core will be primarily composed of the projects leaders, which give direction and guidance for the Center as well as the integration and promotion of research findings for the benefits of our society. The Outreach Core will allow the incorporation and collaboration of outside organizations, within and outside of the government agencies, with the key institutions. These organizations may be involved with research as well as the education and training cores. The Training and Education Core's purpose is to provide training to students as well as professionals in the masters, Doctoral and Post-Doctoral levels, regarding methods to prevent these intentional and unintentional injuries. Finally, the Research Core will contain one exploratory project as well as 3-4 research projects to be completed during the first few years of the established Injury Prevention Center. The focus of these projects will include one of the following topics: Preventing Child Maltreatment, Motor Vehicle Injuries, Unintentional Drug Overdoses and Poisonings, Youth Violence, as well as Traumatic Brain Injury.

Results: It is expected that the establishment of an Injury Prevention Center at Children's Hospital Oakland will help reduce the number of unintentional and intentional deaths amongst the East Bay Area for children and adolescents, through the help and collaboration of other outside organizations and programs.

Conclusions: An Injury Prevention Center will be fully developed, organized and initiated. Through this center, the problems presented amidst the bay area's diverse community, from both intention and unintentional injuries among youth and adolescents, will be addressed and reduced through research and education.

KATIE REGET

Funded by Children's Hospital Los Angeles (National Heart, Lung and Blood Institute, Basic and Translational Research Program)

Osseo Senior High, Osseo, Minnesota, Junior

Mentor: Ellen Fung, PhD, CCD, RD

Throughout my life I have been interested in helping people. The field of medicine is one of the best fields to be in for helping others. I fell in love with the human body when I was in third grade and we learned about bones. From that point on I knew that this was the place for me.

Currently I am attending Osseo Senior High in Osseo, Minnesota. Osseo is a medical magnet school which means that it offers introductory medical classes during the school day. Some of the classes are Medical Terminology, Nursing Assistant and an EMT class. Given this extended medical curriculum I feel blessed to have the opportunity to further in my passion for helping others everyday at school.

In the next few years, I plan to attend college and later continue on to med school. It is important to me that I not only help people clinically, but also through research. I believe that research is a very important aspect in helping people all over the world. Along the way I want to continue my participation in community outreach programs and community service.

I am extremely grateful that Children's Hospital Oakland Research Institute (CHORI) has given me the opportunity to live out my dream at such a young age. Coming to CHORI all the way from Minnesota was a bit freighting, but within a day I felt right at home in the wonderful learning and aspiring atmosphere that CHORI offers to all its summer interns and volunteers. During this entire project I felt full of excitement to find new data and information about the fascinating disease of Thalassemia. The research that I have completed here has really taught me great characteristics that I know I will use throughout my career. Working at CHORI and with the CHORI staff is a beautiful experience that I will cherish for the rest of my life.

Pain and Bone Mineral Deficits in Thalassemia: Is there a Link?

Introduction: Contrary to popular belief osteoporosis is not simply a concern of post-menopausal women; it is present in many children with the chronic disease including those with hemoglobinopathies. Low bone mass has been described in as many as 60% of children and adults with thalassemia (Thal) and sickle cell disease (SCD). Bone pain is also frequently reported in both disorders, however few have explored the relationship between low bone mass and bone pain.

Objectives: The objectives of this study were to determine the prevalence of low bone mass and vertebral height abnormalities in patients with hemoglobinopathies cared for at Children's Hospital Oakland (CHRCO). The secondary objective was to evaluate the relationship between bone mineral density, patient demographics and bone pain with vertebral height abnormalities.

Methods: Data for this analysis were collected from two sources: the Thalassemia Clincal Research Network (TCRN) Pain Survey and the CHRCO Clinical Bone Density Clinic database. The TCRN used a validated 10 page pain survey form to collect data on 45 patients at multiple time points. Bone mineral density (BMD: spine, hip, whole body) Z-scores were abstracted along with patient demographics. Additionally, a full lateral spine scan was conducted at the time of BMD scan in a sub-set of subjects. All VFA scans were re-analyzed by one observer (KR), and scored according to Genant for vertebral abnormalities (crush, wedge, biconcavity; mild to severe).

Results: A total of 231 VFA scans were re-analyzed from 137 patients with Thal or SCD (24.7 ± 12.4 yrs, 57% female, 66.4% Thal). The patients with Thal were primarily Asian (78%) while 98% of the SCD patients were Black. Of the 91 patients with Thal who had VFA scans, 25 (27.5%) had at least one vertebral abnormality, compared to 16 (38.8%) of the 46 patients with SCD (p=NS). SCD patients had significantly more vertebral abnormalities compared to healthy controls (p=0.04). The average number of vertebrae with abnormalities was 1.6±0.2 in Thal compared to 2.8 ± 0.4 in SCD (p=0.003). The most common location for vertebral abnormalities was the lumbar (75%) compared to the thoracic region of the spine (25%). Of the patients with multiple VFA scans, 12 progressed toward vertebral abnormality during a 7 year period, all with Thal. The change of a vertebral abnormality increased with age (p=0.017), but was not related to BMD Z-score. Two-thirds of the Thal patients reported significant pain within the past month, 16% severe and 27% reported pain localized in the lower back.

Conclusions: A surprisingly high percentage of both SCD and Thal patients had significant vertebral abnormalities, which increased with age. The prevalence of abnormality (27%) observed in the CHRCO Thal patients is twice that previously reported from the TCRN (12%). Prevalence has never before been reported in SCD. It is conceivable that the high rate of lower back pain in Thal is related to the observed abnormal vertebrae, these relationships are under investigation and will be presented.

MADELEINE SCOTT

Funded by the Jolyce Hardesty Fund

M.I.T., Freshman

Mentor: Sachiko Takayam, PhD

I was first introduced to the idea of working in a lab by my father. A molecular biologist by trade, many of my earliest memories were of him surrounded by glass beakers full of multicolored liquids. To me, the lab invoked some of the same feeling that a tour of an alien spaceship might – lots of wonder but little understanding.

Today, the lab feels much less alien; it actually feels more like home. My work with epigenetics has been fascinating, and along the way I have picked up some useful techniques as well as life advice from my mentor, Sachiko Takayama. Next year, I head off to MIT, where I hope to continue my scientific studies with a bioengineering major. Many thanks to Dario Boffelli, as well as those who run the summer student program, for allowing me to take part in such a wonderful opportunity.

Investigation of Variation of DNA Methylation States

Introduction: Epigenetics is the study of heritable changes in gene function that occur without a change in the sequence of nuclear DNA. Methylation was the first discovered epigenetic marker, and remains one of the most studied. DNA methylation functions to repress transcription, possibly through physically impeding transcription or by functioning in concert with repressive proteins. Methylation has been shown to be critical in development as well as many other normal processes of the cell. However, should this process become unregulated, diseases such as cancer and cardiovascular dysfunction can result.

Objectives: In this study, we look at the methylation states of the promoters 6 of genes that are involved in lipid processing. The genes under study are HLA3, TRIB, PLEC1, DDX18 and AURKB. DNA sequence variation in these genes is associated with variation in plasma lipid levels, and their expression levels have been shown to be variable in human b-lymphocytes. We sought to use 120 samples from 66 individuals to compare methylation patterns at these promoters to the expression of the corresponding gene. Specifically, we hypothesize that there is a correlation between the level of methylation of a gene's promoter and the subsequent gene expression.

Methods: DNA was obtained from b-lymphocytes, which were previously isolated from whole blood and frozen. The cells were lysed, and the DNA purified. To measure the methylation level of DNA, we used the bisulfite conversion method which converts unmethylated cytosines to thymines. Primers not biased towards a specific methylation state were used to selectively amplify areas of interest. The primers do not contain any CpG sites to avoid discrimination against methylated DNA. The converted DNA was then be amplified using polymerase chain reaction (PCR). PCR will serve to both provide enough DNA for sequencing and convert uracil into thymine. Amplified DNA from the 6 regions of interest will be sequenced using the Illumina Paired-End method. The methylation status can be determined by counting the number of unconverted cytosines (i.e. methylated) and comparing it to the number of cytosines that were converted to thymine (i.e. unmethylated) at all cytosines defined by the reference sequence.

Results: While the sequencing process has not commenced, most of the 120 samples have successfully undergone the bisulfite treatment and been amplified in preparation for sequencing.

Conclusions: Ideally, there will be a statistically relevant correlation between the methlyation status of the gene and the subsequent gene and phenotypic expression. The more methylated the gene is, the less gene expression is expected.

BISRAT TEKIE

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

Sarah Lawrence College, Sophomore

Mentor: Barbara Staggers, MD

My name is Bisrat Tekie and I am a rising junior at Sarah Lawrence College, Bronxville, New York, concentrating in International and Public Relations, Public Policy and Public Health. Focusing primarily at Children's Hospital Oakland, my goal for this summer is to explore how Health Policy is applied here at Children's, by reviewing the Pediatric Adolescence Health Care Data for Alameda County and looking at an analysis of existing countywide programs and see how they are designed to address these needs. In addition, I plan to review data, programming, community benefits plan, and interview the Governmental Relations person at the hospital to complete a draft of a Health Policy.

I've wanted to be involved in the medical field since I was young, and by joining this program my passion for it has taken shape as I learned the multiple ways to be involved in healthcare. This is my second year at CHORI Summer Student Research Program, and it is an honor and a privilege to be part of it on its 30th Anniversary.

I would not be where I am today if it wasn't for my mother, as she is my number one support system, my backbone, the first person I look up to, my number one inspiration and role model. I also would like to all my family and friends for their love and support throughout my journey.

I would have not met the wonderful people here at CHORI and be part of this wonderful and enlightening program if it wasn't for Vicki Laden, it is because of her that I am able to step out of my comfort zone and expand my horizons. It is amazing to learn the many different talents within one vicinity, and I hope that one-day in the nearest future to follow that legacy.

I would like to thank the wonderful people that I have come to know and had the privilege of working with. I would like to start with my mentor Dr. Barbara Staggers, Director and Division Chief, Adolescent Medicine and Medical Staff President, a wonderful woman whom I have had the privilege of knowing; a woman who has demonstrated her true potential that has multiple functions at Children's Hospital. It is because of Dr. Staggers that my passion for medicine, the act and the idea of helping people took shape. I would also give many thanks to CHORI's manager of Government Relations and Public Policy Bernadette Arellano, and it is thanks to her that I am able to get a full grasp on Health Policy and Community Relations. I would like to thank CHORI Summer Student Program Coordinators Debora Ellen and Philip Bollinger: for working hard in making this program possible and enduring with us. We underestimate the work and energy they put forth in order for this program to be successful; I want to thank them for giving us the opportunity to attend lectures regarding many diversified topics in the medical field through doctors, scientists, activists and intellectuals, and having them volunteer their time and share their experiences. It is something that not anyone can experience and be part of. Many thanks to Bertram Lubin, MD President and Chief Executive Officer, Teresa Klask, Vasanthy Narayanaswami, PhD who was extremely encouraging and supportive through this program, and the NIH Foundation for supporting me throughout my time at CHORI.

Health Care Policy

In comparison to other social issues, health is one of the most important factor. The nature of decision making in health involves matters of life and death. Both patients and heal professionals (doctors, nurses, scientists, health-advocates and administrators) come into contact with the health sector as patients seek for assistance by going to hospitals and clinics. Health Policy guides choices about which health technologies to develop and use, how to organize and finance health services, or what drugs will be freely available. To understand these relationships it is necessary to better define what is meant by Health Policy.

Health Care Policy covers a range of health related issues including: the financing of health care, public health, chronic illness and disability, long-term care, and mental health. Health Care Policy also refers to a number of rules, regulations, and guidelines that exist to operate, finance, and shape healthcare. As the World Health Organization defines it "Health policy refers to decisions, plans, and actions that are undertaken to achieve specific health care goals within a society." Nonetheless, health is also affected by many decisions that has nothing to do with health care: poverty, pollution which leads to contaminated water and poor sanitation just to name a few; economic policies, such as: taxes, and consumption of alcohol and cigarettes. Dr. David Killiela, assistant staff scientist at CHORI said in his "Consequences of Micronutrient Deficiencies" talk, that we need to consider social values in the areas we live in. For example, obesity among the young generation that have easy access to fast-food and soft-drinks. Lack of movement also contributes to obesity as we see children playing video-games on a regular basis where parental control is absent due to spending less time at home and more time working to make ends meet.

Understanding the relationship between Health Policy and health is therefore important in order to tackle some of the major health problems: obesity, the epidemic of HIV/AIDS, growing drug resistance, as well as to understand how economic and other policies impact on health.

My goal this summer at CHORI is to do a literary review on Health Policy and finding ways to be involved in Children's Hospital Health Care Policy Arena; that is by reviewing the Pediatric Adolescence Health Care Data for Alameda County and looking at analysis of existing countywide programs and see how they are designed. I will be using Alameda County as my primary reference since it is one of Children's Hospital's potential allies. I also plan to review Data, Programming, Community Benefits Plan, and interview Bernaedette Arellano the manager Governmental Relations and Public Relations at CHRCO.

I would like to combine my concentration International and Public Relations with Health Care. My goal is to be an effective Health Advocate in the future by impacting Health Care Policy that influences the community and individuals' lives. In order to become one, it is essential to know what Health Care Policy is all about. Lastly, the motivation that lead to this research is to answer: why is Health Policy important and what does it take to draft an efficient, comprehensive and accessible Health Policy for all.

TUYEN TRAN

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

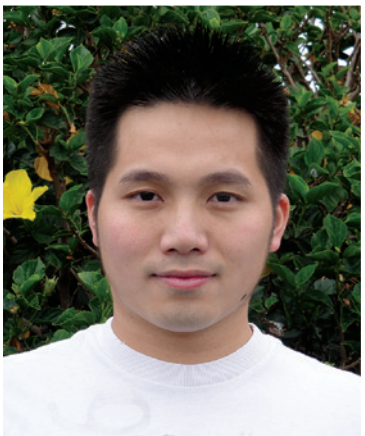
California State University, Long Beach, Non-Graduating Senior

Mentor: Vasanthy Narayanaswami, PhD

Ever since cancer stole my father's life, it is my aspiration to become a researcher and medical practitioner to join the fight against diseases. Although it is too late to save my father, I take solace in knowing that I may someday have the chance to save the lives of parents, children, siblings, and friends. I have the determination and the confidence to achieve my dreams, and CHORI Summer Research Program is a part of these dreams. CHORI Summer Research Program offers an opportunity to sharpen my skills and gain experience in research. Also, as a program participant I will develop knowledge to prepare me for graduate study.

Thanks to the generous support of the program I am able to continue to conduct research under the direction of my mentor, Dr. Vasanthy "Vas" Narayanaswami. Dr. Vas' enthusiasm for encouraging her students to pursue real-world research has dramatically increased my engagement in both my academic studies and undergraduate scientific exploration. Dr. Vas not only taught me how to conduct the research independently, but she also helped to hone my leadership skills. These skills will be extremely helpful for me as a future researcher.

Being a part of the CHORI Summer Research Program would bring me one step closer to achieving my goals, and I greatly appreciate the opportunity to be one of the recipients of this award. Especially, I would like to thank Dr. Vas for her mentorship, patience, and time during the summer.



Potential role of Oxidative Stress in Modulating Cholesterol Homeostasis via Apolipoprotein E

Introduction: Epigenetics is the study of heritable changes in gene function that occur without a change in the sequence of nuclear DNA. Methylation was the first discovered epigenetic marker, and remains one of the most studied. DNA methylation functions to repress transcription, possibly through physically impeding transcription or by functioning in concert with repressive proteins. Methylation has been shown to be critical in development as well as many other normal processes of the cell. However, should this process become unregulated, diseases such as cancer and cardiovascular dysfunction can result.

Objectives: In this study, we look at the methylation states of the promoters 6 of genes that are involved in lipid processing. The genes under study are HLA3, TRIB, PLEC1, DDX18 and AURKB. DNA sequence variation in these genes is associated with variation in plasma lipid levels, and their expression levels have been shown to be variable in human b-lymphocytes. We sought to use 120 samples from 66 individuals to compare methylation patterns at these promoters to the expression of the corresponding gene. Specifically, we hypothesize that there is a correlation between the level of methylation of a gene's promoter and the subsequent gene expression.

Methods: DNA was obtained from b-lymphocytes, which were previously isolated from whole blood and frozen. The cells were lysed, and the DNA purified. To measure the methylation level of DNA, we used the bisulfite conversion method which converts unmethylated cytosines to thymines. Primers not biased towards a specific methylation state were used to selectively amplify areas of interest. The primers do not contain any CpG sites to avoid discrimination against methylated DNA. The converted DNA was then be amplified using polymerase chain reaction (PCR). PCR will serve to both provide enough DNA for sequencing and convert uracil into thymine. Amplified DNA from the 6 regions of interest will be sequenced using the Illumina Paired-End method. The methylation status can be determined by counting the number of unconverted cytosines (i.e. methylated) and comparing it to the number of cytosines that were converted to thymine (i.e. unmethylated) at all cytosines defined by the reference sequence.

Results: While the sequencing process has not commenced, most of the 120 samples have successfully undergone the bisulfite treatment and been amplified in preparation for sequencing.

Conclusions: Ideally, there will be a statistically relevant correlation between the methlyation status of the gene and the subsequent gene and phenotypic expression. The more methylated the gene is, the less gene expression is expected.

AUTUMN TURPIN

Funded by Children's Hospital Los Angeles (National Heart, Lung and Blood Institute, Basic and Translational Research Program

St. Patrick St. Vincent High School, Junior

Mentor: Heidi Flori, MD

My name is Autumn Turpin, and I am a senior in high school at St. Patrick St. Vincent in Vallejo. I have been interested in science for nearly as long as I can remember. I was always curious about how the world around me worked, and I did end up finding out why the sky was blue. In middle school I always enjoyed science class, whether it was early biology or introductory physics. I've continued that interest into high school, where I am on the way to taking all but one of our school's offered science classes.

My junior year, when I took AP Chemistry, I realized I was really passionate about learning about functions at an atomic level. My goal for college is to combine my passion for chemistry with medicine, and to eventually start doing research or engineering. I like learning how things work, and especially being in a lab and seeing how experiments turn out.

This summer, I am working with Heidi R. Flori MD, Natalie Cvijanovich MD, Evan Summers RRT, Katie Sabato RRT, and Julie Simon RN on investigating the effect of helium on high frequency oscillatory ventilators in patients with life-threatening respiratory failure. I am really enjoying being in the hospital environment and seeing so many people working hard to help patients. It is inspiring and making me lean more towards working in a hospital. I am really thankful for this opportunity to do research over the summer, and I am having a lot of fun, too.

Evaluation of Helium Therapy in Combination with High Frequency Oscillatory Ventilation in Pediatric Acute Respiratory Failure

Introduction: The most common diagnosis in the pediatric intensive care unit (PICU) is acute respiratory failure. With moderately severe cases, patients can be supported with "conventional" invasive mechanical ventilation; however, the most severe forms of lung disease require "unconventional" support with high frequency oscillatory ventilation (HFOV) and/or extracorporeal membrane oxygenation (ECMO). These "unconventional" methods of support can be effective in providing adequate pulmonary support while minimizing ventilator-associated lung injury (barotrauma and volutrauma).

The most severe forms of acute respiratory failure involve abnormalities in oxygenation and ventilation due to edema, inflammation, mucus, purulent secretions, etc. These abnormalities can be related to obstructive disease and/or turbulent airflow in the smaller pediatric airways which results in increased resistance to airflow. In these cases, helium may be of benefit. Helium is one-seventh as dense as air, and aids in converting turbulent airflow through obstructed airways to laminar airflow. This may result in decreased work of breathing (Tassaux 2005). Additionally, the more rapid and laminar flow of helium into the distal lung can create a "draft" effect, allowing oxygen as well as medicines to be drawn further into the distal airways (Garner 2006). However, most mechanical ventilators are not calibrated to account for the low density of helium, making it difficult, if not impossible, to exactly determine the volume of gas delivered to the patient. This potentially increases the risk of barotrauma or volutrauma to the lungs. There have been no randomized trials of the use of helium in combination with conventional mechanical ventilation in either adult or pediatric populations, and even fewer reports of the use of helium in combination with HFOV.

Objectives: The objective of this study is to evaluate 1) whether the addition of helium therapy to HFOV will improve oxygenation and ventilation in pediatric patients with acute respiratory failure; and 2) whether addition of helium therapy to HFOV will result in excessive lung hyperinflation, as measured by changes in lung volume on chest radiograph, in the pediatric patients.

Methods: This is a retrospective case series of all pediatric patients treated at CHRCO with helium or Heliox (a mixture of 20% oxygen and 80% helium) therapy in combination with HFOV since 2009. The CHRCO IRB has been notified, in writing, of this case series analysis. The CHRCO billing database was queried for patients receiving both HFOV and helium therapy. Twelve patients were identified meeting the criteria of receiving helium. Meditech reports were reviewed and 3 patients met study criteria including HFOV, for a total of 4 trials of this therapeutic combination. Charts were reviewed for dissolved oxygen levels (PaO2), dissolved carbon dioxide levels (PaCO2), pH, and HFOV settings (mean airway pressure, power, hertz, fraction of inspired oxygen (FiO2); chest radiographs were also reviewed to evaluate for evidence of lung hyperinflation pre- and post-addition of helium.

Results: Three patients were evaluated for four instances of HFOV and helium administration. All patients were treated for acute respiratory distress syndrome associated with pneumonia and sepsis (Pt #1: aspergillus, Pt #2: pandemic H1N1, Pt #3: influenza B and MRSA). Two of the three patients were previously healthy. All patients had very high risk of death (PRISM III 4, 14, 11) with high standardized scores for multiple organ system dysfunction (PELOD: 21, 1, 11) Patient 3 had a trial first of HFOV + Heliox followed by a trial of helium. Patients 1 and 2 had trials of HFOV and helium alone. Review of independent attending radiologist reading of radiographs both pre and post helium administration indicated no evidence of hyperinflation or barotrauma (new pneumothorax) in any of the instances that helium and HFOV were trialed. Three of four instances were associated with an improvement in ventilation as measured by PaCO2 and an associated improvement in acid base status. Oxygenation index was also improved in three out of four instances. Ventilator power and mean airway pressure was able to be decreased in three out of four instances as well.

Conclusions: Controlled use of helium therapy in combination with HFOV may be acutely helpful as a rescue therapy in severe pediatric ARDS. Since tidal volume delivered cannot be measured during the use of this combination therapy, attention to minimizing ventilator settings and fraction of inspired oxygen delivered as well as radiographic findings for evidence of barotrauma and/or hyperinflation is required.

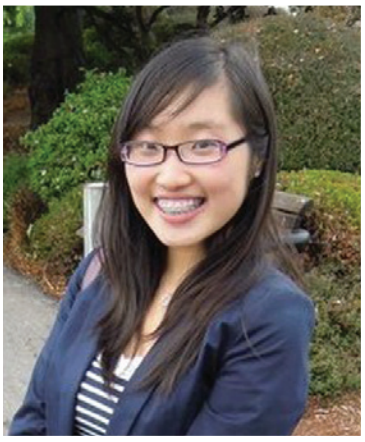
KAREN WONG

Funded by the American Heart Association

Mentors: Robert Ryan, PhD, Trudy Forte, PhD

Why do research? To me, research means a dynamic learning process, creativity, accomplishment of problem –solving, and unlimited possibilities. It allows me to pursue my interests beyond the classroom and challenge my concepts in every way possible. I believe that research is a vital component of a complete and scholarly college education, thus I had been active in seeking for a research position for the last two years until I was offered an opportunity to work in Dr. Ryan's lab studying apolipoproteins. Dr. Ryan recommended me to apply to the AHA Undergraduate Research Program because it offers a precious opportunity for me to become fully involved in a cardiovascular research project of my interest. I can initiate and perform the designed project from start to finish, learning to think like an open-minded scientist. With the funding of this program, I will embark on an exciting science journey to discover the mystery of apolipoproteins in preventing cardiovascular disease. I am confident that the research experience and mentorship network acquired from this fellowship will be assets to realizing my aspiration of becoming a successful health professional.

In addition to my academic life, I enjoy spending time with family and friends because they are my source of support and motivation. They provide me with advice and encouragement when I encounter difficult times. I also like watching movies, singing, and baking to release my stress. I believe that having a well-balanced life style is the key to success.



Determinants of Apolipoprotein A-D Distribution in Plasma

Introduction: Apolipoprotein (apo) A-V is a minor exchangeable apolipoprotein in plasma that appears to have a role in modulating plasma triglcyceride (TG) levels. The protein has been shown to enhance lipoprotein lipase activity and the hydrolysis of TG associated with very low density lipoproteins (VLDL) and chylomicrons; it also plays a role in the removal of VLDL remnants by its ability to bind to low density lipoprotein (LDL) receptor family members.

Objectives: In plasma apoA-V is associated mainly with VLDL and high density lipoprotein (HDL) but there is little information on factors that regulate apoA-V binding to specific lipoprotein classes. We propose to carry out studies to determine the kinetics of binding of apoA-V to plasma lipoproteins.

Methods: To address the binding kinetics of apoA-V to plasma lipoproteins, apoA-V in the form of apoA-V –phospholipid complexes will be incubated with mouse plasma deficient in apoA-V (apoA-V knockout mice that have extremely elevated TG will be used) for periods of 5, 30, and 60 min. At each time point, plasma samples will be fractionated by fast protein liquid chromatography (FPLC) and VLDL, LDL, and HDL fractions will be isolated. ApoA-V in each fraction will be determined by Western blotting for apoA-V following SDS- polyacrylamide electrophoresis. The ability of apoA-V to exchange from VLDL to LDL to HDL or from HDL to LDL to VLDL will also be tested.

Results: Based on immunoblotting results, apoA-V began moving onto VLDL from HDL as early as five minutes of incubation with apoA-V and AV-KO mouse plasma. Chemiluminescence results from incubation periods of 30 and 60 minutes further illustrated that more of apoA-V associated with VLDL rather than HDL. The chemiluminescence film for incubation time of 60 minutes showed that there was virtually no apoA-V detected in the HDL region.

Conclusions: Based on Western blot results, apoA-V distribution in AV-deficient mouse plasma occurs at a faster pace than what we initially expected. The data indicate that apoA-V does not exchange back onto the HDL region afterward. More experiments are underway to narrow down the incubation period to as early as one minute to see if an exchange of apoA-V from HDL to VLDL occurs. Current results give rise to the question of whether the apoA-V exchange reaction stops after incubation in the water bath or it continues even when the incubation mixture has been transferred onto ice. This question can be answered by running the incubation mixture on the FPLC right after incubation in water bath instead of keeping it on ice to control the reaction time.

RATHANA YIM

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

University of California, Berkeley, Junior

Mentors: Ronald Cohen, MD, and Sumi Hoshiko, MPH, CDPH-EHIB

Rathana Yim, or as many people who are familiar with him, prefers to call him Rat a pseudonym bestowed on him by shortening the first name. Rathana is senior at UC Berkeley studying Molecular Toxicology. A child of the "Killing Fields" in Cambodia, Rathana will be the first male out of 12 siblings to obtain a Bachelor's Degree within in his family. This is his first summer participating in CHORI, working concurrently with Dr. Ronald Cohen at Children's Hospital in Oakland and Sumi Hoshiko at the California Department of Health in Richmond studying CT exposures in pediatric populations.

When is he is not bound by countless hours of textbooks and lab work, Rat can be found fighting gravity repetitively for physical superiority, perfecting his jump shot in hopes of one day playing for the Golden State Warriors, enjoying post-apocalyptic flesh-eating zombie films, or creating scrumptious culinary cuisine for his extended family and friends.

As an active member of the Biology Scholars Program (BSP) and Environmental Leadership Pathway (ELP), Rathana plans on pursuing a career in medicine as a foundation for his philanthropic desires in curbing hunger, and lack of quality health care in impoverished places. Armed with the priceless and significant experiences he gained at CHORI, Rathana plans on providing the same experience for those who are from similar background to give them a fair opportunity and platform for reaching their dreams. In all, he attributes his success in educational journey to the many, such as the directors at CHORI, for providing students like him an opportunity to become a scientist.

Determinants of Apolipoprotein A-D Distribution in Plasma

Medical radiation through the utilization of computed tomography (CT) has been increasing in the US. The use of CT for diagnostic evaluation has been increased dramatically over the past two decades in the field of pediatric radiography. CT is associated with higher radiation exposure than conventional radiography. [iv,v] Furthermore, children are more susceptible to detrimental health effects from ionizing radiation than adults. Abdominal and craniocerebral (head) CT are among the most commonly performed CT procedures among pediatric patients. In this study of population exposures, we will look at abdominal and craniocerebral CT use within patients hospitalized or visiting emergency departments in the state of California for the years 2005–2009. We will characterize the frequency of these CT procedures in pediatric populations (0-17 years) by diagnosis, age group, demographics, and other descriptive factors of patients that are exposed to CT. Results from this study will also be used to inform development of future epidemiological studies of CT exposure and health outcomes in pediatric populations.

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Notes

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2011 CHORI SUMMER STUDENT SYMPOSIUM

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