



THE SAMUELS FAMILY LATINO AND AFRICAN-AMERICAN HIGH SCHOOL INTERNSHIP PROGRAM

Annual Report 2013-2014

**// IN THE END,
IT'S THE PEOPLE WHO
ARE CURIOUS WHO
CHANGE THE WORLD. //**

-NEIL DEGRASSE TYSON

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MEET THE SAMUELS FAMILY LA-HIP STAFF



Program Director

Emil Bogenmann, PhD, EdD, is an associate professor in the Department of Pediatrics and holds a secondary appointment in the Department of Molecular

Microbiology and Immunology at the Keck School of Medicine of the University of Southern California (USC). His laboratory research focused on the biology of neuralcrest-derived tumors such as retinoblastoma and neuroblastoma. Over the last two decades he has been involved in the training of high school students, undergraduate students, graduate students and postdoctoral fellows. Since 1995, Bogenmann has been the director for Research Education at The Saban Research Institute of Children's Hospital Los Angeles.

Bogenmann completed his Doctor of Education degree in 2008 with a subspecialty in educational psychology from the Rossier School of Education at USC. He established the Samuels Family Latino and African-American High School Internship Program (LA-HIP) in 2005. Bogenmann is also a director for the National Institutes of Health-sponsored Short Term Research Experience Program for Underrepresented Persons (STEP-UP), a research training program for undergraduate students.



Program Coordinator

Mercedes Gonzalez joined The Saban Research Institute of Children's Hospital Los Angeles in 2008. Mercedes received a Bachelor of Science in human

services from the University of Phoenix. Her previous experience includes a position as a case manager for the city of El Monte, where she focused on high school students from inner-city schools. Mercedes is responsible for the organization and coordination of research training programs, including the Samuels Family LA-HIP.

Gonzalez also acts as program coordinator for the National Institutes of Health-funded Short Term Research Experience Program for Underrepresented Persons (STEP-UP) at Children's Hospital.

A MESSAGE FROM THE DIRECTOR

The Samuels Family Latino and African-American High School Internship Program (LA-HIP) at The Saban Research Institute of Children's Hospital Los Angeles will soon enter its ninth year. A new class has already been selected for 2014, while the students from the class of 2013 have all received their acceptances to some of the nation's best colleges and universities. Students passing through the program, designed to expose incoming high school seniors to the world of biomedical research, have carried the message to friends, peers and family that doing research is exciting and fun. Thanks to our many committed and dedicated supporters, donors and friends, we are able to offer this unique program to these promising students.

The Samuels Family LA-HIP, a cornerstone of the research training programs at The Saban Research Institute, is well-known among high school students in Los Angeles; the program even received applications for the class of 2013 from as far away as San Bernardino and Palmdale. There are many talented, underserved students with an interest in the sciences and medicine who would benefit greatly from an opportunity like the Samuels Family LA-HIP; each year it becomes more difficult for us to determine the final awardees. The class of 2013 was no exception.

The interns of the class of 2013 got to know each other at a bowling alley, where they mingled with the alums of the class of 2012. They had a lot of fun; however, students were all business when working in the lab. "Hell Week," where they learned the proper way to do biomedical experimentation, was followed by five weeks of mentored research under the guidance of a principal investigator and laboratory personnel. I would like to thank the mentors—the program could not exist without them.

The culmination of the summer program was the Science Symposium. The interns all ended on a high note with their presentations! Interns also worked hard in SAT prep classes, and immersed themselves in the long and arduous process of applying to college, with help from our college counselors. The fruits of their efforts were numerous acceptance letters from outstanding schools.

Looking back, our students have always had the opportunity to study at some of the best schools our nation has to offer. However, coming from a public school that often is under-resourced presents a challenge to most of our graduates. They struggle with the academic demands of higher education and often alums talk about experiencing social isolation. Hearing their stories prompted me to look for ways to alleviate some of these challenges. Together with two talented teachers from The Princeton Review, we developed an Academic Boot Camp for the interns of the class of 2012. These incoming college freshmen sacrificed their summer to study chemistry, biology and math, write

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A MESSAGE FROM THE DIRECTOR (continued)

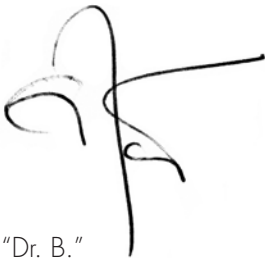
scientific papers about topics discussed in class and read primary scientific literature. They loved those five weeks! Did we alleviate some of the freshman pain? Initial evaluations suggest that the boot camp helped tremendously, although more training is needed for our alums to become competitive students.

The Samuels Family LA-HIP also received national exposure when we were invited to host the inaugural directors meeting for the Clinical Research Experience for High School Students program, a national consortium of nine centers supported by the Doris Duke Charitable Foundation. In-depth, insightful discussions confirmed to me that the Samuels Family LA-HIP is among the very best research training programs for underserved high school students.

As I look ahead, I already see 14 new students who have been accepted to the class of 2014 and I cannot wait to teach them the intricacies of research. I am sure they too will have life-changing experiences in the laboratories of The Saban Research Institute, thanks to all of our supporters and friends.

I hope you enjoy reading the report.

Sincerely,

A handwritten signature in black ink, appearing to be 'Dr. B.', with a stylized, flowing script.

"Dr. B."
Emil Bogenmann, PhD, EdD
Program Director – LA-HIP

2013 PROGRAM HIGHLIGHTS

Application and Selection of the Class of 2013

Online Applications due Feb. 3, 2013

Interested Latino and African-American students from Greater Los Angeles submitted an online application, a letter of recommendation and transcripts to be considered as a candidate.

The online application for the summer program opened Oct. 1, 2012, and closed Feb. 3, 2013. The application enables students to provide their personal and academic information, describe their extracurricular activities and submit a personal statement that elaborates on their career interests. During the open application period, Mercedes Gonzalez, program coordinator, visited 11 high schools and spoke with students, counselors and science teachers about the program, provided handouts and answered questions.

Final Selection, March 2013

A total of 79 completed applications were received. The selection committee, which included Emil Bogenmann, PhD, EdD, Barbara Driscoll, PhD, Cara Esposito, Alexa Margalith, Mercedes Gonzalez and Charlene Liebau, narrowed down the applicant pool to 31 and conducted face-to-face interviews. Each candidate was interviewed for 15 minutes. After considering the applicants' academic strengths, demonstrated interest in science, the strength of their letters of recommendation and the quality of their interviews, the committee selected 14 students and two alternates. They each received a letter in the mail announcing their acceptance into the program.

Class Orientation

March 30, 2013

The summer program began with a class orientation, held at The Saban Research Institute, where students and their families as well as members of the Board of Trustees of Children's Hospital Los Angeles met Samuels Family LA-HIP officials. The agenda included introductions of the director, coordinator and interns, program expectations, on-boarding and workshop attendance.

Programmatic details were discussed and performance expectations explained, and attendees had a chance to visit the Institute's research laboratories. Co-chair of the Board of Trustees Ted Samuels (also the program's largest benefactor) greeted the new class and reminded the students that participating in the Samuels Family LA-HIP is a privilege, and that interns have an obligation to do everything they can to succeed. Several alums from the class of 2012 were on hand to settle the nerves of the new recruits. The event was an opportunity for families and their children to meet each other, get a glimpse of the professional environment in which their kids would be working and familiarize themselves with the paperwork required for the internship.

2013 PROGRAM HIGHLIGHTS (continued)

Class of 2013 interns (seen in the official blue Samuels Family LA-HIP polo shirts) on a tour of the Claremont Colleges ▶

Class of 2012 Farewell Luncheon

June 26, 2013

As is our tradition, we said goodbye to the class of 2012 and celebrated with students, their families and friends in the Anita S. Watson Courtyard with a farewell luncheon. Students were all dressed up and chatted with members of the Board of Trustees in attendance. Interns received the final portion of their stipend, to be used for college-related purposes. It was bittersweet; this tightly bonded group of youngsters had a tough time saying goodbye to the place they called home for the summer of 2012.

The Summer Research Program

Many new features were introduced to the program in 2012, including daily lectures in biology, a pre- and post-internship biology test, the reading of primary scientific articles relevant to pediatric research, research with planaria (a non-parasitic flatworm often used in research) and pre- and post-internship surveys about student learning; these elements were continued in 2013. In particular, the additional instruction in biology, which helped the interns to better understand biological concepts, was very much appreciated and helped the interns with their mentored research project.

Laboratory Prep Course (aka “Hell Week”),

June 25-July 5, 2013

Interns attended a laboratory prep course during which they worked in small groups under the supervision of Bogenmann to learn basic experimentation skills.

The eight-day course, affectionately known as “Hell Week,” introduced the students to hands-on research. The course teaches basic laboratory skills and provides an opportunity

for students and the program director to get to know each other. The students faced a steep learning curve, since most schools don’t offer the opportunity to perform basic biomedical research procedures. The interns received instructions from class of 2012 alums Carolina Herrera (University of California, Irvine) and Roxana Rodriguez (Williams College). Performing an experimental procedure, keeping records in a lab notebook and understanding the underlying concepts are a few of the skills learned in this course. By the end of the training, the students were laboratory-savvy and happy with their accomplishments.

Summer Internship, July 8-Aug. 12, 2013

The interns conducted research with their assigned mentors Monday through Friday, 8:30 a.m. to 5 p.m. The details of the project and the research were left up to the individual mentor.

Experiments performed during a laboratory course are designed to give a known outcome, while mentored research is intended to discover new knowledge. Thus, research trainees must learn the scientific background of the investigations performed in their mentors’ labs, and they must read primary literature, where every other word is something to be looked up on the web, and get familiar with the scientific method. Developing a research hypothesis, performing tricky experiments and analyzing data to reach a conclusion is difficult for graduate students, let alone high school seniors. Working with precious biological material only adds to the pressure our interns were under while in the mentor’s lab. Yet, they all quickly learned the

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2013 PROGRAM HIGHLIGHTS (continued)

ropes and soon seamlessly fit into the research environment (complete with their own white lab coats).

Interns presented their research projects to their peers at Morning Research Rounds. Students introduced the clinical problem, provided background information from the primary literature and presented their experimental procedures used to address the research question. They received valuable feedback from their peers about their presentation skills and learned to answer scientific questions. These “chalk talks” prepared them well for the highlight of the program, the Science Symposium.

2013 Samuels Family LA-HIP Science Symposium – Aug. 12, 2013

A two-hour Science Symposium was held in the auditorium of The Saban Research Building, where all interns presented their research accomplishments. Each student prepared an eight-minute oral presentation and PowerPoint slide. Hospital leadership attended the students’ presentations and Brent Polk, MD, director of The Saban Research Institute, personally handed out the well-deserved certificates of participation and completion, as well as part of the students’ stipends for the program.

College Preparation

The Samuels Family LA-HIP is also a comprehensive college preparatory program in which students receive professional SAT prep training, participate in writing, college and financial aid workshops, and visit the Claremont Colleges. Increasing their SAT scores, together with the counseling they get during the college application process, helps the

high school seniors become competitive college applicants, and, ultimately, students at some of the nation’s best institutions of higher education.

LA-HIP Holiday Reunion Luncheon Dec. 20, 2013

Samuels Family LA-HIP classes come together at this annual luncheon to reconnect with their friends and staff at CHLA. This year we celebrated with students and their mentors at a cozy restaurant near the hospital. Alumni from every class attended and reunited with friends they hadn’t seen for a long time. The college freshmen had many stories to tell, while the interns from the class of 2013 seemed nervous around their predecessors.

Academic Boot Camp

Our interns are accepted to some of the nation’s most elite colleges and universities. While this is a great achievement, it comes with high academic expectations and considerable social demands that pose significant challenges for our students, who can be less prepared than their college peers, academically and socially. Thus, we determined that additional instruction and college preparation would be beneficial for our alums when they matriculate as freshmen.

Teachers from The Princeton Review provided instruction in chemistry, biology, math and English to the interns from the class of 2012 in the summer following their high school graduation. Eleven of the 16 interns gave up five weeks of their last summer before college, Monday through Friday from 8:30 a.m. to 5 p.m., and worked diligently to improve their skills. Stephanie Landicho and Keegan Wood enthusiastically taught the students college-level material,

provided one-on-one tutoring and talked with them about college life. Study skills, time management, note taking and public speaking were also addressed, while guest lecturers discussed research in public health and neuroscience. Students received a stipend, free transportation and meals. The costs for Academic Boot Camp were covered by a grant from the Rose Hills Foundation and by Emil's Pottery Scholarship Award.

A student evaluation was conducted after the first semester of college, to investigate the effect of the extra instruction. Students overwhelmingly indicated that the boot camp prepared them for the rigor of college chemistry and biology classes, as well as the demands of reading primary scientific literature. However, students also expressed the need for further coaching in time management and priority setting.



Doris Duke Charitable Foundation Directors Meeting

In 2012, the Doris Duke Charitable Foundation initiated a program for underserved high school students to be exposed and trained in clinically relevant biomedical research. Following a highly competitive application process, nine research institutions from across the nation, including The Saban Research Institute, were awarded three-year grants, called the Clinical Research Experience for High School Students (CREHSS). The CREHSS program at The Saban Research Institute funds up to eight Samuels Family LA-HIP students.

In 2013, CHLA was asked to host the inaugural CREHSS Directors Meeting in Los Angeles. Directors and administrators from eight of the nine centers attended the meeting, in addition to the program director and administrators from the Doris Duke Charitable Foundation. The agenda of the meeting focused on the work done by the various centers, their experiences and program outcomes. The two-day meeting highlighted the importance of the goals of the centers, but also demonstrated the diversity of approaches taken by the different programs. Strategies to perform student tracking and evaluation were discussed. The meeting was a great opportunity to gauge how our work compares at the national level, and it was obvious that the Samuels Family LA-HIP is a leader in many ways.

◀ Class of 2012 "Boot Campers" pose in front of the iconic blocks on CHLA's campus

**// THE SAMUELS FAMILY
LA-HIP IS ONE OF THE BEST
EXAMPLES OF MENTORING
AND EDUCATING YOUNG
MINDS THAT I HAVE
EVER BEEN EXPOSED TO. //**

**-D. BRENT POLK, MD
DIRECTOR, THE SABAN RESEARCH INSTITUTE,
AND A SAMUELS FAMILY LA-HIP MENTOR**



SAMUELS FAMILY LA-HIP MENTORS



Shahab Asgharzadeh, MD

Shahab Asgharzadeh, MD, is a physician-scientist in the Cancer Program at The Saban Research Institute of Children's Hospital Los

Angeles and an associate professor of Pediatrics and Pathology at the Keck School of Medicine of the University of Southern California (USC). His research is directed toward understanding pathogenesis of neuroblastoma, medulloblastoma and Ewing's sarcoma, and involves identification of molecular features associated with cancer development and identification of risk groups using microarray and next-generation sequencing technologies. Asgharzadeh received his bachelor's degree from Northwestern University in 1992, majoring in biomedical engineering with specialization in genetic engineering. He pursued his medical degree from the University of Illinois, followed by training in pediatrics at the University of Chicago. He completed his pediatric hematology-oncology fellowship program at Children's Hospital Los Angeles prior to joining the faculty of USC in 2005. Asgharzadeh has been a mentor since 2010.



Sebastian G. Bouret, PhD

The research laboratory of Sebastian G. Bouret, PhD, focuses on metabolic programming and the neurobiology of obesity. His research has led

directly to several breakthroughs in the understanding of the complex hormonal signals and neurodevelopmental substrates responsible for appetite regulation. Bouret received his scientific training in France and joined The Saban Research Institute in 2007. He has mentored three graduate students and three postdoctoral fellows. He has also acted as a mentor for minority undergraduate students. He has been a Samuels Family LA-HIP mentor since 2008.



David Cobrinik, MD, PhD

David Cobrinik, MD, PhD, is a principal investigator at The Saban Research Institute and associate professor of Ophthalmology at the Keck

School of Medicine of USC. He majored in biology at Amherst College and pursued graduate training in medicine and biochemistry at Case Western Reserve University. He pursued a postdoctoral fellowship in cancer biology at the Whitehead Institute for Biomedical Research and MIT. He was recruited to CHLA following positions at Columbia University College of Physicians and Surgeons, Weill Cornell Medical College and Memorial Sloan-Kettering Cancer Center. The Cobrinik laboratory focuses on relationships between retinal development and retinoblastoma tumorigenesis using mouse, human and stem cell model systems. Cobrinik has been a mentor since 2013.

SAMUELS FAMILY LA-HIP MENTORS (continued)



Yves DeClerck, MD

Yves DeClerck, MD, is a pediatrician caring for children with cancer and blood diseases at Children's Hospital Los Angeles, the Richard Call Family

Endowed Chair in Pediatric Research and Innovation at The Saban Research Institute and a professor of Pediatrics and Biochemistry at the Keck School of Medicine of USC. DeClerck completed medical school in his hometown of Brussels, Belgium. He developed a career as a physician-scientist, combining clinical care with laboratory research to find new treatments for children with cancer, in particular neuroblastoma. His laboratory focuses on the role of the tumor microenvironment in the progression of tumors and uses this understanding to develop treatment strategies for various childhood cancers. DeClerck has been a mentor since 2010.



Barbara Driscoll, PhD

Barbara Driscoll, PhD, has focused much of her scientific career on understanding the mechanisms of cell and tissue regeneration. Her

graduate work at the University of Arizona using DNA tumor (papilloma) viruses, and initial postdoctoral work at USC on the regulation of the pRb tumor suppressor protein, laid the foundation for inquiries into the molecular mechanisms that control stem and progenitor cell function. Her later postdoctoral work at USC immersed her in lung cell biology and lung physiology, which interested her so much that she decided to focus on stem/progenitor cell queries on the process of lung regeneration. Her laboratory is particularly interested in the mechanisms that underlie

lung progenitor cell turnover and the exhaustion of the regenerative capacity of lungs, either through disease or aging. Driscoll has been a mentor since 2006.



Muller Fabbri, MD, PhD

Muller Fabbri, MD, PhD, is a principal investigator at The Saban Research Institute and assistant professor of Pediatrics at the Keck

School of Medicine of USC. He joined CHLA in June 2012 and holds a secondary appointment in the Department of Molecular Microbiology and Immunology at USC. Fabbri received his medical degree and doctorate in Italy, where he also specialized in medical oncology and practiced medicine for seven years. In 2003, he joined the lab of Carlo Croce, MD, at the Wistar Institute in Philadelphia. Fabbri provided the first evidence of the existence of epi-miRNAs (a group of miRNAs able to regulate epigenetically modulated genes through their targeting effects on effectors of the epigenetic machinery). More recently, Fabbri has identified a completely new mechanism of action for miRNAs as ligands of tolllike receptors, thereby discovering an unsuspected new mechanism of action used by cancer cells to grow within their tumor microenvironment and disseminate. Fabbri has been a mentor since 2013.



Mark Frey, PhD

Mark Frey, PhD, is a researcher in The Saban Research Institute and assistant professor of Pediatrics and of Biochemistry and Molecular

Biology at the Keck School of Medicine of USC. He performed his graduate studies at the University of Buffalo, followed by postdoctoral training at Vanderbilt University, and joined Children's Hospital Los Angeles in 2010. His lab, housed in The Saban Research Institute, studies protein growth factors used by the intestine to repair itself after injury or inflammation. These repair-inducing factors are often altered or lost in chronic inflammatory disorders such as Crohn's disease or ulcerative colitis, and thus may be good targets for therapeutic intervention. Frey has been a mentor since 2011.



Senta Georgia, PhD

Senta Georgia, PhD, is an investigator in the Division of Endocrinology at CHLA and assistant professor of Pediatrics at the Keck School of

Medicine of USC. She attended Stanford University, earning her bachelor's degree in biological sciences with a minor in philosophy. She earned dual departmental honors in biological sciences and ethics in society. She earned her doctorate at the University of California, Los Angeles (UCLA), in molecular biology. During her doctoral studies, she became interested in diabetes and wanted to find a way to increase a patient's insulin-producing cell population so the patient could make his or her own insulin. Her dissertation focused on how cell division regulated the differentiation, expansion and maintenance of insulin

cells. Georgia served as an adjunct assistant professor of Medicine at UCLA's David Geffen School of Medicine, where her research focused on how DNA methylation defines and restricts the identity of insulin-producing cells. At CHLA, her laboratory is focused on devising new methods of expanding insulin-producing cells as a potential cellular therapy for patients with diabetes. Georgia has been a mentor since 2013.



Charles J. Gomer, PhD

Charles J. Gomer, PhD, is vice chair of Pediatrics for Faculty Development at Children's Hospital Los Angeles and a professor of Pediatrics and

Radiation Oncology at USC. He has served on numerous National Institutes of Health grant review committees and was elected president of the USC faculty for the 2013-14 academic year. Gomer received his doctorate in radiation biology and completed a postdoctoral fellowship at the Los Alamos National Laboratory. His laboratory investigates the effects of radiation and laser-induced oxidative stress on tumors. Current studies are examining mechanisms and procedures to improve treatments for retinoblastoma, a pediatric eye tumor. Gomer has been a mentor since 2009.

SAMUELS FAMILY LA-HIP MENTORS (continued)



Prasadarao Nemani, PhD

Prasadarao Nemani, PhD, is a scientist with broad expertise in biological and chemical sciences, and his interest is in finding solutions

to combat neonatal meningitis, pneumonia and necrotizing enterocolitis caused by bacterial pathogens. The focus of his research is understanding the underlying mechanisms involved in the pathogenesis of these diseases, and to combine this knowledge with applied technology to develop therapeutic or preventive strategies. His lab studies the molecular interactions of bacterial ligands and their cognate receptors. Computer simulations are used to model these interactions in order to develop small molecular therapeutics, delivered by nanoparticle technology. Nemani has been a mentor since 2006.



Brent Polk, MD

Brent Polk, MD, is a pediatric gastroenterologist with a research laboratory focused on the regulation of growth and development of the

intestinal cell as it relates to ontogeny and disease. His laboratory uses molecular, cellular, genetic and mouse models to understand how these processes relate to human conditions such as Crohn's disease, ulcerative colitis, necrotizing enterocolitis and other types of intestinal injury and disease. Polk is also chair of the Department of Pediatrics at Children's Hospital Los Angeles and director of The Saban Research Institute, as well as professor and chairman of Pediatrics and vice dean for Child Health at USC. He has been a mentor since 2012.

STUDENT ABSTRACTS



MERCEDES ADAME



Mercedes Adame of Edward R. Roybal Learning Center is interested in math and science and their applications to our daily lives. She is amazed by the human body's complexity, and aspires to either become a surgeon or obtain her medical degree and

concentrate on oncology research. Because her immediate goal is to become valedictorian of her high school class, Mercedes was excited to take part in the Samuels Family LA-HIP, which gave her "work, college and medical experience." Mercedes will attend Scripps College in the fall.

Research Abstract:

DNMT1 Is Important for the Expansion of Postnatal Beta Cell Mass

Mentor: Senta Georgia, PhD

Key Words: Beta Cells, DNMT1, P53, ki67

Problem: In the U.S., there are 25 million people who have diabetes, and there are 45 million undiagnosed cases. Diabetes is a chronic disease characterized by hyperglycemia that is a result of insufficient insulin production by pancreatic beta cells. Current therapy for treating diabetes is insulin supplementation by multiple daily injections. However, multiple insulin injections decreases a patient's quality of life, and can be fatal if miscalculated. The

Georgia lab focuses on how to expand a patient's own beta cells to make sufficient insulin and what molecules are important to regulate beta cell replication. The lab is interested in DNMT1, which is a protein that adds methyl groups to cytosines in DNA to silence gene expression. I analyzed a pancreas-specific knockout of DNMT1 that had a decrease in the expression of p53, which is an oncogene, to understand if DNMT1 is important for the expansion of beta cell mass.

Hypothesis: DNMT1 is important for the proliferation of the beta cells.

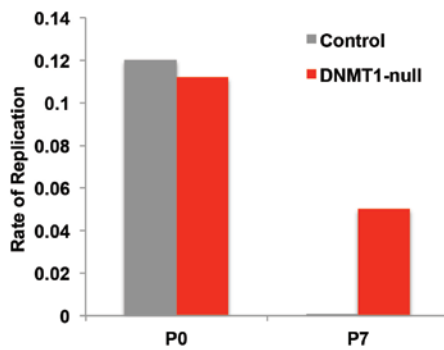
Methodology: I analyzed pancreatic tissue from postnatal 0-, 7- and 15-day-old wild type and DNMT1^{-/-} mice using immunohistochemistry and fluorescence microscopy. I used imaging software to quantify beta cell area, islet diameter and beta cell proliferation index.

Results: There was a significant statistical change of islet diameter between the control and the experimental, such that the mutant islets were smaller than the wild type, but proliferation rates were increased in comparison to the wild type. Interestingly, there was an increase in single cells in the mutant pancreas, which suggests that single beta cells may be differentiating from unidentified stem cells.

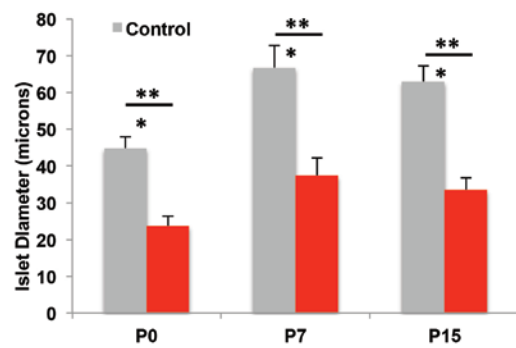
Conclusion: DNMT1 is important for the expansion of postnatal beta cell mass. In the future, it would be interesting to investigate why DNMT1 null mice have increased proliferation but no change in islet diameter. Understanding why this occurs can take us a step further toward regenerative therapy for diabetic patients.

Results

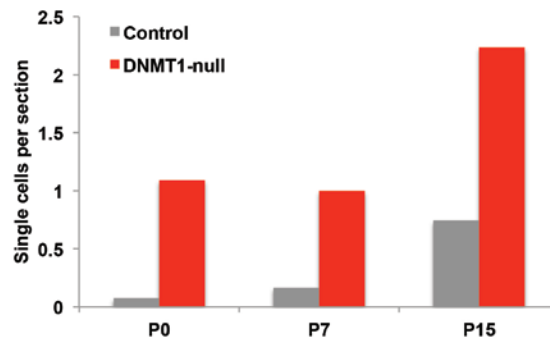
Beta Cell Replication



Islet Diameter



Single Cells



JOSSELYN BARAHONA



Josselyn Barahona of John H. Francis Polytechnic High School brings a passion for medicine and anatomy to the Samuels Family LA-HIP. She is eager to continue her studies of the intricate human body, and plans to pursue a career “in pediatric oncology, in hopes of making an everlasting impact on a child’s life.” As a proud Latina, Josselyn is determined to rise to her full potential and be a role model for young girls in her community. Josselyn will attend Williams College in the fall.

Research Abstract:

The Role of Epidermal Growth Factor Receptor (EGFR) Signaling in Lung Injury

Mentor: Barbara Driscoll, PhD

Lab Personnel: Orquidea Garcia, PhD, Michael Hiatt, PhD, Joeeun Lee, Raghava Reddy, PhD

Key Words: lung, injury, fibrosis, epidermal growth factor receptor

Problem: The occurrence of lung disease in the industrialized world is an increasing public health problem, with 60,000 cases of pulmonary fibrosis reported annually in the United States. The cause of the most common types of pulmonary fibrosis (idiopathic pulmonary fibrosis, chronic obstructive pulmonary disease [adults] and bronchopulmonary dysplasia [neonates]) is currently unknown, but may be connected to lung injury, followed by permanent

changes in surviving cells. Because the molecular factors that initiate lung fibrosis are unknown, targeted therapies cannot be developed. Consequently, there is no cure, though symptoms can be alleviated. One significant abnormality in fibrosis is uncontrolled proliferation of lung fibroblasts. Because lung fibroblasts proliferate in response to signals from surrounding cells, we wished to determine if epidermal growth factor receptor (EGFR) signaling in the lung, a known modulator of cellular proliferation, plays a role in the development of fibrosis.

Hypothesis: Epidermal growth factor receptor signaling plays a critical role in the fibrotic response to lung injury.

Methodology: Whole lungs were harvested at 0, 7, 14, 28 and 56 days post-injury. Western blotting, followed by densitometry quantification, was used to determine activated epidermal growth factor protein levels in control and injured lung tissue. Fixed, embedded and sectioned injured lung tissue from wild type and EGFR knockout mice was analyzed for differences in morphology by H&E staining and in lung cell marker expression by immunohistochemistry.

Results: Western Blots showed elevated, phosphorylated EGFR in injured lung tissue at 28 days post-injury. At this same time point, wild type tissue appears mostly repaired, with the exception of some immune cell infiltrate. However, EGFR knockout tissue exhibits increased immune infiltration, thickening of alveolar walls and significantly larger lung progenitor cells.

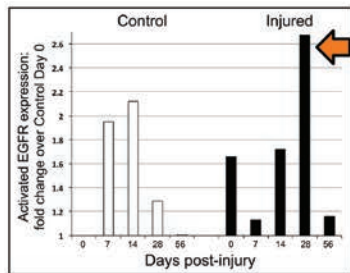
Conclusion: Phosphorylated epidermal growth factor receptor plays a role in response to lung injury, though its role in development of fibrosis is not yet known.

Lung fibrosis

epidermal growth factor receptor

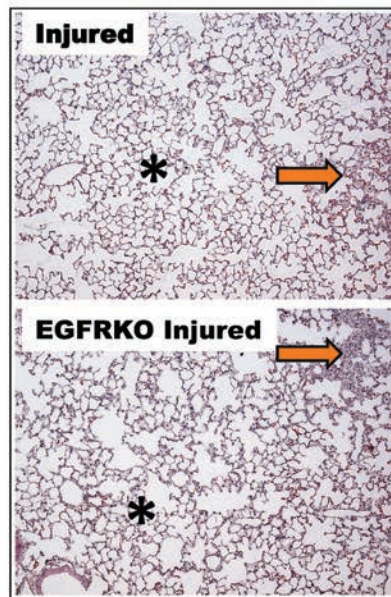
Results

Western Blot



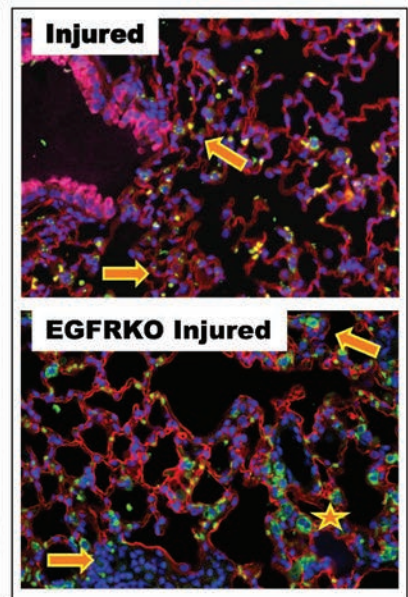
0 - 56 Days
Post-Injury

H&E Stain



Immunohistochemistry

Airways / Epithelia / Nuclei / Progenitors



28 Days Post-Injury

ROGELIO CARO

Doris Duke Scholar



Rogelio Caro of the California Academy of Mathematics and Science High School (CAMS) is passionate about medicine and participates in several science-related clubs to immerse himself in the field. He also holds leadership positions in the Biomed Club and

on the CAMS debate team, and “enjoys working in a team to bring about positive results.” As part of the Samuels Family LA-HIP, he was eager to investigate childhood diseases and establish lasting relationships with mentors at The Saban Research Institute. Rogelio will attend the University of Pennsylvania in the fall.

Research Abstract:

Targeting the Tumor Microenvironment of Neuroblastoma Cells

Mentor: Yves DeClerck, MD

Lab Personnel: Lucia Borriello, PhD

Key Words: Microenvironment, STAT-3, Ruxolitinib, Neuroblastoma

Problem: Neuroblastoma is a childhood cancer that often becomes drug resistant and thus is prone to treatment failure. This makes discovering new treatments for neuroblastoma imperative. Drug resistance is induced from the tumor microenvironment, where there is a reciprocal dialogue of soluble factors between the tumor cells and microenvironment cells; the most relevant factor is Interleukin-6 (IL-6). IL-6 binds to receptors on the tumor cells and induces the activation/phosphorylation of the signal

transducer and activator of transcription-3 (STAT-3) pathway. This pathway is associated with the upregulation of proteins involved in survival, proliferation and drug resistance.

Hypothesis: Inhibition of STAT-3 phosphorylation with Ruxolitinib will prevent drug resistance.

Methodology: Conditioned medium (CM) was generated from a co-culture of CHLA-255 neuroblastoma cells in direct contact with human bone marrow mesenchymal stem cells for 48 hours. As a control, the CM of CHLA-255 cells cultured alone was obtained. Next, an enzyme linked immunosorbent assay (ELISA) was performed to detect the level of IL-6 in each CM. To evaluate the effect of the CM on cell survival, the cells were treated with Etoposide, a chemotherapeutic drug, and Ruxolitinib in the two CM prepared earlier; a cell viability assay was then conducted. Finally, a Western Blot was performed to determine the presence of pSTAT-3 in cells after being treated with the same two drugs in the co-culture.

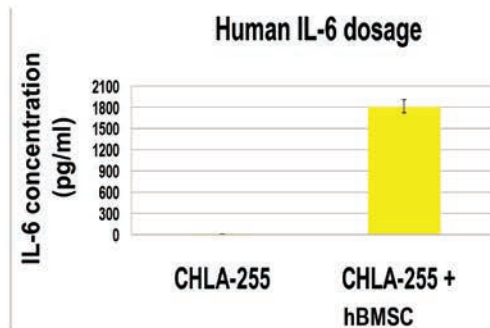
Results

1. The ELISA showed a higher secretion of IL-6 in the co-culture.
2. Treatment showed that the co-culture protects the cells from apoptosis induced by Etoposide and that Ruxolitinib does not significantly increase sensitivity to chemotherapy.
3. The Western Blot showed no presence of pSTAT-3 in neuroblastoma treated with Ruxolitinib.

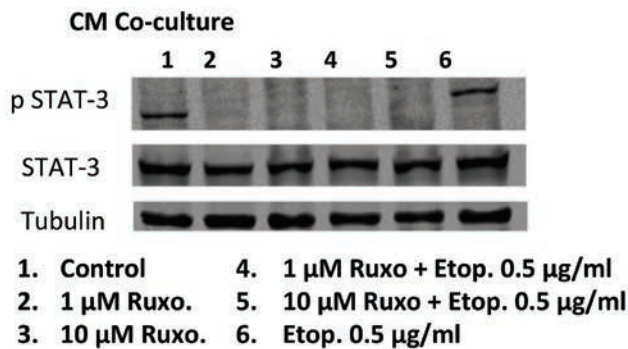
Conclusion: The results suggest that Ruxolitinib is effective in blocking STAT-3 phosphorylation but is not effective in increasing sensitivity to chemotherapy in the co-culture.

Results

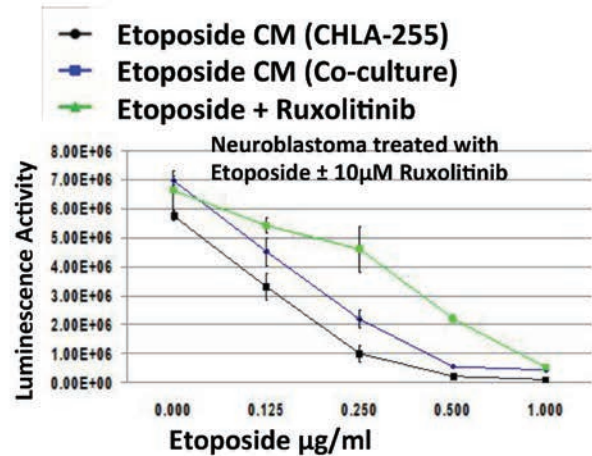
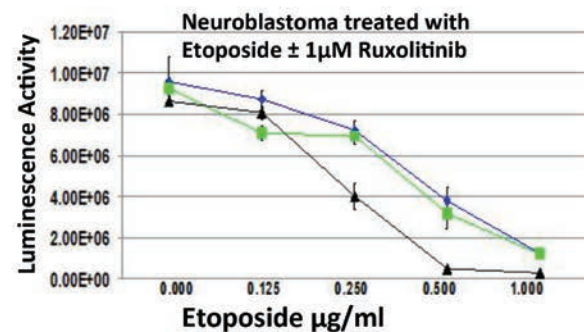
1. ELISA



2. Western Blot



3. Cell Viability Assay



LUIS CUIRIEL



Luis Curiel of John H. Francis Polytechnic High School is interested in microbiology and immunology and how microscopic elements are able to significantly affect the macroscopic world. In college, he plans on majoring in biochemistry and then earning a doctorate in immunology. He is excited about “learning and partaking in research methods” that will better prepare him to pursue a research career. Luis will attend Johns Hopkins University in the fall.

Research Abstract:

Altered Lung Fibroblast Gene Expression in Lung Injury

Mentor: Barbara Driscoll, PhD

Lab Personnel: Taylor Brown, Michael Hiatt, PhD,
Raghava Reddy, PhD

Key Words: Lung, Fibroblast, Injury, Cell Cycle, Fibrosis

Problem

New cases of pulmonary fibrosis are diagnosed in 60,000 people each year. The majority of these cases occur in adults, and include idiopathic pulmonary fibrosis and the fibrotic component of chronic obstructive pulmonary disease. A small number of neonatal cases of fibrotic bronchopulmonary dysplasia also occur. These diseases can be treated for symptoms but currently there is no cure. One reason for the lack of a cure is the

poor understanding of how lung fibrosis begins. If the cause of fibrosis can be determined, the possibility of developing therapies that target said cause is improved. We wish to determine how lung injury stimulates lung fibroblast proliferation, senescence and acquisition of a myofibroblast phenotype, and whether these changes in fibroblast function are due to changes in specific gene expression.

Hypothesis

Proliferation, senescence and myofibroblast-related gene expression in lung fibroblasts changes as a result of lung injury.

Methodology

We isolated messenger RNA from lung fibroblast cells that were harvested from control and injured lungs. RT-PCR analyses enabled us to amplify the genes of interest (P16, P19, Tp53BP2, smooth muscle actin (SMA) and actin as an internal control). Agarose gel electrophoresis was used to visualize gene expression, which was quantified by densitometry analysis using ImageJ.

Results

Fibroblasts isolated at acute time frames after the injury (0 or 7 days) showed no change in expression of P16, Tp53BP2 or SMA, but notably reduced expression of P19. At a later time point (56 days following injury) P19 expression was brought back to normal.

Conclusion

Results suggest that some cell cycle and myofibroblast-related genes are not affected by lung injury at acute or chronic time points, but the cell cycle checkpoint/senescence gene P19 is downregulated.

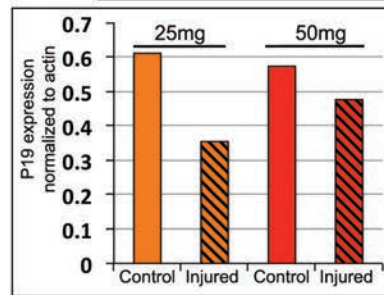
Results

Inject drug
(25mg/kg or 50mg/kg)
1/day for 3 days
to cause lung injury

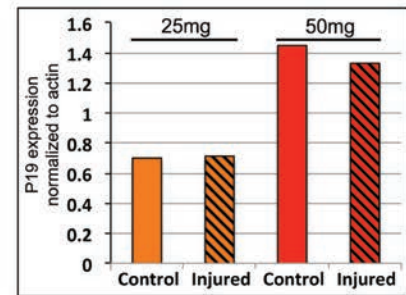
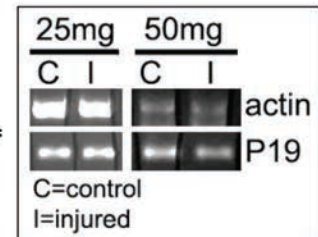
Days following injury



Acute



Chronic



ROCIO DEL CID



Rocio Del CID of John Marshall High School has already gotten her hands dirty in science by conducting her own experiments focusing on a cure for plant cancer. She is driven to develop “new and efficient medical procedures that are affordable to people in developing countries,” and was eager to experience science outside of the classroom as part of the Samuels Family LA-HIP. Rocio will attend Crown College at the University of California, Santa Cruz, in the fall.

Research Abstract:

Cell Type-Specific Signaling Pathways That Collaborate With RB1 Inactivation in Retinoblastoma

Mentor: David Cobrinik, MD, PhD

Lab Personnel: Dong Lai Qi, PhD

Key Words: Retinoblastoma, RB1 Inactivation, Stabilization of MDM2, Protein Expression

Problem

Retinoblastoma is a childhood eye cancer that develops due to mutations that inactivate an important tumor suppressor gene, RB1. If both alleles of RB1 are mutated early in life, RB1 is unable to inhibit progression from the G1 to S phase of the cell cycle and excessive cell proliferation. Little is known about the type of retinal cells the cancer emerges from or the features that make the cell sensitive to RB1 mutations. It is important to study

the cell type-specific signaling pathway that cooperates with the inactivation of RB1 that results in retinoblastoma. Future data could help further studies in other types of cancer that are also a result of RB1 inactivation as well as the possible development of more specific cancer therapies.

Hypothesis

By studying retinoblastoma cell-signaling, I hypothesized that inhibition of the p53 cell apoptosis in retinoblastoma is due to an increased expression of MDM2 (a regulator of p53) and stabilization of MDM2 by the deubiquitinase USP47.

Methodology

An observational approach was taken where four different retinoblastoma cell lines (Rb176, Rb177, Y79, CHLA Rb43) were tested for MDM2 and USP47 expression. The four different cell lines were cultured at 37°C for two weeks and then lysed to break their cellular membrane to release their protein. The protein was then separated based upon size through gel electrophoresis, transferred onto a membrane (Western Blot) and probed with primary and secondary antibodies.

Results

Membrane development on film showed a clear expression of both MDM2 and USP47 in each of the cell lines examined, supporting my hypothesis.

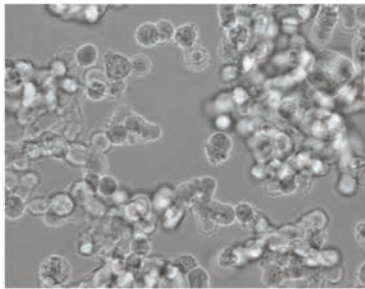
Conclusions

The data was not sufficient to prove my hypothesis correct. Further experimentation would be needed, such as a re-observation of the same cell lines and USP47 suppression in the retinoblastoma cells.

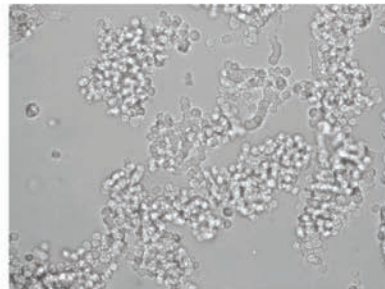
Stabilization of MDM2

Protein Expression

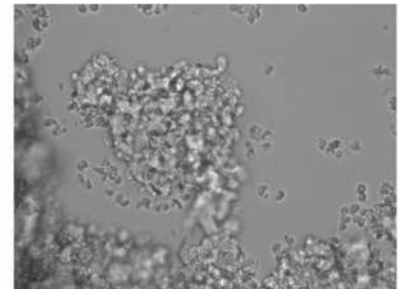
Results



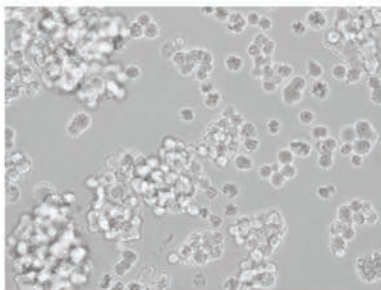
Rb176 40x



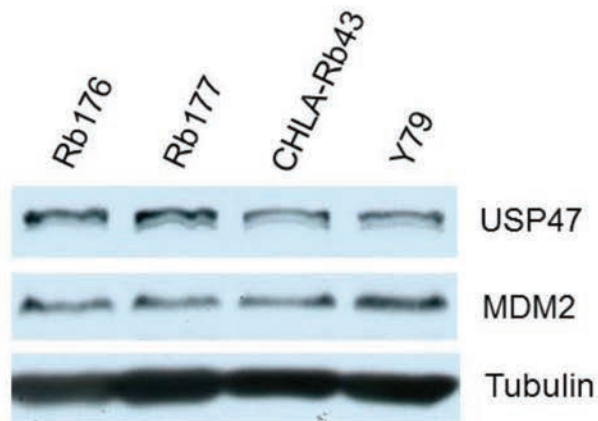
Y79 20x



CHLA Rb43 20x



Rb177 20x



ANDREW GONZALEZ

Doris Duke Scholar



Andrew Gonzalez from Bravo Medical Magnet High School brought dedication and “a thirst for science” to the Samuels Family LA-HIP. He co-created a youth-led nonprofit organization, Multi-Taskers Los Angeles Youth Council, in 2009 and aspires

to help adolescents make volunteering a lifelong commitment. In the future, he hopes to advance his understanding of human disease and treatments, work with computers and other laboratory equipment and improve individual health worldwide. Andrew will attend the University of California, Los Angeles, in the fall.

Research Abstract:

Lipopolysaccharides Affect the Gastrointestinal Tract in a Region-specific Manner

Mentor: Mark Frey, PhD

Key Words: Lipopolysaccharides, Apoptosis, Ileum and Colon, Inflammatory Bowel Disease

Problem

Inflammatory bowel disease (IBD) is both a chronic and incurable disease that affects approximately 1.4 million people in the U.S., with 10 percent under the age of 18. Also, recent data has shown that the incidence of children with IBD is increasing. The two main causes of IBD are Crohn’s disease, which affects the ileum and colon, and ulcerative colitis, which affects only the

colon. In IBD, the epithelial layer, the cell lining that separates the body from the inside of the gut, becomes inflamed, causing cell death. This causes the degradation and loss of viability of the epithelial cell barrier.

Hypothesis

Lipopolysaccharides (LPS) are large molecules composed of lipids and polysaccharides that are found on the outer layers of gram-negative bacteria, such as *E. coli*, that elicit strong immune responses in humans. LPS induces acute colitis and serves as a model for inflammation-induced cell death. In my project, we looked at the difference in the responses of the two areas of the bowel, the colon and the ileum.

Methodology

In order to test our hypothesis, colon and ileum tissues were treated with LPS for 90 minutes and stained for apoptosis, or cell death, using an In Situ Oligo Ligation (ISOL) stain, in which antibodies bind to the ends of fragmented strands of DNA that are present during apoptosis. The apoptotic cells appeared brown and were then counted under a microscope per 100 crypts or 100 crypt/villus units.

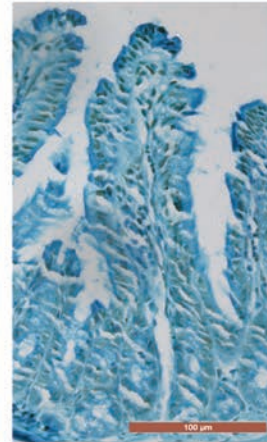
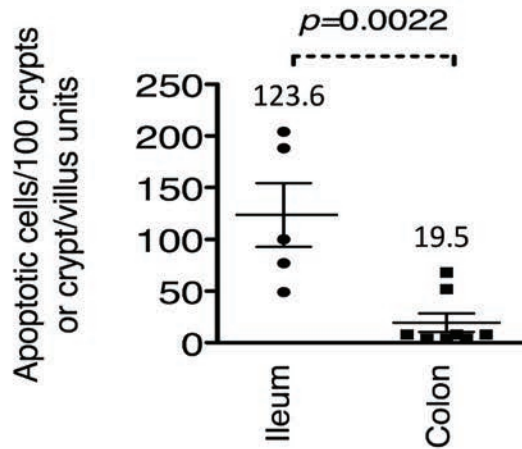
Results

The cell counts revealed that there was a 10x greater average amount (196 vs. 19.5) of apoptotic cells present in the ileum than in the colon.

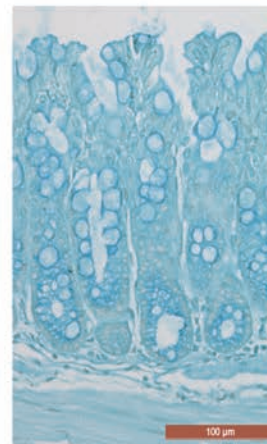
Conclusion

We were able to conclude that the ileum is sensitive to, and the colon is resistant to, LPS-induced apoptosis.

Results



Ileum
(small intestine)



Colon

NALLELY LOPEZ



Nallely Lopez of South East High School strives to achieve her full potential, especially in the field of neurology. After meeting with top neurologists at the University of California, Los Angeles, she was eager to feed off the excitement of researchers and other students as a part of the Samuels Family LA-HIP. In the future, Nallely plans on pursuing her passion and becoming a neurologist. Nallely will attend Williams College in the fall.

Research Abstract:

Anatomical Link Between the Brain and Diabetes

Mentor: Sebastien G. Bouret, PhD

Lab Personnel: Sophie Croizier, PhD

Key Words: Obesity, Diabetes, Insulin, Hypothalamus, Brain

Problem

In 2013, approximately 23.9 million children and adolescents were considered obese or overweight in the United States. Children with obesity have an 80 percent chance of becoming obese as adults, increasing their risk of developing type 2 diabetes. However, we still know little about the mechanisms that underlie the development of obesity and diabetes.

Proopiomelanocortin (POMC) is a neurohormone secreted by neurons located in a region of the brain called the hypothalamus. These neurons are partially responsible for maintaining our

body weight by regulating the amount of food that we eat. We recently found that deletion of a class of molecules called “micro-RNAs” in POMC neurons causes obesity and diabetes.

Hypothesis

We hypothesize that the loss of micro-RNAs in POMC neurons causes structural alterations in the pancreas, an organ that plays an essential role in regulating blood sugar, and that may contribute to the development of diabetes.

Methodology

Sections of pancreatic tissue from mutant (diabetic) and normal mice were cut using a cryostat and mounted onto slides. Immunohistochemistry was performed on these sections using specific antibodies against insulin, a pancreatic hormone that is critical to maintaining blood glucose levels. Confocal microscopy was then used to visualize and quantify the mass of insulin-producing cells in the pancreas.

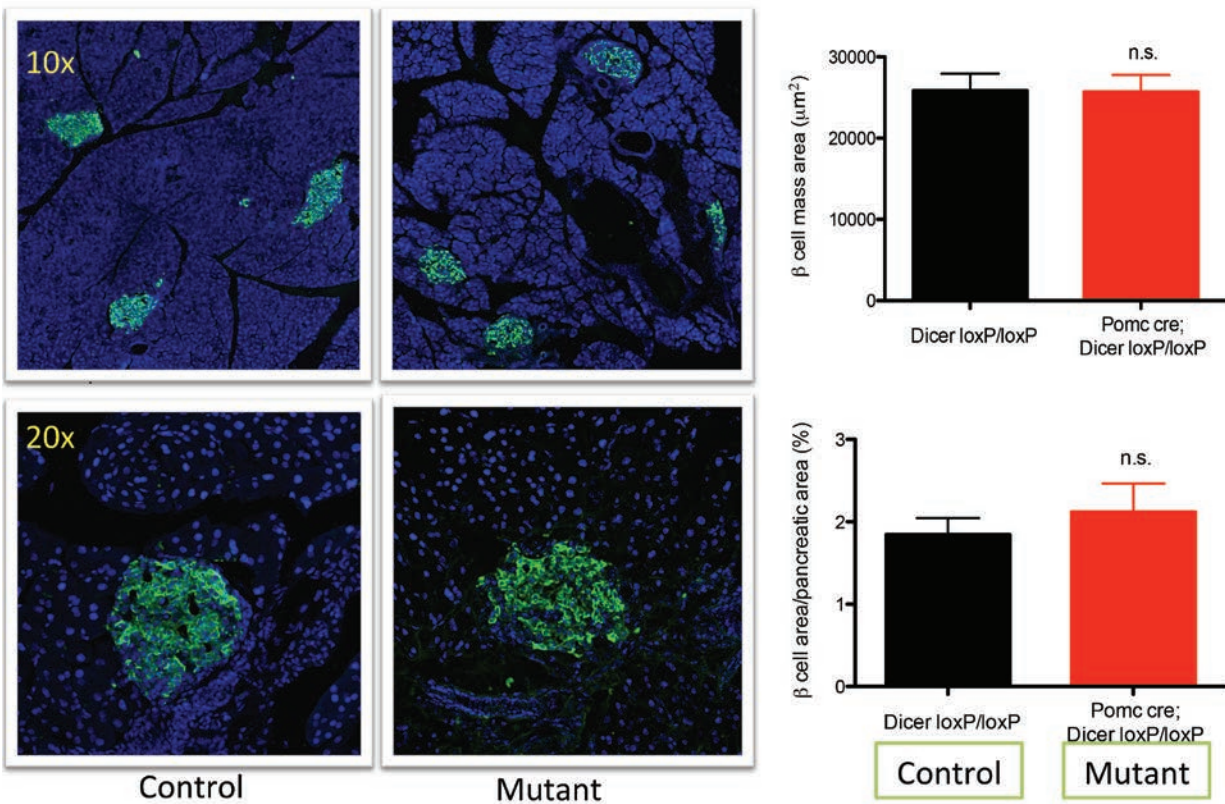
Results

The results indicate that the average mass of insulin-producing cells is not significantly different between control and mutant mice. Moreover, there are no morphological differences in the size and morphology of insulin-producing cells in mutant mice.

Conclusion

The deletion of micro-RNAs in POMC neurons is not associated with major changes in the overall quantity of insulin-producing cells in the pancreas. These data suggest that pancreatic function may be relatively normal in mutant mice and indicate that the diabetes observed in mutant mice may be caused by disruption of other peripheral processes involved in glucose regulation.

Results



MONICA LOZA

Doris Duke Scholar



Monica Loza of the California Academy of Mathematics and Science High School enjoys participating in her school's Key Club, as it allows her to give back to her community. She dreams of finding cures for debilitating diseases and making a direct, positive impact on people's lives. As a member of the Samuels Family LA-HIP, she was eager to learn about the jobs of researchers and make her own scientific discoveries. Monica will attend Grinnell College in the fall.

Research Abstract:

Role of miR-155 in Neuroblastoma

Mentor: Muller Fabbri, MD, PhD

Lab Personnel: Petra Wise, PhD

Key Words: miR-155, Neuroblastoma, BRG-1, Monocyte

Problem

Neuroblastoma (NB) is a cancer that develops from nerve tissue. It is most commonly diagnosed in children less than 5 years of age. In the United States, there are about 700 cases each year; however, the cause of neuroblastoma has not been understood. The research question that will be addressed is, "What is the role of microRNA, miR-155 that is derived from immune cells, in regulating the progression of neuroblastoma?"

Hypothesis

MicroRNA, miR-155 derived from immune cells, regulates the progression of neuroblastoma by targeting BRG-1 in NB cells and upregulates the c-Myc oncogene.

Methodology

IMR-32 was the neuroblastoma cell line that was used in this study because it does not express the BRG-1 gene. A polymerase chain reaction was conducted to amplify the BRG-1 gene with the binding site of miR-155 on the 3' untranslated region. The amplified BRG-1 fragment was then cloned into a TOPO-10 vector and transformed into *E. coli*. The BRG-1 fragment was then subcloned into a pGL-3 vector and transformed into *E. coli*. This pGL-3 vector with the BRG-1 fragment was transfected into the IMR-32 cells and a luciferase assay was conducted.

Results

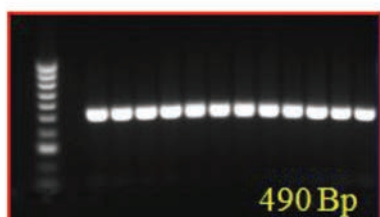
The custom-made primers to amplify the BRG-1 fragment were successful. The BRG-1 fragment was successfully cloned into a TOPO vector and verified by sequencing. The BRG-1 fragment was successfully subcloned into a pGL-3 vector and verified by sequencing; however, the fragment was in antisense orientation. The pGL-3 vector with the BRG-1 fragment in antisense was successfully transfected into the IMR-32 cells.

Conclusion

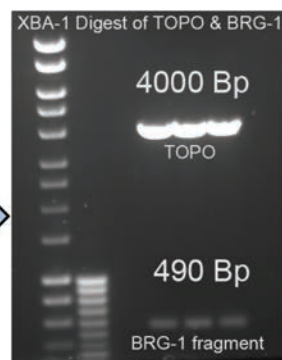
IMR-32 cells can be transfected with a foreign vector. The next step would be to transfect the IMR-32 cells with the vector with the BRG-1 fragment in sense orientation and a miR-155 to analyze the effects of the miR-155 on the BRG-1 fragment.

Results

1) PCR with custom primers

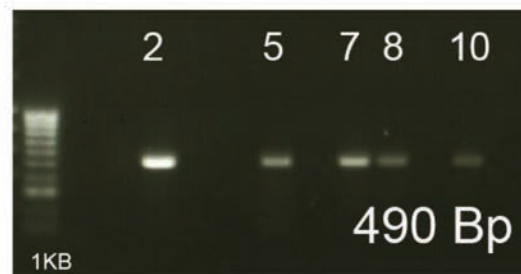


2) TOPO Cloning



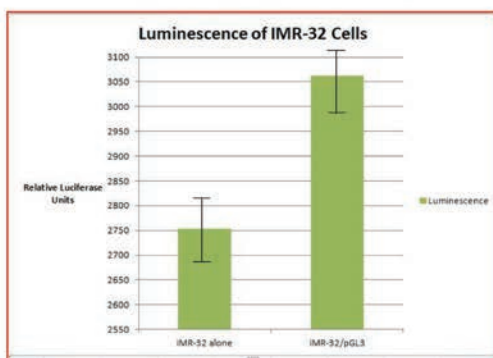
100% match after sequencing

3) pGL-3 Subcloning



100% match after sequencing but in antisense, and still need to screen and sequence 16 positive colonies

4) NB cell transfection & Luciferase Assay



DONNA MEDEL AND ANGEL ORTIZ

Doris Duke Scholars



Donna Medel of Wallis Annenberg High School loves being active outdoors, has volunteered at her local elementary school and hospital, and started a community garden. In addition to her extracurricular pursuits, she is fascinated by the human body

and hopes to have a career in either engineering or medicine. She is grateful for the guidance that the Samuels Family LA-HIP provided in the college-application process, and was eager to participate in biomedical research at The Saban Research Institute. Donna will attend Columbia University in the fall.



Angel Ortiz of James A. Garfield High School is an active volunteer, and spends his time feeding and helping the homeless and visiting the elderly. In the future, he hopes to “help the most people” by becoming a doctor. Through the Samuels Family LA-HIP,

Angel was eager to absorb as much knowledge as possible about the science and medical fields from The Saban Research Institute’s top investigators. Angel will attend Brown University in the fall.

Research Abstract:

Induction of Survivin and Vascular Endothelial Growth Factor in Retinoblastoma Cells Following Benzoporphyrin Derivative Mediated Photodynamic Therapy

Mentor: Charles Gomer, PhD

Lab Personnel: Angela Ferrario, PhD, Marian Luna, Natalie Rucker, Sam Wong

Key Words: Retinoblastoma, Photodynamic Therapy, Benzoporphyrin Derivative, Survivin

Problem

Retinoblastoma (Rb) is an eye tumor of the developing retina presenting in children before the age of 5 and occurring at a frequency of 1/15,000 live births. Photodynamic therapy (PDT) is a treatment that uses photosensitizing agents and laser light to destroy cancer cells. PDT is an ideal treatment for the reduction of the Rb tumor, since the tumor can be targeted very precisely and it has significantly fewer side effects than chemotherapy. BPD is a second-generation photosensitizer that has been approved for clinical use and has a faster clearance from the body than first-generation photosensitizers. The purpose of this research was to determine if BPD-mediated PDT was an effective method of treating Rb cells.

Hypothesis

BPD-mediated PDT is an effective method of treating retinoblastoma cells, but can induce survivin and VEGF.

Methodology

Retinoblastoma cells, Y-79 and CHLA 215, were treated with 0.1 $\mu\text{g}/\text{ml}$ and then exposed to non-thermal laser light. The Y-79 cells were treated with PDT at light doses of 135 and 435 mJ/cm^2 while the CHLA 215 Rb cells were treated at light doses of 135 and 580 mJ/cm^2 . After 24 hours of the cells undergoing PDT, survivin was determined by a Western Blot assay, VEGF was determined with a VEGF assay, and apoptosis was determined by a cell death assay.

Results

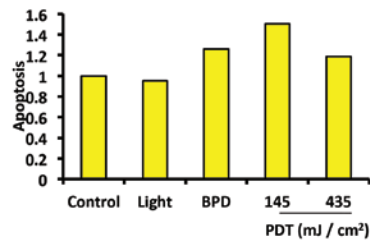
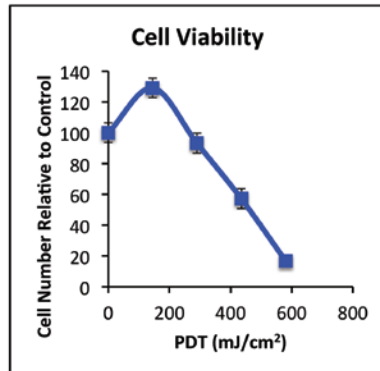
It was determined that as the dosage of PDT increases, the cell viability decreases in both of the cell lines. The Y-79 cells did not show significant apoptosis in the highest amount of dosage in PDT as compared to the CHLA 215 cells. In both cell lines, there was an increase of survivin at the light dose of 145 mJ/cm^2 and an increase of VEGF as the PDT dosage increased.

Conclusion

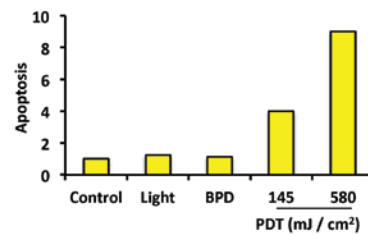
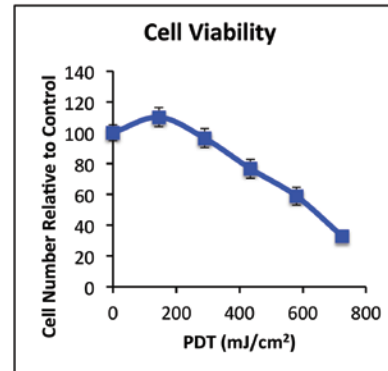
BPD-PDT effectively kills retinoblastoma cells and induces survivin and VEGF.

Results

Y-79

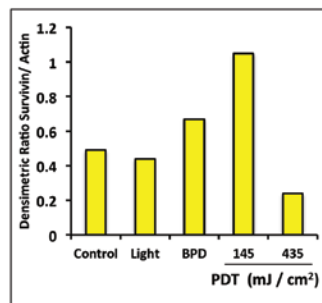
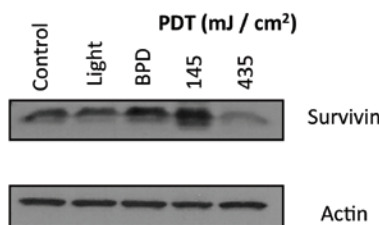


CHLA 215

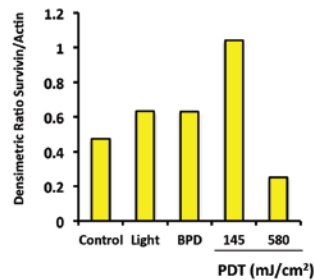
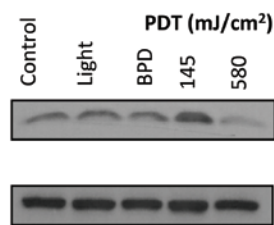


Western Analysis of Survivin

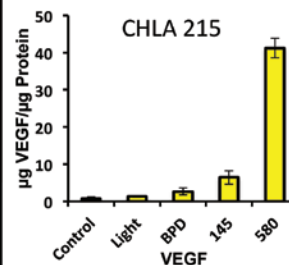
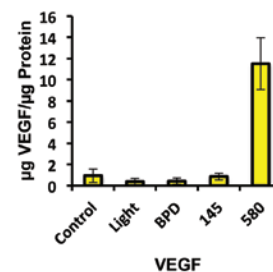
Y-79



CHLA 215



VEGF Assay



LUIS ANGEL OCON



Luis Angel Ocon of Renaissance Arts Academy is inspired by the complexity of science. He dreams of working as a physician in hematology and oncology and finding new solutions to help patients in this complex field. As a young child, he was enthralled by visits to the hospital and doctor's office, and he was excited to be guided by Children's Hospital Los Angeles physician-researchers as part of the Samuels Family LA-HIP. Luis Angel will attend Furman University in the fall.

Research Abstract:

The Role of TNF α in Wound Healing

Mentor: D. Brent Polk, MD

Lab Personnel: Philip E. Dubé, PhD, Cambrian Liu, PhD, Shivesh Punit, PhD, Claudio Alberto Rivera, MD, MPH, Unice Soh, PhD

Key Words:

Tumor Necrosis Factor (TNF), Inflammatory Bowel Disease (IBD), Epithelial Cells, Wound Healing

Problem

Inflammatory bowel disease (IBD) involves chronic inflammation of all or part of the gastrointestinal (GI) tract. IBD affects greater than 1.4 million people in the US. IBD primarily includes ulcerative colitis (UC) and Crohn's disease; they are similar diseases but the main distinction is the location of the inflammation and the extent of it.

Inflammatory bowel diseases are considered autoimmune diseases, in which the body's own immune system attacks elements of the digestive system. Impaired wound healing is a significant clinical problem in IBD patients. TNF is a ubiquitous inflammatory mediator released by activated macrophages. TNF has acquired a negative connotation; however TNF also can promote cell migration and proliferation.

My research involves the relationship between wound healing and tumor necrosis factor α (TNF α), which is a pro-inflammatory cytokine; it has an antineoplastic effect but causes inflammation and apoptosis (cell death).

Hypothesis

Large quantities of TNF inhibit wound healing, and small amounts of TNF promote wound healing.

Methodology

To address my hypothesis I conducted a wound healing assay to measure cell migration and proliferation. I plated epithelial cells on a Petri dish. I created eight different wounds using a drill press, then treated these wounds with TNF at different doses and measured the size of wounds remaining at 0hr, 6hr and 24hr with a microscope.

Results

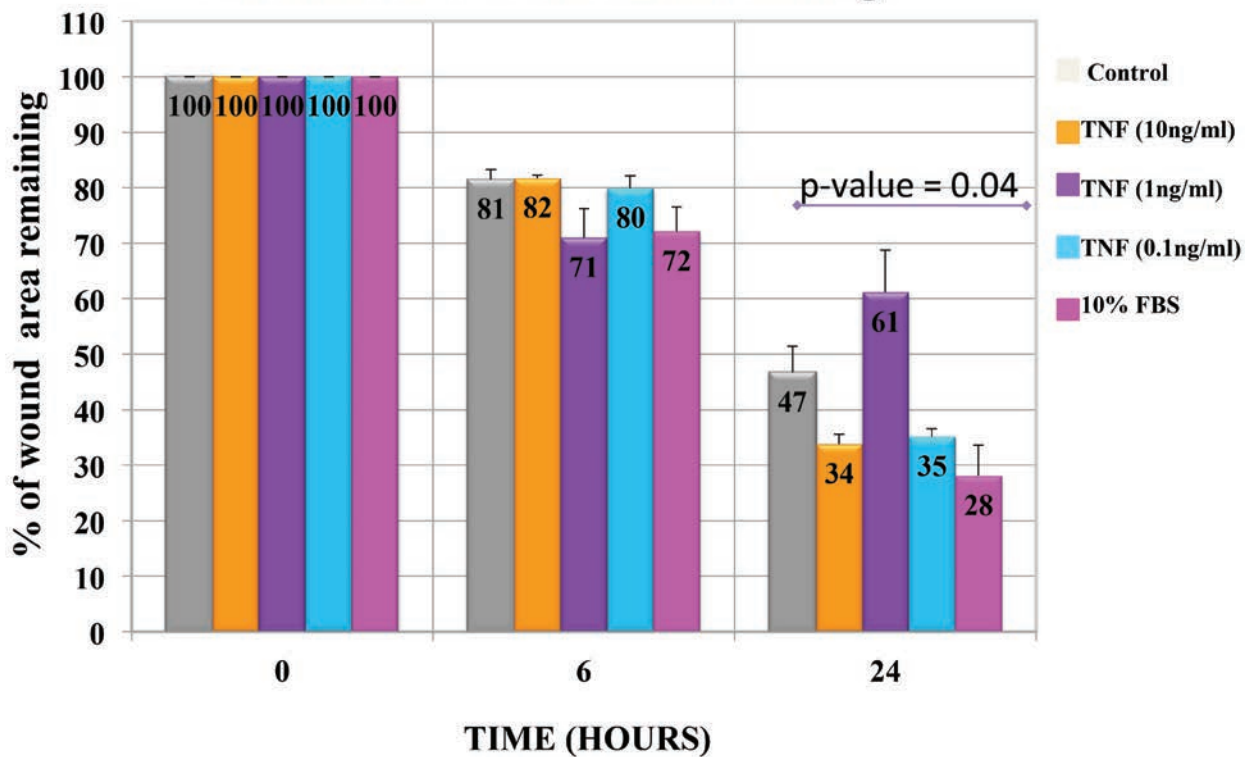
The results were varied due to the number of times I did the experiment, but I found that TNF still helps in the process of wound healing in a trend line and at specific doses.

Conclusions

As hypothesized, I found that TNF at specific doses promotes wound healing, so TNF could help to treat IBD. My future direction is to determine how TNF and anti-TNF therapy could be used to treat patients with IBD.

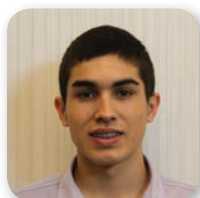
Results

The effect of TNF on wound healing



EDUARDO ROMO

Doris Duke Scholar



Eduardo Romo of Warren High School is passionately curious. He continuously searches for solutions in life, from how to do his best academically to conducting research on medical diagnoses. He reflects back on the unanswered questions of his childhood, and aspires to become a pediatrician in order to “help any child who needs answers.” He sees the Samuels Family LA-HIP as a starting point for his career in the medical field and was excited to pursue this research opportunity, as it will prepare him to “continue his lifelong quest for knowledge.” Eduardo will attend Johns Hopkins University in the fall.

Research Abstract:

Effects of Trametinib on Medulloblastoma

Mentor: Shahab Asgharzadeh, MD

Lab personnel: Long Hung

Key Words: Trametinib, MAPK Pathway, Mek, Medulloblastoma

Problem

Medulloblastoma is a highly malignant brain tumor originating in the cerebellum or posterior cranial fossa. Current treatments that are used for medulloblastoma are chemotherapy, radiation and surgery. Trametinib is a Mek inhibitor drug, which means that it

inhibits the Mek protein in the MAPK pathway by not allowing it to activate other proteins. The MAPK pathway is a chain of proteins in a cell being activated through phosphorylation so that the cell can grow, which is vital for many cancers. My research question is: Can Trametinib be used as therapy in combination with other standard treatments to treat medulloblastoma?

Hypothesis

Trametinib will inhibit the MAPK pathway, causing proliferation to be prevented or slowed down.

Methodology

We ran the protein of treated (with Trametinib) and untreated cells on a Western Blot. Then we probed for Mek, Erk and GAPDH; GAPDH was used as a loading control, since it is a housekeeping gene. The second methodology involved counting the amount of cells after treating them.

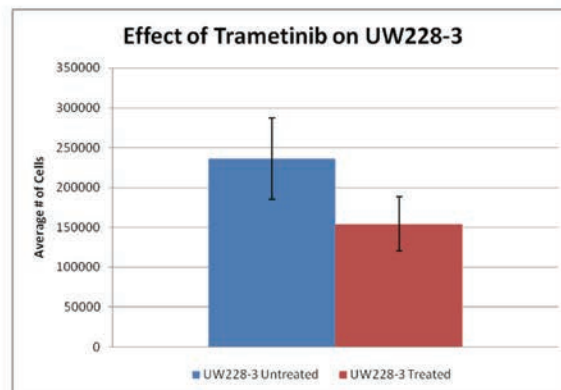
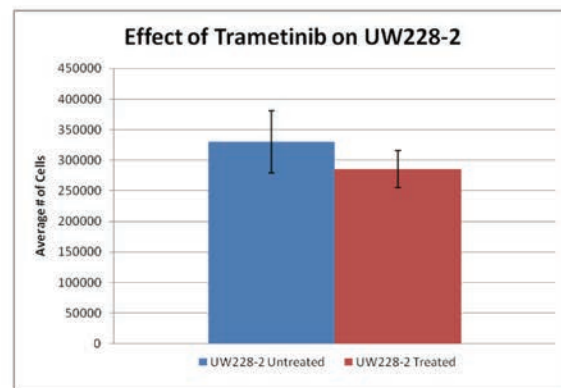
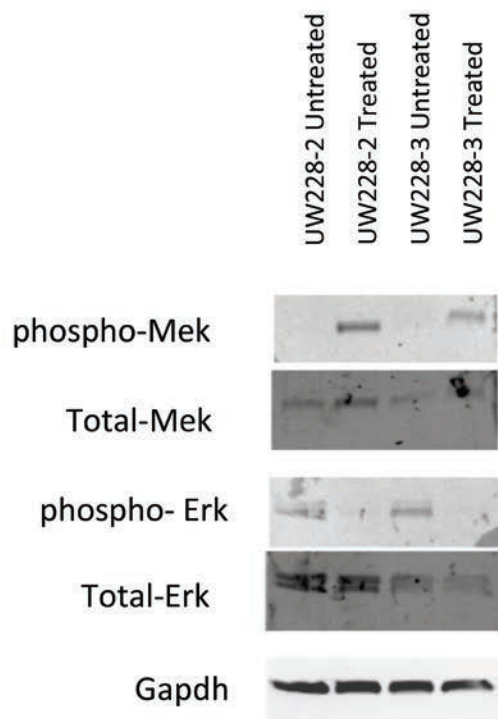
Results

GAPDH levels were equal for treated and untreated cells. Phosphorylated Mek was greater in treated cells in comparison to untreated cells. Phosphorylated Erk was at a low level in treated. Phospho-Erk was at a low level because phospho-Mek was not able to activate Erk. The cell count demonstrated that there were fewer cells treated than untreated.

Conclusion

Trametinib does affect the MAPK pathway by inhibiting phospho-Mek and causing cell proliferation to slow down.

Results



MANISHA SAJNANI AND SOMTOCHUKWU 'SOMTO' UZOEGBU

Doris Duke Scholars



Manisha Sajnani of Bravo Medical Magnet High School is a talented and dedicated ballerina who brings her persistent spirit to the fields of math and science. After high school, she dreams of attending a university that will allow her intellectual curiosity to

flourish. Manisha was excited to be a part of the Samuels Family LA-HIP and believes that it "is an amazing opportunity in which I will be able to expand my scientific knowledge via hands-on activities." Manisha will attend the University of Southern California in the fall.



Somtochukwu 'Somto' Uzoegwu of King/Drew Magnet High School of Medicine and Science is plagued by the question "as to why some prenatal diseases cannot be cured." To answer this question, he dreams of being a pathologist and conducting

research that will discover treatments for disease. He looked forward to the lab experience that the Samuels Family LA-HIP gave him, as well as the chance to learn from leading researchers. Somtochukwu will attend Pomona College in the fall.

Research Abstract:

The Role of Cytotoxic Necrotizing Factor 1 (CNF1) in the Pathogenesis of E.coli K1-Mediated Neonatal Meningitis

Mentor: Prasadarao Nemani, PhD

Lab Personnel: Alex Chang, PhD

Key Words: Meningitis, CNF1, Macrophages, E.coli K1

Problem

Neonatal meningitis is a disease caused by inflammation of the meninges. There were 4,100 cases reported in the U.S. between 2003 and 2007. Symptoms include fever, headache, soft spots on the head and abnormal reflexes. The mortality rates for treated neonatal meningitis range from 20-30 percent. If left untreated, mortality rates can reach 100 percent. In addition, 50 percent of survivors of neonatal meningitis suffer long-term consequences such as mental retardation, hearing impairment and cortical blindness. Studying neonatal meningitis is important due to the emergence of antibiotic-resistant strains of bacteria, which has led to fewer viable treatment options in clinical settings. Escherichia coli K1 is the second-most prevalent cause of bacteria-mediated neonatal meningitis. Neonatal meningitis occurs when E. coli K1 enters the blood and invades a macrophage by using outer membrane protein A (OmpA) to attach to the macrophage receptor protein CD64, causing the macrophage to internalize the bacteria. After multiplication, the bacteria exit the macrophage and enter the bloodstream to the blood-brain barrier.

Hypothesis

CNF1 plays a critical role in the invasion of macrophages by Escherichia coli K1.

Methods

We used a Western Blot to verify the expression of CNF1 in our panel of bacterial strains. We used an invasion assay to compare the different rates of invasion for each bacterial strain into macrophages and human brain microvascular endothelial cells (HBMECs).

Results

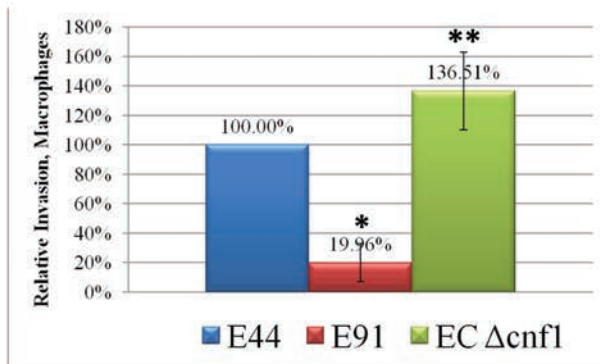
The mutant strain lacking CNF1 (Δ cnf1) invaded more than the wild type E44 strain in both macrophages and HBMECs.

Conclusion

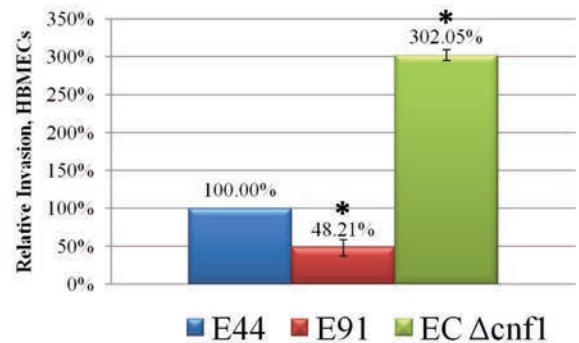
Unexpectedly, the Δ cnf1 strain invaded more than the wild type E44 strain, suggesting that CNF1 plays an inhibitory role in the invasion of E. coli K1 into both macrophages and HBMECs.

Results

Macrophages



Human Brain Microvascular Endothelial Cells



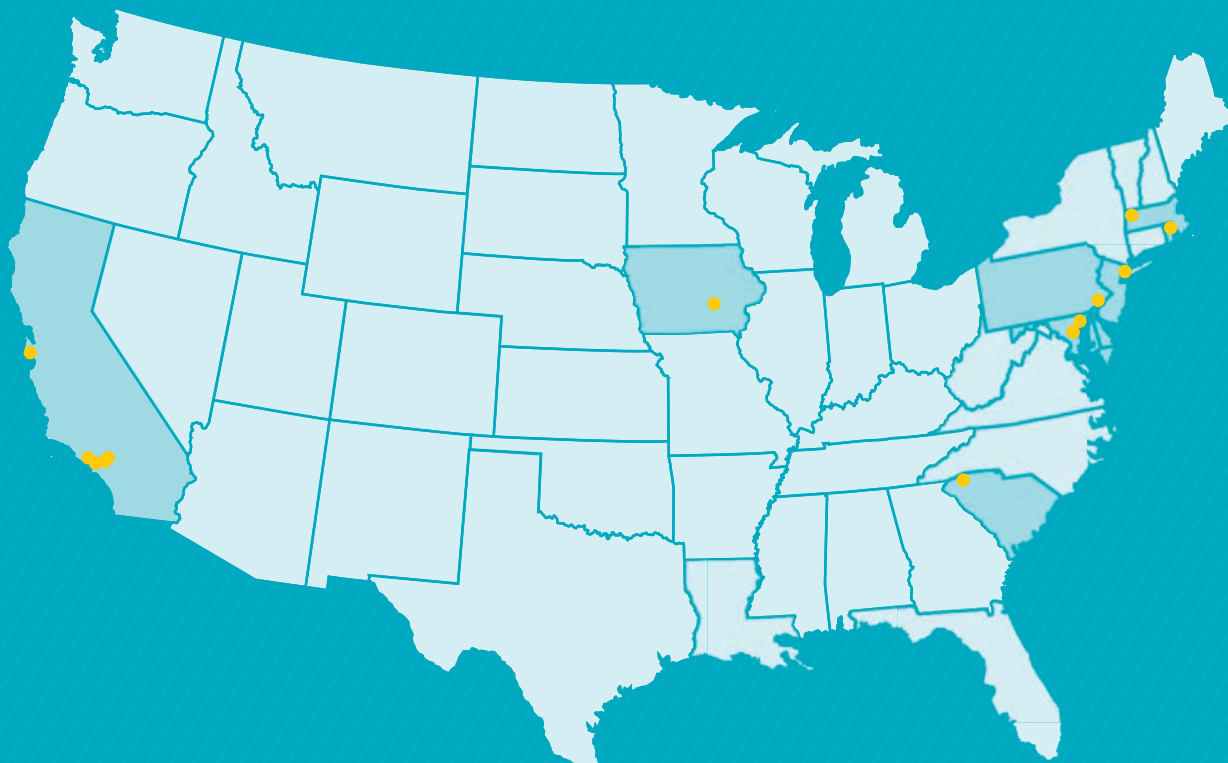
- The E91 (OmpA-) mutant strain invades **LESS** than the wild-type E44 *E. coli* K1 strain.
- The Δcnf1 (CNF1-) strain invades **MORE** than E44.

$p < 0.05$ compared to WT by Student's *t*-test; ** $p = 0.0747$

Assays were performed at least three times, averages are shown above.

COLLEGE MATRICULATION LA-HIP CLASS OF 2013

INTERN	HIGH SCHOOL	COLLEGE
Mercedes Adame	Edward R. Roybal Learning Center	Scripps College
Josselyn Barahona	John H. Francis Polytechnic High School	Williams College
Rogelio Caro	California Academy of Math and Science	University of Pennsylvania
Luis Curiel	John H. Francis Polytechnic High School	Johns Hopkins University
Rocio Del Cid	John Marshall High School	Crown College at the University of California, Santa Cruz
Andrew Gonzalez	Bravo Medical Magnet High School	University of California, Los Angeles
Nallely Lopez	South East High School	Williams College
Monica Loza	California Academy of Math and Science	Grinnell College
Donna Medel	Wallis Annenberg High School	Columbia University
Luis Angel Ocon	Renaissance Arts Academy	Furman University
Angel Ortiz	James A. Garfield High School	Brown University
Eduardo Romo	Warren High School	Johns Hopkins University
Manisha Sajani	Bravo Medical Magnet High School	University of Southern California
Somtochukwu Uzoegwu	King/Drew Magnet High School of Medicine and Science	Pomona College



SPECIAL THANKS



Bowling with the interns from the classes of 2012 and 2013, June 2013

High School Supporters

Gene Almeida

Dean of Students
California Academy of Math
and Science

Jayne Couchois

Magnet Coordinator
John H. Francis Polytechnic
Magnet High School

Millicent Dypiangco

Magnet Coordinator
Bravo Medical Magnet High School

Special Thanks

Alejandro Sanchez Alverado, PhD
Reginald Belhomme
Hayden Betts
Emil Bogenmann, PhD, EdD

Reneé A. Bianco, MEd
Santiago Chambers
Barbara Driscoll, PhD
Cara Esposito
Mercedes Gonzalez
Miguel Gonzalez
Carolina Herrera

Jim Jenkins
Jennifer Jing
Wendi Kellaris
Charlene Liebau
Ellie Malchione
Alexa Pearl Margalith
Jessica Medina
Justin Meloni
Alex Ostroff
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The Princeton Review
Leo Rangel
Roxana Rodriguez
Susan Rubin
Ben and Bobby Samuels
Lori and Theodore Samuels
Anand Upadhyaya
Kevin Walls
Sara Delgadillo



Mercedes Gonzalez (left) and D. Brent Polk, MD (right), present Somtochukwu "Somto" Uzoegwu with his certificate at the Science Symposium.

SPECIAL THANKS (continued)

CHLA Departments

Commuter Services
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Food Services
Foundation Department
Marketing Communications
Parking Office
Safety and Security
The Saban Research Institute
Transportation Department
Volunteer Office

Mentors

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Sebastian G. Bouret, PhD
David Cobrinik, MD, PhD
Yves DeClerck, MD
Barbara Driscoll, PhD
Muller Fabbri, MD, PhD
Mark Frey, PhD

Senta Georgia, PhD
Charles Gomer, PhD
Prasad Rao Nemani, PhD
D. Brent Polk, MD

Lab Personnel

Lucia Borriello, PhD
Taylor Brown
Alex Chang, PhD
Sophie Croizier, PhD
Philip E. Dubé, PhD
Angela Ferrario, PhD
Orquidea Garcia, PhD
Michael Hiatt, PhD
Long Hung
Dong Lai Qi, PhD
Joeeun Lee
Cambrian Liu, PhD
Marian Luna
Shivesh Punit, PhD

Raghava Reddy, PhD
Claudio Alberto Rivera, MD, MPH
Natalie Rucker
Unice Soh, PhD
Petra Wise, PhD
Sam Wong

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Barbara Driscoll, PhD
Cara Esposito
Mercedes Gonzalez
Charlene Liebau
Alexa Pearl Margalith

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Marianna and David Fisher
The Fletcher Jones Foundation
Leonetti/O'Connell Family Foundation
Mary Adams O'Connell and
Kevin O'Connell
The Rose Hills Foundation
The Samuels Family



Betsy Meyers, PhD, program director for Medical Research at the Doris Duke Charitable Foundation, addresses the participants at the Directors Meeting (see page 9 for more information)

SAMUELS FAMILY LA-HIP ADVISORY BOARD



**Mary Adams
O'Connell, MBA**

Mary Adams O'Connell has been a member of the Children's Hospital Los Angeles Board of Trustees since 2002. She serves on the Audit, Investment and The Saban Research Institute committees. Adams O'Connell is a member of First Families, and also a former president of Las Madrinas. Mary is president and CEO of Adams O'Connell, Inc., a family investment management company serving several generations of Adams family clients. She founded and chairs HealthyCity.org, a project using innovative data analysis and GIS mapping techniques to provide services for the underserved and to support policy, research and planning efforts for collaborating organizations. Healthy City expanded statewide in February 2010. Adams O'Connell graduated from Smith College and serves on the President's Council. She received her Master of Business Administration from the University of Missouri.



**Emil Bogenmann,
PhD, EdD**

Emil Bogenmann, PhD, EdD, is an associate professor in the Department of Pediatrics and holds a secondary appointment in the Department of Molecular Microbiology and Immunology at the Keck School of Medicine of the University of Southern California (USC). His laboratory research focused on the biology of neuralcrest-derived tumors such as retinoblastoma and neuroblastoma. Over the last two decades he has been involved in the training of high school students, undergraduate students, graduate students and postdoctoral fellows. Since 1995, Bogenmann

has been the director for Research Education at The Saban Research Institute of Children's Hospital Los Angeles.

Bogenmann completed his Doctor of Education degree in 2008 from the USC Rossier School of Education with a subspecialty in educational psychology. He established the Samuels Family Latino and African-American High School Internship Program (LA-HIP) in 2005. Bogenmann is also a director for the National Institutes of Health-sponsored Short Term Research Experience Program for Underrepresented Persons (STEP-UP), a research training program for undergraduate students.



Gus Dalis, EdD

Gus Dalis, EdD, has spent his career in education with an emphasis on health education. His interest is in developing new instructional approaches to teaching people health-related topics. Dalis has been an associate professor in the Department of Health Science at California State University, Northridge, and he served as a member of the Curriculum Development Writing Team of the national School Health Education Study. He also served as chair of the state of California Department of Education Curriculum Development Commission, and he is the past president of the American Association for Health Education.

Dalis received both his Bachelor of Science degree in physical education and his Doctor of Education degree from the University of California, Los Angeles.

SAMUELS FAMILY LA-HIP ADVISORY BOARD (continued)



Joe Duardo

Joe Duardo spent 24 years as a research scientist at the Xerox Corp. in Pasadena, where he specialized in the field of laser technology. His experimental and theoretical research advanced the understanding of the physics of lasers and led to the improvement of their design. He also served as evaluator of the application of lasers in government space and defense projects. Duardo also was principal investigator of a research project funded by NASA.

Duardo pioneered Xerox's Social Service Leave program, serving as a volunteer for a year at Lincoln High School in northeast Los Angeles. His exposure to the world of education prompted him to serve as a board member of the Whittier School District and as a member of the California School Board Association.

Duardo grew up in East Los Angeles, graduated from East Los Angeles Community College and completed his graduate studies at the California Institute of Technology (Caltech).



Stuart E. Gothold, EdD

Stuart E. Gothold, EdD, served for more than 20 years as school district and Los Angeles County superintendent. This leadership role connected Gothold with local, state and national educational leaders, and he continues to this day to serve as a consultant and advisor to many different organizations. He is an executive coach for the leadership team of a large group of California charter schools, and consults with school organizations and corporate

leaders on issues related to leadership and schools of the future. Gothold is clinical professor emeritus at the USC Rossier School of Education, where he teaches courses in leadership and school governance. He leads research teams of doctoral students in education studying the performance of urban schools.

Gothold graduated from Whittier High School and earned a Doctor of Education degree from the University of Southern California.



Charlene Liebau, MA

Charlene Liebau, MA, is currently the director of College Counseling Services after a 20-year career in college admissions. Most recently she served as director of Admissions at California Institute of Technology (Caltech), and prior to that as dean of Admission at Occidental College. Professional activities include service on committees to select National Merit, corporate and foundation scholars, and as a panel member at regional College Board and Western Association for College Admission Counseling (WACAC) seminars and conferences. In addition to her extensive experience in college counseling and admissions, she is a certified career counselor. Liebau is well-known for her years of dedicated service on many community, foundation, independent school and university boards of directors. Her leadership role in these organizations is noteworthy. Liebau has served as college counselor to Samuels Family LA-HIP students since 2008.

Liebaw holds a bachelor's degree from the University of California, Berkeley, and a master's degree in counseling from Stanford University.



DeAnn S. Marshall, MHA

DeAnn Marshall, MHA, serves as senior vice president, chief development and marketing officer at Children's Hospital Los Angeles. Prior to joining

Children's Hospital, she served as the chief marketing communications officer for Health Sciences at the University of California, San Diego. Marshall served as executive vice president and chief development officer for the Children's Hospital of Pittsburgh Foundation, providing executive leadership, strategic planning and operational direction for the \$300 million private foundation. She also served as director of Public Relations (1995-99), executive director of Public and Government Affairs (2000-02) and finally as vice president of Public and Government Affairs (2002-04) for the 235-bed Children's Hospital of Pittsburgh.

Marshall was named Communicator of the Year in 2003 by the Public Relations Society of America, and received the Touchstone Award from the American Hospital Association. She received a bachelor's degree in journalism (1988) with a minor in business administration from Duquesne University in Pittsburgh, and a Master of Health Administration (2012) from the University of Southern California.



Dave Master

Dave Master has probably guided more young people to careers in the arts than anyone else alive.

Internationally recognized as one of the premier educators in the field of animation, he has lectured throughout the world and has served on numerous educational advisory boards.

Master founded the ACME Animation Virtual Training Network while he was director of Artist Development at Warner Bros. Feature Animation. Master has worked extensively with young people while at various educational institutions, including California State Polytechnic University, Pomona, and Rowland High School, where he established the DaVinci Project, a collaborative, student-centered learning program for math and science. Master continues to be active in education and lectures on the topic of animation as a tool to educate and teach.



Bonnie McClure

Bonnie McClure has been a member of the Children's Hospital Los Angeles Board of Trustees since 2005. She serves as chairman of the Associates and Affiliates.

McClure chairs the Associates and Affiliates Advisory Committee and the Chaplaincy Advisory Board. In addition, she is vice chair of The Saban Research Institute

(continued)

SAMUELS FAMILY LA-HIP ADVISORY BOARD (continued)

Committee and serves as a member of the Development Advisory Campaign Cabinet, the Executive Committee and the Safety, Quality and Service Committee.

McClure is a member of First Families and the Emma Phillips Society. She is a former president of Children's Chain. She also oversees CHLA's tour docent training. In 2001, McClure helped coordinate Children's Hospital Los Angeles' Centennial Celebration.



Cheryl Saban, PhD

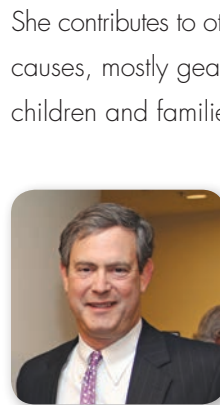
Cheryl Saban, PhD, has authored several books about self-worth, community service and personal involvement. But she doesn't just talk about these issues—she lives them.

Along with her husband, Haim, Dr. Saban is a longtime supporter of Children's Hospital Los Angeles. In 2003, the Sabans generously donated \$40 million to the Children's Hospital Los Angeles Research Institute—now named The Saban Research Institute—to support pediatric research. They are founding members of the Children's Fund 100, a core group of donors who support the hospital's mission-based giving program, the Children's Fund, with pledges of \$100,000 or more. Dr. Saban is currently an honorary member of the hospital's Board of Trustees and serves on The Saban Research Institute Committee.

Dr. Saban has a doctorate in psychology and is a member of the American Psychological Association. As part of her training, she had the unique opportunity of seeing Children's Hospital "at work" when she participated in an externship program at the Children's Center for Cancer and Blood

Diseases. She has also volunteered as a "cuddler" in the hospital's Newborn and Infant Critical Care Unit.

Dr. Saban is also affiliated with the Board of Overseers of the Keck School of Medicine of the University of Southern California, The Saban Free Clinic, The Nathanson Family Resource Center at the University of California, Los Angeles, and The Everychild Foundation.



Theodore (Ted) Samuels, MBA

She contributes to other domestic and international charitable causes, mostly geared toward the welfare of women, children and families.

Ted Samuels is president and director of Capital Guardian Trust Company and co-chair of the Children's Hospital Los Angeles Board of Trustees. He has been a member of the Board of Trustees since 2004. He received his bachelor's degree and Master of Business Administration from Harvard University. He is co-chair of the executive committee and serves on the governance, advancement and nominating committees. He and his wife, Lori, are significant contributors to the hospital and Second Century 200 members. The Samuels family made a gift to endow the program, naming it the Samuels Family Latino and African-American High School Internship Program and ensuring its longevity.

Members of the class of 2012 during their 2013 Summer BootCamp, sporting shirts from their chosen colleges and universities.



Samuels Family LA-HIP Mission Statement:

To inspire change and self-determination by igniting
a passion for scientific discovery.



Louis Curiel (left), Rogelio Caro and Manisha Sadjnani in the lab during "Hell Week"



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