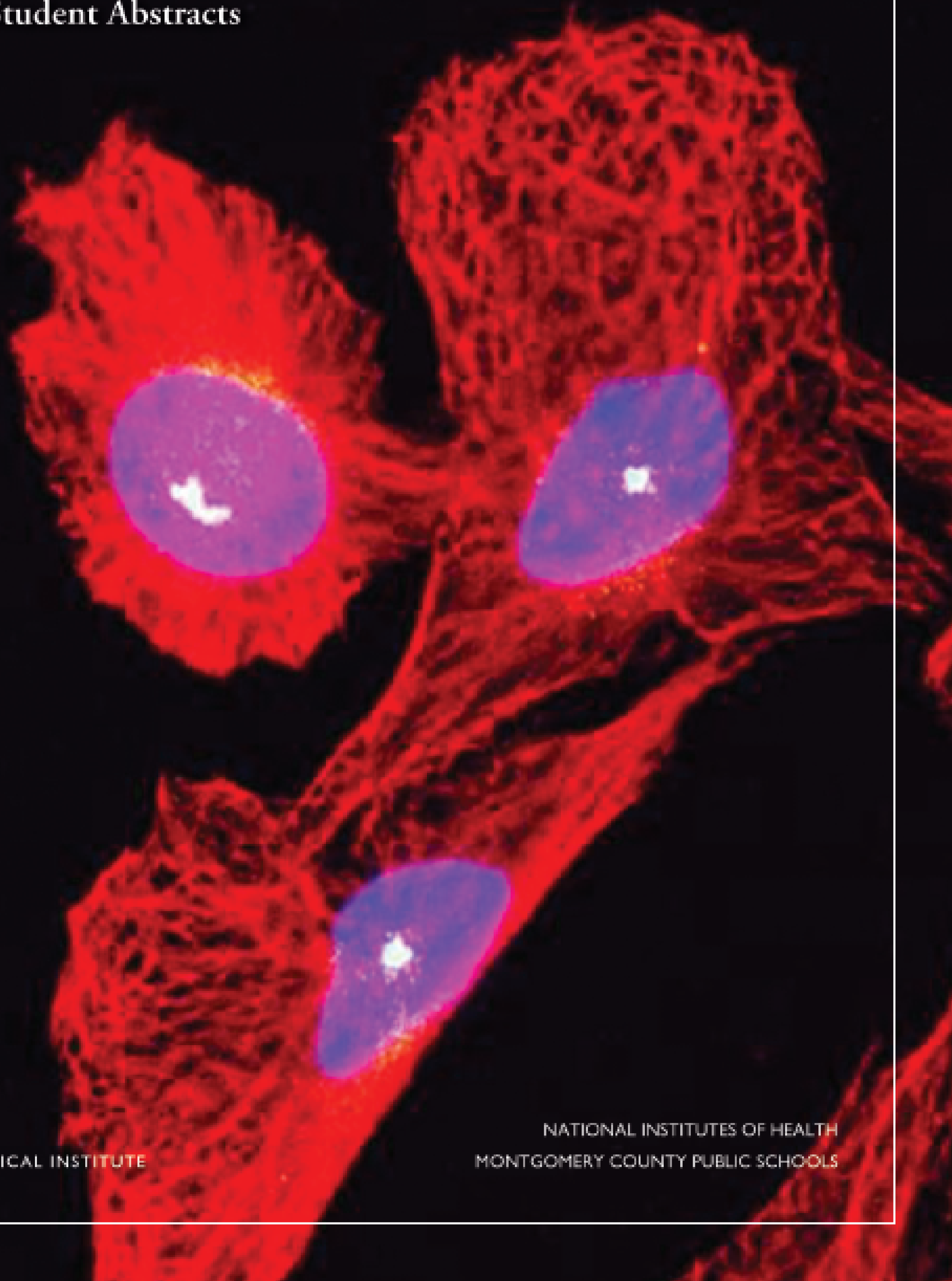
2009 Student *and* Teacher Internship Program

Program *and* Student Abstracts

May 7, 2009



HHMI
HOWARD HUGHES MEDICAL INSTITUTE

NATIONAL INSTITUTES OF HEALTH
MONTGOMERY COUNTY PUBLIC SCHOOLS

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Howard Hughes Medical Institute
www.hhmi.org

HHMI Office of Grants and Special Programs
www.hhmi.org/grants

National Institutes of Health
www.nih.gov

NIH Office of Science Education
http://science.education.nih.gov

Montgomery County Public Schools
www.montgomeryschoolsmd.org

Cover: Hamster cells stained with ant-tubulin-rhodamine conjugated antibody and pericentrin show centrosomal amplification. See abstract on page 14. The image was created using immunohistochemistry, visualized and captured with confocal microscopy. *(Courtesy of Ofelia Olivero, Ph.D., Laboratory of Cancer Biology and Genetics, National Cancer Institute)*

Photos: Paul Fetters

Student and Teacher Internship Program

Student Participants

2008–2009

Brent Abel, Paint Branch High School
Kavi Anandalingam, Walt Whitman High School
Mohammad Omar Bukhari, Northwest High School
Shivali Choxi, Sherwood High School
Ana Gabriela Coello, Albert Einstein High School
Tania Delgado, Colonel Zadok Magruder High School
Alma C. Gonzalez, Montgomery Blair High School
Sayeh Gorjifard, Thomas S. Wootton High School
Vidushani Jayalal, Gaithersburg High School
Philip Kong, Thomas S. Wootton High School
Michael Kovacs, Winston Churchill High School
Stephanie Kuo, Quince Orchard High School
Uzoamaka Okunji, Paint Branch High School
Kayla Perry, James Hubert Blake High School
Elie G. Pommier, Walt Whitman High School
Jean Ra, Walter Johnson High School
Sydney Rosebraugh, Sherwood High School
Shraddha Sheth, Paint Branch High School
Edward Sullivan, Poolesville High School
Peter Sylvers, Damascus High School
Seda Tolu, Colonel Zadok Magruder High School
Andrea Vaught, Bethesda–Chevy Chase High School
Samrawit Yalewayker, Wheaton High School

2009–2010

Tyler Babich, Rockville High School
Alex Clark, Colonel Zadok Magruder High School
Julian Curiel, Winston Churchill High School
Craig D'Cruz, Quince Orchard High School
Ramatullah Deme, James Hubert Blake High School
Danielle Dhillon, Northwest High School
Dieynaba Diagne, James Hubert Blake High School
Bianca Marie Ignacio, John F. Kennedy High School
Abigail Klein, Bethesda–Chevy Chase High School
Nicholas Kovacs, Winston Churchill High School
William Kovacs, Winston Churchill High School
Sarthak Kumar, Clarksburg High School
Andrew Li, Poolesville High School
Claire McWhite, Thomas S. Wootton High School
Tom Mou, Walter Johnson High School
Thomas Nehring, Damascus High School
Tam Nguyen, Gaithersburg High School
Victoria Poon, John F. Kennedy High School
Puja Sheth, Thomas S. Wootton High School
Konrad Slepoy, Walt Whitman High School
Jigisha Srivastav, Poolesville High School
Anh Truong, Sherwood High School
Amy Tuttle, Northwood High School
Mikias Wolde, Paint Branch High School
Leuk Woldeyohannes, Wheaton High School
Anna Zakas, Montgomery Blair High School
Krishan Zaveri, Seneca Valley High School

Teacher Participants

Summer 2008

Carrie Black, Westland Middle School
Chujor S. N. Chujor, Ph.D., Albert Einstein High School
Joel I. Cohen, Ph.D., Parkland Magnet Middle School for Aerospace Technology
Kimberly de la Cerda, Paint Branch High School
Brendon Friedman, Clarksburg High School
Jacob Hall, Bethesda–Chevy Chase High School
Selin Mammen, Ph.D., Seneca Valley High School
Terri Nostrand, Thomas S. Wootton High School
Donald J. Walker, Bethesda–Chevy Chase High School

Summer 2009

Franco Canet, Quince Orchard High School
Chujor S. N. Chujor, Ph.D., Albert Einstein High School
Joel I. Cohen, Ph.D., Parkland Magnet Middle School for Aerospace Technology
Kimberly de la Cerda, Paint Branch High School
John Ernst, Winston Churchill High School
Brendon Friedman, Clarksburg High School
Shelly Malik, Colonel Zadok Magruder High School
Terri Nostrand, Thomas S. Wootton High School

Introduction

Peter J. Bruns, Ph.D.
Vice President for Grants and Special Programs
Howard Hughes Medical Institute

I am pleased to welcome you to the 19th annual dinner symposium of the Montgomery County Public Schools (MCPS) Student and Teacher Internship Program (STIP) at the National Institutes of Health (NIH). This successful program enables students and teachers to become part of the NIH research community and work in state-of-the-art laboratories alongside some of the world's leading biomedical researchers.

Nine teachers who completed their internships were recognized at an event held at summer's end. Tonight's symposium honors the 23 high school students who recently completed their internships. The students will present the results of their investigations into areas such as obesity in children, bipolar disorder, endometriosis, stress-related diseases, fibroid tumors, autism, and malaria.

Participants in this program must demonstrate the commitment and perseverance that good science requires. In return, students learn how to design and conduct experiments professionally and then analyze and interpret the results. They gain a clearer understanding of what it means to be a scientist and contribute to a research team.

Teachers in the program are able to deepen their enthusiasm for science, learn current methods of laboratory research, and find better ways to communicate key principles of today's biology to students. Teachers who return for a second summer develop original laboratory inquiry-based lessons that are shared on the MCPS website and on HHMI's "For Educators" resource site on Cool Science (*www.hhmi.org/coolscience/resources/SPT--Home.php*).

Our guest speaker tonight is Robert M. Kao, a 2001 STIP intern who is now a National Science Foundation fellow in the laboratory of Andrew McMahon, Ph.D., in the Molecular and Cellular Biology Department at Harvard University. Bob came to his STIP laboratory work with a burning desire to answer a particular question: could a soybean leachate that inhibits plant growth selectively inhibit cancer cell growth? In the laboratory of Michael Birrer, M.D., Ph.D., at the National Cancer Institute, he pursued research in this important area—research that earned him the "best in category" prize in botany at the 2001 Intel International Science and Engineering Fair. The STIP program gave Bob a taste of professional-level research, and we are so pleased that he is continuing his graduate studies and has returned to inspire this year's STIP students.

I would like to recognize the parents and NIH preceptors and mentors whose enthusiasm, encouragement, and guidance make these achievements possible. Finally, this program could not happen without the dedicated work of Anita O'Neill, MCPS supervisor of science and engineering, and Bruce Fuchs, Ph.D., director, NIH Office of Science Education.

On behalf of the Howard Hughes Medical Institute, I extend to all of you a warm welcome. To the 32 program participants, we extend our heartiest congratulations and best wishes for your future endeavors.

Program Schedule

Student and Teacher Internship Program
Dinner Symposium
Thursday, May 7, 2009
HHMI Headquarters and Conference Center

5:30–6:00 p.m.	**Welcome Reception** *Great Hall*
6:00–6:45 p.m.	**Dinner** *Dining Room*
7:00–8:15 p.m.	**Research Presentations by Students** *Meeting Rooms D-115, D-116, D-124, D-125, Rathskeller*
8:15 p.m.	**Official Ceremony** *Auditorium*
	Welcome Peter J. Bruns, Ph.D. Vice President for Grants and Special Programs, Howard Hughes Medical Institute
	Opening Remarks Robert Tjian, Ph.D. President, Howard Hughes Medical Institute
	Remarks by a STIP Alumnus Robert M. Kao Class of 2001
	Presentation of Certificates to Program Participants Bruce A. Fuchs, Ph.D. Director, Office of Science Education, National Institutes of Health Gloria A. Seelman, M.A. Instructional Specialist, Office of Science Education, National Institutes of Health
	Concluding Comments Peter J. Bruns, Ph.D. Vice President for Grants and Special Programs, Howard Hughes Medical Institute
9:30 p.m.	**Adjournment**

Schedule of Student Presentations

Room D-115
Bruce A. Fuchs, Ph.D., convener

7:00 p.m.

STEPHANIE KUO, QUINCE ORCHARD HIGH SCHOOL
Oxygenase mechanism of retinal pigment epithelial specific protein, RPE65
Preceptor: T. MICHAEL REDMOND, PH.D., LABORATORY OF RETINAL CELL AND MOLECULAR BIOLOGY, NATIONAL EYE INSTITUTE

7:15 p.m.

SYDNEY ROSEBRAUGH, SHERWOOD HIGH SCHOOL
HIV-1 integrase double mutant, G140S/Q148H, and its components' resistance to raltegravir in vitro
Preceptor: YVES POMMIER, M.D., PH.D., LABORATORY OF MOLECULAR PHARMACOLOGY, NATIONAL CANCER INSTITUTE

7:30 p.m.

SAYEH GORJIFARD, THOMAS S. WOOTTON HIGH SCHOOL
A novel mechanism of genotoxicity induced by antiretroviral nucleoside reverse transcriptase inhibitors (NRTIs) and non-nucleoside reverse transcriptase inhibitors (NNRTIs) in *Erythrocebus patas* bone marrow
Preceptor: MIRIAM POIRIER, M.SC., PH.D., LABORATORY OF CANCER BIOLOGY AND GENETICS, NATIONAL CANCER INSTITUTE

7:45 p.m.

SHRADDHA SHETH, PAINT BRANCH HIGH SCHOOL
Role of variable region A of porcine endogenous retrovirus in binding and infection of human cells
Preceptor: TAKELE ARGAW, D.V.M., CENTER FOR BIOLOGICS EVALUATION AND RESEARCH, U.S. FOOD AND DRUG ADMINISTRATION

8:00 p.m.

PETER SYLVERS, DAMASCUS HIGH SCHOOL
Natural polyreactive antibodies bind to apoptotic cells
Preceptor: STEVEN KOZLOWSKI, M.D., CENTER FOR DRUG EVALUATION AND RESEARCH, U.S. FOOD AND DRUG ADMINISTRATION

Room D-116
Rashimi Gopal-Srivastava, Ph.D., convener

7:00 p.m.

Tania Delgado, Colonel Zadok Magruder High School
Effect of liarozole on uterine leiomyoma cells
Preceptor: William H. Catherino, M.D., Ph.D., Obstetrics and Gynecology, Uniformed Services University of the Health Sciences

7:15 p.m.

Uzoamaka Okunji, Paint Branch High School
Effects of AKAP13 gene mutation on cardiac function and output in mice models
Preceptor: James Segars, M.D., Program on Reproductive and Adult Endocrinology, Eunice Kennedy Shriver National Institute of Child Health and Human Development

7:30 p.m.

Andrea Vaught, Bethesda–Chevy Chase High School
The use of retroviral vectors for therapeutic gene delivery to hematopoietic stem cells
Preceptor: Maribeth V. Eiden, Ph.D., Laboratory of Cellular and Molecular Regulation, National Institute of Mental Health

7:45 p.m.

Samrawit Yalewayker, Wheaton High School
Effect of *Mest* on somatic growth regulation
Preceptor: Jeffrey Baron, M.D., Section on Growth and Development, Eunice Kennedy Shriver National Institute of Child Health and Human Development

Room D-124
John Glowa, Ph.D., convener

7:00 p.m.

MICHAEL KOVACS, WINSTON CHURCHILL HIGH SCHOOL
Effect of lymphatic filariasis on the immune response to malaria
Preceptor: THOMAS B. NUTMAN, M.D., LABORATORY OF PARASITIC DISEASES, NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

7:15 p.m.

SEDA TOLU, COLONEL ZADOK MAGRUDER HIGH SCHOOL
Pharmacological treatment of mouse models of autism
Preceptor: JACQUELINE N. CRAWLEY, PH.D., LABORATORY OF BEHAVIORAL NEUROSCIENCE, NATIONAL INSTITUTE OF MENTAL HEALTH

7:30 p.m.

KAYLA PERRY, JAMES HUBERT BLAKE HIGH SCHOOL
Peer intervention in the BTBR T+tf/J mouse model of autism
Preceptor: JACQUELINE N. CRAWLEY, PH.D., LABORATORY OF BEHAVIORAL NEUROSCIENCE, NATIONAL INSTITUTE OF MENTAL HEALTH

7:45 p.m.

EDWARD SULLIVAN, POOLESVILLE HIGH SCHOOL
COMT, Dysbindin, and their interaction: impact on social behavior and recognition memory
Preceptor: FRANCESCO PAPALEO, PH.D., CLINICAL BRAIN DISORDERS BRANCH, NATIONAL INSTITUTE OF MENTAL HEALTH

8:00 p.m.

BRENT ABEL, PAINT BRANCH HIGH SCHOOL
Suppression of the transcriptional activity of glucocorticoid receptor (GR) by liver X receptors (LXRs): crosstalk between two receptor molecules
Preceptor: TOMOSHIGE KINO, M.D., PH.D., UNIT ON PEDIATRIC ENDOCRINOLOGY, EUNICE KENNEDY SHRIVER NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

Room D-125
Charles Dearolf, Ph.D., convener

7:00 p.m.	ELIE G. POMMIER, WALT WHITMAN HIGH SCHOOL Identification and cloning of a new ADAMTS13 alternative splicing form: analysis of expression and function **Preceptor:** CHAVA KIMCHI-SARFATY, PH.D., CENTER FOR BIOLOGICS EVALUATION AND RESEARCH, U.S. FOOD AND DRUG ADMINISTRATION
7:15 p.m.	PHILIP KONG, THOMAS S. WOOTTON HIGH SCHOOL Elucidating nuclear localization of ADAMTS13, a secreted thrombotic protease **Preceptor:** CHAVA KIMCHI-SARFATY, PH.D., CENTER FOR BIOLOGICS EVALUATION AND RESEARCH, U.S. FOOD AND DRUG ADMINISTRATION
7:30 p.m.	VIDUSHANI JAYALAL, GAITHERSBURG HIGH SCHOOL Protein interaction with the Rep-P region of human β-globin locus control region in myelogenous leukemia cells **Preceptor:** MIRIT ALADJEM, PH.D., LABORATORY OF MOLECULAR PHARMACOLOGY, NATIONAL CANCER INSTITUTE
7:45 p.m.	JEAN RA, WALTER JOHNSON HIGH SCHOOL Interactions of *p53, SMAD4,* and E-cadherin on the differentiation and aggressiveness of breast cancer **Preceptor:** JEFFREY GREEN, M.D., LABORATORY OF CANCER BIOLOGY AND GENETICS, NATIONAL CANCER INSTITUTE
8:00 p.m.	KAVI ANANDALINGAM, WALT WHITMAN HIGH SCHOOL Associations between the *FTO* gene and eating behavior in children **Preceptor:** JACK A. YANOVSKI, M.D., PH.D., PROGRAM IN DEVELOPMENTAL ENDOCRINOLOGY AND GENETICS, EUNICE KENNEDY SHRIVER NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

Rathskeller
Barry Komisarak, Ph.D., convener

7:00 p.m.

MOHAMMAD OMAR BUKHARI, NORTHWEST HIGH SCHOOL
Positron emission tomography and bipolar disorder:
radiotracer development for the imaging of protein kinase C
Preceptor: VICTOR W. PIKE, PH.D., MOLECULAR IMAGING BRANCH,
NATIONAL INSTITUTE OF MENTAL HEALTH

7:15 p.m.

ANA GABRIELA COELLO, ALBERT EINSTEIN HIGH SCHOOL
Stress and the regulation of the corticotropin releasing hormone
Preceptor: GRETI AGUILERA, M.D., SECTION ON ENDOCRINE PHYSIOLOGY, EUNICE
KENNEDY SHRIVER NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

7:30 p.m.

SHIVALI CHOXI, SHERWOOD HIGH SCHOOL
Identification of structural determinants on PEDF-R responsible for
binding PEDF
Preceptor: S. PATRICIA BECERRA, PH.D., LABORATORY OF RETINAL CELL AND
MOLECULAR BIOLOGY, NATIONAL EYE INSTITUTE

7:45 p.m.

ALMA C. GONZALEZ, MONTGOMERY BLAIR HIGH SCHOOL
Endometrial stem cells and their relationship to the development of
endometriosis and chronic pelvic pain
Preceptor: ALAN DECHERNEY, M.D., REPRODUCTIVE BIOLOGY AND MEDICINE BRANCH,
EUNICE KENNEDY SHRIVER NATIONAL INSTITUTE OF CHILD HEALTH AND
HUMAN DEVELOPMENT

Research
Abstracts

Room D-115
7:00 p.m.

Oxygenase mechanism of retinal pigment epithelial specific protein, RPE65

STEPHANIE KUO, QUINCE ORCHARD HIGH SCHOOL

Preceptor: T. MICHAEL REDMOND, PH.D., LABORATORY OF RETINAL CELL AND MOLECULAR BIOLOGY, NATIONAL EYE INSTITUTE

Mentor: EUGENIA POLIAKOV, PH.D., LABORATORY OF RETINAL CELL AND MOLECULAR BIOLOGY, NATIONAL EYE INSTITUTE

STEPHANIE KUO
QUINCE ORCHARD HIGH SCHOOL

SUMMARY

We are studying the mechanisms of the retinoid isomerase, RPE65, which is vital for vision. Using heavy isotope labels, we hope to determine whether the enzyme works as an oxygenase. Ultimately, with a more comprehensive knowledge of the mechanisms of the enzyme, we may apply and enrich our understanding of RPE65's role in eye diseases such as Leber's congenital amaurosis type 2.

ABSTRACT

Retinal pigment epithelial-specific protein, RPE65, is the important retinoid isomerase of the visual cycle. In the visual cycle, the enzyme lecithin retinol acyltransferase esterifies all-trans retinol into all-trans retinyl esters, which RPE65 isomerizes to 11-cis retinol. Specific mutations in RPE65 can knock out the isomerase function of the enzyme and, as a result, can lead to severe early-onset eye diseases such as Leber's congenital amaurosis type 2 and retinitis pigmentosa type 20. The enzymatic mechanism of RPE65 is still not completely understood. RPE65 is closely related to the carotenoid oxygenases, which suggests that RPE65 is itself an oxygenase. To test this hypothesis, we made isotopically labeled [15-2H, 18O] all-trans retinol and purified it through normal phase high-pressure liquid chromatography (HPLC) and analyzed it by mass spectrometry, which revealed a peak of three mass units higher than unlabeled retinol. The "heavy" retinol was given to human HEK293 cells transfected with RPE65 and LRAT DNA in culture. Retinol was later extracted from the cells, and the isomers were separated and purified by normal phase HPLC. The 11-cis isomer was collected and then mixed with 2,5-dihydroxybenzoic acid matrix for mass spectrometry characterization (MALDI-TOF). The mass spectrometry analysis revealed a large peak of two mass units lower than the "heavy" retinol; while the retinol kept the deuterium, it did not maintain the heavy oxygen label. The exchange of 18O to 16O suggests that the enzyme is incorporating 16O to the retinol product, which suggests that RPE65 is an oxygenase.

HIV-1 integrase double mutant, G140S/Q148H, and its components' resistance to raltegravir in vitro

Room D-115
7:15 p.m.

SYDNEY ROSEBRAUGH, SHERWOOD HIGH SCHOOL

Preceptor: YVES POMMIER, M.D., PH.D., LABORATORY OF MOLECULAR PHARMACOLOGY, NATIONAL CANCER INSTITUTE

Mentor: CHRISTOPHE MARCHAND, PH.D., LABORATORY OF MOLECULAR PHARMACOLOGY, NATIONAL CANCER INSTITUTE

SYDNEY ROSEBRAUGH
SHERWOOD HIGH SCHOOL

SUMMARY

The enzyme integrase prepares the DNA of HIV and inserts it into the host's DNA. Previous studies have found that the rate of HIV's replication decreases with the inhibition of integrase. The first approved integrase inhibitor, raltegravir, has revolutionized HIV treatment as therapy for patients who have developed multiple resistance to other antiretroviral drugs. Despite major success, mutations for resistance to raltegravir have already been reported in these patients. The aim of the present study is to understand raltegravir resistance mechanisms and to identify novel integrase inhibitors that will circumvent such resistances.

ABSTRACT

Several compounds have been found to inhibit HIV-1 integrase, thus decreasing the rate of HIV replication. However, HIV, being a retrovirus, is capable of quickly generating different mutations that are resistant to these drugs. Raltegravir, the only approved inhibitor of integrase, has become a novel therapy for patients with multiple resistances to other retroviral drugs. Despite major success, mutations with resistance to raltegravir have already been reported in these patients, who then experience treatment failure. A double mutation (G140S/Q148H) responsible for raltegravir resistance has been identified in the integrase gene of several patients. It has been recently suggested that the single mutation, G140S, does not confer resistance to raltegravir alone, but instead rescues the viral fitness of the otherwise catalytically inactive mutation, Q148H. This double mutant exacts one of the highest resistance levels to raltegravir (7- to 8-fold decrease in sensitivity), and its catalytic activity level is almost identical to that of the wild type. We have expressed and purified each single and double mutant and compared the catalytic activity of these enzymes to the wild type. Preliminary results seem to confirm the fitness rescue of Q148H by G140S. We plan to investigate raltegravir resistance mechanisms by further characterizing this double mutant in biochemical assays. We also plan to study cross-resistance to other integrase inhibitors and to implement a high-throughput screening assay using G140S/Q148H to overcome resistance to raltegravir.

Room D-115
7:30 p.m.

A novel mechanism of genotoxicity induced by antiretroviral nucleoside reverse transcriptase inhibitors (NRTIs) and non-nucleoside reverse transcriptase inhibitors (NNRTIs) in *Erythrocebus patas* bone marrow

SAYEH GORJIFARD, THOMAS S. WOOTTON HIGH SCHOOL

Preceptor: MIRIAM POIRIER, M.SC., PH.D., LABORATORY OF CANCER BIOLOGY AND GENETICS, NATIONAL CANCER INSTITUTE

Mentor: OFELIA OLIVERO, PH.D., LABORATORY OF CANCER BIOLOGY AND GENETICS, NATIONAL CANCER INSTITUTE

SAYEH GORJIFARD
THOMAS S. WOOTTON
HIGH SCHOOL

SUMMARY

Evidence of DNA damage was observed in bone marrow cells taken from the offspring of Erythrocebus patas *monkey mothers given human-equivalent doses of anti-AIDS drugs. It has been demonstrated that some of these drugs are transplacental carcinogens, meaning that the drug is given to a pregnant individual and the offspring are subject to an increase in cancer risk. This study seeks to understand the mechanisms underlying the carcinogenicity of the anti-AIDS drugs.*

ABSTRACT

Antiretroviral therapy, which includes nucleoside reverse transcriptase inhibitors (NRTIs) and non-nucleoside reverse transcriptase inhibitors (NNRTIs), virtually eliminates maternal-fetal HIV-1 transmission when given to HIV-1-infected mothers. However, the NRTI zidovudine (AZT) is a transplacental carcinogen in mice. Also, in utero exposure to the NRTI combination AZT plus lamivudine (3TC) results in multiple genotoxic effects in the offspring of exposed CD-1 mice and *Erythrocebus patas* monkeys. Here, we studied bone marrow (mesenchymal cells) taken from monkey infants exposed in utero to human-equivalent protocols containing either no drugs (n=3), AZT/3TC (n=3), AZT/3TC plus the NRTI abacavir (ABC) (n=3), or AZT/3TC plus the NNRTI nevirapine (NVP) (n=3). Infant bone marrow cells were examined at birth, 1 day, and 3 years of age for genotoxicity in the form of micronuclei, and micronuclei containing kinteochore material. Examination of 1,000–5,000 cells total for each treatment in the monkeys revealed that approximately 1.0% of cells from unexposed monkeys and approximately 2.0–6.5% of cells from antiretroviral drug-exposed monkeys contained micronuclei. The rate of kinetochore-positive micronuclei was 0.15% in cells from unexposed monkeys and 0.75–3.5% in cells from drug-exposed monkeys. Thus, not only did the NRTI/NNRTI exposures result in more frequent micronucleus formation, but these exposures also induced a novel abnormal chromosomal segregation, as evidenced by the micronuclei containing kinetochore material. The cellular biologic consequences of these events are currently unclear, but malfunction of the mitotic spindle could result in missegregation of chromosomes, thereby producing micronuclei containing kinetochore material. We therefore studied centrosomal amplification (more than two centrosomes) to validate micronuclei and kineteochore analysis. Further consequences could include genomic instability, mutagenesis, and increased cancer risk.

Role of variable region A of porcine endogenous retrovirus in binding and infection of human cells

Room D-115
7:45 p.m.

SHRADDHA SHETH, PAINT BRANCH HIGH SCHOOL

Preceptor: TAKELE ARGAW, D.V.M., GENE TRANSFER AND IMMUNOGENICITY BRANCH, CENTER FOR BIOLOGICS EVALUATION AND RESEARCH, U.S. FOOD AND DRUG ADMINISTRATION

Mentor: CAROLYN WILSON, PH.D., GENE TRANSFER AND IMMUNOGENICITY BRANCH, CENTER FOR BIOLOGICS EVALUATION AND RESEARCH, U.S. FOOD AND DRUG ADMINISTRATION

SHRADDHA SHETH
PAINT BRANCH HIGH SCHOOL

SUMMARY

Porcine products (pig cells, tissues, and organs) have been identified as a possible donor source to remedy the organ shortage crisis. However, previous studies indicate that the use of porcine products in humans poses the risk of human infection with the porcine endogenous retrovirus (PERV). Studying the characteristics of viral entry of PERV in human cells is essential to understanding the compatibility of porcine products in humans.

ABSTRACT

The recent interest in the clinical use of porcine organs for xenotransplantation (the transplant of living cells, tissues, or organs from one species to another) has created the possibility of using pig cells, tissues, and organs as a donor source to remedy the current shortage of organs for human patients. Unfortunately, previous studies have shown that xenotransplantation of porcine organs poses the risk of human infection with the porcine endogenous retrovirus (PERV). Thus, understanding the biology of PERV in human cells is critical to facilitating the safe use of porcine products in humans.

PERV has three receptor classes based on its envelope gene: PERV-A, -B, and -C. Previous studies indicate that both PERV-A and PERV-B are infectious to both human and porcine cells; PERV-C, however, is infectious only to pig cells.

The PERV envelope is a glycoprotein. It is cleaved into two subunits: the surface envelope polyprotein (SU), harboring the receptor binding domain (RBD), and the transmembrane protein (TM).

Using knowledge obtained from previous studies, we used the chimeric PERV-A/C envelope as a starting point for our mutagenesis studies. The mutant chimeric PERV-A/C envelope, with only two single amino acid substitutions, Q374R and I412V, has the ability to restore infectivity to human cells to a titer equivalent of PERV-A. In an attempt to make PERV-C infectious, we substituted the two amino acids, Q374R and I412V, into it. However, no infectivity was observed in human cells, suggesting that other regions were required for human cell infection.

Since then, we have shifted our focus to the RBD. Identifying the amino acids of the RBD that influence the infectivity and tropism of PERV is essential to understanding the binding properties and infection properties of PERV in human cells.

The purpose of our study is to swap parts of the RBD, variable region A (VRA), into mutant Q374R I412V PERV-C to identify the role of the VRA on PERV infection and cell tropism in human cells. From this study, we hope to be able to identify the specific sequences necessary to change the tropism of PERV-C.

Determining the specific regions and sequences of the PERV envelope necessary for human cell infection is critical for vaccine research. The creation of a vaccine is vital in efforts to eliminate the risk of infection via xenotransplantation of porcine products.

Room D-115
8:00 p.m.

PETER SYLVERS
DAMASCUS HIGH SCHOOL

Natural polyreactive antibodies bind to apoptotic cells

PETER SYLVERS, DAMASCUS HIGH SCHOOL

Preceptor: STEVEN KOZLOWSKI, M.D., CENTER FOR DRUG EVALUATION AND RESEARCH, U.S. FOOD AND DRUG ADMINISTRATION

Mentor: ZHAOHUA ZHOU, PH.D., CENTER FOR DRUG EVALUATION AND RESEARCH, U.S. FOOD AND DRUG ADMINISTRATION

SUMMARY

In every human being, a hundred thousand cells are produced every second by mitosis, and a similar number die by apoptosis. Apoptosis, also known as programmed cell death, is a natural cellular mechanism that destroys cells. If apoptotic cells are not cleared from the body, they will accumulate. It is estimated that the dysregulation of apoptosis contributes to half of all the major medical illnesses that currently lack adequate therapy or prevention. Clearance of the apoptotic cells in mammalian systems is regulated by numerous engulfment ligands or "eat me" signals, including lipids, sugars, and proteins, which are exposed on the surface of apoptotic cells. These newly exposed signals then become targets of the immune system, including natural antibodies, of which the majority are polyreactive. Using human T cells as a model, we found by flowcytometry assay that monoclonal polyreactive antibodies bound to apoptotic but not to live cells. Further imaging techniques, including fluorescence microscopy and ImageStream analysis, showed that polyreactive antibodies could recognize different parts or sites of apoptotic cells. Binding of natural polyreactive antibodies with ligands exposed on or in the apoptotic cells may provide "bridging" with macrophages that will engulf the apoptotic cells.

ABSTRACT

Apoptosis, or programmed cell death, is a highly regulated process of cell deletion and plays a fundamental role in the maintenance of tissue homeostasis. Tissue homeostasis is dependent not only on the degree of mitosis and apoptosis, but also on the balance between cell death and cell clearance. It has been widely shown that ligands or "eat me" signals, including lipids, sugars, and proteins, are exposed on the surface of apoptotic cells. Since natural polyreactive antibodies can bind to a variety of self- and non-self-antigens, it was hypothesized that polyreactive antibodies may have a role in the clearance of apoptotic cells. In this study, we used various methods, including ultraviolet (UV) light, receptor ligation (activation-induced cell death, AICD), and HIV infection to make human peripheral blood T cells apoptotic. Then, live cells and apoptotic cells were incubated with a panel of monoclonal monoreactive antibodies or polyreactive antibodies and evaluated by flowcytometry assay. It was found that the polyreactive antibodies dramatically bound to apoptotic cells but not to live cells. The monoreactive antibodies did not bind to either live cells or apoptotic cells. Fluorescence microscopy and ImageStream techniques were then used to localize the binding sites of polyreactive antibodies within the apoptotic cells. For example, in cells made apoptotic by UV treatment, the polyreactive antibody clone 2E4 bound to the nucleus of 8.15% of the cells, to the membrane of 4.07% of the cells, and to the cytoplasm of 87.8% of the cells. These data indicated that the natural polyreactive antibodies can bind to various ligands exposed on or in the apoptotic cells and thus may provide "bridging" with macrophages to engulf the apoptotic cells.

Effect of liarozole on uterine leiomyoma cells

Tania Delgado, Colonel Zadok Magruder High School

Preceptor and Mentor: William H. Catherino, M.D., Ph.D., Obstetrics and Gynecology, Uniformed Services University of the Health Sciences

Room D-116
7:00 p.m.

Tania Delgado
Colonel Zadok Magruder High School

Summary

Uterine leiomyomas are the most frequently diagnosed uterine tumors in women of reproductive age, occurring in 20–50% of women older than 30 years. In an effort to stop the growth of leiomyomas, a drug was used to inhibit an upregulated gene that could be responsible for the development of these tumors. We are currently studying the effects of the drug to further understand the developmental activity of uterine leiomyomas.

Abstract

Uterine leiomyomas are benign tumors commonly found in women of reproductive age, occurring in 20–50% of women older than 30 years. These tumors are clinically significant, as their enlargement can cause pelvic pain, menorrhagia, reduced fertility, miscarriage, and other serious gynecological problems. Currently, the sole definitive treatment is hysterectomy, the surgical removal of the uterus. Uterine leiomyomas are characterized by an extracellular matrix (ECM) that is atypical in its volume, content, density, and structure compared to that of myometrium, the normal uterine tissue. We have recently identified molecular alterations resulting in decreased intracellular all-trans retinoic acid (ATRA) concentration in leiomyoma cells that may induce the abnormal characteristics of the tumors. Genes involved in the production of retinoic acid (RA), the oxidized form of vitamin A, have been found to be reduced in leiomyoma surgical specimens, while the RA metabolizing genes were found to be increased. The imbalance results in a reduced amount of active RA available to regulate important pathways in the cell. Cytochrome P450 26A1 (*CYP26A1*), a gene responsible for RA metabolism to inactive metabolites, is overexpressed in leiomyomas compared to myometrium. The overexpression of *CYP26A1* causes a reduced amount of active RA. In this study, the drug liarozole, a *CYP26A1* inhibitor, was used on immortalized leiomyoma cell lines to determine the effect of treatment on leiomyoma cell proliferation. A cell proliferation study was conducted using liarozole at a range of different concentrations. The percent growth of cells treated with liarozole was then compared to the percent growth of leiomyoma cells that proliferated under no treatment. We found that after treatment with liarozole, leiomyoma cells proliferation was inhibited, potentially by inhibiting *CYP26A1*, and the growth of leiomyoma cells was decreased. These results demonstrate that increasing RA exposure inhibits leiomyoma cell proliferation. They also suggest that liarozole could be used as a treatment for uterine leiomyomas.

Room D-116
7:15 p.m.

Effects of AKAP13 gene mutation on cardiac function and output in mice models

UZOAMAKA OKUNJI, PAINT BRANCH HIGH SCHOOL

Preceptor: JAMES SEGARS, M.D., PROGRAM ON REPRODUCTIVE AND ADULT ENDOCRINOLOGY, EUNICE KENNEDY SHRIVER NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

Mentor: CATHERINE GUO, B.S., PROGRAM ON REPRODUCTIVE AND ADULT ENDOCRINOLOGY, EUNICE KENNEDY SHRIVER NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

UZOAMAKA OKUNJI
PAINT BRANCH HIGH SCHOOL

SUMMARY

I am researching the effects from a mutation of AKAP13, a protein that is essential in heart cell development, by using mice models. I am measuring whether the mutation increases or decreases cardiac rates and also measuring the weight and size of the mutant hearts for signs of hypertrophy, the enlargement of the heart.

ABSTRACT

My study investigates the effects of cardiac output and heart rate in a mouse model with half the amount of AKAP13 expressed (heterozygotes). AKAP13 is an α-kinase anchoring protein, which functions to bind to the regulatory subunit of protein kinase A (PKA) and to confine it to discrete locations within the cell. A complete knockout (homozygous recessive) of the AKAP13 gene results in embryonic death at day 9.5–10.5 due to failure in heart formation. Specifically, AKAP13 is associated with actin and is required for sarcomere development in cardiomyocytes. Since AKAP13 is required for heart formation and is present in adult hearts, I examined adult heterozygous mice for abnormalities in heart function and compared the data with data from adult wild-type mice. Through DNA extraction, purification, and amplification, I determined which mice were heterozygous and therefore had an insufficient amount of AKAP13. The wild-type and heterozygous mice underwent magnetic resonance imaging (MRI) to evaluate cardiac output and to observe any abnormalities in heart anatomy due to hypertrophy, the enlargement of a targeted organ. Blood pressure recordings and electrocardiogram (ECG) scans were used to average the resting heart rate for both genotypes. Heterozygous mice for mutant AKAP13 showed a significant decrease in systolic and diastolic blood pressure and heart rate due to inhibition of the cardiomyocytes, thus resulting in lower cardiac output. This knowledge can be used to study similar patterns in human models linked to AKAP13, which will be significant in treating illnesses such as heart disease.

The use of retroviral vectors for therapeutic gene delivery to hematopoietic stem cells

Room D-116
7:30 p.m.

ANDREA VAUGHT, BETHESDA–CHEVY CHASE HIGH SCHOOL

Preceptor: MARIBETH V. EIDEN, PH.D., LABORATORY OF CELLULAR AND MOLECULAR REGULATION, NATIONAL INSTITUTE OF MENTAL HEALTH

Mentor: MEIHONG LIU, PH.D., LABORATORY OF CELLULAR AND MOLECULAR REGULATION, NATIONAL INSTITUTE OF MENTAL HEALTH

ANDREA VAUGHT
BETHESDA–CHEVY CHASE
HIGH SCHOOL

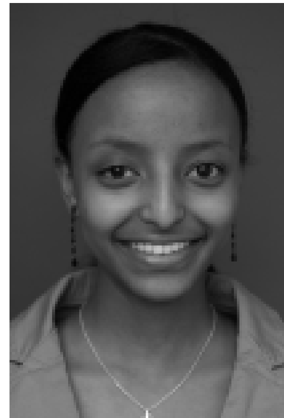
SUMMARY

Gene therapy is the treatment of a disease by expressing a therapeutic gene in the defective cell. Retroviral vectors are particularly useful as therapeutic gene delivery tools because of their ability to integrate and stably express genes in the genome of target cells. However, they do exhibit some deleterious properties that compromise their efficiency. Our goal is to investigate how helpful some possible solutions to this problem and others may be so we can create a safer tool for gene therapy.

ABSTRACT

Retroviral vectors are based on RNA viruses that use the enzyme reverse transcriptase to transcribe their RNA genome into double-stranded DNA, which then integrates into the host's cell genome. Vectors made from some of these viruses have been useful in the past for various gene therapies, but problems arose from their use in the treatment of X-linked severe combined immunodeficiency (X-SCID). Several years after patients were treated with retroviral vector-mediated gene delivery into their hematopoietic stem cells, they developed cancer. It has been determined that the problem with these retroviral vectors was that they integrated adjacent to an oncogene, thereby inappropriately activating its expression. We are trying to offset these effects by making a self-inactivating vector that will not affect the surrounding genes. In many cases, the vectors are silenced as well when the stem cells differentiate into their final cell types. To counter this, we will insert a human replicator that has been shown to regulate gene expression. The replicator will also allow the vector to integrate into areas in the genome that are usually inaccessible. The vector will be synthesized using mutagenesis to make it self-inactivating and ligation to insert the replicator. The vector will then be transfected into human bone marrow stem cells. The mCherry gene will allow the infected cells to be viewed with immunofluorescence microscopy. Using this technique, we can monitor the infection and expression levels of these vectors and compare them with regular vectors to determine the effectiveness of self-inactivation and the human replicator. If the new vectors are more effective, they could be used in the treatment of X-SCID and other diseases currently treated with retroviral-mediated gene delivery.

Room D-116
7:45 p.m.



SAMRAWIT YALEWAYKER
WHEATON HIGH SCHOOL

Effect of *Mest* on somatic growth regulation

SAMRAWIT YALEWAYKER, WHEATON HIGH SCHOOL

Preceptor: JEFFREY BARON, M.D., SECTION ON GROWTH AND DEVELOPMENT, EUNICE KENNEDY SHRIVER NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

Mentor: KEVIN BARNES, PH.D., SECTION ON GROWTH AND DEVELOPMENT, EUNICE KENNEDY SHRIVER NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

SUMMARY

It is not known why growth in body size slows down with age and eventually stops, so that adults do not continue to grow larger. We have previously identified some genes that may be responsible for this growth deceleration. In our current study, we have generated mice with an extra copy of one of these genes to study its effect on growth. The overall goal of these experiments is to improve our understanding of childhood growth disorders and gain insights into the unregulated growth of cancers.

ABSTRACT

In mammals the rate of somatic growth is rapid in early postnatal life but decelerates with age and eventually stops. Using microarray analysis, our group previously identified a set of 11 imprinted genes that show marked downregulation of mRNA expression with age postnatally in multiple tissues. One of these genes, *Mest* (mesoderm-specific transcript), is a hydrolase of unknown substrate specificity. Targeted ablation of *Mest* in mice results in decreased body size, suggesting that the gene positively regulates somatic growth. We therefore hypothesized that the decrease in expression of *Mest* with age contributes to postnatal growth deceleration. To test this hypothesis, our group generated transgenic mice that overexpress *Mest*. Heterozygous transgenic mice were bred with wild-type mice, and the offspring were genotyped by extracting DNA from tail samples and PCR amplifying the transgene. Subsequent real-time RT-PCR demonstrated that the transgene was expressed in liver, kidney, and lung of 4-week-old mice at levels equal to or exceeding levels found in 1-week-old wild-type mice. Preliminary data (combining mice from different transgenic founders) showed that, in male mice, body weight was unaffected, and in females, the body weight of transgenic mice was actually less than that of wild-type mice (13.0 ± 0.2 vs. 13.6 ± 0.2, mean ± SEM, $P < 0.04$, at 4 weeks of age; 17.6 ± 0.4 vs. 19.0 ± 0.4, $P < 0.03$, at 8 weeks of age). Thus, the preliminary data do not support the hypothesis that *Mest* positively regulates somatic growth. However, we plan to breed additional mice to study the individual transgenic lines and to assess growth of specific organs.

Effect of lymphatic filariasis on the immune response to malaria

MICHAEL KOVACS, WINSTON CHURCHILL HIGH SCHOOL

Preceptor: THOMAS B. NUTMAN, M.D., LABORATORY OF PARASITIC DISEASES, NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Mentor: SIMON METENOU, PH.D., LABORATORY OF PARASITIC DISEASES, NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Room D-124
7:00 p.m.

MICHAEL KOVACS
WINSTON CHURCHILL
HIGH SCHOOL

SUMMARY

In many regions of Africa, immunity against malaria may be modulated in the presence of coincident lymphatic filariasis. By modeling the interactions between these two parasites and measuring the immune response they elicit, we hope to show that immune responses against filarial parasites directly limit the production of proteins essential for fighting malarial infection.

ABSTRACT

Malaria, a disease caused by protozoan *Plasmodium* spp., affects more than 500 million people each year. Unfortunately, in many of the same regions of the world where malaria is found, lymphatic filariasis—a disease caused by the parasitic nematodes *Wuchereria bancrofti, Brugia timori,* and *Brugia malayi*—is coendemic with malaria. Because filarial infections generate host responses that are highly regulatory in nature, modulation of the host's immune responses to other pathogens can occur, such that immunity against malaria may be weakened. Previous studies have shown that the regulatory environment generated in response to chronic filarial infection results from an increase in interleukin-10 (IL-10) production by regulatory T cells, which in turn interferes with the host's ability to produce the two cytokines key to fighting malarial infection: interleukin-12 (IL-12) and interferon-gamma (IFN-γ).

To understand more precisely the mechanisms underlying the modulation of malarial-specific IL-12 and IFN-γ by coexistent filarial infection, we measured malaria and filarial antigen-specific immune responses in cultures of whole blood obtained from filarial-positive and filarial-negative patients in Mali, a malaria-endemic region of West Africa.

Using quantitative real-time RT-PCR, our results demonstrated that expression of the interferon regulatory factor 1 (IRF1)—a transcription factor that initiates the production of IL-12, which in turn promotes IFN-γ—was significantly downregulated in filarial-positive samples as compared with the filarial-negative samples. Conversely, the expression of the IL-12 receptor (IL-12R) was not significantly different between the two groups. These data suggest that the inhibited IL-12 and IFN-γ production that occurs in chronic lymphatic filariasis results from IRF1 downregulation and the failure to initiate the production of IL-12 rather than by influencing IL-12R expression. Additional pathways are currently under study in hopes of developing a better understanding of how lymphatic filariasis (a chronic helminth infection) modulates the host response to malaria in areas where both infections are coendemic.

Room D-124
7:15 p.m.

Pharmacological treatment of mouse models of autism

SEDA TOLU, COLONEL ZADOK MAGRUDER HIGH SCHOOL

Preceptor: JACQUELINE N. CRAWLEY, PH.D., LABORATORY OF BEHAVIORAL NEUROSCIENCE, NATIONAL INSTITUTE OF MENTAL HEALTH

Mentor: JILL SILVERMAN, PH.D., LABORATORY OF BEHAVIORAL NEUROSCIENCE, NATIONAL INSTITUTE OF MENTAL HEALTH

SEDA TOLU
COLONEL ZADOK MAGRUDER
HIGH SCHOOL

SUMMARY

Autism is a neurodevelopmental disorder with no known cures or treatments; however, pharmacological drugs may have the potential to reduce some of its symptoms. Using the BTBR T+tf/J mouse models of autism, we administered injections of two of these drugs, risperidone and MPEP, and followed with the social approach and self-grooming tasks to discern the effects of the drugs. We expect that the two drugs will reduce low sociability and repetitive behaviors, which are two out of the three symptoms characteristic of autism.

ABSTRACT

Autism is a neurodevelopmental disorder characterized by an impairment of growth in the brain or central nervous system. It is distinguished by abnormal social interactions, communication impairment, and repetitive behaviors. BTBR T+tf/J (BTBR) mice are a naturally occurring inbred strain that exhibit at least two out of the three autistic-like behavioral traits: 1) low sociability and 2) high levels of restrictive, repetitive self-grooming behaviors. Risperidone is the only accepted drug on the market that has been approved by the Food and Drug Administration to help decrease irritability in autistic patients. MPEP, an mGluR5 antagonist receptor, has been found to treat some of the symptoms of fragile X syndrome, which has 50% comorbidity with symptoms of autism. Using the BTBR mouse model, we are trying to discern the effects of the drugs risperidone and MPEP on the low-sociability and repetitive behavior symptoms of autism. To test the hypothesis that risperidone and MPEP increase sociability and decrease repetitive behaviors, we evaluated data from the social approach (which measures sociability) and self-grooming (which measures this repetitive behavior) tasks. Open-field data were also evaluated to determine the effect of risperidone and MPEP on locomotor activity. Results showed that risperidone does not increase sociability of BTBR mice. However, both risperidone and MPEP reduced repetitive self-grooming behavior. Results obtained from the open-field data revealed that risperidone caused sedating side effects, whereas MPEP did not show any significant changes in locomotor activity in mice. In conclusion, MPEP would seem to be the better potential drug treatment for autism because it has significantly reduced repetitive behaviors in mice, and unlike risperidone, it does not have any side effects on locomotor activity in the BTBR mouse model of autism. Neither risperidone nor MPEP drug treatments have been found to increase sociability in mice.

Peer intervention in the BTBR T+tf/J mouse model of autism

Kayla Perry, James Hubert Blake High School

Preceptor: Jacqueline N. Crawley, Ph.D., Laboratory of Behavioral Neuroscience, National Institute of Mental Health

Mentor: Mu Yang, Ph.D., Laboratory of Behavioral Neuroscience, National Institute of Mental Health

Room D-124
7:30 p.m.

Kayla Perry
James Hubert Blake
High School

Summary

Autism is a neurodevelopmental disorder characterized by abnormal social interaction, communication deficits, and high levels of restricted and repetitive behaviors. This study aims to investigate whether mice with low sociability will show improved social scores after living with mice with high sociability. The outcome of this experiment could have clinical implications on the effectiveness of peer intervention in autism.

Abstract

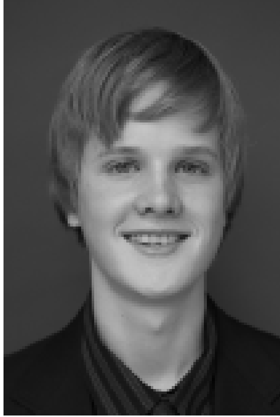
Autism is a behaviorally defined neurodevelopmental disorder diagnosed by three main symptoms: impairments in social interaction, communication deficits, and restricted and repetitive behaviors. While there is no known effective medical treatment for the diagnostic symptoms of autism, well-structured behavioral interventions produce beneficial effects. Notably, peer-mediated intervention programs have been found to improve social skills in some children with autism, indicating the importance of frequent social interaction with social peers as part of the behavioral treatment program. An inbred strain of mice called BTBR T+tf/J (BTBR) displays symptoms with face validity to the core symptoms of autism. In the social approach test, C57BL/6J (B6) mice exhibit high levels of sociability whereas BTBR mice score poorly, indicating that these two strains might be used to test the effects of peer-mediated behavioral treatments. The intervention procedure began by forming mixed-strain cage mates. Two BTBR and two B6 of the same sex were paired at the time of weaning (postnatal day 21) and allowed to interact freely as juveniles and adults. Control animals were B6 that lived with B6 cage mates and BTBR that lived with BTBR cage mates. Animals were tested for social approach at 8 weeks of age. Results showed that both male and female BTBR mice were significantly more social after living with B6 cage mates for 40 days, similar to the B6 controls. The BTBR controls did not exhibit significant sociability. These data indicate that the profound social deficits in BTBR mice are significantly improved by constant social interaction with highly social B6 "peer" cage mates, suggesting that the BTBR mouse model of autism could be used to explore intervention strategies to improve autism-relevant symptoms.

Room D-124
7:45 p.m.

COMT, Dysbindin, and their interaction: impact on social behavior and recognition memory

EDWARD SULLIVAN, POOLESVILLE HIGH SCHOOL

Preceptor and Mentor: FRANCESCO PAPALEO, PH.D., CLINICAL BRAIN DISORDERS BRANCH, NATIONAL INSTITUTE OF MENTAL HEALTH



EDWARD SULLIVAN
POOLESVILLE HIGH SCHOOL

SUMMARY

Through a diverse array of symptoms, schizophrenia disturbs the emotions, sociability, and cognition of approximately 4/1,000 people, yet no biological definition or practical treatments exist. By testing the social and cognitive behaviors of genetically modified mice, we may identify the influences of corresponding schizophrenia-related genes in humans. Identification of genes' roles may eventually assist in better understanding and perhaps treatment of the illness.

ABSTRACT

Activity of the neurotransmitter dopamine may influence social and cognitive behavioral deficits that characterize schizophrenia. The catecheol-O-methyltransferase (COMT) is an enzyme involved in dopamine trafficking. We have previously shown that genetic modification resulting in lower COMT enzyme activity, which increases dopamine levels, results in cognitive advantages but emotional disadvantages. Conversely, genetic modification bringing about higher COMT enzyme activity results in cognitive disadvantages and blunted stress reactions. Dysbindin is another gene that could contribute to the development of schizophrenia, possibly via regulation of the dopamine system. To investigate the affects of COMT and Dysbindin and their interaction on sociability and recognition memory, we tested COMT overexpressing, COMT knockout, Dysbindin knockout, and Dysbindin × COMT double-knockout mice in the social approach and novel object recognition tasks. The social approach task quantifies sociability by comparing the amount of time that a subject mouse explores a novel conspecific and a novel inanimate object. It similarly examines preference for social novelty by comparing time spent exploring a familiar conspecific and a completely novel conspecific. Data demonstrated that increased COMT enzyme activity selectively reduced preference for social novelty, yet reduction in COMT enzyme activity has no influence on sociability or preference for social novelty. We further hypothesize a trade-off between short- and long-term memory from preliminary results using the novel object recognition task, which compares a subject mouse's exploration of a novel and a familiar object. We conclude that increased COMT may impair social behavior, yet perhaps have a different impact on long- versus short-term memory.

Suppression of the transcriptional activity of glucocorticoid receptor (GR) by liver X receptors (LXRs): crosstalk between two receptor molecules

Room D-124
8:00 p.m.

BRENT ABEL, PAINT BRANCH HIGH SCHOOL

Preceptor: TOMOSHIGE KINO, M.D., PH.D., UNIT ON PEDIATRIC ENDOCRINOLOGY, EUNICE KENNEDY SHRIVER NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

Mentors: NANCY NADER, PH.D., AND ALAN DECHERNEY, M.D., PROGRAM IN REPRODUCTIVE ENDOCRINOLOGY AND SCIENCE, EUNICE KENNEDY SHRIVER NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

BRENT ABEL
PAINT BRANCH HIGH SCHOOL

SUMMARY

Glucocorticoid receptor (GR) and liver X receptors (LXRs) are receptor molecules implicated in glucose and cholesterol metabolism, inflammation, and immunity. Because these two proteins have similar metabolic effects, I tested to see whether there is any crosstalk between the metabolic activities of the proteins by using transfection experiments and an animal study. My results showed that LXRs repress the transcriptional activity of GR and can affect the expression of GR-regulated genes in a gene-specific way.

ABSTRACT

Glucocorticoids are steroid hormones that increase glucose and cholesterol levels, decrease inflammation, and strengthen immunity. Glucocorticoid-action in the cell relies entirely on the action of glucocorticoid receptor (GR), a protein that upon binding to glucocorticoids moves from the cytoplasm to the nucleus in order to activate the transcription of genes linked to the effects of glucocorticoids. Liver X receptors (LXRs) are other proteins that decrease glucose and cholesterol levels, decrease inflammation, and strengthen immunity. Since some metabolic actions of GR and LXRs overlap, our laboratory hypothesized that LXRs might have antiglucocorticoid activity.

To test whether LXRs affect the activity of GR, I performed several transfection experiments and an animal study. For the transfection experiments, I introduced various plasmids expressing GR and/or LXRs into HCT116 human colon cancer cells. I treated the transfected cells with either dexamethasone (a synthetic glucocorticoid that activates GR), GW3965 or TO901317 (synthetic molecules shown to activate LXRs), or 22-R-hydroxycholesterol (a cholesterol metabolite naturally produced by the body that activates LXRs). By measuring the activity of luciferase expressed under the control of the mouse mammary tumor virus promoter (MMTV) containing glucocorticoid response element (GRE), I was able to determine whether LXRs affect the GR-related transcription activity. In my animal study, the rats were divided into four different treatment groups: no drug, dexamethasone, GW3965, and a combination of dexamethasone and GW3965. Following treatment and asphyxiation, I collected different tissues of the rats and studied the expression of different genes to see the effects of the drugs.

The results showed that LXRs repress the transcriptional activity of GR. These results could lead to future drug studies targeting the adverse effects of glucocorticoids (obesity, diabetes, and high cholesterol) by using a molecule stimulating LXRs. The results also help the scientific community further understand the relationships between receptor molecules such as GR and LXRs and their effect on the human body.

Room D-125
7:00 p.m.

Identification and cloning of a new ADAMTS13 alternative splicing form: analysis of expression and function

Elie G. Pommier, Walt Whitman High School

Preceptor: Chava Kimchi-Sarfaty, Ph.D., Center for Biologics Evaluation and Research, U.S. Food and Drug Administration

Mentors: Nobuko Katagiri, Ph.D., and Klilah Hershko, M.D., Center for Biologics Evaluation and Research, U.S. Food and Drug Administration

Elie G. Pommier
Walt Whitman High School

Summary

My project focuses on a human protein, ADAMTS13, that ensures proper blood clot formation by regulating one of the major clotting factors found in the blood stream. Like most proteins, ADAMTS13 has numerous variations that result from naturally occurring mutations in the body. Recently, we discovered a new variation, which arises from alternative splicing of ADAMTS13 in liver cells. I will be cloning the new form of ADAMTS13 so that we can measure the expression and function of the alternative splicing form.

Abstract

Much of blood clotting in the body is the result of major clotting factors aiding platelets to adhere to one another. Cleaving proteases regulate the body's production of clots and ensure that an excess of clots in the bloodstream does not occur by regulating clotting factors. Von Willebrand factor (VWF) is a major blood-clotting factor and its activity is regulated by ADAMTS13 (a disintegrin and metalloprotease with a thrombospondin type 1 motif, member 13) also known as von Willebrand factor-cleaving protease (VWFCP). ADAMTS13 is a secreted protein that has a number of genetic variations. This project examines a recently discovered intron retention splicing form with a retained intron containing a stop codon between exons 25 and 26. The stop codon causes the loss of exons during translation, which may lead to a protein product with very different characteristics. To be able to study the new splicing form, one must first be able to transfect cells with the new form of ADAMTS13 DNA. To this end, the form must be cloned into an expression plasmid. The intron retention splicing form has never been researched or synthesized, and to clone it directly from the liver cells in which it was first discovered would be a difficult process. Instead, our approach has been to produce the intron retention splicing form by modifying the wild-type ADAMTS13 plasmid to include the intronic region between exons 25 and 26. Once the intron retention splicing form is attained, it will be tested for subcellular localization, activity levels, and secretion levels.

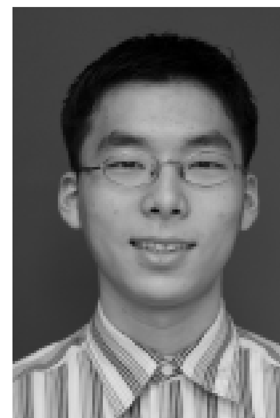
Elucidating nuclear localization of ADAMTS13, a secreted thrombotic protease

PHILIP KONG, THOMAS S. WOOTTON HIGH SCHOOL

Preceptor: CHAVA KIMCHI-SARFATY, PH.D., CENTER FOR BIOLOGICS EVALUATION AND RESEARCH, U.S. FOOD AND DRUG ADMINISTRATION

Mentor: RYAN HUNT, CENTER FOR BIOLOGICS EVALUATION AND RESEARCH, U.S. FOOD AND DRUG ADMINISTRATION

Room D-125
7:15 p.m.



PHILIP KONG
THOMAS S. WOOTTON HIGH SCHOOL

SUMMARY

ADAMTS13 (a disintegrin-like and metalloprotease thrombospondin type-1 motif, member 13) is understood to cleave a glycoprotein responsible in blood coagulation and clotting cascade. Despite the protein's secretion in normal human cells, confocal imaging studies have shown ADAMTS13 localizing to the nucleus. My project is to demystify its nuclear localization by 1) testing a putative nuclear localization sequence that brings ADAMTS13 to the nucleus and 2) identifying and analyzing all the ADAMTS13 protein bands in the nucleus.

ABSTRACT

This research seeks to unveil the mechanism and the effects of nuclear localization of ADAMTS13 (a disintegrin-like and metalloprotease thrombospondin type-1 motif, member 13). ADAMTS13 is a secreted protease in the blood responsible for cleaving a prothrombotic glycoprotein called von Willebrand. Mutations in the *ADAMTS13* gene or the development of antibodies against the ADAMTS13 protein often lead to blood-clotting diseases such as thrombotic thrombocytopenic purpura (TTP). In an effort to understand the mechanism of ADAMTS13's recently discovered nuclear localization, we sought to investigate a potential nuclear localization signal within the prodomain region. The work was facilitated by the fact that this region can be cleaved off by another protein, Furin. Our findings show that ADAMTS13 without the prodomain localizes less to the nucleus than the ADAMTS13 wild type does. Upon further investigation of ADAMTS13 nuclear localization, we found both full-length ADAMTS13 and smaller segments of the protein in transfected nuclear extracts. Our bioinformatics analysis of ADAMTS13 domains that could correspond to these smaller fragments revealed that the CUB-domain of ADAMTS13 may share similar characteristics to a protein involved in DNA unbinding and transcription regulation processes. These studies promise an innovative approach to prevention and treatment of blood-clotting diseases and could be useful in the production of a recombinant drug to combat TTP.

Room D-125
7:30 p.m.

Protein interaction with the Rep-P region of human β-globin locus control region in myelogenous leukemia cells

VIDUSHANI JAYALAL, GAITHERSBURG HIGH SCHOOL

Preceptor: MIRIT ALADJEM, PH.D., LABORATORY OF MOLECULAR PHARMACOLOGY, NATIONAL CANCER INSTITUTE

Mentor: CINDY TSENG, M.S., LABORATORY OF MOLECULAR PHARMACOLOGY, NATIONAL CANCER INSTITUTE

VIDUSHANI JAYALAL
GAITHERSBURG HIGH SCHOOL

SUMMARY

Cancer killed more than 7.6 million people in the year 2007. The main characteristic shared by all cancer cells is uncontrollable growth. The cell cycle controls when cells divide, and because DNA replication is the first step of the cell cycle, locating the origin could lead to drugs and treatment that would be able to disturb the proliferation of cancer cells.

ABSTRACT

Cancer is a disease characterized by the inability of cells to control their growth. Cancerous cells ignore instructions that would cause normal cells to stop growing and/or to undergo apoptosis. DNA replication is a critical checkpoint stage in the cell cycle that responds to those instructions. Because cancer cells constantly proliferate, it is thought that if we understand the instruction that triggers DNA replication, we might be able to interfere with the proliferation of cancer cells.

One known region where replication may initiate is at the human β-globin locus. The initiation region is broken into two different sections: Rep-P and Rep-I. Previous studies have shown that replication cannot initiate within the Rep-P region without a particular 45-base-pair (bp) sequence. Studying protein interaction within this 45-bp sequence can further enhance the understanding of how the initiation region starts replication. The search for proteins that bind to the Rep-P region may provide researchers with a clue as to the nature of the instructions DNA receives to start replication.

Our goal is to isolate from the myriad of nuclear proteins a select few that bind to the region of interest, Rep-P. Using myelogenous leukemia cells as a model system, we collected nuclear protein and then fractionated it according to electrical charge. To test whether the proteins collected after fractionation bind to the Rep-P region, we used electromobility shift assay (EMSA). Oligonucleotides, which have the same 45 bps as the Rep-P region, are mixed with the protein. Then, using a gel electrophoresis apparatus, we can determine whether the protein binds to the Rep-P region. Because DNA oligonucleotides that are free of protein migrate faster in this assay than those complexed with proteins, the binding of protein to DNA can be visualized. Once we identify proteins that bind the 45-bp Rep-P sequence, we will investigate how these proteins transmit the instructions that control the replication process.

Interactions of *p53, SMAD4,* and E-cadherin on the differentiation and aggressiveness of breast cancer

Room D-125
7:45 p.m.

JEAN RA, WALTER JOHNSON HIGH SCHOOL

Preceptor: JEFFREY GREEN, M.D., LABORATORY OF CANCER BIOLOGY AND GENETICS, NATIONAL CANCER INSTITUTE

Mentor: HARK K. KIM, M.D., PH.D., LABORATORY OF CANCER BIOLOGY AND GENETICS, NATIONAL CANCER INSTITUTE

JEAN RA
WALTER JOHNSON HIGH SCHOOL

SUMMARY

*We have explored the roles of three genes—*p53, SMAD4, *and E-cadherin, known to be altered often in human breast cancer—by studying their interactions in promoting mammary tumors in genetically engineered mice. Loss of* p53 *and* SMAD4 *leads to adenosquamous mammary tumors, but the additional loss of E-cadherin results in an adenocarcinoma mammary tumor phenotype. Additionally, mice with the loss of all three genes developed very aggressive tumors and increased metastatic disease. These new models of mammary cancer will help us understand the signaling pathways that determine tumor histology and metastases.*

ABSTRACT

Breast cancer is a malignant disease characterized by uncontrollable proliferation of breast cells. This condition may be caused by a deletion of genes in the DNA. Under normal circumstances, the expression of the genes *SMAD4, p53,* and E-cadherin helps maintain normal cellular functions. However, when these genes are mutated or lost, cells may transform into cancer cells.

SMAD4 is a tumor suppressor and an intracellular mediator of transforming growth factor-β and bone morphogenic protein signal transduction pathways. Protein expression of *SMAD4* is decreased in many breast cancer patients, as is that of E-cadherin. E-cadherin is a calcium-dependent glycoprotein whose deletion has been extensively implicated in the progression and dissemination of human cancer. The *p53* gene, located on chromosome 17, encodes a 53-kilodalton tumor-suppressor protein that acts to prevent the formation of tumors. To date, the effects of combined *SMAD4*/E-cadherin loss on the differentiation and progression of mammary tumors have not been documented.

We used the conditional gene knockout method to genetically engineer mice with loss of various combinations of these genes. To examine the interactions of these genes in the development and differentiation of tumor cells, we generated targeted deletions of one or both alleles of *SMAD4* and E-cadherin in a *p53*-null background. The complete loss of *SMAD4* and *p53* resulted in mammary squamous carcinomas in most of the mice, whereas the triple loss of *SMAD4/p53*/E-cadherin primarily resulted in mammary adenocarcinomas. A small number of triple-knockout mice developed adenosquamous tumors, in which only partial loss of E-cadherin was demonstrated. These results suggest that E-cadherin expression is an important regulator of mammary cancer differentiation, but this effect may be modified by *SMAD4* expression. Further studies are being performed to determine what biologic differences in mammary cancer progression and metastases are regulated by the loss of each gene, and how *SMAD4* and E-cadherin may interact to affect mammary cancer differentiation.

Room D-125
8:00 p.m.

KAVI ANANDALINGAM
WALT WHITMAN HIGH SCHOOL

Associations between the *FTO* gene and eating behavior in children

KAVI ANANDALINGAM, WALT WHITMAN HIGH SCHOOL

Preceptor: JACK A. YANOVSKI, M.D., PH.D., PROGRAM IN DEVELOPMENTAL ENDOCRINOLOGY AND GENETICS, EUNICE KENNEDY SHRIVER NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

Mentor: JOAN C. HAN, M.D., PROGRAM IN DEVELOPMENTAL ENDOCRINOLOGY AND GENETICS, EUNICE KENNEDY SHRIVER NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

SUMMARY

My project examines the effect of a base-pair change (polymorphism) from T to A in the FTO *gene, which has been found to be associated with obesity. I genotyped a population of 203 children and compared this result to body mass index (BMI), body fat percentage, and reported eating behavior. I found that children with the A allele were more likely to have a higher BMI and were less able to control their eating habits. This means that the* FTO *gene could affect food intake, but more studies examining actual intake are warranted.*

ABSTRACT

Obesity is a disease associated with an imbalance in energy homeostasis. It has a strong genetic component, and one gene found to be associated with excess weight gain is *FTO*. *FTO* is highly expressed in regions of the brain important for appetite regulation. Therefore, one possibility is that a gene near *FTO* exerts its influence on weight by altering eating behavior. My project examined the relationship between a single base-pair change of T to A in the *FTO* gene at the rs9939609 location, body composition, and eating behaviors in children.

I genotyped 210 children from ages 8 to 18 years by TaqMan assay to determine the presence of an A allele, a T allele, or both. Using questionnaires, children self-reported measures of eating in the absence of hunger (EAH, the tendency to eat when full) and loss-of-control eating (LOC, the experience that one cannot control what or how much is being eaten). Parents completed corresponding questionnaires to assess their child's behavior. Children were also interviewed to assess LOC eating patterns.

Because few qualitative or quantitative differences existed between AA and AT children, they were grouped together for analysis. AA+AT children were found to have higher body mass index (BMI) scores than the TT children. Compared to the TT group, AA+AT children did not self-report greater EAH, but parents of AA+AT reported that their children were more likely to eat even though they were not hungry, in response to negative affect and feeling fatigued or bored. Based on both child self-report and child interview assessment, we found that AA+AT youth were also significantly more likely to report LOC.

Our preliminary data suggest that genetic variation at *FTO* rs9939609 is associated with differences in BMI and alterations in child-reported and parent-reported eating behaviors. These data are consistent with the hypothesis that the relevant gene at the *FTO* location important for body weight likely affects the control of food intake, perhaps through stimulating eating in the absence of hunger and loss of control over eating.

Positron emission tomography and bipolar disorder: radiotracer development for the imaging of protein kinase C

MOHAMMAD OMAR BUKHARI, NORTHWEST HIGH SCHOOL

Preceptor: VICTOR W. PIKE, PH.D., MOLECULAR IMAGING BRANCH, NATIONAL INSTITUTE OF MENTAL HEALTH

Mentor: LISHENG CAI, PH.D., MOLECULAR IMAGING BRANCH, NATIONAL INSTITUTE OF MENTAL HEALTH

Rathskeller
7:00 p.m.

MOHAMMAD OMAR BUKHARI
NORTHWEST HIGH SCHOOL

SUMMARY

Bipolar disorder is an elusive disease that is extremely hard to track in its early stages. To view the early progress of this disease, we created a carbon-11-radiolabeled compound and used it in conjunction with positron emission tomography to detect for the density of protein kinase C (PKC) in the brain; PKC has been associated with bipolar disorder. If successful, this method could potentially be used to detect the early progress of bipolar disorder in humans.

ABSTRACT

Bipolar disorder is a psychological disease that causes changes in one's ability to function normally. These changes are seen as mental episodes, or mood swings, that can be manic or depressive. Recent neurological studies have shown a relatively high density of protein kinase C (PKC) in patients who have exhibited bipolar tendencies. In addition, scientists, including Husseini Manji, M.D. (National Institute of Mental Health [NIMH]), have shown that the inhibition of PKC lowers the frequency of manic emotions. For these reasons, we imaged PKC using a radiotracer and positron emission tomography (PET).

Our objective in this study was to create a radiolabeled tracer to measure the quantity and distribution of PKC in the brain, using PET. Our initial goal was to radiolabel a preexisting compound of Go 6976, which has already shown a high binding affinity for PKC. We adapted existing methods to synthesize this compound, improve the chemical yield of each step, and separate each individual isomer for its own testing purposes. The precursor was radiolabeled using [11C]MeI, a common radiolabeling agent, which was produced from a cyclotron a few minutes before radiolabeling. The radiolabeled compound was evaluated using the NIMH animal PET imaging facility to determine whether it was suitable for PET imaging and whether it has potential for further development to monitor PKC in patients suffering from bipolar disorder.

Rathskeller
7:15 p.m.

Stress and the regulation of the corticotropin releasing hormone

ANA GABRIELA COELLO, ALBERT EINSTEIN HIGH SCHOOL

Preceptor: GRETI AGUILERA, M.D., SECTION ON ENDOCRINE PHYSIOLOGY, EUNICE KENNEDY SHRIVER NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

Mentor: YING LIU, M.D., SECTION ON ENDOCRINE PHYSIOLOGY, EUNICE KENNEDY SHRIVER NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

ANA GABRIELA COELLO
ALBERT EINSTEIN HIGH SCHOOL

SUMMARY

The hypothalamic peptide corticotropin releasing hormone (CRH) mediates endocrine, autonomic, and behavioral responses to stress. Elucidation of the mechanisms controlling CRH production is necessary for understanding the origin, diagnosis, and treatment of stress-related diseases. At the gene level, stress stimulates CRH transcription by inducing phosphorylation and interaction of the protein cyclic AMP response element binding (CREB) with the promoter. However, recent studies show that phosphorylated CREB (pCREB) alone cannot activate CRH transcription, suggesting that an additional factor (coactivator) is required. This study tests the hypothesis that the protein transducer of regulated CREB activity (TORC) acts as a CREB coactivator driving CRH transcription.

ABSTRACT

The hypothalamic peptide corticotropin releasing hormone (CRH) mediates endocrine, autonomic, and behavioral responses to stress, which is a prevalent issue for most people. Excessive or insufficient CRH production in the brain can lead to pathology; therefore, understanding the mechanisms controlling CRH expression affects the prevention, diagnosis, and treatment of stress-related diseases. Stress regulates CRH by increasing its secretion and gene transcription, with the latter depending on activation of cyclic AMP/PKA signaling leading to phosphorylation of the protein cyclic AMP (cAMP) response element binding (i.e., phosphorylated CREB, or pCREB). However, pCREB alone is insufficient for transcriptional activation of the CRH gene, suggesting the need for a coactivator. The role of the protein transducer of regulated CREB activity (TORC) as a coactivator during regulation of CRH transcription was studied in the hypothalamic cell line 4B by either increasing TORC expression or knocking out endogenous TORC by using siRNA (silencing RNA) on CRH promoter activity. Forskolin (stimulator of cAMP production and CREB phosphorylation) stimulated CRH promoter activity and nuclear translocation of TORC. In contrast, the phorbol ester PMA (which also phosphorylates CREB) sequestered TORC in the cytosol and failed to stimulate CRH promoter activity. TORC 1 and 2 overexpression potentiated the stimulation by forskolin but had no effect with PMA. The siRNA knock out of TORC 2 and 3 reduced and prevented forskolin-stimulated CRH promoter activity. The study shows that TORC 2 and 3 are required for cAMP-dependent activation of CRH transcription. The data support the hypothesis that TORC can serve as the coactivator of pCREB for transcriptional activation of CRH. This provides a basis for further studies to elucidate the physiological regulation of CRH during stress and to develop new tools for the management of stress-related diseases.

Identification of structural determinants on PEDF-R responsible for binding PEDF

SHIVALI CHOXI, SHERWOOD HIGH SCHOOL

Preceptor: S. PATRICIA BECERRA, PH.D., LABORATORY OF RETINAL CELL AND MOLECULAR BIOLOGY, NATIONAL EYE INSTITUTE

Mentors: SILVIA LOCATELLI-HOOPS, PH.D., AND PREETI SUBRAMANIAN, PH.D., LABORATORY OF RETINAL CELL AND MOLECULAR BIOLOGY, NATIONAL EYE INSTITUTE

Rathskeller
7:30 p.m.

SHIVALI CHOXI
SHERWOOD HIGH SCHOOL

SUMMARY

Pigment epithelium-derived factor (PEDF) is a protein naturally present in the retina, a tissue where the essential processes of vision take place. PEDF is involved in retinal cell survival. A novel receptor for PEDF, known as PEDF-R, was recently identified. Our purpose is to study the interactions between PEDF and PEDF-R. This study will enhance the understanding of the interaction between PEDF and retinal cells to better exploit PEDF for future treatments of various diseases that cause blindness.

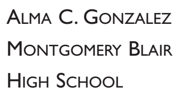
ABSTRACT

The retina is a multilayered sensory tissue found in the back of the eye that is essential for vision processes. Retinal degeneration refers to a general body of diseases that contribute to vision loss due to photoreceptor and retinal cell death. Pigment epithelium-derived factor (PEDF), a member of the serine protease inhibitor superfamily (SERPINS), is a multifunctional protein naturally present in the retina that enhances retinal cell survival. A receptor for PEDF, termed PEDF-R, has been identified on plasma membranes of retinal cells. The hydrophobicity plot predicts that PEDF-R contains four transmembrane domains, three intracellular regions (L1, L3, and L5), and two extracellular loops (L2 and L4). We are interested in studying the interactions between PEDF and PEDF-R in order to fully understand and determine the mechanism by which PEDF acts on retinal cell survival. The goal of this study is to identify the region on PEDF-R responsible for binding PEDF.

To investigate the binding of PEDF to PEDF-R, we carried out ligand blot experiments with fluoresceinated PEDF (Fl-PEDF) and synthetic peptides. Fl-PEDF is a chemically modified protein version. Synthetic peptides E4a, E4b, E5a, E5+6a, and E7a were designed from the longest extracellular loop (L4) of PEDF-R. Among all the peptides tested, PEDF showed the highest binding affinity to immobilized E4b followed by E5+6a, while the remaining did not bind. Blocking experiments confirmed that E4b:Fl-PEDF interactions also occurred when both were in solution. Unlabeled PEDF partially competed with Fl-PEDF for binding to E4b, suggesting that unlabeled PEDF has lower affinity for E4b binding than the Fl-PEDF. Other modified PEDF versions have been prepared to better understand the difference in binding affinity between Fl-PEDF and PEDF to E4b. Three PEDF variants with alterations in specific domains were generated. These variants were purified using ion-exchange column chromatography. They will be tested using ligand blot assays to determine the affinity of these altered proteins on the binding to PEDF-R.

Thus, we have identified a specific region within the extracellular loop L4 on PEDF-R to which PEDF binds with high affinity. This study provides insight into the specific interactions between PEDF and PEDF-R, thereby leading to better therapeutic interventions of PEDF for retinal degeneration.

Rathskeller
7:45 p.m.



ALMA C. GONZALEZ
MONTGOMERY BLAIR
HIGH SCHOOL

Endometrial stem cells and their relationship to the development of endometriosis and chronic pelvic pain

ALMA C. GONZALEZ, MONTGOMERY BLAIR HIGH SCHOOL

Preceptor: ALAN DECHERNEY, M.D., REPRODUCTIVE BIOLOGY AND MEDICINE BRANCH, EUNICE KENNEDY SHRIVER NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

Mentor: PAMELA STRATTON, M.D., GYNECOLOGY CONSULT SERVICE, EUNICE KENNEDY SHRIVER NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

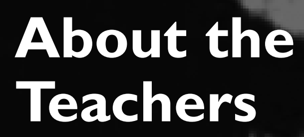
SUMMARY

Endometriosis occurs when endometrium-like tissue grows outside of pelvic organs. It is associated with pain and may arise from endometrial fragments deposited during menstruation. In our study, we obtained endometrial biopsies from women with endometriosis and chronic pelvic pain, women with pelvic pain only, and healthy volunteers. We then isolated stem cells by using cell culture, and we plan to analyze these cells to determine whether they differ among our study cohorts. This may further our understanding of endometriosis and how pain is associated with this condition.

ABSTRACT

Up to 15% of all women of reproductive age in the United States suffer from chronic pelvic pain (CPP). CPP has been attributed to endometriosis, a medical condition in which endometrium-like tissue grows outside of the uterus. Endometriosis adheres to other pelvic organs and induces a local inflammation reaction. Many believe that the pain experienced results from these disease characteristics. We hypothesize that the extra-uterine tissue may be caused by endometrium that is deposited by the reflux of menses into the pelvic cavity. Why the endometrium survives and attaches in some women (those who develop endometriosis) but not others is a focus of our research. We are isolating and culturing stem cells from menstrual endometrial biopsy specimens in three cohorts of women: those with endometriosis and pelvic pain, those with pelvic pain and no endometriosis, and healthy volunteers. Others have shown that these cells have the potential to mature into mesenchymal or supporting tissue cell types such as cardiomyocytes, endothelial cells, hepatocytes, adipocytes, and respiratory epithelial cells. We plan to test these stem cell samples to look for differences in neuronal growth markers between the cohorts of women. In addition, we plan to delineate their differing stem cell characteristics, confirming that they are stem cells of endometrial origin and have potential for angiogenesis. With this information, we hope to learn more about the pathophysiology of endometriosis and the pain associated with it.

About the Teachers



About the Teachers

Carrie Black, Westland Middle School

Lab: Margaret Bash, M.D., M.P.H., Laboratory for Bacterial Polysaccharides, Center for Biologics Evaluation and Research, U.S. Food and Drug Administration

Research: Worked with DNA from *Neisseria gonorrhoeae* (GC), the bacteria that cause the sexually transmitted disease gonorrhea, and used polymerase chain reaction and checkerboard hybridization to type the gene of the outermembrane protein PorB

I loved being back in a lab again because it reminded me of why I studied science and cellular and molecular biology to begin with, and I miss that kind of intellectual stimulation. But the most rewarding part of the experience was building relationships with the other members of my lab. I am now able to share anecdotes with my students of what it's like to work in a real lab on a daily basis. I am also trying to incorporate lab notebooks into some of my inquiry-based labs in class. Although I had a great time during my internship, I still missed the kids, so the lab experience helped to get me excited about a new school year.

Chujor S. N. Chujor, Ph.D., Albert Einstein High School

Lab: Rajat Varma, Ph.D., Laboratory of Cellular and Molecular Immunology, National Institute of Allergy and Infectious Diseases

Research: Worked to verify cDNA sequences for some cytokine receptors and helped design additional internal primers to allow further sequencing of the unverified cDNAs, contributing to the development of tools to study cell surface dynamics, signaling, and trafficking of cytokine receptors

I enjoyed an exciting, intellectually stimulating research environment and the interpersonal interaction with outstanding scientists who are willing to share their wealth of professional experiences and achievements. The internship has enhanced my ability to skillfully integrate practical applications of scientific knowledge into teaching in order to provide my students with the connection and relevance between scientific principles and practice.

Joel I. Cohen, Ph.D., Parkland Magnet Middle School for Aerospace Technology

Lab: Chava Kimchi-Sarfaty, Ph.D., Center for Biological Evaluation and Research, U.S. Food and Drug Administration

Research: Studied variation in gene expression in the von Willebrand gene; used gel electrophoresis to look for DNA fragment combinations using primers across specific exons of the gene; and performed digests working within these various exons, followed by gel electrophoresis

I enjoyed being a part of Dr. Kimchi-Sarfaty's lab group, as there was a real team approach to the science. Weekly team meetings, where colleagues commented on one another's progress and difficulties, were challenging yet very helpful. I gained a lot from listening to group members, from high school students to postdocs, as to how I might perform better and contribute more. I also gained valuable exposure to human genetic conditions and blood disorders, both new areas of knowledge for me. The lab experience provided me with examples to use in classroom science units. In addition, it prepared me for "running" two DNA-based laboratories in seventh-grade middle school. I can show students that these are not just lab exercises, but technologies serving real purposes in the area of human health care and pharmaceutical development.

Kimberly de la Cerda, Paint Branch High School

Lab: Carolyn Wilson, Ph.D., Center for Biologics Evaluation and Research, U.S. Food and Drug Administration

Research: Worked to help propagate the animal cell lines that are used in the testing of the process of developing a vaccine for the Ebola virus and helped to produce the vectors used in the research

I enjoyed working with the scientists and other interns in the lab. It is a great way to "do" the science that we discuss in school. I enjoyed working with and learning from the scientists completing the necessary research on a daily basis. I'm able to share stories with my students about my firsthand experiences at NIH. I have also completed different classroom activities and labs with techniques learned during the summer internship.

Brendon Friedman, Clarksburg High School

Lab: Susan Gottesman, Ph.D., Laboratory of Molecular Biology, Center for Cancer Research, National Cancer Institute

Research: Searched for small RNAs in *Escherichia coli* to study their role in regulating translation and messenger RNA stability

I very much enjoyed the people in the lab with whom I worked. They were very friendly and helpful. The lab experience has given me a better perspective on the relationship between a secondary education in science and the application of it in a real lab setting. I would advise other teachers to apply if they are interested in gaining important lab skills, expanding their knowledge in the field, being exposed to true professionals in science, and having fun while getting paid.

Jacob Hall, Bethesda–Chevy Chase High School

Lab: Lisheng Cai, Ph.D., PET Radiopharmaceutical Sciences Section, Molecular Imaging Branch, National Institute of Mental Health

Research: Worked on the development of a radiotracer for use with positron emission tomography (PET)

The best part about working at NIH was being surrounded by such great minds and being able to learn from my colleagues. Expanding on my existing knowledge of chemistry and making it practical was a wonderful feeling. I also really enjoyed mentoring students who were exceptionally bright and eager to learn. I've become able to give my students a sense of how science works in the real world, especially the importance of patience, persistence, and creative problem solving.

Selin Mammen, Ph.D., Seneca Valley High School

Lab: Lewis Hsu, M.D., Ph.D., Molecular Medicine Branch, National Institute of Diabetes and Digestive and Kidney Diseases

Research: Investigated the bioavailability of nitric oxide by nitrite supplementation, via drinking water in the whole blood, brain, and liver of mice after different time courses

In the process of seeking your own answers to questions, you sometimes come up with totally new answers, and that arouses your curiosity on the subject further. The warm and collegial atmosphere truly fostered the perfect environment to enhance my lab skills. The internship provided a combination of experience, skills, and resources that have helped me tackle challenges in labs. Also, the second year of internship allowed more independent lab work than the first. Altogether, it was truly a productive and enjoyable experience. I have learned how to bridge the gap between students' learning during a science lecture and the process they are involved in during lab work. This makes science more meaningful and real to them. The interdisciplinary approach to teaching now has a broader meaning for my students. They have become more inquisitive and creative in their approach to learning science as they practice the methodology of research, coupled with the process of logic.

Terri Nostrand, Thomas S. Wootton High School

Lab: Ofelia Olivero, Ph.D., Laboratory of Cancer Biology and Genetics, National Cancer Institute

Research: Studied the relationship between administration of the AIDS drug AZT (Zidovudine) and nuclear centrosomal amplification

I had the best lab mates with whom to work. Teaching can be very isolating at times, so it was a treat to have daily professional interactions that stretch one's brain. Getting into the lab and being in a research team means that I am part of science as it is happening. It was a one-of-a-kind professional growth opportunity to work alongside top-notch scientists in a world-class facility. As the program coordinator for the Wootton Science, Technology, and Research Signature Program, I advise hundreds of science students. I really appreciated the chance to recharge my intellectual batteries, which will have a positive effect on my work with students.

Donald J. Walker, Bethesda–Chevy Chase High School

Lab: Sankar Adhya, Ph.D., and Dale Lewis, Ph.D., Laboratory of Molecular Biology, National Cancer Institute

Research: Examined the influence that asymmetric binding of c1 repressor had on the gene regulation region of lambda DNA

Although I was a novice in terms of gene regulation of lambda DNA, the entire group treated me as if I were truly a part of the research team. Most importantly, group members gave me the support I needed to master the techniques essential to complete my research and share my summer experience with fellow colleagues at the HHMI/MCPS closing ceremony. Through the experience and support I received, I was able to sharpen my laboratory skills. I have insisted that my students keep thorough notes during lab experiments to ensure that they produce efficient results.

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Office of Grants and Special Programs
4000 Jones Bridge Road, Chevy Chase, Maryland 20815-6789
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