



# 2006 Student *and* Teacher Internship Program

Program *and* Student Abstracts

May 18, 2006

**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.mcps.k12.md.us*

Cover: Avian influenza virus (James Cavallini/Photo Researchers, Inc.)

## Student and Teacher Internship Program

### STUDENT PARTICIPANTS

#### 2005–2006

Ambareen Zeenat Ahmed, Damascus High School  
César C. D. Baëta, Wheaton High School  
Thomas Chen, Winston Churchill High School  
Everis Clarke Jr., Walter Johnson High School  
Namisha Dhillon, Northwest High School  
Dipankar Dutta, Paint Branch High School  
Dana Gale, Sherwood High School  
Abby Goldman, Montgomery Blair High School  
Grace Han, Thomas S. Wootton High School  
Susan Han, Thomas S. Wootton High School  
Christopher M. Hill, John F. Kennedy High School  
Leon Lew, Quince Orchard High School  
Szu-Wen (Amy) Liou, Thomas S. Wootton High School  
Sara Moghaddam-Taaheri, Rockville High School  
Thoi Ngo, Walter Johnson High School  
Ernika Quimby, Sherwood High School  
Noelle Singh, Seneca Valley High School  
Alina Starchenko, Winston Churchill High School  
Kabir Teja, Walt Whitman High School  
Belachew Telahun, Wheaton High School  
Richard Washburn, Walt Whitman High School\*  
Didia Zhou, Walter Johnson High School

#### 2006–2007

Anushka R. Aqil, Walt Whitman High School  
Tiffany M. Andersen, Gaithersburg High School  
Millicent I. Bright, Montgomery Blair High School  
Matthew Bushman, Poolesville High School  
Rachel Chen, Thomas S. Wootton High School  
Roberto E. Figueroa, Seneca Valley High School  
Anike K. Freeman, Damascus High School  
Cory Gu, Quince Orchard High School  
Jessica E. Hill, Paint Branch High School  
Greg L. Iannuzzi, Damascus High School  
Hi Joo Karen Kim, Col. Zadek Magruder High School  
Gloria Koskey, Wheaton High School  
Laura J. Li, Rockville High School

\* Not presenting

Daksh Malhotra, Thomas S. Wootton High School  
Maanasi S. Mistry, Winston Churchill High School  
Maria M. Rivera, Wheaton High School  
Maria Isabella O. Roma, Wheaton High School  
Julia L. Sampson, Albert Einstein High School  
Saumil N. Sheth, Paint Branch High School  
Irina D. Tchania, Winston Churchill High School  
Vladimir Zhodzishsky, Thomas S. Wootton High School  
Rahul R. Venkateshwara, Winston Churchill High School

### TEACHER PARTICIPANTS

#### SUMMER 2005

Nova C. Cobble, Seneca Valley High School  
Deborah L. Copeland, Colonel Zadok Magruder High School  
Jennifer L. Jarosinski, Forest Oak Middle School  
Rosetta A. Jordan, Colonel Zadok Magruder High School  
Stephanie N. Malone, Walter Johnson High School  
Emily J. Robinson, Northwest High School  
Stephen D. Shifflett, Walter Johnson High School  
Carol J. Shilling, Watkins Mill High School  
May Y. Shlash, Poolesville High School  
Christie N. Wolfgang, Lakelands Park Middle School  
Shana M. Yudowitch, Colonel Zadok Magruder High School

#### SUMMER 2006

Elaina A. Berres, Albert Einstein High School  
Patrick H. Bilock, Roberto Clemente Middle School  
Alicia M. Campbell, Watkins Mill High School  
Jessica R. Engle, Seneca Valley High School  
Jason A. Jefferson, Silver Spring International Middle School  
Philip A. Johnson, Montgomery Blair High School  
Emily J. Robinson, Northwest High School  
Carol J. Shilling, Watkins Mill High School  
Nikki Snyder Watkins Mill High School  
Christie N. Wolfgang, Lakelands Park Middle School

## Introduction

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

It is my great pleasure to welcome you to the 16th annual dinner symposium of the Montgomery County Public Schools (MCPS) Student and Teacher Internship Program at the National Institutes of Health (NIH), which honors the 22 high school students and 11 teachers who have completed their internships. The program enables students and teachers to become part of the NIH research community, working in state-of-the-art laboratories alongside some of the world's leading biomedical scientists. This booklet presents the students' abstracts describing their projects. This evening we will hear about their investigations into areas such as DNA replication and cancer, koala retrovirus host range, autism, schizophrenia, Alzheimer's disease, hormonal link between osteoporosis and depression, pathogenesis of plague, and genetic causes of obesity.

I want to congratulate the students and teachers on their accomplishments. Participants in the program must not only meet the intellectual challenges of their scientific investigations but also demonstrate the commitment and perseverance that good science requires. In return, students learn how to design and conduct experiments and then analyze and interpret the results. They gain a clearer understanding of what it's like to be a scientist and contribute as part of a research team. And most importantly, they learn how creative, fun, and exciting research can be. Teachers are able to pursue their enthusiasm for science, learn current methods of laboratory research, and find better ways to communicate key principles of today's biology to their students.

I want to recognize the parents and NIH preceptors and mentors whose enthusiasm, encouragement, and guidance make these achievements possible. In particular, this year we are recognizing four preceptors—Dr. Jacqueline N. Crawley, Dr. Steven Kozlowski, Dr. Yves Pommier, and Dr. Thomas Hyde—who have each hosted more than 10 students in their labs over the years. We are also recognizing two long-serving conveners, Dr. John Finerty, who began participating in the program in 1999, and Dr. Bruce A. Fuchs, who began in 1997. Finally, I want to acknowledge Sandra R. Shmookler, special assistant to the superintendent, MCPS, and Gloria A. Seelman, NIH's coordinator of the program, who do such a superb job in organizing the program each year and ensuring a rewarding experience for everyone involved.

On behalf of the Howard Hughes Medical Institute, I extend to all of you our warmest congratulations and best wishes in your future endeavors.

## Program Schedule

*2006 Student and Teacher Internship Program  
HHMI Headquarters and Conference Center*

4:15–5:30 p.m.

### **Student Photographs**

*Outside Terrace*

5:30–6:00 p.m.

### **Welcome Reception**

*Great Hall*

6:00–7:30 p.m.

### **Research Presentations by Students**

*Meeting Rooms A, B, C, and D*

7:30–8:15 p.m.

### **Dinner**

*Dining Room*

8:15 p.m.

### **Official Ceremony**

*Auditorium*

### **Welcome and Opening Remarks**

THOMAS R. CECH, PH.D.

PRESIDENT, HOWARD HUGHES MEDICAL INSTITUTE

### **Remarks by a Former Intern**

HENRIETTA OCHENI BRIGHT

CLASS OF 1999

### **Remarks by a Preceptor**

JACQUELINE N. CRAWLEY, PH.D.

### **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

SANDRA R. SHMOOKLER, M.A.

SPECIAL ASSISTANT TO THE SUPERINTENDENT FOR RESOURCE AND INTERNSHIP DEVELOPMENT,  
MONTGOMERY COUNTY PUBLIC SCHOOLS

### **Special Awards**

### **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 A*

*Bruce A. Fuchs, Ph.D., convener*

- 6:00 p.m. DIDIA ZHOU, WALTER JOHNSON HIGH SCHOOL  
Interaction of LIM kinase 1 and neuregulin 1  
**Preceptor:** CYNTHIA SHANNON-WEICKERT, PH.D., CLINICAL BRAIN DISORDERS BRANCH, NATIONAL INSTITUTE OF MENTAL HEALTH
- 6:15 p.m. SUSAN HAN, THOMAS S. WOOTTON HIGH SCHOOL  
*CHRNA7* transcription in patients with schizophrenia and control subjects  
**Preceptor:** THOMAS HYDE, M.D., PH.D., CLINICAL BRAIN DISORDERS BRANCH, NATIONAL INSTITUTE OF MENTAL HEALTH
- 6:30 p.m. CÉSAR C. D. BAËTA, WHEATON HIGH SCHOOL  
Development of radiotracers for positron emission tomography imaging of  $\beta$ -amyloid aggregates  
**Preceptor:** VICTOR W. PIKE, PH.D., MOLECULAR IMAGING BRANCH, NATIONAL INSTITUTE OF MENTAL HEALTH
- 6:45 p.m. BELACHEW TELAHUN, WHEATON HIGH SCHOOL  
Determining the amino acid residues on the koala retrovirus (KoRV) envelope that defines KoRV's host range  
**Preceptor:** MARIBETH V. EIDEN, PH.D., SECTION ON MOLECULAR VIROLOGY, NATIONAL INSTITUTE OF MENTAL HEALTH
- 7:00 p.m. THOI NGO, WALTER JOHNSON HIGH SCHOOL  
Interaction between the ribosome and translation initiation factor eIF5B  
**Preceptor:** THOMAS DEVER, PH.D., LABORATORY OF GENE REGULATION AND DEVELOPMENT, NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT
- 7:15 p.m. ALINA STARCHENKO, WINSTON CHURCHILL HIGH SCHOOL  
Signal pathways of Dlk and stem cells  
**Preceptor:** STEVEN R. BAUER, PH.D., DIVISION OF CELLULAR AND GENE THERAPIES, FOOD AND DRUG ADMINISTRATION

*Room B*  
*John Finerty, Ph.D., convener*

- 6:00 p.m. CHRISTOPHER M. HILL, JOHN F. KENNEDY HIGH SCHOOL  
Chemokine receptor redistribution to leading edge during neutrophil polarization and migration  
**Preceptor:** STEVEN KOZLOWSKI, M.D., OFFICE OF BIOTECHNOLOGY PRODUCTS, CENTER FOR DRUG EVALUATION AND RESEARCH, FOOD AND DRUG ADMINISTRATION
- 6:15 p.m. KABIR TEJA, WALT WHITMAN HIGH SCHOOL  
Role of *Yersinia* protein kinase A in the pathogenesis of plague  
**Preceptor:** JOHN O'SHEA, M.D., MOLECULAR IMMUNOLOGY AND INFLAMMATION BRANCH, NATIONAL INSTITUTE OF ARTHRITIS AND MUSCULOSKELETAL AND SKIN DISEASES
- 6:30 p.m. DIPANKAR DUTTA, PAINT BRANCH HIGH SCHOOL  
Protection of microtubules from destabilization by intracellular urea  
**Preceptor:** DAN SACKETT, PH.D., LABORATORY OF INTEGRATIVE AND MEDICAL BIOPHYSICS, NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT
- 6:45 p.m. ERNIKA QUIMBY, SHERWOOD HIGH SCHOOL  
Human growth and transformation-dependent protein gene expression in malignant and benign pheochromocytomas  
**Preceptor:** KAREL PACAK, M.D., PH.D., D.Sc., REPRODUCTIVE BIOLOGY AND MEDICINE BRANCH, NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT
- 7:00 p.m. AMBAREEN ZEENAT AHMED, DAMASCUS HIGH SCHOOL  
Protein stability of a double-mutant melanocortin-3 receptor, a genetic cause for obesity  
**Preceptor:** JACK A. YANOVSKI, M.D., PH.D., DEVELOPMENTAL ENDOCRINOLOGY BRANCH, NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT
- 7:15 p.m. DANA GALE, SHERWOOD HIGH SCHOOL  
Corticotropin-releasing hormone and bone cell physiology: link between depression and osteoporosis?  
**Preceptor:** SALVATORE ALESCI, M.D., PH.D., CLINICAL NEUROENDOCRINOLOGY BRANCH, NATIONAL INSTITUTE OF MENTAL HEALTH

*Room C*

*Barry Komisaruk, Ph.D., convener*

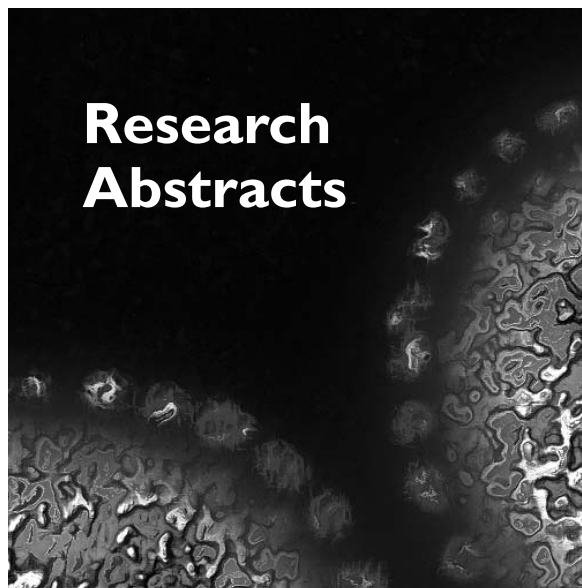
- 6:00 p.m. THOMAS CHEN, WINSTON CHURCHILL HIGH SCHOOL  
Absence of oxytocin alters mouse social behaviors relevant to autism  
**Preceptor:** JACQUELINE N. CRAWLEY, PH.D., LABORATORY OF BEHAVIORAL NEUROSCIENCE, NATIONAL INSTITUTE OF MENTAL HEALTH
- 6:15 p.m. LEON LEW, QUINCE ORCHARD HIGH SCHOOL  
Influence of cyclin-dependent kinase 5 on the transcriptional activity of the glucocorticoid receptor  
**Preceptor:** TOMOSHIGE KINO, M.D., PH.D., REPRODUCTIVE BIOLOGY AND MEDICINE BRANCH, NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT
- 6:30 p.m. SZU-WEN (AMY) LIU, THOMAS S. WOOTTON HIGH SCHOOL  
Role of stored calcium pools in pulsatile activity of gonadotropin-releasing hormone neurons  
**Preceptor:** SUSAN WRAY, PH.D., CELLULAR AND DEVELOPMENTAL NEUROBIOLOGY SECTION, NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE
- 6:45 p.m. NOELLE SINGH, SENECA VALLEY HIGH SCHOOL  
ErbB4-positive white matter neurons in the frontal cortex of normal individuals versus patients with schizophrenia  
**Preceptor:** CYNTHIA SHANNON-WEICKERT, PH.D., CLINICAL BRAIN DISORDERS BRANCH, NATIONAL INSTITUTE OF MENTAL HEALTH

*Room D*

*Charles Dearolf, Ph.D., convener*

- 6:00 p.m. GRACE HAN, THOMAS S. WOOTTON HIGH SCHOOL  
Replication timing of DNA in the human  $\beta$ -globin locus  
**Preceptor:** MIRIT I. ALADJEM, PH.D., SECTION OF LABORATORY OF MOLECULAR PHARMACOLOGY, NATIONAL CANCER INSTITUTE
- 6:15 p.m. EVERIS CLARKE JR., WALTER JOHNSON HIGH SCHOOL  
Genetic mosaic screening for eye-brain connectivity mutants in *Drosophila*  
**Preceptor:** CHI-HON LEE, M.D., PH.D., LABORATORY OF GENE REGULATION AND DEVELOPMENT, NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT
- 6:30 p.m. SARA MOGHADDAM-TAAHERI, ROCKVILLE HIGH SCHOOL  
Modulation of pigment epithelium-derived factor in the eye by matrix metalloproteinases  
**Preceptor:** S. PATRICIA BECERRA, PH.D., LABORATORY OF RETINAL CELL AND MOLECULAR BIOLOGY, NATIONAL EYE INSTITUTE
- 6:45 p.m. NAMISHA DHILLON, NORTHWEST HIGH SCHOOL  
Subcellular location of breast receptor-binding auxiliary protein  
**Preceptor:** JAMES SEGARS, M.D., REPRODUCTIVE BIOLOGY AND MEDICINE BRANCH, NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT; DEPARTMENT OF OBSTETRICS AND GYNECOLOGY, UNIFORMED SERVICES UNIVERSITY OF THE HEALTH SCIENCES
- 7:00 p.m. ABBY GOLDMAN, MONTGOMERY BLAIR HIGH SCHOOL  
TRAIL induces apoptotic topoisomerase I-DNA complexes by a mechanism dependent on caspase-3 and reactive oxygen species  
**Preceptor:** YVES POMMIER, M.D., PH.D., LABORATORY OF MOLECULAR PHARMACOLOGY, NATIONAL CANCER INSTITUTE

# Research Abstracts



Room A  
6:00 p.m.

## Interaction of LIM kinase 1 and neuregulin 1

DIDIA ZHOU, WALTER JOHNSON HIGH SCHOOL

**Preceptor and Mentor:** CYNTHIA SHANNON-WEICKERT, PH.D., CLINICAL BRAIN DISORDERS BRANCH,  
NATIONAL INSTITUTE OF MENTAL HEALTH

### SUMMARY

*Approximately 1% of the population has the brain disorder schizophrenia, and recent evidence has implicated the growth factor signal neuregulin 1 (NRG1) as being related to its cause. The focus of this project is to determine whether patients with schizophrenia and normal individuals express NRG1 or LIM kinase 1 differently. By examining the frontal cortex and hippocampus via quantitative polymerase chain reaction, we found that patients with schizophrenia have altered levels of the mRNA encoding these neurodevelopmentally important proteins.*

### ABSTRACT

Schizophrenia is a disease that is characterized by psychotic symptoms and cognitive deficiencies. The onset of the disease occurs during late adolescence or early adulthood and impairs a person's ability to do many high-level functions. Through linkage studies, neuregulin 1 (NRG1) was found to be a schizophrenia susceptibility gene. NRG1 plays a large role in intercellular and intracellular signaling. One particular intracellular signaling pathway is between NRG1 and LIM kinase 1 (LIMK1; an intracellular kinase), which together control aspects of cell migration in the brain and regulate microtubule networks in cells.

This study looks at whether abnormal gene expression occurs in NRG1 itself or in LIMK1. Our hypothesis is that the gene expression of NRG1 and LIMK1 is different in patients with schizophrenia and normal individuals because of or leading to the irregular cellular migration and/or signaling.

Comparisons of LIMK1 and NRG1 in the frontal cortex and hippocampus are done using quantitative real-time polymerase chain reaction. Differences in the cycle threshold value for each transcript from each postmortem brain sample indicate differences in gene expression. Our preliminary data show no significant changes in the NRG1 mRNA level between patients with schizophrenia and normal individuals. However, LIMK1 mRNA levels are higher in the hippocampus in normal subjects than in patients with schizophrenia. We also detected gender dimorphic gene expression levels in the hippocampus for LIMK1 mRNA, with males having significantly higher levels than females. From these results we conclude that NRG1-LIMK1 signaling may be altered in schizophrenia, which may cause problems in neuronal communication and possibly neuronal migration.



DIDIA ZHOU  
WALTER JOHNSON HIGH SCHOOL

## *CHRNA7* transcription in patients with schizophrenia and control subjects

SUSAN HAN, THOMAS S. WOOTTON HIGH SCHOOL

**Preceptor:** THOMAS HYDE, M.D., PH.D., CLINICAL BRAIN DISORDERS BRANCH,  
NATIONAL INSTITUTE OF MENTAL HEALTH

**Mentor:** SHINY MATHEW, PH.D., CLINICAL BRAIN DISORDERS BRANCH,  
NATIONAL INSTITUTE OF MENTAL HEALTH

### SUMMARY

*Schizophrenia is a severe mental disorder characterized by hallucinations, delusions, thought disorder, and cognitive dysfunction. Many probable susceptibility genes have been identified in schizophrenia. The focus of our group is to better understand the involvement of the nicotinic acetylcholine receptor  $\alpha 7$  (*CHRNA7*) gene.*

### ABSTRACT

Schizophrenia is a polygenic illness affecting approximately 1.5 million Americans. As compared with the normal population, individuals with schizophrenia are 4 times as likely to be cigarette smokers. Nicotine from cigarettes and the endogenous ligand acetylcholine can bind to and alter the properties of nicotinic acetylcholine receptors, which are pentameric, ligand-gated cation channels distributed throughout the body and the brain. Within the brain, these receptors may be found postsynaptically on the cell soma and cause the depolarization of the neuron or presynaptically on the axon terminals modulating neurotransmitter release.

Of the variety of subunits ( $\alpha 2$ - $\alpha 7$  and  $\beta 2$ - $\beta 4$ ) that assemble to form functional receptors, the homomeric  $\alpha 7$  receptor (*CHRNA7*) gene has been implicated as a probable susceptibility gene in schizophrenia. *CHRNA7* is involved in cognitive functions such as learning and memory, which are impaired at the onset of schizophrenia. A study conducted in a small cohort of patients with schizophrenia reported that the protein product of *CHRNA7* is significantly lower within the hippocampus. On the basis of this finding, we hypothesized that the mRNA transcript of *CHRNA7* will also be lowered in patients with schizophrenia.

To test this hypothesis, we used postmortem hippocampal RNA extracts from 63 normal control subjects and 30 patients with schizophrenia to perform real-time quantitative polymerase chain reaction to determine the transcript abundance of *CHRNA7*. We found no significant differences in mRNA levels between normal control subjects and patients with schizophrenia.

Although a negative finding, these data indicate that the transcription of this susceptibility gene in schizophrenia may be normal. Our data further suggest that the differences in protein observed by previous researchers may have been due to inefficient translation of this gene or faster degradation of the *CHRNA7* protein in patients with schizophrenia. Studies are underway to better understand this lack of correlation between *CHRNA7* mRNA and protein levels in schizophrenia.

Room A  
6:15 p.m.



SUSAN HAN  
THOMAS S. WOOTTON  
HIGH SCHOOL

Room A  
6:30 p.m.

## Development of radiotracers for positron emission tomography imaging of $\beta$ -amyloid aggregates

CÉSAR C. D. BAËTA, WHEATON 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



CÉSAR C. D. BAËTA  
WHEATON HIGH SCHOOL

### SUMMARY

*Our objective is to create radioactively labeled small molecules (radiotracers) for use in positron emission tomography (PET) imaging of lesions putatively responsible for Alzheimer's disease (AD). We are looking for radiotracers that will effectively attach to  $\beta$ -amyloid aggregates that characteristically feature in AD. We inject our candidate radiotracers into normal and transgenic rodents and, with the help of PET imaging, look at the  $\beta$ -amyloid protein targets. The effectiveness of the radiotracer is gauged by whether  $\beta$ -amyloid is measured accurately. The purpose of this research effort is to contribute to ongoing research in the diagnosis and monitoring of AD patients.*

### ABSTRACT

Our objective is to design and create radiotracers that bind specifically with  $\beta$ -amyloid plaques that are believed to be the lesions responsible for Alzheimer's disease (AD). We are searching for ligands with the optimum binding potential. Positron emission tomography (PET) imaging of these protein targets will determine the stage of the disease and benefit the monitoring of therapeutic treatments under development.

The process begins with the design of small molecules that bind with amyloid plaques efficiently and selectively in an in vitro assay of AD brain homogenates. The selected small molecules, known as ligands, are labeled with radioisotopes capable of being used in PET, such as  $^{11}\text{C}$  and  $^{18}\text{F}$ . We then inject such candidate radiotracers into normal animals to evaluate their pharmacokinetic and pharmacodynamic properties. Effective radiotracers will ultimately be used in human clinical studies.

We are studying a group of 4-(6-iodoH-imidazo[1,2-a]pyridin-2-yl)-*N,N*-dimethylbenzenamines to select promising ligands for further study. One was identified before my entry into the laboratory. We synthesized a precursor of this compound for labeling with  $^{11}\text{C}$ , using [ $^{11}\text{C}$ ]methyl triflate as the labeling agent. The labeled compound is to be studied using an animal PET scanner to obtain PET images and to determine its pharmacokinetic and pharmacodynamic properties.

## Determining the amino acid residues on the koala retrovirus (KoRV) envelope that defines KoRV's host range

BELACHEW TELAHUN, WHEATON HIGH SCHOOL

**Preceptor:** MARIBETH V. EIDEN, PH.D., SECTION ON MOLECULAR VIROLOGY,  
NATIONAL INSTITUTE OF MENTAL HEALTH

**Mentor:** NIDIA OLIVEIRA, PH.D., SECTION ON MOLECULAR VIROLOGY,  
NATIONAL INSTITUTE OF MENTAL HEALTH

### SUMMARY

*This project focuses on an emerging retrovirus, koala endogenous retrovirus (KoRV), and the broad range of cell types from the diverse species it infects. We have chosen to compare KoRV with gibbon ape leukemia virus (GALV), its closest relative. GALV has a more restricted host range, which should help to pinpoint which genetic sequences are important in defining the range of cells the viruses can infect. This project has broad implications for our better understanding the methods of defining who viruses can infect, giving us a powerful tool to combat species jumping and other related phenomena. More immediately, the project allows us to investigate the similarities between the two viruses and to better define KoRV, thus laying the foundation for future vaccines and diagnostics.*

### ABSTRACT

Mutations in the genome of RNA viruses have caused a myriad of problems throughout recent history and have presented a significant threat to the health and sustenance of humans and other organisms. The emerging threat from RNA viruses, specifically the scourges resulting from their adaptability, reflected by species jumping, has served as an impetus to spur research on the mechanics of such occurrences. One such emerging virus, koala endogenous retrovirus (KoRV), has displayed a remarkable ability to infect different types of cells.

The promiscuity of KoRV is at odds with its closest genomic relative, gibbon ape leukemia virus (GALV). These viruses have 72% identical amino acids in the receptor binding domain of the viral envelope, yet GALV has a much more limited ability to infect different cells.

We are investigating the specific residues responsible for this disparity in infection. We hope to discover more about the interesting relationship between GALV and KoRV, which defies the consensus that taxonomic similarities result in host range similarities.

To begin the process, we identified 19 residue differences between the receptor binding domains of the KoRV and GALV envelopes. We will introduce mutations to change those 19 differences on the KoRV envelope to mirror those of GALV. Through comparative analysis, we will be able to determine which mutation or combination of mutations was most influential for determining the host range of KoRV. Our results have yet to yield conclusive information on what changes are most important, but we are making progress.

Room A  
6:45 p.m.



BELACHEW TELAHUN  
WHEATON HIGH SCHOOL

Room A  
7:00 p.m.

## Interaction between the ribosome and translation initiation factor eIF5B

THOI NGO, WALTER JOHNSON HIGH SCHOOL

**Preceptor:** THOMAS DEVER, PH.D., LABORATORY OF GENE REGULATION AND DEVELOPMENT,  
NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

**Mentor:** JEANNE FRINGER, PH.D., LABORATORY OF GENE REGULATION AND DEVELOPMENT,  
NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT



THOI NGO  
WALTER JOHNSON HIGH SCHOOL

### SUMMARY

*Translation, also known as protein synthesis, is the final step of gene expression in which the language of DNA and nucleic acids is converted into the language of protein composed of amino acids. At the beginning of translation, several proteins called translation initiation factors aid the assembly of the protein-synthesizing machine, the ribosome, into a competent state. Yeast cells that lack the translation initiation factor eIF5B have an impaired ability to synthesize proteins. We are identifying and characterizing mutations in the ribosome itself that improve protein synthesis in cells lacking eIF5B. This basic research will help to define the function of eIF5B and the ribosome. As misregulation of protein synthesis is observed in a number of diseases, our studies may identify new pharmaceutical targets to overcome illnesses related to this essential biological process.*

### ABSTRACT

During the initiation phase of protein synthesis, the 40S ribosomal subunit binds to an mRNA and moves to the start codon where the 60S subunit joins, forming a competent 80S ribosome. This process is aided by initiation factors. Our research examines the initiation factor eIF5B, encoded by the gene *FUN12* in the yeast *Saccharomyces cerevisiae*. eIF5B stimulates the joining of the 60S ribosomal subunit to a 40S subunit. Yeast lacking the *FUN12* gene grow much slower than normal cells because of a defect in translation.

Because eIF5B facilitates ribosomal subunit joining, we focused on the ribosome and searched for mutations that lessen the requirement for eIF5B. The ribosome is composed of ribosomal proteins and ribosomal RNA (rRNA), which is the critical functional component of the ribosome. We searched for mutations in the rRNA that could suppress the slow growth of yeast cells lacking eIF5B.

For our studies we used a yeast strain in which we could shut off expression of eIF5B and the normal (wild-type) rRNA by growing cells on medium containing glucose. After randomly mutating a plasmid containing the rDNA gene encoding for rRNA, we generated a library of mutant plasmids, which was introduced into the yeast strain. We then screened for cells that grew well on glucose medium. Although cells containing an unmutated rDNA plasmid grew poorly because of the lack of eIF5B, some cells grew well because the rDNA contained a mutation enabling translation to initiate without eIF5B.

To further characterize the rRNA mutations, we will sequence the mutant plasmids and biochemically characterize the ribosomes from the mutants. These studies will enhance our understanding of the mechanism of translation initiation and may help identify targets for drugs to prevent illnesses caused by defects in protein synthesis.

## Signal pathways of Dlk and stem cells

ALINA STARCHENKO, WINSTON CHURCHILL HIGH SCHOOL

**Preceptor and Mentor:** STEVEN R. BAUER, PH.D., DIVISION OF CELLULAR AND GENE THERAPIES,  
FOOD AND DRUG ADMINISTRATION

### SUMMARY

*Dlk (delta-like homolog) is a transmembrane molecule that takes part in cellular signaling and causes cells to differentiate along certain paths. We are using Dlk1-deficient mice in order to better understand the Dlk pathway. We succeeded in establishing Dlk1-deficient cell lines and found that Dlk affects adipose stem cell proliferation and differentiation, suggesting that Dlk can be used to manipulate and/or control adipose-derived stem cells in the future.*

### ABSTRACT

Stem cell therapies are an important emerging field in the medical and scientific communities. The ability to control and manipulate these cells has implications in medicine and science. Unfortunately, control is still difficult because of limited knowledge about specific differentiation patterns. Often, patterns are triggered by specific molecules. Dlk (delta-like homolog) is a transmembrane protein that seems to be involved in numerous differentiation processes such as adipogenesis (fat cells) and fetal liver hematopoiesis (red and white blood cells). Dlk is highly expressed by preadipose cells and neuroendocrine tumors.

To find the pathways affected by Dlk, we are comparing mice lacking the *Dlk1* gene with normal mice and looking for psychological and physiological differences. Because the pathway that Dlk affects is important for neuronal differentiation, we are using the Morris water maze to explore the notion that Dlk plays a role in the formation of nerve cells controlling long-term memory storage. So far, we have seen no difference between the two groups, implying that Dlk has little to no effect on memory storage.

Because Dlk was shown to affect fat cell differentiation, we compared adipose-derived stem cells (ASCs) from normal mice and *Dlk1*-deficient mice in two different tests: one testing their ability to form bone and the other testing their proliferation rate. Our experiments show that viable lines can be established from adipose stem cells lacking Dlk. Preliminary studies suggest that *Dlk1*-deficient ASCs multiply and differentiate more rapidly into bone than do ASCs from normal mice. This implies that Dlk acts as a negative regulator of both differentiation and division pathways of ASCs. Our results suggest that Dlk can be used to enable us to better understand and control ASCs.

Room A  
7:15 p.m.



ALINA STARCHENKO  
WINSTON CHURCHILL  
HIGH SCHOOL

Room B  
6:00 p.m.

## Chemokine receptor redistribution to leading edge during neutrophil polarization and migration

CHRISTOPHER M. HILL, JOHN F. KENNEDY HIGH SCHOOL

**Preceptor:** STEVEN KOZLOWSKI, M.D., OFFICE OF BIOTECHNOLOGY PRODUCTS,  
CENTER FOR DRUG EVALUATION AND RESEARCH, FOOD AND DRUG ADMINISTRATION

**Mentor:** KAMALPREET ARORA, PH.D., DIVISION OF IMMUNOLOGY AND MONOCLONAL ANTIBODIES,  
CENTER FOR DRUG EVALUATION AND RESEARCH, FOOD AND DRUG ADMINISTRATION



### SUMMARY

*Inflammation is the first response of the immune system to an infection or irritation. When a part of our body becomes inflamed, a chemical signal—a chemokine—is released. Cells known as neutrophils are constantly circulating in our blood; when they learn through the chemical signals that there is an infection, they leave our blood vessels and migrate to the site of infection. The migration is caused by a redistribution of the surface proteins on neutrophils. We are investigating the redistribution of these surface proteins, known as chemokine receptors, to better understand how neutrophils migrate to the inflammatory sites.*

CHRISTOPHER M. HILL  
JOHN F. KENNEDY HIGH SCHOOL

### ABSTRACT

Resting polymorphonuclear leukocytes (neutrophils) circulating in the blood rapidly activate in response to inflammatory signals and migrate to inflamed areas. Migrating neutrophils adopt a polarized morphology in response to chemotactic stimuli (chemokines) that are released during inflammation. Polarized migrating neutrophils form a leading edge (lamellipodia) and a rear end tail (uropod). These separate regions take on different properties to carry out specialized functions. Chemokine receptors and adhesion molecules together direct the migration of neutrophils into inflamed areas. CD43, a sialoglycoprotein adhesion molecule, redistributes to the rear end tail. This redistribution of CD43 is related to neutrophil polarity and locomotion.

We are studying the redistribution of chemokine receptors to the leading edge of polarized neutrophils and their role in neutrophil migration. We isolated the peripheral neutrophils from the murine blood (BALB/C strain) using histopaque 1077 and 1119 gradient. Diff quick staining after cytopsin established 90% neutrophil purity. We are studying the expression of chemokine receptors CXCR4, CCR5, and CCR7 on these neutrophils using fluorescence-activated cell sorting. The surface redistribution of these receptors will be studied using immunofluorescence confocal microscopy in the presence of chemoattractants, for example, bacterial products and chemokines such as fMLP (*N*-formyl-MET-LEU-PHE), SDF1 $\alpha$ , Rantes, and CCL21.

Information obtained from this study will help shed light on the role of chemokine receptor redistribution to the leading edge and its relation to neutrophil polarity and locomotion.

# Role of *Yersinia* protein kinase A in the pathogenesis of plague

KABIR TEJA, WALT WHITMAN HIGH SCHOOL

**Preceptor:** JOHN O'SHEA, M.D., MOLECULAR IMMUNOLOGY AND INFLAMMATION BRANCH,  
NATIONAL INSTITUTE OF ARTHRITIS AND MUSCULOSKELETAL AND SKIN DISEASES

**Mentor:** HEIYOUNG PARK, PH.D., MOLECULAR IMMUNOLOGY AND INFLAMMATION BRANCH,  
NATIONAL INSTITUTE OF ARTHRITIS AND MUSCULOSKELETAL AND SKIN DISEASES

## SUMMARY

*Yersinia pestis*, the causative agent of plague, is a major bioterrorism threat and is still endemic in parts of the world. It functions by injecting 6 proteins that interfere with various cellular functions into immune cells. The purpose of our research is to determine the significance and functions of one of these proteins, *Yersinia* protein kinase A (YpkA). We found that YpkA acts as a direct killer by causing programmed cell death (apoptosis) in target cells. By studying the pathway that YpkA uses, we may find an effective way to block it and create a new therapy for plague.

## ABSTRACT

*Yersinia pestis*, the causative agent of plague, is still endemic in many parts of the world and is a potential bioterrorism agent. Through evolutionary and genetically engineered pathways, antibiotic-resistant strains of plague have become a major threat. Unfortunately, there are no other effective therapies for treating plague. To develop an alternative therapy, we must study the mechanisms that the bacteria use.

*Yersinia* attacks immune cells by injecting 6 effector proteins, known as Yops (*Yersinia* outer proteins). One of these Yops, *Yersinia* protein kinase A (YpkA), plays a critical role in the termination of target cells. When cells expressing YpkA were examined under a microscope, they showed signs of apoptosis (programmed cell death). We hypothesized that YpkA killed immune cells by causing apoptosis.

To test this hypothesis, we quantified apoptosis by staining active caspase-3 using flow cytometry analysis. Apoptotic activity was significantly increased in the YpkA-expressing cells compared with control cells. Because YpkA is directly related to apoptosis, it is very likely that it is a direct killer Yop in plague. If YpkA could be inhibited or prevented from functioning, new therapies could be created to prevent, slow, or treat the *Yersinia* infection.

By continuing to study YpkA and the specific pathways it uses to induce apoptosis, we will be better able to understand how to prevent it from doing so.

Room B  
6:15 p.m.



KABIR TEJA  
WALT WHITMAN HIGH SCHOOL

Room B  
6:30 p.m.

## Protection of microtubules from destabilization by intracellular urea

DIPANKAR DUTTA, PAINT BRANCH HIGH SCHOOL

**Preceptor and Mentor:** DAN SACKETT, PH.D., LABORATORY OF INTEGRATIVE AND MEDICAL BIOPHYSICS,  
NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT



DIPANKAR DUTTA  
PAINT BRANCH HIGH SCHOOL

### SUMMARY

*The purpose of this study is to understand the mechanisms that allow self-organizing protein polymers such as microtubules to function properly even in the presence of molecular destabilizers such as urea. We predict that a set of small organic solutes, termed compatible or compensating osmolytes, and the crowded environment in the cell itself are responsible for microtubule protection from destabilization. We investigated how tubulin is affected by the osmolytes present in mammalian kidneys as well as how the crowded interior of a cell can influence microtubule formation. We also investigated why these factors were or were not sufficient to allow for microtubule formation and protection.*

### ABSTRACT

Osmolytes are small solutes found in osmotically stressed tissues that allow cell volume to be maintained. Trimethylamine *N*-oxide (TMAO) is a common osmolyte present in sharks. TMAO can counteract the effects of urea and other compounds that disrupt various cell activities, including the formation of protein polymers such as microtubules. Since mammals do not have TMAO, it is of interest to understand how microtubules are still able to polymerize in mammalian kidney cells, where urea is present in high concentrations.

This study measured the promotion or inhibition of polymerization of cow brain tubulin by various natural intracellular molecules, especially those found in mammalian kidneys. Tubulin was incubated with the test compounds, the microtubules that formed were centrifuged, and the pellets were quantified, giving the percentage polymerization of the original protein.

Mammals have several osmolytes that show little promotion of polymerization, and most provide little protection from the depolymerization caused by urea. However, when all the mammalian osmolytes were combined in the relative concentrations found in the kidney, we found that they increased polymerization by 20–25% and provided some protection from urea. Macromolecules such as Ficoll, which mimics the crowded state in a cell, substantially increase polymerization and, like the osmolytes, Ficoll also provides marginal protection against urea. When Ficoll was combined with the osmolyte mixture that resembled the inside of a mammalian kidney cell, the effect on polymerization was additive, but the counteracting ability of urea became more than additive, allowing tubulin to polymerize more than in the urea-osmolytes or urea-Ficoll control. The combination was also able to recover tubulin previously exposed to urea.

We conclude that an additive relationship in polymerization and a more than additive relationship in counteracting ability of molecular destabilizers allow for microtubules to form and function properly, enabling mammalian kidney cells to function normally even in the presence of urea and other toxic substances.

# Human growth and transformation-dependent protein gene expression in malignant and benign pheochromocytomas

ERNIKA QUIMBY, SHERWOOD HIGH SCHOOL

**Preceptor:** KAREL PACAK, M.D., PH.D., D.Sc., REPRODUCTIVE BIOLOGY AND MEDICINE BRANCH,  
NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

**Mentors:** SHOICHIRO OHTA, M.D., AND EDWIN W. LAI, B.S., REPRODUCTIVE BIOLOGY AND MEDICINE BRANCH,  
NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

## SUMMARY

*Expression of the growth and transformation-dependent protein gene has been implicated in malignancy of pheochromocytoma (pheo) from microarray analysis. My project involves the use of quantitative real-time polymerase chain reaction to confirm the gene expression levels of human growth and transformation-dependent protein in malignant and benign pheos. The protein is presumed to play a role in allowing cells to die naturally, a characteristic that is lacking in metastatic cancer. If this presumption holds, related genes will be also be investigated.*

## ABSTRACT

Pheochromocytoma (pheo), a rare tumor of the adrenal gland, has an annual incidence of three to eight cases per million people. Pheo has a diverse manifestation but can be classified based on tumor presentation as either malignant or benign. Comparing the expression levels of genes in malignant tumors with levels in benign tumors may help us to better understand and possibly predict the metastatic potential of these tumors.

Our study investigated the difference in the expression of human growth and transformation-dependent protein (HGTD-P) between malignant and benign pheos. A recently completed microarray indicated that *HGTD-P* expression was significantly different between malignant and benign tumor samples ( $p < 0.05$ ). We synthesized cDNA from the RNA extracted from 6 malignant and 7 benign pheo patient samples. We then performed quantitative reverse-transcription polymerase chain reaction and compared the results with an 18s rRNA internal control, using the standard curve method and a standard manufacturer's protocol. The predicted result is that *HGTD-P* is more highly expressed ( $p < 0.05$ ) in benign pheos, verifying the microarray results.

Previous research showed that the ability for cancerous cells to evade apoptosis is an important factor in metastasis, and *HGTD-P* has been classified as pro-apoptotic. If the expression of *HGTD-P* facilitates apoptosis such as occurs naturally in normal cells, and most likely to a slightly higher degree in benign pheos, it could be an important gene for future study into the prevention of malignancy potential and metastasis. Further analysis should be done to detect differences based on such characteristics of the pheo sample population as their location (adrenal/extradrenal) or mutations (SDHB positive/negative) for more specific results. Investigation into the role of other pro-apoptotic genes with pathways similar to that of *HGTD-P* would be helpful for more insight into the necessary underlying genetic factors to help develop earlier detection of and treatment for malignant pheo.

Room B  
6:45 p.m.



ERNIKA QUIMBY  
SHERWOOD HIGH SCHOOL

Room B  
7:00 p.m.

## Protein stability of a double-mutant melanocortin-3 receptor, a genetic cause for obesity

AMBAREEN ZEENAT AHMED, DAMASCUS HIGH SCHOOL

**Preceptor:** JACK A. YANOVSKI, M.D., PH.D., DEVELOPMENTAL ENDOCRINOLOGY BRANCH,  
NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

**Mentor:** JA-SHIN KOO, PH.D., DEVELOPMENTAL ENDOCRINOLOGY BRANCH,  
NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT



### SUMMARY

*Approximately 15% of children and teens in the United States are overweight. A double-mutant variant of the melanocortin-3 receptor may be a genetic cause for obesity because it is associated with high body fat in children and causes lower protein expression. My project will study whether this lower expression comes from lower protein production or altered protein stability.*

AMBAREEN ZEENAT AHMED  
DAMASCUS HIGH SCHOOL

### ABSTRACT

Obesity is a major problem in economically developed countries, affecting approximately 15% of the children and adolescent population in the United States alone. The melanocortin-3 receptor (MC3R) plays an important role in the regulation of energy balance. Knockout mouse models suggest that MC3R is important for nutrient partitioning and that its effects of body adiposity are additive with mutations in other obesity genes.

A previous study from our laboratory found that 8.2% of 355 overweight and nonoverweight children were double homozygous for a pair of MC3R sequence variants (Thr6Lys and Val81Ile). Children with this double-mutant variant were significantly heavier and had greater plasma leptin and insulin concentrations than did children with wild-type MC3R or heterozygous MC3R. The study also found that this double-mutant variant generated less downstream signaling activity than did wild type and that the mechanism for the lower activity may involve less receptor protein expression. The lower receptor protein levels for this mutant did not depend on transfection efficiency or mRNA levels but appeared to be due solely to posttranslational events. It remains unclear whether the lower protein expression is due to decreased synthesis or increased degradation.

We will compare the translational efficiency and protein stability of wild-type and double-mutant MC3R proteins. We will begin by transfecting an HEK293 cell line with wild-type and double-mutant MC3R genes tagged with green fluorescent protein. We will then study the effects of a protein translation inhibitor (cycloheximide) on protein expression by monitoring fluorescence via fluorescent-activated cell sorting and Western blot analysis. To study whether degradation is altered, we will examine the effects of proteasome inhibitors (MG-132 and Lactacystin) and lysosome inhibitors (Bafilomycin A1 and ammonium chloride). Our results will reveal whether the reduced protein production comes from protein translation efficiency or protein degradation.

# Corticotropin-releasing hormone and bone cell physiology: link between depression and osteoporosis?

DANA GALE, SHERWOOD HIGH SCHOOL

**Preceptor:** SALVATORE ALESCI, M.D., PH.D., CLINICAL NEUROENDOCRINOLOGY BRANCH, NATIONAL INSTITUTE OF MENTAL HEALTH

**Mentors:** LULU Z. LIAO, B.S., AND ANGELA D. TAYLOR, M.S., CLINICAL NEUROENDOCRINOLOGY BRANCH, NATIONAL INSTITUTE OF MENTAL HEALTH

## SUMMARY

*I am studying the role of the stress hormone corticotropin-releasing hormone (CRH) on osteoblast (bone-forming cell) physiology as a possible link between major depression and osteoporosis. CRH plays a key role in depression, and women with depression have an increased risk of developing bone loss. We will use polymerase chain reaction to determine whether osteoblasts express the genes for CRH and/or CRH receptors. If any of these genes is present, then it is likely that bone cells are influenced by CRH. We speculate that increased levels of CRH may contribute to the bone mineral loss associated with major depression.*

## ABSTRACT

Major depression (characterized by symptoms of loss of interest, sleep disturbance, low energy, weight change, low self-esteem, poor concentration, and thoughts of suicide) affects 1–6% of the world's population, costing \$44 billion to treat in the United States alone. Depression is a disease of the mind as well as the body because it increases the risk of heart attacks, diabetes, and osteoporosis.

Research done at the Clinical Neuroendocrinology Branch has shown the importance of corticotropin-releasing hormone (CRH) dysregulation in depression. Research has also shown that premenopausal women with depression have a higher risk of developing osteoporosis (condition of skeletal fragility characterized by reduced bone mass and microarchitectural deterioration of bone tissue). We hypothesize that the two phenomena are linked.

Our project is to study the effects of CRH (a stress hormone secreted by the hypothalamus that affects multiple organs) on osteoblasts (bone-forming cells). If the osteoblasts have receptors for CRH, then CRH may modulate their proliferation as well as the release of important regulators of bone turnover, such as the cytokine interleukin-6 (IL-6), a potent stimulator of bone resorption.

We used two osteosarcoma cell lines (MG63 and SaOS-2) as models of human osteoblasts. We isolated RNA and performed polymerase chain reaction (PCR) and real-time reverse-transcription PCR to determine the presence of and quantify the expression of the genes for CRH and CRH receptors in these cells. In addition, we are performing functional studies by exposing osteoblasts to various CRH concentrations for different time intervals to determine whether CRH modulates the production of IL-6. PCR results have shown the presence of CRH and its receptor genes in MG63 cells.

Room B  
7:15 p.m.



DANA GALE  
SHERWOOD HIGH SCHOOL

Room C  
6:00 p.m.



THOMAS CHEN  
WINSTON CHURCHILL  
HIGH SCHOOL

## Absence of oxytocin alters mouse social behaviors relevant to autism

THOMAS CHEN, WINSTON CHURCHILL HIGH SCHOOL

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

### SUMMARY

*Autism is a developmental disorder of the brain that affects 60 in 10,000 births worldwide. Our laboratory investigates the genetic components of autism by analyzing social approach behaviors in genetically modified mice. My experiments tested mice with mutations in the gene for the hypothalamic neuropeptide oxytocin. Male oxytocin heterozygotes (mice that produce less than normal levels of oxytocin) and null mutants (mice that cannot produce any oxytocin) as well as female heterozygotes failed to show the normal preference for social novelty. These results support a role for oxytocin in social recognition, which may be relevant to the deficits in reciprocal social interactions that define autism.*

### ABSTRACT

Autism is characterized by deficits in social interaction, social communication, and repetitive behaviors. Our laboratory uses social-approach behavioral assays on mutant lines of mice to model deficits in social interaction. Using an automated three-chambered apparatus, the sociability measure determines whether the subject mouse would rather spend time with a stranger mouse (placed in an inverted wire cage) or an unfamiliar, inanimate object (an identical but empty inverted wire cage). Normal, wild-type mice spend more time interacting with the new peer than with a nonsocial novel object. Autistic-like behavior is the interpretation if mice stay away from the stranger or spend more time with the empty wire cage. The measure of preference for social novelty determines whether the subject mouse would rather spend time with a familiar mouse (the stranger from the sociability measure, or stranger 1) or a new stranger (stranger 2).

The mutant mice used in this study were  $+/+$ ,  $+/-$ , or  $-/-$  for the gene that codes for oxytocin, a hypothalamic neuropeptide that mediates social affiliation in rodents. My experiments compared mice with a mutation in the oxytocin gene with their wild-type littermate controls on the social tasks and other procedural behaviors. Social contact is scored by an observer using two stopwatches, one recording time spent sniffing the stranger mouse, the other recording time spent sniffing the empty cage; time spent is computer scored.

Oxytocin knockouts showed a specific deficit in the preference for social novelty portion of the task. Male heterozygotes and null mutants and female heterozygotes failed to show a significant preference for stranger 2 over stranger 1. Normal scores on general health, home cage behaviors, neurological reflexes, olfaction, vision, hearing, touch, locomotion, and motor coordination confirmed the specificity of the social deficit. Our results confirm the relationship between oxytocin and social recognition. Our approach will be useful for further investigations of other genes that may contribute to the symptoms of autism.

# Influence of cyclin-dependent kinase 5 on the transcriptional activity of the glucocorticoid receptor

LEON LEW, QUINCE ORCHARD HIGH SCHOOL

**Preceptor and Mentor:** TOMOSHIGE KINO, M.D., PH.D., REPRODUCTIVE BIOLOGY AND MEDICINE BRANCH, NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

## SUMMARY

*Glucocorticoids are steroid hormones that maintain homeostasis so that the body can function normally. My research concerns how cyclin-dependent kinase 5 (CDK5), which is important in brain development, affects activity of the glucocorticoid receptor (GR, which is a protein in the cytoplasm and nucleus). I will determine whether the CDK5 affects GR and, if it does, use the data to estimate how much transcriptional activity will occur because of the interaction between CDK5 and GR.*

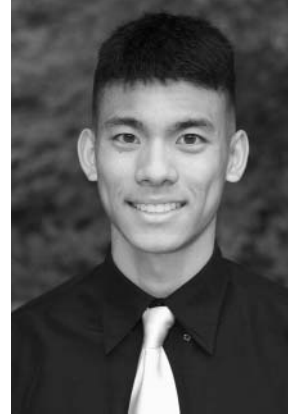
## ABSTRACT

Cyclin-dependent kinase 5 (CDK5) is a kinase specific to the brain that plays an important role in brain development. Deregulation of its activity also plays a significant role in the pathogenesis of Alzheimer's disease. We are focusing on how CDK5 affects the biological activity of glucocorticoid receptor (GR). CDK5 and GR were found previously to interact with each other. I will perform transfection with plasmids expressing CDK5 to determine whether the CDK5 overexpression modulates GR-induced transcriptional activity.

We will first introduce several plasmids into HCT116 human colon cancer cells so that GR and CDK5 are expressed. By measuring the activity of luciferase expressed under the control of the mouse mammary tumor virus promoter (MMTV) containing glucocorticoid response element, we can determine whether CDK5 affects GR-induced transcriptional activity. We will add dexamethasone (a synthetic glucocorticoid) to the transfected cells to stimulate GR. Activated GR then translocates from the cytoplasm to the nucleus, binds the promoter region of the MMTV-Luc, and finally stimulates the transcription of the downstream luciferase gene, creating a signal. Because we cannot measure the transcriptional activity directly, we will estimate it from activity of the expressed luciferase. For this purpose, we will use a luminometer, which measures the amount of activated, light-producing luciferene that is catalyzed by the luciferase. From there, we can determine whether CDK5 influences GR.

We have determined that CDK5 has a profound effect on GR: the higher the dexamethasone dosage, the higher the transcriptional activity that is recorded. CDK5 strongly suppressed GR-induced transcriptional activity. Using this information, we can assess the effect other diseases have on GR. My results will help the laboratory further advance its study of the physiological causes of diseases.

Room C  
6:15 p.m.



LEON LEW  
QUINCE ORCHARD HIGH SCHOOL

Room C  
6:30 p.m.



SZU-WEN (AMY) LIU  
THOMAS S. WOOTTON  
HIGH SCHOOL

## Role of stored calcium pools in pulsatile activity of gonadotropin-releasing hormone neurons

SZU-WEN (AMY) LIU, THOMAS S. WOOTTON HIGH SCHOOL

**Preceptor:** SUSAN WRAY, PH.D., CELLULAR AND DEVELOPMENTAL NEUROBIOLOGY SECTION,  
NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE

**Mentor:** STEPHANIE CONSTANTIN, PH.D., CELLULAR AND DEVELOPMENTAL NEUROBIOLOGY SECTION,  
NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE

### SUMMARY

*We are trying to determine what initiates pulsatile hormone secretion in a specific neuron of the brain important for reproduction. Data have suggested that calcium concentration in the endoplasmic reticulum plays a key role in this process. To test this theory, we added a drug to the neurons that depletes the calcium stores and recorded its effects over time.*

### ABSTRACT

Gonadotropin-releasing hormone-1 (GnRH-1) neurons are neuroendocrine cells essential for reproduction. GnRH-1 is released into the portal circulation of the pituitary gland in a pulsatile manner. Data suggest that pulsatility is an innate capability of GnRH-1 neurons, independent of cues in the central nervous system and dependent on synchronization of cells. GnRH-1 neurons maintained in mouse nasal explants display significant calcium peaks that synchronize at 20-minute intervals, a temporal interval similar to that of pulsatile GnRH-1 secretion. In such explants, changes in intracellular calcium in GnRH-1 neurons can be monitored using calcium imaging because an elevation of intracellular calcium concentration is associated with neurosecretion. Calcium in the axon terminal is involved in neurosecretion, and calcium oscillation in the cell body is pulsatile. Thus, in this model we can evaluate signals used to synchronize GnRH-1 activity and, potentially, GnRH-1 secretion.

We do not know what initiates the opening of the voltage-gated sodium channels that depolarize the cells and lead to action potentials. One theory is that the intracellular calcium stores in the endoplasmic reticulum are emptied, which leads to a phase of extracellular calcium influx caused by calcium release-activated channels located on the plasma membrane. Calcium-ATPase reuptakes the calcium into the endoplasmic reticulum and allows repetitions of action potential to occur.

We tested this theory using thapsigargin, a calcium-ATPase reuptake inhibitor that depletes the calcium stores of the endoplasmic reticulum. We hypothesize that the depletion of the calcium stores will lead to a decrease of synchronized pulses while simultaneously decreasing the amplitude of calcium oscillations over time. These findings will be beneficial to our understanding of the underlying neuronal secretion mechanisms of neurons and, specifically, pulsatile secretion of neuroendocrine cells.

## ErbB4-positive white matter neurons in the frontal cortex of normal individuals versus patients with schizophrenia

NOELLE SINGH, SENECA VALLEY HIGH SCHOOL

**Preceptor:** CYNTHIA SHANNON-WEICKERT, PH.D., CLINICAL BRAIN DISORDERS BRANCH, NATIONAL INSTITUTE OF MENTAL HEALTH

**Mentors:** SENDA BELTAIFA, M.D., AND MIA THOMPSON, B.S., CLINICAL BRAIN DISORDERS BRANCH, NATIONAL INSTITUTE OF MENTAL HEALTH

### SUMMARY

*The purpose of our work is to determine whether the susceptibility gene NRG1 can be linked to neuropathological changes in brains of patients with schizophrenia. We are interested in determining whether neurons buried within the white matter of the human frontal cortex can be NRG1 responsive. We specifically look at the NRG1 receptor, ErbB4, by conducting immunohistochemistry experiments, which stain specific proteins expressed in cells. We then compare the interstitial white matter neurons in the brain tissue of normal individuals and patients with schizophrenia to ascertain whether there is a difference in their expression of ErbB4. This research will help us determine the cellular routes by which NRG1 may be involved in developing schizophrenia.*

### ABSTRACT

Schizophrenia is a chronic, severe, and disabling brain disease that affects approximately 1% of the population. More than 2 million Americans have schizophrenia in a given year. Some common symptoms of schizophrenia are hallucinations, delusions, social isolation, withdrawal, and unusual speech or behavior. Underlying cellular and molecular changes occur in brains of patients with schizophrenia and evidence suggests that the density or number of neurons is altered in the white matter. We are currently trying to compare the differences between the interstitial white matter neurons in normal individuals and patients with schizophrenia. We hypothesize that patients with schizophrenia fail to undergo certain NRG1-mediated developmental brain changes, causing them to have abnormal neuronal migration.

Using immunohistochemistry, I am focused on finding which immunohistochemical markers will work best for identifying interstitial white matter neurons. I use frozen sections of brain tissue and follow a typical immunohistochemical protocol of blocking nonspecific sites, applying the primary antibody, and incubating with the secondary antibody-enzyme conjugate. This procedure allows me to visualize the location of specific proteins and analyze the density of the protein's expression in cells. I am looking for differences in the structure, shape, and location of the immunostained cells in patients with schizophrenia compared with normal individuals. I tested p75, NeuN, and calbindin. I found that p75 is the best at identifying interstitial white matter neurons. Next, I used an antibody specific for ErbB4 to determine whether the interstitial white matter neurons contain the NRG1 receptor.

This research will allow us to determine whether this population of neurons remains NRG1 responsive into adult life and to identify any differences between ErbB4-positive interstitial white matter neurons in normal individuals compared with patients with schizophrenia.

Room C  
6:45 p.m.



NOELLE SINGH  
SENECA VALLEY HIGH SCHOOL

Room D  
6:00 p.m.

## Replication timing of DNA in the human $\beta$ -globin locus

GRACE HAN, THOMAS S. WOOTTON HIGH SCHOOL

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

**Mentor:** CHII MEI LIN, M.Sc., SECTION OF LABORATORY OF MOLECULAR PHARMACOLOGY,  
NATIONAL CANCER INSTITUTE



### SUMMARY

*Over 200 different types of cancers affect more than 1 million individuals in the United States each year. The focus of our project is to find out what controls DNA replication through the study of DNA sequences in the human  $\beta$ -globin locus, which play an important role in DNA replication. We are studying how the timing of DNA replication is regulated by taking sequences from the  $\beta$ -globin locus from their natural location and placing them next to other sequences that replicate at different times during the cell cycle. In doing so, we hope to better understand the regulation of DNA replication in normal cells and abnormal cancerous cells.*

### ABSTRACT

Cancer cells form when DNA replication becomes uncontrollable. DNA replication occurs during the S (synthesis) phase of the cell cycle. However, some parts of the genome replicate early during the cell cycle and other parts replicate late during the cell cycle. Exactly how cells decide which sequences should replicate early and which should replicate late is unknown. The purpose of this study was to see whether specific sequences called replicators, which regulate the location at which DNA replication starts inside the  $\beta$ -globin locus, also play a role in the regulation of DNA replication timing.

First, we selected a segment of DNA from the human  $\beta$ -globin locus, which functions as a replicator, and inserted it into a specific site in murine erythro-leukemia cells. This transformation was performed to study whether the replicators affected the timing of DNA replication when placed next to early- or late-replicating DNA outside their natural location. Next, we exposed cells for a short time to a compound that incorporated into newly replicated DNA. We then used a fluorescence-activated cell sorter to obtain cells in the early or late phase of the cell cycle. Immunoprecipitation assays with specific antibodies that recognized only DNA that contained the compound were then performed on the cells grouped according to stage of cell cycle. Next, we extracted DNA from each cell group. This DNA represented genes that were replicated during the specific phases of the cell cycle. Finally, we used real-time polymerase chain reactions to identify the genes that replicated during the different cell cycle stages.

Using these techniques, we are elucidating the role of specific sequences in cell cycle control of DNA replication.

GRACE HAN  
THOMAS S. WOOTTON  
HIGH SCHOOL

# Genetic mosaic screening for eye-brain connectivity mutants in *Drosophila*

EVERIS CLARKE JR., WALTER JOHNSON HIGH SCHOOL

**Preceptor:** CHI-HON LEE, M.D., PH.D., LABORATORY OF GENE REGULATION AND DEVELOPMENT,  
NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

**Mentor:** SHUYING GAO, PH.D., LABORATORY OF GENE REGULATION AND DEVELOPMENT,  
NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

## SUMMARY

*The overall purpose of my research is to isolate mutations that disrupt neural connectivity of the R7 and R8 photoreceptor neurons in the Drosophila visual system. We do this by generating eye-mosaic animals in which the retina is rendered mutant while the rest of the animal remains wild type. This system allows us to screen for the genes that function in the photoreceptor neurons to establish proper connections with the brain. To identify connectivity defects, we expressed a red fluorescent protein in the mutant photoreceptor neurons and examined their projection pattern using immunohistochemistry. In over 2000 lines screened, we have isolated 6 loci that affect R7 or R8 connectivity: 3 are involved in the establishment of R7 and R8 connections during development; the other 3 likely play a role in the maintenance of these connections in adults.*

## ABSTRACT

We have screened ~2000 lines of *Drosophila* treated with ethane methyl sulfonate mutagen and ~150 lines of existing behavioral mutants for eye-brain connectivity defects. We have identified 6 mutants that exhibit various defects in the R7 and/or R8 connection pattern. Complementation tests revealed that these mutations affect independent loci, indicating that the screen has not yet reached saturation. Three mutations disrupt the topographic map of R7 and/or R8 connections immediately after eclosion, indicating that they are involved in establishing the connection pattern during development. Mutations in 3 distinct loci appear to cause retina or afferent degeneration; the connections are normal immediately after eclosion, but the photoreceptor neurons and their axons begin to lose their structural integrity after 5 days. We are currently testing whether the degeneration depends on light exposure.

To clone these mutations, we are establishing a single nucleotide polymorphism (SNP) mapping technique for the relevant chromosomes (2L and 3R). Using sequence analysis tools, we mapped 37 known SNP markers on the genomic sequences (on the 2L chromosomal arm). Based on the chromosomal locations and restriction enzyme availability, we selected 13 markers for further characterization and were able to reproducibly amplify 8 of them by polymerase chain reaction. Surprisingly, only 4 markers show differential restriction digestion patterns between the experimental and mapping strains. We are now collecting and testing more SNP markers on 2L and mapping available markers on 3R.

Room D  
6:15 p.m.



EVERIS CLARKE JR.  
WALTER JOHNSON HIGH SCHOOL

Room D  
6:30 p.m.

## Modulation of pigment epithelium-derived factor in the eye by matrix metalloproteinases

SARA MOGHADDAM-TAAHERI, ROCKVILLE HIGH SCHOOL

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

**Mentor:** LUIGI NOTARI, PH.D., LABORATORY OF RETINAL CELL AND MOLECULAR BIOLOGY, NATIONAL EYE INSTITUTE

### SUMMARY

*Pigment epithelium-derived factor (PEDF) is an extracellular protein that plays a critical role in the normal functioning of the vascular and neural retina. Progression of neovascular retinal diseases correlates inversely to PEDF levels and directly to matrix metalloproteinase (MMP) types 2 and 9. The MMP enzymes can degrade extracellular protein components. The purpose of this study is to determine whether MMP inhibitors can preserve PEDF from MMP degradation in the eye and to explore the relationship between PEDF and MMP levels in neural retinal damage.*

### ABSTRACT

An antiangiogenic and neurotrophic protein, pigment epithelium-derived factor (PEDF), is implicated in inhibiting the progression of damaging neovascular ocular pathologies and retinopathies such as age-related macular degeneration and diabetic retinopathy. Therefore, it is of interest to determine the factors involved in regulating PEDF in the eye. Matrix metalloproteinases (MMPs) are proteolytic enzymes that degrade proteins of the extracellular matrix. Two types of MMPs, MMP-2 and MMP-9, degrade the PEDF protein in vitro.

The corticosteroid dexamethasone (DEX) can repress MMP activity and was tested as a possible protector of PEDF against MMP degradation in an ocular organotypic culture. Western blots of eluates from DEX-treated ocular organotypic cultures showed significantly higher levels of PEDF than in non-DEX-treated control samples. Zymograms showed that ~95-kDa MMP-like zymogens in DEX-treated samples decreased relative to controls. These results indicate an inverse correlation between ~95-kDa MMP-like zymogens and PEDF.

In the native retina, PEDF is present at low levels (less than 1% of total protein). Methods for measuring PEDF in mouse tissues had not been established. We developed a reproducible and sensitive method for quantifying PEDF in mouse eye tissues that uses cation-exchange column chromatography with macrospin columns, polyacrylamide gel electrophoresis, protein electrotransfer, immunoreactions with anti-PEDF antibodies, and enzyme-linked immunosorbent assay. We found quantifiable levels of PEDF in the choroid-retinal pigment epithelium complexes and lower amounts in the retina and interphotoreceptor matrix. We also found that protein from mouse ocular tissues can be extracted in a high-throughput fashion.

Quantification of PEDF in the eye has implications for the regulation of PEDF in relation to other factors. Ongoing experiments include determination of PEDF levels in mice treated with doxycycline and in mouse models of photoreceptor cell degeneration induced by intense light.



SARA MOGHADDAM-TAAHERI  
ROCKVILLE HIGH SCHOOL

## Subcellular location of breast receptor-binding auxiliary protein

NAMISHA DHILLON, NORTHWEST HIGH SCHOOL

**Preceptor:** JAMES SEGARS, M.D., REPRODUCTIVE BIOLOGY AND MEDICINE BRANCH, NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT; DEPARTMENT OF OBSTETRICS AND GYNECOLOGY, UNIFORMED SERVICES UNIVERSITY OF THE HEALTH SCIENCES

**Mentors:** WILLIAM CATHERINO, M.D., PH.D., AND PAUL DRIGGERS, PH.D., DEPARTMENT OF OBSTETRICS AND GYNECOLOGY, UNIFORMED SERVICES UNIVERSITY OF THE HEALTH SCIENCES

### SUMMARY

*Breast receptor-binding auxiliary protein (Brx) is required for proper heart development. In mice that lack Brx, the muscle cells of the heart do not develop properly and the heart ruptures during fetal development because of failure of cardiac cell (cardiomyocyte) differentiation. The objective of this project was to determine the location of Brx within the cardiomyocytes of normal mice. These studies will contribute to understanding the role of Brx in normal cardiomyocyte function and perhaps explain the abnormalities of mice lacking Brx.*

### ABSTRACT

Breast receptor-binding auxiliary protein (Brx) is a multifunctional protein that coordinates multiple signaling pathways in hormone-responsive reproductive, immune, and cardiac tissues. Targeted deletion of the *brx* gene in mice (the creation of a null *brx* allele, or a knockout mouse) showed that a lack of Brx was lethal because cardiac development was arrested at 9.5 days after conception. Because Brx increases p38 MAP-kinase activity, which in turn is required for sarcomere formation (a key structure in cardiac cell development), the objective of this project was to examine the sarcomere structure in wild-type and *brx* null mice. In addition, we sought to identify the location of Brx within normal cardiac cells.

We dissected wild-type C57BL/6 mice and stained sections from the heart with antisera directed against Brx using a standard immunohistochemistry protocol. The regions of interest highlighted by immunohistochemistry were then further examined using electron microscopy and immunogold labeling. These studies revealed that sarcomere development is abnormal in the Brx knockout mice.

Immunogold labeling will be used to identify the subcellular location of Brx and may suggest how Brx influences sarcomere organization. Future studies are planned to elucidate the precise signaling pathways coordinated by Brx to influence development of cardiac muscle cells.

Room D  
6:45 p.m.



NAMISHA DHILLON  
NORTHWEST HIGH SCHOOL

Room D  
7:00 p.m.

## TRAIL induces apoptotic topoisomerase I-DNA complexes by a mechanism dependent on caspase-3 and reactive oxygen species

ABBY GOLDMAN, MONTGOMERY BLAIR HIGH SCHOOL

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

**Mentor:** OLIVIER SORDET, PH.D., LABORATORY OF MOLECULAR PHARMACOLOGY, NATIONAL CANCER INSTITUTE

### SUMMARY

*Topoisomerase I (Top1), an essential enzyme in higher eukaryotes, removes DNA supercoiling generated during transcription and replication. Using leukemia and colon cancer cells treated by TRAIL (a promising anticancer therapeutic agent), we unexpectedly found that high levels of Top1 covalently bind to nuclear DNA. Our project is to determine the mechanism by which Top1 binds to DNA in cells exposed to TRAIL and the biological significance of these Top1-DNA complexes.*

### ABSTRACT

Topoisomerase I (Top1) is an essential enzyme in higher eukaryotes. Top1 removes DNA supercoiling generated during transcription and replication and can be trapped by anticancer drugs (camptothecins) as well as by endogenous and exogenous DNA lesions. We found that TRAIL, a potent and selective inducer of apoptosis in cancer cells, induces the formation of cellular Top1-DNA complexes.

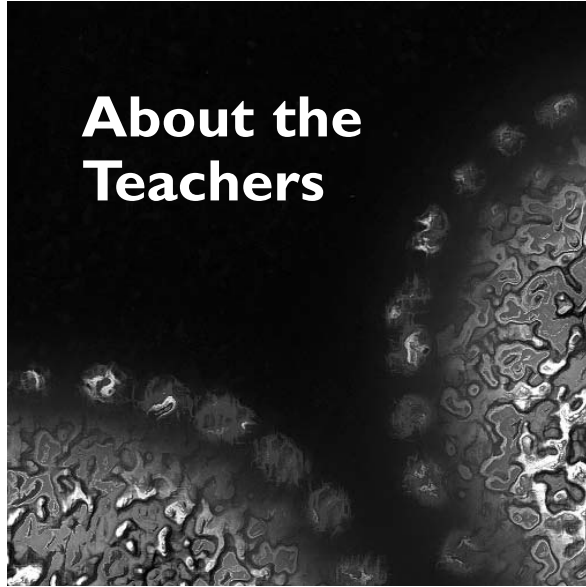
We performed bioassays (slot blots) to test for the presence of the Top1 cleavage complexes and DNA fragmentation assays and sub G1 peaks to quantify levels of apoptosis. Inhibition of TRAIL-induced apoptosis by the caspase peptide inhibitor z-VAD-fmk or by knocking down the *Bax* gene also prevents the formation of Top1-DNA complexes, indicating that these complexes are closely related to apoptosis in cells exposed to TRAIL. The formation of these apoptotic Top1-DNA complexes is inhibited by the antioxidant *N*-acetyl-L-cystein, which indicates that oxidative DNA lesions are likely involved in their formation. The cleavage of Top1 during apoptosis also contributes to the formation of Top1-DNA complexes because the 80-kDa caspase-3-processed form of Top1 (but not the 100-kDa native Top1) binds to nuclear DNA of cells exposed to TRAIL. Thus, we propose that the apoptotic Top1-DNA complexes induced by TRAIL are preferentially formed by the 80-kDa carboxy-terminal fragment of Top1 (generated by caspase-3) covalently bound to damaged DNA (oxidized bases).

Experiments using stable Top1siRNA cell lines (HCT116 and MCF-7 cells) and cell-free systems are ongoing to elucidate the functional role of Top1-DNA complexes in chromatin processing during apoptosis.



ABBY GOLDMAN  
MONTGOMERY BLAIR  
HIGH SCHOOL

# About the Teachers



## About the Teachers



NOVA C. COBBLE  
SENECA VALLEY HIGH SCHOOL

**Lab:** CONSTANCE NOGUCHI, PH.D., AND ZHI-YONG CHEN, PH.D., LABORATORY OF MOLECULAR MEDICINE, NATIONAL INSTITUTE OF DIABETES AND DIGESTIVE AND KIDNEY DISEASES

**Research:** EFFECTS OF NORMOXIC AND HYPOXIC CONDITIONS ON NT2 CELL PROLIFERATION AND EpoR EXPRESSION

*I always knew communication was a key to successful teaching; however, my summer experience solidified this for me. Clear communication is so important in a lab where people have varying levels of English proficiency. I will use the experiences I had to help foster a change in my method of communication, especially with my ESOL classes.*



DEBORAH L. COPELAND  
COLONEL ZADOK MAGRUDER HIGH SCHOOL

**Lab:** PAUL RANDAZZO, M.D., PH.D., LABORATORY OF CELLULAR ONCOLOGY, NATIONAL CANCER INSTITUTE

**Research:** CLONING OF ASAP3

*Collaborating with so many knowledgeable scientists on a wide variety of topics, ranging from scientific methods to science education to philosophy, was gratifying. Overall, the experience enhanced my laboratory proficiency and was an incredible opportunity for professional and personal development.*



JENNIFER L. JAROSINSKI  
FOREST OAK MIDDLE SCHOOL

**Lab:** SUDESHNA KAR, PH.D., AND SANKAR ADHYA, PH.D., LABORATORY OF MOLECULAR BIOLOGY, NATIONAL CANCER INSTITUTE

**Research:** THE EFFECTS OF AN ALTERED HISTONE-LIKE BACTERIAL PROTEIN, HU, ON *E. COLI* INVASION OF HUMAN INTESTINAL EPITHELIAL CELLS

*I was excited when my results confirmed our initial hypothesis that the mutant *E. coli* was able to invade mammalian hosts. I enjoyed learning new techniques and now feel more confident when demonstrating techniques in the classroom and teaching them to my students. I would highly recommend this interesting, rewarding, and worthwhile experience. I have learned so much and am very thankful for the opportunity to work alongside some of the top research scientists in the world.*



**ROSETTA A. JORDAN**  
**COLONEL ZADOK MAGRUDER HIGH SCHOOL**

**Lab:** PAUL RANDAZZO, M.D., PH.D., AND VI LUAN HA, PH.D.,  
LABORATORY OF CELLULAR ONCOLOGY, NATIONAL CANCER INSTITUTE

**Research:** EXPRESSION AND PURIFICATION OF ADD-RIBOSYLATION FACTOR (ARF)  
GTPASE ACTIVATING PROTEINS (GAPs) ASAP3 AND ARF 5

*I enjoyed working with scientists in a cutting-edge laboratory environment and taking part on a small level in scientific discovery on a grand scale. This experience has helped renew my passion for science, provided me with tools to increase my level of competency, and inspired me to become a better scientist and a better teacher. I hope to instill in my students this passion for scientific discovery.*



**STEPHANIE N. MALONE**  
**WALTER JOHNSON HIGH SCHOOL**

**Lab:** HEE-YONG KIM, PH.D., AND YANG-SUK KIM, PH.D., LABORATORY OF MEMBRANE  
BIOCHEMISTRY AND BIOPHYSICS, SECTION OF MASS SPECTROMETRY,  
NATIONAL INSTITUTE ON ALCOHOL ABUSE AND ALCOHOLISM

**Research:** THE RELATIONSHIP BETWEEN DHA DEFICIENCY AND  
FETAL ALCOHOL SYNDROME, ATTENTION DEFICIT HYPERACTIVITY DISORDER,  
DEPRESSION, ALZHEIMER'S DISEASE, AND CYSTIC FIBROSIS

*I enjoyed working in an intellectually stimulating environment that encouraged individual thought and truly valued the differences in each of its researchers. It inspired me to teach my students to think on their feet. Simply saying "The experiment didn't work" isn't good enough. Students should ask why. They should be able to determine what was wrong with their logic, techniques, or procedures; why they didn't get the expected outcome; and, if possible, how to fix it.*



**EMILY J. ROBINSON**  
**NORTHWEST HIGH SCHOOL**

**Lab:** OFELIA OLIVERO, PH.D., LABORATORY OF CELLULAR CARCINOGENESIS  
AND TUMOR PROMOTION, NATIONAL CANCER INSTITUTE

**Research:** ANALYSIS OF MICRONUCLEI IN LONG-TERM AZT-EXPOSED MOLT-3 CELLS  
TO ASSESS THE GENOTOXICITY OF AZT

*The best parts of this internship were being exposed to current research, being able to become a part of that research, learning new lab techniques, and meeting new people. My experience reaffirmed for me the importance of exposing my students to inquiry and current research as much as possible. This was an amazing opportunity. I gained so much from it and had a great time doing it.*



STEPHEN D. SHIFFLETT  
WALTER JOHNSON HIGH SCHOOL

**Lab:** CAROLYN WILSON, PH.D., CENTER FOR BIOLOGICS EVALUATION AND RESEARCH,  
FOOD AND DRUG ADMINISTRATION

**Research:** EBOLA VIRUS GLYCOPROTEIN EXPRESSION VECTOR SYSTEM

*This was a great experience for me—truly the chance of a lifetime. I thoroughly enjoyed working with the scientists in my lab. As a result of this experience, I am planning to add more molecular biology labs to my curriculum, and I will start using lab notebooks with my students.*



CAROL J. SHILLING  
WATKINS MILL HIGH SCHOOL

**Lab:** LISHENG CAI, PH.D., CYCLOTRON PET SCAN LAB,  
NATIONAL INSTITUTE OF MENTAL HEALTH

**Research:** ELISA TO DETERMINE THE CONCENTRATION OF HUMAN TAU,  
A PROTEIN THAT MAY BE INVOLVED IN ALZHEIMER'S DISEASE

*This was a phenomenal experience for me. The lab and its personnel were awesome, and I enjoyed the opportunity to dissect a human brain. As a result, I have a deeper understanding of antibody antigen interactions to take back to my classroom.*



MAY Y. SHLASH  
POOLESVILLE HIGH SCHOOL

**Lab:** DIANE ADLER-WAILES, M.S., UNIT ON OBESITY AND GROWTH,  
NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

**Research:** DETERMINING WHETHER A CORRELATION EXISTS BETWEEN THE  
NONESTERIFIED FREE FATTY ACID CONCENTRATION IN A PATIENT'S BLOOD PLASMA  
AND WEIGHT LOSS DURING A SIX-MONTH TIME COURSE

*I appreciated having an organized, meticulous, and supportive mentor, and I enjoyed the real-life application of biotechnology concepts. This experience has given me greater insight on how science takes place in the real world that I can share with my students with greater confidence and appreciation.*



**CHRISTIE N. WOLFGANG**  
**LAKELANDS PARK MIDDLE SCHOOL**

**Lab:** MARJAN HUIZING, PH.D., NATIONAL HUMAN GENOME RESEARCH INSTITUTE

**Research:** PURIFIED AND SEQUENCED DNA TO SCREEN PATIENTS  
WHO HAD OPTIC ATROPHY

*Learning the process behind the content helped me better understand protein synthesis. Also, I enjoyed working in the lab and learning from the experienced staff. This experience will help me to help my students understand content better by presenting it using visual, auditory, and tactile media.*



**SHANA M. YUDOWITCH**  
**COLONEL ZADOK MAGRUDER HIGH SCHOOL**

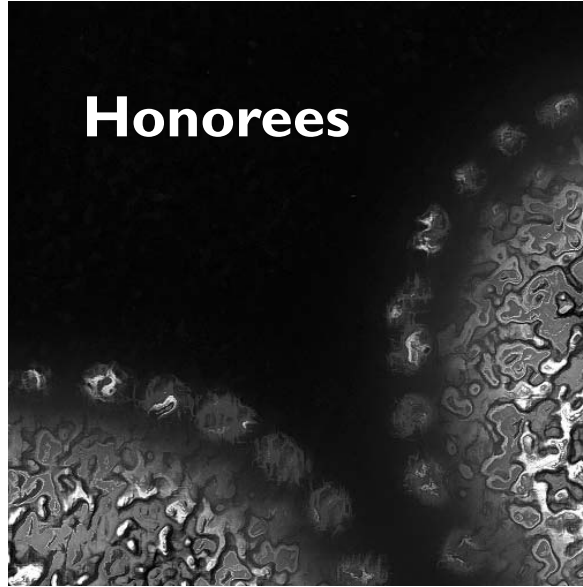
**Lab:** D. SCOTT MERRELL, PH.D., MICROBIOLOGY DIVISION, UNIFORMED SERVICES  
UNIVERSITY OF THE HEALTH SCIENCES

**Research:** IDENTIFYING GENES THAT PLAY A ROLE IN ACID SENSITIVITY  
AND ACID RESISTANCE IN THE BACTERIA *HELICOBACTER PYLORI*

*I would tell someone applying to this program to expect to make mistakes, keep trying, ask good questions, and write all details down. And remember to have fun. I enjoyed meeting new people and learning a new way of thinking about the process of science research. I will bring back to my classes some personal stories, a greater understanding of lab safety, confidence in my understanding of the process of science, and a greater ability to model the lab environment.*



# Honorees



## Honorees

### PRECEPTORS



#### JACQUELINE N. CRAWLEY, PH.D.

LABORATORY OF BEHAVIORAL NEUROSCIENCE,  
NATIONAL INSTITUTE OF MENTAL HEALTH

Each year, our high school student interns from the Student and Teacher Internship Program (STIP) seem better than the last. Of the 78 students that I have mentored during my more than 20 years at the National Institute of Mental Health, the most outstanding have been the 25 STIP students. Since joining the program in 1992, I have been amazed at the motivation, intellect, and laboratory skills of these students. Selection must be remarkably rigorous. Leadership by Gloria Seelman, Bruce Fuchs, Sandra Shmookler, and the HHMI directors provides these students with intensive training in writing scientific reports, talking about their experimental data, and delivering polished 15-minute presentations on their research findings at the prestigious STIP symposium.

STIP students are integral to the research efforts of our Laboratory of Behavioral Neuroscience. Their experiments contributed to our discoveries of learning and memory using a mouse model of Alzheimer's disease, anxiety-like phenotypes in serotonin transporter knockout mice, and new assays of mouse social behaviors that model the symptoms of autism.

Because the program spans a full-time paid summer position and half time in the lab during the academic year, students complete substantive research projects and become coauthors on papers in scientific journals. Authorship on publications from NIH labs is likely to help their college applications and future careers. Special examples of students' independence and unsolicited volunteering, like Selen Tolu's photographs and digital videos of mouse behaviors that I now use in PowerPoint presentations at international conferences, and Jordan Cohen's unsolicited independent search of GenBank for functional descriptions of genes involved in William's syndrome on his first day in the lab, and Tommy Chen's coauthorship on three publications in preparation, must impress the college admissions offices when they read the letters of recommendations that I am honored to write.

On a personal level, it has been tremendously rewarding to follow the progress of our students. They often choose a science major and pursue a biomedical career. Congratulations to each student and each member of the Howard Hughes Medical Institute, the NIH Office of Science Education, and the Montgomery County Public Schools collaborative team for supporting this superlative internship program.



**THOMAS HYDE, M.D., PH.D.**

CLINICAL BRAIN DISORDERS BRANCH, NATIONAL INSTITUTE OF MENTAL HEALTH

I have had a wonderful experience mentoring STIP students. They are bright, creative, and hard working. I have been consistently amazed at their level of interest and motivation. Uniformly, they have integrated themselves seamlessly into our research team, displaying social and intellectual maturity beyond their years. In fact, the STIP students have become so embedded in our operation that many of our research projects would not have reached fruition without their input and assistance.

It has been gratifying to see these young minds blossom and grow over the course of the year with our team. Many of them have gone on to major in one of the biological sciences in college. Several of them have stayed in touch with me and are planning careers in either medicine or the biological sciences as Ph.D. candidates.

This program has been an enriching experience for me, the members of my research group, and, apparently, for the students who have worked in my laboratory. I look forward to the continuation of this program and my participation in it.



**STEVEN KOZLOWSKI, M.D.**

OFFICE OF BIOTECHNOLOGY PRODUCTS, CENTER FOR DRUG EVALUATION  
AND RESEARCH, FOOD AND DRUG ADMINISTRATION

In addition to a broad range of interests, the raw intelligence of the STIP student interns has been striking. Our lab published three papers based on work primarily done by student interns. Five students shared lead authorships on these papers. Overall, eight students have been authors on papers from our lab.

Although learning science and an occasional publication are important fringe benefits of the program, the true reward is the yearly dinner symposium at HHMI headquarters. Before the meal, students present their findings to their peers, parents, and preceptors, as well as the NIH director and HHMI president (at various times, the NIH director or HHMI president has also been a Nobel laureate). Many career scientists never get an audience of similar stature. Despite this audience, the students present with poise and clarity and answer questions with ease.

Large numbers of people are on medications or medical treatments. The safety, efficacy, availability, and future development of medicines are critical issues. Those of us who do research at the FDA are very aware of the link between good science and good medicines. Science education is a critical component of an effective public health policy. From the training of those who will develop and regulate cutting-edge therapeutics to the education of those who prescribe or consume them, the dissemination of science can improve health.

My thanks to Huiming (Sooki) Hon, Juanna Tingem, Mary Whitman, Yakita Wilkinson, Jason Strohmaier, Andrea Hebert, Dawn Hill, Tina Kasliwal, Tiffany Nguyen, Shaleen Vira, Nirav Joshi, and Chris Hill for participating in the program with my lab. They are in college, postbaccalaureate NIH fellowships, applying to grad school, in med school, in pharmacy school, and in M.D./Ph.D. programs. And thanks to Gloria Seelman and Sandy Shmookler for their long involvement in the program.



**YVES POMMIER, M.D., PH.D.**

LABORATORY OF MOLECULAR PHARMACOLOGY, NATIONAL CANCER INSTITUTE

I have had the privilege and pleasure of hosting STIP students since 1998. I initially became involved in this program because I wanted to give high school students the opportunity to experience what science really is. The program is unique; I don't believe one like it exists anywhere else. These students in Montgomery County are really fortunate to have this opportunity.

The reason I keep welcoming high school students into my lab is that my experience with these highly motivated students has been rewarding. They contribute to our research goals with their hard work and scientific input. It is a great reward to list them as coauthors on scientific publications and to contribute to their acceptance to Ph.D. and M.D. programs at top universities. One former student came back to talk to me two months ago because she is applying for a clinical fellowship at NIH. This is what pleases me most.

Because NIH does not have a graduate program, STIP also affords us a great opportunity to have young people to teach. Teaching is learning. We learn as much by teaching as by doing, and this is good for all of us, especially NIH postdocs who may later become teachers or professors and who otherwise would not be exposed to what teaching is all about.

## CONVENERS



### JOHN FINERTY, PH.D.

DEPARTMENT OF IMMUNOLOGY AND MICROBIOLOGY,  
FOUNDATION FOR ADVANCED EDUCATION IN THE SCIENCES

In the many years that I have participated in the program and mentored a variety of students, I have been astounded by their creativity, intellect, and talents. Their research projects range from basic to clinical in human diseases. The ultimate goal is to take lab results to the patient—that is, bench to bedside. However, the students' ultimate goal is to present their year of research as a 15-minute public presentation.

This can be a real eye-opener. Having to balance completing a presentation with filling out college applications, going on college interviews, and keeping up with school projects is challenging. But every year, the students meet this challenge and give excellent presentations at the symposium. In addition, over the years, many students have continued the internship at NIH and applied to graduate and professional schools.

There is a saying “By your students you’ll be taught.” The students I have mentored exposed me to areas of biomedical research with which I was not familiar. Thus, my scientific acumen was broadened and we all became educated. I am honored to participate and to be “taught” by my students through this outstanding program.



### BRUCE A. FUCHS, PH.D.

OFFICE OF SCIENCE EDUCATION, NATIONAL INSTITUTES OF HEALTH

I have been involved with this program for nine years. The experience has been both enjoyable and enlightening. I enjoy advising the students in one-on-one meetings to help them clarify and organize their presentations. Surrounded with the details of their day-to-day research activities, students sometimes find themselves deep in the jargon of science. They need to be guided in translating that specialized language and communicating their ideas to a general audience. This means that the students must truly understand their research and how it fits into the bigger picture or mission of their lab.

My enlightenment comes when students exceed my expectations. They often have a deep understanding of the research being conducted in their labs. Even more remarkable, some of these exceptionally bright students gain a broad view of the current research in a particular field, such as immunology. That they comprehend the science in such depth is impressive. I have enjoyed keeping my hand in teaching through the personal contact with these young science students.

## PROGRAM COORDINATORS



**GLORIA A. SEELMAN, M.A.**

OFFICE OF SCIENCE EDUCATION, NATIONAL INSTITUTES OF HEALTH

It has been a privilege and pleasure to work with the wonderful students and teachers in this program. STIP has evolved from a very small program with just a few student and teacher interns into a program with 22 students and 10 teachers each year. Many of the students have gone on to prestigious colleges and graduate schools, and some are now practicing research scientists. The teacher interns, as a result of their research experience in National Institutes of Health laboratories, have been beneficial to all Montgomery County Public Schools students by providing them with more science labs and the opportunity to take a molecular biology course.

When one STIP student at a practice talk described the results of his research as “beautiful,” I knew he had reached a true understanding of his research and that he had found his passion. In their one year of research, students grow from naive teens to very sophisticated young adults who can speak the language of science. Over the years, I have seen some legacies as the younger brothers or sisters of former interns are coming in as the new student interns.



**SANDRA R. SHMOOKLER, M.A.**

MONTGOMERY COUNTY PUBLIC SCHOOLS

Overseeing this program has been like watching a child grow and develop. Initiated in 1990 as a pilot project designed to encourage educational advancement in science and increase the opportunities for motivated high school students to perform hands-on scientific research, STIP began with three teams consisting of one teacher and five students each.

The program is a model for young people to show that they are like sponges: “Show me, teach me, I can do it.” The teacher interns bring their experiences and excitement back to their classrooms, exposing their students to higher-level science. Over the years, this demanding but very rewarding program has grown to be the most highly respected science internship program in the United States, and the only high school program where students have “NIH” on their transcripts.

**Photo Credits**

Students: Paul Fetters

Teachers: Branson Bros., NIH; Bill Mills, MCPS

Crawley, Fuchs, Hyde, Kozlowski, Pommier, Seelman: Branson Bros., NIH

Finerty: Courtesy of John Finerty

Shmookler: Bill Mills, MCPS

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