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ABSTRACT

This document reports on a science education reform program sponsored by the Howard Hughes Medical Institute. The program is an attempt to overhaul the reform efforts of the Montgomery County Public Schools in Maryland, and participation in the project has been underway since 1994. Funds from the institute support teacher training in the use and evaluation of curricular materials, a summer science camp for middle school girls, an outdoor environmental education program for students and teachers, a week-long summer program for biology teachers at the outdoor education site on the Chesapeake Bay, the Holiday Lectures on Science Series, and programs that provide state-of-the-art training in molecular biology and chemistry. Program details are provided on the Holiday Lectures on Science; precollege science education grants in the Washington, D.C. metropolitan area; regional awards in the national grants program in the Washington, D.C. and Baltimore areas; the 1995-1996 participants in institute-funded projects in the Washington, D.C. and Baltimore areas; and background information about the Howard Hughes Medical Institute. (DDR)

Howard Hughes Medical Institute

Community Partnerships in Science Education

Holiday Lectures on Science

Washington, D.C., Metropolitan Area Precollege Science Education Initiatives

January 1997

Office of Grants and Special Programs

Community Partnerships in Science Education

Holiday Lectures on Science
December 9–10, 1996

Precollege Science Education Initiatives in the Washington, D.C., Metropolitan Area

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Howard Hughes Medical Institute Programs

The Howard Hughes Medical Institute was founded in 1953 by aviator-industrialist Howard R. Hughes. Its charter, in part, reads:

The primary purpose and objective of the Howard Hughes Medical Institute shall be the promotion of human knowledge within the field of the basic sciences (principally the field of medical research and medical education) and the effective application thereof for the benefit of mankind.

Biomedical Research Program

The Howard Hughes Medical Institute is a nonprofit medical research organization dedicated to basic biomedical research and education. Its principal objectives are the advancement of fundamental knowledge in biomedical science and the application of new scientific knowledge to the alleviation of disease and the promotion of health.

Through its program of direct conduct of medical research in conjunction with hospitals, it employs over 270 independent investigators at its laboratories in more than 60 leading academic medical centers, universities, and hospitals throughout the United States. The Institute conducts research in five broad areas: cell biology, genetics, immunology, neuroscience, and structural biology.

To aid these research efforts, the Institute is involved in the training of graduate and postgraduate students in its investigators' laboratories, has given substantial support to the international genome mapping program, provides research training to medical students through the Research Scholars Program (conducted jointly with the National Institutes of Health), and organizes scientific conferences, workshops, and program reviews.

Grants and Special Programs

To complement its research program, the Institute has a grants program dedicated to strengthening education in the biological and related sciences. Administered by the Office of Grants and Special Programs, the Institute grants are designed to enhance science education at the graduate, undergraduate, and precollege levels; to increase public understanding and appreciation of science; and to support fundamental biomedical research abroad and research resources in U.S. medical schools. In addition, a comprehensive assessment effort is under way. The grants reach a wide range of institutions involved in formal and informal science education, including colleges and universities, medical schools, research institutes, elementary and secondary schools, and museums.

Since 1988 the Institute's grants program has provided about $95 million in fellowship support to 1,400 students and physician scientists who have shown strong promise of becoming tomorrow's leading biomedical researchers.

The undergraduate program has awarded $335 million to strengthen

life sciences education at 220 public and private colleges and universities. These awards are intended to enrich educational opportunities for science majors and enhance the general scientific literacy of students who major in nonscience subjects.

In addition to precollege activities in the undergraduate program, the Institute has awarded $11 million to 51 museums, aquaria, botanical gardens, and zoos to support innovative education programs and to interest youngsters in science. In 1994 the precollege program was extended by awards totaling $10 million to 42 biomedical research institutions.

The Institute's local science education initiatives provide opportunities in the Washington, D.C., area for precollege students at all levels to gain experience in the science classroom and laboratory. A holiday lecture series on science for high school students, held each December, is telecast via satellite throughout North America to more than 8,000 junior and senior high schools.

A research resources competition for U.S. medical schools was held in 1995. A total of $80 million was awarded to 30 U.S. medical schools. Annual payments of $550,000–$1 million will be made over four years for junior faculty startup, core facilities, pilot projects, emergency funds, and other activities that will help the schools sustain their commitment to research. The research resources program also provides support to research organizations serving the biomedical community as unique resource laboratories and teaching facilities.

Through a grants initiative launched in 1991, the Institute supports the research of outstanding biomedical scientists abroad. Altogether, more than $38 million in five-year grants has been awarded to 143 international research scholars.

The Institute has a home page on the World Wide Web, with direct links to the grant sites. The universal resource locator (URL) is <http://www.hhmi.org>.

Preface

Purnell W. Choppin, M.D. □ President □ Howard Hughes Medical Institute

Peter C. Doherty and Rolf M. Zinkernagel were awarded this year's Nobel Prize in Physiology or Medicine for discovering how the immune system recognizes virus-infected cells. Their discovery, made nearly 20 years ago, laid a foundation for an understanding of general mechanisms used by the cellular immune system to recognize both foreign microorganisms and self molecules. This knowledge has led to a search for methods to strengthen the immune response against invading microorganisms and certain forms of cancer, and efforts to diminish the effects of autoimmune reactions in inflammatory diseases, such as rheumatic conditions, multiple sclerosis, and diabetes.

Coincidentally, our speakers for the Institute's 1996 Holiday Lecture Series for high school students are two prominent immunologists, whose work has augmented and expanded the work of Doherty and Zinkernagel. HHMI Investigators John W. Kappler and Philippa Marrack, a husband-and-wife research team at the National Jewish Center for Immunology and Respiratory Medicine in Denver, Colorado, have produced a steady stream of advances in our understanding of how the immune system operates, punctuated by major discoveries that have earned them a global reputation as immunologists of the highest caliber.

The work of all these scientists relies on special assets: intellect, ambition, forbearance, and cooperation. When asked what makes a great scientist, Marrack and Kappler answer that determination, flexibility, patience, working well with your peers, and luck are all as useful as raw brain power in building a successful scientific career. Kappler points out that another important

Institute Vice President Dr. Joseph G. Perpich and Institute President Dr. Purnell W. Choppin commend Dr. John Glowa, National Institute of Diabetes and Digestive and Kidney Diseases, for his exemplary dedication and service as a mentor of Montgomery County students and teachers.

trait is the ability to forge productive scientific collaborations: "Almost nobody succeeds in this business all by themselves."

Clearly, being a good scientist requires many of the same traits it takes to be a good citizen. Through its local grants program, the Institute aims to help the children in our community become both good scientists and good citizens. The Institute-sponsored programs described in this report illustrate some of the best the Washington, D.C., metropolitan area has to offer in terms of students, teachers, and community volunteers. These include teachers who spend their summers in molecular biology and chemistry courses so they can offer their students state-of-the-art knowledge; students who spend their summers and after-school hours working side by side with scientists at the National Institutes of Health; scientists who enthusiastically and freely give of their time and talent; and educators and staff of the Audubon Naturalist Society and the Chesapeake Bay Foundation who believe that children are best taught to appreciate the natural world through inquiry-based, hands-on study. Through all these programs children learn the values of observation, perseverance, and teamwork—values that will serve them on whatever path they take.

We are impressed with the seemingly infinite capacity our youngest citizens bring to the scientific enterprise. A prime example is Jamalah Munir, a graduate of Oxon Hill High School and now a junior at Brown University. In 1996 Ms. Munir spent her third consecutive summer as an HHMI Summer Research Fellow at the National Institutes of Health. There she worked in the laboratory of Dr. W. Jay Ramsey of the National Center for Human Genome Research. Her three-year effort paid off this year when she developed a more efficient method of preparing viral vectors for gene therapy. Now a junior at Brown University, she is planning a career in medicine and science. Just beginning her career as a scientist, this one student has already made a contribution to the field. Think of what we can look forward to from the thousands of other students engaged in these newly invigorated science education efforts!

The primary mission of the Howard Hughes Medical Institute is to support biomedical research. Science is not a subject or "thing"; it is a process of inquiry conducted by human beings. Without the human intellect and will, there is no science. Through support of science education at all levels, from kindergarten to postdoctoral training, we aim to nourish developing intellects and boost the will to succeed. Whether the young people portrayed in this publication go on to careers in science is, in some ways, immaterial. Of course, we hope they will. But if they don't, they have "done science," and will forever understand its processes. As citizens, they will have a better grasp of how science is changing their lives.

Introduction: New Roads to Science Learning

Joseph G. Perpich, M.D., J.D. □ Vice President for Grants and Special Programs

According to Greek mythology, the first ship, Argo, set sail with visions of wonderful new horizons yet unseen and new civilizations yet to be discovered. The myth, however, also presents the "other side" of those visions, that is, the community's concern about how they would interact with and be affected by contact with people of a new world.

This myth has significance today as we pursue new horizons in science. There seems to be no end of great visions, but increasingly we are faced with the realities of how to pursue them. Once faced, we must be prepared to deal with the consequences, both positive and negative. Fortunately, scientists are an optimistic bunch. They obviously believe the voyage is worth taking, even though the stakes are high and the outcomes uncertain. It is critical, however, that the general public not only share and support the pursuit of scientific knowledge, but also examine the types of questions asked by those who watched Argo set sail.

As a medical research organization, the Howard Hughes Medical Institute embraces all aspects of the scientific journey by supporting investigators who have the vision, by providing the supplies and environment needed to pursue new horizons, and by educating the next generation so that it, too, can pursue new visions.

Where Journeys Begin

In 1997 the Institute enters the eighth year of an active program to support science education efforts in the Washington, D.C., metropolitan area, home of HHMI headquarters. This year cumulative support for local grants surpassed $4 million. Although the Institute supports science education nationally through programs at the precollege,

Montgomery County School Board member Dr. Alan Cheung and Institute Vice President Dr. Joseph G. Perpich at the 1996 Student Interns Dinner Symposium.

With an abundance of scientific and educational resources already established in the Washington area, our children are plainly starting their educational voyages with unique advantages.

undergraduate, and graduate levels, we are also committed to providing as many children as possible in our own community with science education experiences that will open up new horizons.

With an abundance of scientific and educational resources already established in the Washington area, our children are plainly starting their educational voyages with unique advantages. The programs we fund take advantage of local scientific resources, such as the laboratories of the National Institutes of Health, the classrooms of our local colleges and universities, the living collections of the National Zoo and National Aquarium, and the vast waters of the Chesapeake Bay. We believe these are tremendous places with extraordinary resources for students to discover the worlds of science.

Since 1994 the Institute has financed, in part, an overhaul of the Montgomery County Public Schools elementary science education reform efforts. Thus far we have committed $640,000 to the year 2000 for the development, purchase, and replacement of science education kits for use in the County's elementary schools. The Institute grant also supports teacher training in the use and evaluation of these curricular materials.

At the middle school level, the Institute sponsors a summer science camp for girls. For three weeks, 25 students from around the county are involved in an intensive (and fun) immersion in molecular biology and biotechnology at the Thomas Edison High School for Technology in Wheaton, Maryland. Such opportunities have proven to be a highly successful way of maintaining enthusiasm for science among middle school girls, especially those from minority populations.

Now in its third year, and extended to the year 2000, the Institute has provided $598,000 in support of a program offered by the Chesapeake Bay Foundation that provides environmental science education experiences for county students and teachers, including a week-long summer program for high school biology teachers. This year we were pleased to augment this type of educational programming for Montgomery County teachers by supporting the development of a GREEN LABS teacher education program at the Audubon Naturalist Society, our nearby neighbor. This program is especially valuable because it provides local teachers with curricula and resources to conduct science education programs in their own schoolyard.

County teachers also participate in three one-week courses that provide them with state-of-the-art training in molecular biology and chemistry and ready them for integrating their newfound knowledge into the classroom. During the molecular biology course teachers work side-by-side with students, a unique experience that is, by all accounts, mutually beneficial and gratifying.

A New Generation of Explorers

Two of our longest running local programs provide intensive research experiences for area high school and college students in the laboratories of the National Institutes of Health. A summer research program enrolls about 40 students each year. We have delighted in their progress. Many of the students started in the program three or four years ago while in high school and are now completing their undergraduate degrees. They have overwhelmingly continued to opt for science, both in college and as a career option.

Another program enlists 15 students each year for a summer research experience followed by an academic-year program, which requires after-school time in the laboratory. We are humbled by the sacrifices these students make, often giving up other activities and social events to spend time with career scientists in busy laboratories.

Just when we think we might be asking too much of these students, they set us straight. Clay Ackerly, a senior at St. Albans School, spent the summer in the laboratory of Dr. Alan Wolffe in the National Institute of Child Health and Human Development. There he participated in efforts to purify a protein that is hypothesized to play an important role in activating DNA transcription. Later, Clay wrote to us that "when I first walked into Dr. Wolffe's lab, I possessed only two very wide eyes and a few words of family advice; 'Do whatever you're told and listen up.' My first weeks were filled with wonder, awe, and mistake after mistake after mistake. However, my mentor never gave up on me. Now I actually understand the specific area of molecular cloning and protein purification and I understand the patience required of all researchers. Thank you."

Clay's words are a testimonial to his own unique abilities and the value of this type of learning. They also serve as a monument to the devoted scientists and postdoctoral students who provide advice and information as role models to aspiring young scientists.

The caliber of these students is further demonstrated each spring when the Institute hosts a dinner at which student participants in a year-round research program present their research. Their expositions are representative of the expansive nature of biomedical science. Through their presentations they take us through explorations of the world of the cell, where they are molecular voyagers on a journey, adding bit by bit to the puzzle of how cells grow, divide, live, and die. They are contributing to insights into how cancer and diseases affect the immune and nervous systems. Other students reported on their work in genetics—how genes are turned off and on and how harmful mutations in genes can lead to diseases like breast cancer. Still others worked in laboratories exploring the last frontier: the brain.

"My first weeks were filled with wonder, awe, and mistake after mistake after mistake. However, my mentor never gave up on me."

–Clay Ackerly

There is no doubt that these are exceptional students. But we want these worlds of science opened not only to the 1 per cent of young people who will pursue research and science teaching careers, but also to the 99 percent who will not. At the very least we want each generation of students to be given the opportunity of a lifetime of science learning. To achieve this, it is essential that children be exposed to a wide variety of learning experiences. What works for one child might not work for the next. Creativity takes many forms.

Any teacher will tell you that their greatest reward is a student who "gets it." Teachers describe that gratifying moment when a connection is made and a child's face lights up. Good teachers are always struggling to find new ways of reaching their students, unwilling to give up on a child's chance to make the learning voyage. At the Institute we live vicariously through teachers who tell us of their successes and students who demonstrate that they "get it."

Julie Goldberg is one such example. A freshman at Wesleyan Univer-

Table 1

Summary of Washington, D.C., Metropolitan Area Grants

Year(s)	Science Education Grants	Total Awarded†
1990–1999*	Howard Hughes Medical Institute Summer Research Fellowship Program at the National Institutes of Health	$760,000
1990–1997*	Montgomery County Public Schools Student and Teacher Intern Program at the National Institutes of Health	1,332,000
1990–1993*	Cold Spring Harbor Biotechnology Program with the Montgomery County Public Schools	219,500
1994–1999*	Montgomery County Public Schools Elementary Science Education	640,000
1993–1994	Edison Career Center Biotechnology Program	14,000
1993–1998*	Edison Career Center Middle School Biotechnology Summer Focus Program	85,000
1993–1999*	Chesapeake Bay Foundation/ Montgomery County Public Schools	598,000
1996–1999	Audubon Naturalist Society/ Montgomery County Public Schools	37,000
1992–1995*	Maryland Science Week	35,000
1990–1995*	Carnegie Institution of Washington First Light Program	65,000
Year	**Other Grants**	**Total Awarded†**
1991	American Association for the Advancement of Science	5,000
1988–1990	University of Maryland Education Center	225,000
1989–1995*	Washington Area United Way	200,000
	Total	**$4,215,500**

*Multiple awards

†Cumulative amounts paid and/or committed for calendar years shown

"Life is a dance with just a few steps known. If those few steps are enough to catch one's breath, imagine the wonder of the entire choreographed performance."

–Julie Goldberg

sity and a graduate of Montgomery Blair High School, she spent last summer in the laboratory of Dr. Sharon Powell of the National Institute of Dental Research, where she investigated potential therapeutic agents for developmental disorders and injuries to the nervous system. In describing her appreciation of science, she wrote, "Life is a dance with just a few steps known. If those few steps are enough to catch one's breath, imagine the wonder of the entire choreographed performance."

Local Destinations for Discovery

In addition to local programs supported through our grants programs, the Institute makes awards through a variety of national competitions at the precollege, undergraduate, and graduate levels. Many of the institutions supported through these national competitions are based in the Washington, D.C., metropolitan area (Table 1).

Through the Institute's precollege initiative, Georgetown University Medical Center, Johns Hopkins University School of Medicine, and the Carnegie Institution of Washington have opened their doors to area students and teachers for a variety of educational and enrichment activities. The National Zoo, the National Aquarium in Baltimore, and the Irvine Natural Science Center sponsor a wonderful and innovative assortment of educational activities for their communities.

The Institute's undergraduate initiative provides funds for biological sciences education at 220 colleges and universities nationwide, 7 of which are in Maryland and the District of Columbia. All of these institutions of higher education have made a commitment to improving science education, not just at the undergraduate and graduate levels, but also at the K–12 level. Nearly 25 percent of the funds awarded to these institutions have gone to students and teachers in precollege outreach programs.

Local awards also support students at the predoctoral and postdoctoral levels. Through national fellowship programs, medical students and pre- and postdoctoral fellows receive research training at Catholic University, Georgetown University, Johns Hopkins University, the University of Maryland, and the National Institutes of Health.

Electronic Expeditions

This year the Grants Program is fully exploiting electronic technology to broadcast the Holiday Lectures for high school students, now in their fourth year. The annual holiday lectures on science will be held at the Institute's conference center on December 9–10, 1996, for approximately 200 high school students in the Washington metropolitan area.

Last year's lecture series reached 7,000 schools by satellite and an additional 10,000 schools by the Classroom Channel, making a total of approximately 800,000 teachers and students. This year's lectures, "The Immune System—Friend and Foe" will be presented by HHMI

The Holiday Lectures home page will ... provide invaluable content and over 100 links for obtaining immunology research information and educational materials, including an on-line virtual lab...

Investigators John W. Kappler and Philippa Marrack.

Once again the four lectures will be available to classrooms in the United States and Canada live via satellite. They will also be rebroadcast over Channel One in early 1997. Various public education cable television stations, such as SC-ETV in South Carolina, have also agreed to broadcast the lectures. These stations are handling publicity in their own areas, by printed, televised, and Web advertising. SC-ETV covers all colleges, universities, and public schools in the state.

In addition, a *Teacher and Student Resources* guide was developed by grants staff and consultants in conjunction with a panel of high school science teachers and three student interns. The guide provides background information on Drs. Kappler and Marrack, curricular materials tailored to each of the four lectures, information about the Holiday Lectures home page, and some immunology resources available on the World Wide Web. The Holiday Lectures home page will also provide invaluable content and over 100 links for obtaining immunology research information and educational materials, including an on-line virtual lab, which will allow students to perform immunology experiments and view animations that detail the immune response to bacterial and viral infections.

One of the interns who assisted us on Web site development is Jason Carroll, a graduate of Sidwell Friends School and a freshman at Harvard University. We were not the only beneficiaries of his computer knowledge. Jason also served as a summer research intern at the National Institute of Diabetes and Digestive and Kidney Diseases. In the laboratory of Dr. Julianna Barsony, Jason generated the world's first map of glucocorticoid receptor target genes and captured this extraordinary structure in a movie. Jason is on the edge of a new frontier that combines computers and biology to map new horizons yet unimaginable. He is proof that our students can teach us well.

Conclusion

The teachers, scientists, and students described in these pages are on a journey that will bring them, in the words of the Greek poet C.P. Cavafy, "to ports seen for the first time." Cavafy reminds us that when we start on our journey we should pray for a road that is long, full of adventure, and full of knowledge.

We are proud to be a partner in launching these journeys and we sense that no matter what road these young people choose in life, they are headed in the right direction. I am reminded of the mouse in E. B. White's *Stuart Little*, who heads out to find the love of his life, Margalo, a little hen-bird. He chooses a fork in the road, knowing that this road will take him to wonderful places and that he will travel to the end of his days headed in the right direction. It is that optimism that propels scientists to pursue their intuition, students to become active in extracurricular and demanding science programs, and teachers to teach. As another year comes to an end, we look back with pride on our community and hope for the important journeys to come.

When we start on our journey we should pray for a road that is long, full of adventure, and full of knowledge.

–adapted from "Ithaca" by C.P. Cavafy

Howard Hughes Medical Institute Holiday Lectures on Science

In 1993 the Institute established a series of holiday lectures on science for high school students. The lectures build on traditions established in 1827 in London by the British scientist Michael Faraday and, more recently, on a science lecture series offered annually by Rockefeller University. The holiday lectures are held for two days in the conference center at Institute headquarters. The speakers are scientists known to be effective in communicating science to the general public and reaching out to students at the precollege level.

The lectures are part of the Institute's grants program, which complements the Institute's research activities. Through its grants, the Institute is a major contributor to the enhancement of science education, extending from the students' earliest years to graduate or medical school and beyond. Since 1988 the Institute has granted about $593 million, including $461 million expended through fiscal year 1996 and the rest committed to four- and five-year annual awards. The awards have reached a wide range of institutions, including colleges, universities, medical schools, research institutes, science museums, and elementary and secondary schools, covering an extensive array of educational activities.

Approximately 190 students from 80 high schools in the Washington, D.C., area attend the lectures annually in December at the Institute's headquarters in Chevy Chase, Maryland. Science department chairs and principals in each area high school nominate students for participation on the basis of their demonstrated interest in science. The inaugural lectures in 1993 entitled "Da Vinci and Darwin in the Molecules of Life" were given by Stephen Burley, M.D., D.Phil., and John Kuriyan, Ph.D., both HHMI investigators at the Rockefeller University. These lectures discussed the three-dimensional structure of biologically important molecules and their role in health and disease. In 1994, Shirley Tilghman, Ph.D., HHMI Investigator at Yale University, and Robert L. Nussbaum, M.D., of the National Center for Genome Research at the National Institutes of Health, spoke on "Genes, Gender, and Genetic Disorders," which discussed the latest findings on sex

John W. Kappler, Ph.D., and Philippa Marrack, Ph.D.

Howard Hughes Medical Institute Investigators

The Department of Medicine, National Jewish Center for Immunology and Respiratory Disease

Denver, Colorado

Table 2

Howard Hughes Medical Institute Holiday Lectures on Science, 1993–1995

- December 20–21, 1993
  Stephen Burley, M.D., D.Phil.,* The Rockefeller University
  John Kuriyan, Ph.D.,† The Rockefeller University
  Da Vinci and Darwin in the Molecules of Life
  The speakers explored relationships between modern structural biology and the work of Leonardo da Vinci and Charles Darwin, who helped establish the intellectual foundation for the biological sciences.

- December 19–20, 1994
  Shirley M. Tilghman, Ph.D.,† Princeton University
  Robert L. Nussbaum, M.D., National Institutes of Health
  Genes, Gender, and Genetic Disorders
  Dr. Tilghman explained the latest findings on how gender is determined in humans and other mammals, and Dr. Nussbaum discussed how mutations and chromosome disorders affect the genes involved in this process and lead to clinical disorders.

- December 18–19, 1995
  Thomas Cech, Ph.D.,† University of Colorado, Boulder
  The Double Life of RNA
  The discovery that RNA can play a dual role in the cell, serving both as messenger and catalyst, was discussed and illustrated; new therapeutic agents based on RNA's dual role were suggested; and a novel theory involving RNA was offered to explain the origin of life on earth.

*HHMI Associate Investigator
†HHMI Investigator

determination in humans and other mammals. In 1995, Thomas R. Cech, Ph.D., presented "The Double Life of RNA," in which he described the discovery of a catalytic function for RNA that may help fight viruses, cancer, and genetic disease (Table 2).

Dr. Cech's lectures were televised live across the United States and Canada. They reached an audience of 7,000 junior and senior high schools via satellite and were rebroadcast to an additional 10,000 schools by the Classroom Channel. As such, the lectures reached approximately 800,000 students and teachers.

This year John W. Kappler, Ph.D., and Philippa Marrack, Ph.D., HHMI Investigators and members of the Department of Medicine at the National Jewish Center for Immunology and Respiratory Medicine in Denver, Colorado, will present "The Immune System—Friend and Foe." Their lectures will discuss how vertebrates defend themselves against infectious organisms through receptors on the surfaces of lymphocyte cells. As each lymphocyte develops, it randomly expresses only one of trillions of possible receptors. Chances are that any invading organism will be targeted. When an infection occurs, the lymphocytes that can react with the invader multiply rapidly and mount an effective defense.

The body must avoid being attacked by its own immune system. Lymphocytes that might harm the host are destroyed during development. Some that escape destruction can attack the host and cause autoimmune diseases. Infectious agents evolve at least as rapidly as the vertebrates they threaten, and many have developed ways to survive their hosts. How these processes occur is still a major unanswered question.

The Institute is strongly committed to enhancing science education nationally. The lecture series this year is supported by materials based on the lectures and provided by the Institute to 10,000 teachers around the country. Additionally, the Institute will once again broadcast the lectures, using advanced satellite and computer technologies, and thereby providing additional means by which the Institute can contribute to encouraging interest in science in students, nationally and internationally.

The Immune System—Friend and Foe

If asked what trait would be most useful to a budding scientist, many people would probably say "being really, really smart." But immunologists Philippa Marrack and John Kappler say that an excess of brains is not necessarily what you need. Instead, they say, determination, flexibility, patience, working well with your peers, and luck are all as useful as raw brain power in building a successful scientific career.

Marrack and Kappler know more than most about what it takes to succeed in science—and about how to get along with laboratory partners. Married since 1974, they have enjoyed a uniquely productive personal and professional partnership for more than two decades. During their careers, they have produced a steady stream of advances in our understanding of how the immune system operates, punctuated by a few major discoveries that have earned them a global reputation as immunologists of the highest caliber.

Marrack cites three traits that have been helpful to her, and which she says many good biologists have. First, she says, you need to be alert, and able to hear what your results—especially unexpected results—are saying. "Accidental discoveries are often the best, but you have to be able to pay attention to the unexpected data," she says. "If you can't, you'll miss the most important findings."

But beyond intellectual flexibility, Marrack says, you need both tenacity and a special kind of patience—the ability to find satisfaction in the smallest details while slowly building a much bigger picture. "In science, you need to know what the most important question is, and be willing to do whatever it takes to answer that question," says Marrack. "John and I have always had a clear idea of what we wanted to find out, and we have pursued it ruthlessly." But really big discoveries

happen rarely, if at all, she continues. "For most of your daily scientific life you have to be satisfied with little things, small satisfactions. Just the fact that the gel ran straight, or that the cell cultures seem healthy for a change, counts as a small triumph."

Kappler agrees, but adds that another important trait is the ability to forge productive scientific collaborations. "Almost nobody succeeds in this business all by themselves, and I owe a lot of my success to the people I've worked with." Kappler also says that the whims of fate play a role in moving a scientist out to the sharpest part of the cutting edge. "Serendipity plays an awfully big role in most scientific careers, and even then only if you're in the right place at the right time and collaborating with good people," says Kappler. "We sometimes don't like to admit it, but to make discoveries you have to be lucky."

School Days

"Chance favors the prepared mind," said nineteenth-century biologist Louis Pasteur. If Marrack and Kappler were lucky, it's only because they earned their good fortune. They met at the University of California, San Diego, in 1971, where they were postdoctoral researchers working on immune cell culture systems in the laboratory of immunologist Richard Dutton. This stint was Kappler's first plunge into immunology. After graduating in 1961 from a science and engineering-oriented high school in Baltimore, Maryland, he went to Lehigh University to study engineering. He soon realized, however, that scientific research, especially biochemistry, was his real love. After taking his B.S. in chemistry from Lehigh, he went to Brandeis University to pursue a Ph.D. There he studied how the attachment of specific chemical groups to DNA (methylation) changes as cells move through the growth cycle.

Kappler says he spent most of his time in graduate school learning how not to do science. "Like most graduate students, I came in with all these great ideas about what I would do, and I slogged away for a long time trying to get some kind of sensible results, without getting anywhere," he recalls. "Then something clicked, and I started to think more clearly about how to approach the problem. I branched out and found something that worked, "probably producing 80 percent of the data for my thesis in my last six months of graduate school."

Marrack, meanwhile, had already taken up the study of the immune system as a graduate student. Born in England, she went to an all-girls boarding school in Winchester, England, and from there moved on to Cambridge University. "My high school was more intellectual than many other girls' schools of the time," says Marrack. "We weren't just being trained to wear fancy gloves and run church bazaars, although, I must admit, it was close. My teachers didn't really know how to deal with a woman who was interested in science, so they shipped me off to various places to have extra

instruction. When I went to University, I took all science courses because that was what I was good at."

From there, she just continued to pursue her scientific education without a clear idea of where it would lead. "At the start I didn't really know there were people who spent their whole lives in research," Marrack continues. "In my last year at University, I met the man who became my Ph.D. thesis adviser, and he persuaded me to come study with him. My father's uncle, John Marrack, was a famous immunologist in the 1930s, and my future adviser (I later learned) thought it would be neat to have a descendant of this curmudgeonly character working in his lab. So I started to study T cells then, and I've been at it ever since."

Kappler and Marrack both recall that they went to San Diego as much for the climate as for the intellectual opportunity. In the laboratory where they met, each independently characterized immune system cells in culture and unraveled the complex interactions that lead to specific immune defenses. Marrack had planned to return to England at the end of her postdoctoral work, but changed her plans and instead joined Kappler in Rochester, New York, where he had landed a job as an assistant professor of microbiology at the University of Rochester.

Building a Partnership

The first few years in Rochester set a tone for their partnership that continues today. When they first arrived, only Kappler had a faculty position; Marrack, with a Ph.D. from Cambridge and three years of postdoctoral training, was officially a technician working in his lab. "But from the very beginning it was clear to both of us, and to anyone who worked with us, that our lab was a complete partnership—we worked together," says Kappler. Also, they decided that all their scientific papers and—as much as possible—grant applications would be joint endeavors. "We figured it didn't matter who did what—whether it was making the supper or running the gel, we both contributed," he says.

Marrack quickly took steps to establish her own scientific credentials. In her second year in Rochester, she won a prestigious research grant from the American Heart Association and began teaching a graduate course in immunology. But most important perhaps, she credits her husband for having the good sense to support her. "John never got in the way—he didn't blanket my achievements. Anyone could see we were a pair of scientists and not a guy and someone working for him."

The first problems the couple took on in their new laboratory were extensions of their postdoctoral projects. They continued to characterize the interactions that occur between immune cells—T cells, which mature in the thymus, and B cells, which mature in the bone marrow and produce antibodies. They showed that there were many specific factors, called cytokines, that are released by helper T cells and exert

profound physiologic effects on their B cell targets. They also showed that various cytokines act together and produce effects far different than when they act alone.

Eventually Marrack and Kappler began to focus on how T cells recognize specific antigens. As is the case with B cells, the body fields an incredibly broad array of T cells, each one displaying receptors capable of binding a different but highly specific chemical antigen. Immunologists at the time knew that T cells, unlike B cells, must recognize their antigen displayed on another cell's surface before they can be activated, and that a set of cell surface proteins encoded by genes of the major histocompatibility complex (MHC) was intimately involved in antigen recognition.

"The burning question at the time was how antigen recognition occurs," says Kappler. "Were there separate receptors on the T cell for antigen and MHC protein, or was there just one receptor for both? How did each receptor manage to so specifically recognize a single antigen? Could each T cell recognize only one specific antigen, or many? Why didn't T cells bind antigens normally present in the body? How did the body generate such a wide diversity of T cell specificities? Structurally and biochemically, what were the T cell receptors like? Those were questions we took on then, and we've been working on them ever since."

One of the technical difficulties is that immune cells taken from an animal only live for a few weeks when cultured in the lab. In the mid-1970s, researchers learned to fuse healthy B cells from mice with cultured cells derived from mouse myeloma—an immune system cancer in which mutated B cells divide indefinitely. The resulting hybridoma cells had the ability to make whatever antibody the healthy B cell encoded, but would also live indefinitely in culture. If one starts a culture with a single B cell/myeloma hybrid, the resulting monoclonal culture will produce only a single type of antibody, with an exquisitely specific affinity for a particular antigen. These monoclonal antibodies are immensely useful as sources of raw material for scientists studying antibody structure and function.

In the late 1970s, Marrack and Kappler worked with Lee Harwell, a technician in their lab, to develop a method of making T cell hybridomas. "It was really Lee's idea, because he was in charge of harvesting mouse T cells for our studies of cytokines," recalls Marrack. "He had learned about B cell hybridoma technology at a scientific conference we attended, and he wanted to adapt it to make immortal T cells, so he'd never have to kill another mouse," she says.

"Lee was a determined character, and he slogged away for a whole year in a corner of the lab, getting plenty of hybrids but no secretion of the T cell factors we needed," Kappler adds. "We were sitting around the lab talking one day, and suddenly one of us—I'm not sure who—had an inspiration: unlike B cell hybridomas that need no urging,

the T cell hybridomas perhaps had to be stimulated to secrete the factors, just like T cells *in vivo*." The next experiment was to add concanavalin A, a potent stimulator of T cells, to the hybridized cultures. "Boom, there it was," recalls Kappler—"the hybridomas made cytokines in abundance." It immediately occurred to the researchers that adding a specific antigen to a mix of T cell hybridomas should only stimulate those hybrids with receptors for that antigen. This should result in a permanent T cell population with a defined binding capability—in short, monoclonal T cells.

Following up on that idea had to wait a bit. Kappler and Marrack had meanwhile added two children to their family—Jim, born in 1974, and Katy, born in 1976. If having children didn't slow them down, it at least made them much busier. Marrack's parents emigrated from England in 1978 to help care for their grandchildren, which both Marrack and Kappler say allowed them to do more in the laboratory than would otherwise have been possible.

The couple had also been looking for a place where both could be full-fledged faculty. Then fate intervened. "A friend called and told us to come look at Denver, where he was, and we never looked back," says Kappler. "There were lots of good people, with plenty of energy, and they gave us each a job we couldn't refuse." Specifically, the offer came from the National Jewish Center for Immunology and Respiratory Medicine, a research institution, and the University of Colorado Health Sciences Center, which encompasses a medical school and graduate programs in several biomedical sciences.

T Cells: Function and Origin

They set up shop in Denver in 1980, and the first experiment was to try stimulating the hybrid T cells with specific antigens. Happily, it worked like a charm, allowing them to grow up many liters of well characterized T cells, with the same antigen specificity. With these defined cultures in hand, they set out to purify and characterize the cell's antigen receptor, using monoclonal antibodies as a tool. They injected the hybridoma cells back into rats and mice, then screened the blood serum of the inoculated animals for antibodies that could either stimulate or block T cell activation in culture. An antibody that stimulated activation would likely do so by binding to the T cell receptor (TCR), in turn signaling the cell that binding had occurred, while one that blocked T cell activation would barricade the antigen-binding site.

After a great deal of tedious screening, Marrack and Kappler found two mouse antibodies that bound the TCR. They used these to help with TCR purification, which they conducted in collaboration with their colleague Ralph Kubo, a protein chemist. Around the same time in the mid-1980s, a technical revolution was sweeping the biomedical labs as the astonishingly powerful

techniques of gene cloning and molecular biology became widely available. Kappler and Marrack's laboratory went on to purify and partially sequence one TCR chain. Competitors Mark Davis and Tak Mak beat them to the complete sequence of the TCR, though not by much.

All the results together showed that the TCR was only vaguely similar to an antibody molecule. Like immunoglobulin, it had two chains, dubbed alpha and beta, each with a so-called constant domain (the same on all T cells) and variable domain (different on T cells with different antigen specificities). The sequences, however, of the TCR chains were different from those of the antibody chains. "Immunologists had been arguing about the chemical nature of the TCR for a decade, and suddenly the controversy was over," Kappler says. "Within two months, our lab and two others had purified and characterized the TCR."

The chemical nature of the TCR was only half the story, though. It was still unclear what the receptor actually bound on the antigen-presenting cells. Researchers did not know if the TCR bound only the antigen molecule on a presenting cell's surface, while something else bound the MHC protein, or if the TCR bound both the antigen and the MHC. To distinguish these possibilities, Marrack and Kappler fused a monoclonal T cell that recognized one specific antigen and MHC complex with another T cell capable of recognizing a different MHC and antigen grouping. Then they presented the fused cells with all possible combinations of these antigens and MHC variants. Rather than binding every complex, the fused cells reacted only with the two original combinations. The researchers interpreted these results as showing that the antigen and MHC variants were recognized, and therefore bound together.

Shortly afterward, says Kappler, Rick Shimonkevitz, one of their graduate students, filled in the rest of the story of how the TCR, antigens, and the MHC intertwine. Shimonkevitz cleaved a protein into short peptide fragments, and allowed the fragments to bind to the surfaces of presenting cells. He then separated out the MHC proteins and showed that the peptide fragments were bound to the MHC. After the peptides had been bound, the presenting cells could readily activate T cells.

"Rick's work finally clarified a whole bunch of fuzzy thinking and gave us a new paradigm," says Kappler. "Antigens were taken inside the presenting cells, broken into fragments, complexed with MHC proteins, and finally shipped back out to the cell surface for display."

Clonal Elimination and Self-Tolerance

"The first few years in Denver were really our turning point from being basically good scientists doing a good job to doing something that was really out at the edge," says

Kappler. "But many of our successes wouldn't have happened without our collaborators in Denver. We really were in the right place at the right time." This right time, however, was not just a brief interlude but a long span of time that continues to this day.

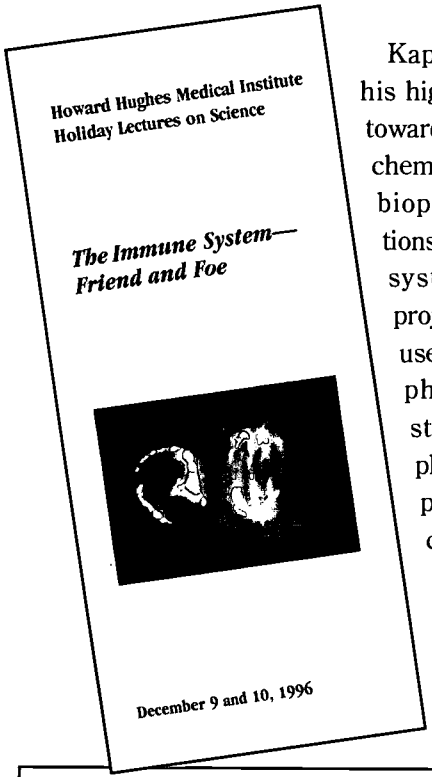
Marrack and Kappler next turned their laboratory's attention to the question of how the immune system manages to create a repertoire of T cells that recognize antigens from every potential pathogen under the sun without making T cells that attack the body's healthy tissues. It was clear that the MHC proteins were intimately involved in marking cells as self or non-self. Indeed, MHC proteins were first noticed because they are extraordinarily potent activators of the immune response: the immune system will quickly destroy tissue transplanted from one animal to another with different MHC variants, even if the two animals are closely related (thus the term histocompatibility). But if MHC molecules are such good targets, why doesn't the body attack its own MHC proteins? What mechanism prevents that from happening?

In 1959 Nobel laureate Joshua Lederberg proposed that any developing T cell that can recognize the body's MHC proteins is somehow eliminated in the thymus. Lederberg's idea of clonal elimination was one of several competing theories to explain self-tolerance. Others suggested that self-reactive T cells are just inactivated, not eliminated, or that the body never makes self-reactive T cells in the first place. Direct proof for any of these theories was still lacking in the mid-1980s.

Marrack and Kappler, however, now had the tools to follow specific T cells as they passed through development in the thymus. One of their monoclonal antibodies, they discovered, bound to a particular region of the TCR. They also found that TCRs containing this region reacted strongly to a particular MHC molecule. Surprisingly, however, when this MHC molecule was present in strains of adult mice, mature T cells containing this TCR region were absent. By using the appropriate fluorescent-labeled monoclonal antibody, the investigators were able to identify immature T cells in the thymus that did contain this region. They also saw that these cell clones disappeared as the T cells matured in the thymus. Clonal elimination had finally been observed.

The Edge of the Envelope

Since their breakthrough work on clonal elimination, Marrack and Kappler have continued to pursue the ins and outs of immune recognition of foreign antigens and the development of self-tolerance, but their research paths have diverged somewhat. "In the last five years or so, our work has taken a different flavor," says Marrack. "Our projects still often converge, but we generally have separate programs now."



Kappler has returned to his high school predilection toward physics and physical chemistry and is working on biophysical characterizations of important immune system molecules. His projects have included the use of x-ray crystallography to determine the structure of the complete TCR-antigen-MHC protein complex. Success in this line of work often hinges on finding just the right conditions for growing high-quality crystals of the protein under study. "It is a very empirical process, with no guarantee of success, and I've been dusting off a lot of my old books on kinetics and biophysics," says Kappler. "You pretty much have to have the heart of a riverboat gambler," he adds—and judging by his enthusiastic tone, he apparently has.

Marrack, meanwhile, has returned to whole animal studies after many years of investigating immune system cells in culture. She is finding important differences between the immune system operating in an intact animal and the immune cells in a Petri dish. "We showed years ago that you make a

Howard Hughes Medical Institute
Holiday Lectures on Science

Monday, December 9, and
Tuesday, December 10, 1996

10:00 a.m. – 12:30 p.m.

HHMI Conference Center
4000 Jones Bridge Road
Chevy Chase, MD 20815-6789

The 1996 Howard Hughes Medical Institute Holiday Lectures on Science for high school students, fourth in an annual series, will be delivered by John W. Kappler, Ph.D., and Philippa Marrack, Ph.D., Howard Hughes Medical Institute investigators and members of the Department of Medicine at the National Jewish Center for Immunology and Respiratory Medicine, Denver. Dr. Kappler and Dr. Marrack are also professors at the University of Colorado Health Sciences Center in Denver.

Monday, December 9

How Immune Cells Create Trillions of Receptors from a Few Hundred Parts
John W. Kappler
10:00 a.m. – 11:00 a.m.

White blood cells of the type called lymphocytes are able to recognize almost any kind of foreign material that enters the body, including bacteria, viruses (such as HIV), and man-made chemicals that did not exist when the immune system was evolving. Lymphocytes are divided into two principal groups, termed B cells and T cells. Both have the ability to identify a wide array of intruders because each bears on its surface a unique receptor, one created by random combinations of relatively few components. Much as random choices from a restaurant menu can lead to meals with a huge number of variations, random combinations of components can lead to trillions of different receptors. The human body therefore has at least a trillion ways of recognizing that something foreign has invaded.

How the Immune System Detects Invaders
Philippa Marrack
11:30 a.m. – 12:30 p.m.

The immune system recognizes invaders in a complex way. The two lymphocyte groups use different strategies. B cells can attack the intruder directly. T cells require assistance from B cells or other white blood cells that ingest and digest foreign invaders. Protein fragments from the processed invader reappear on the surface of these cells, bound in specialized grooves of a complex of proteins. This complex, known as the MHC (major histocompatibility complex) proteins, presents the invader fragments to T cells. The T cell receptors recognize the bound protein complex and initiate a cascade of events, enlisting the B cell army as well as other T cells. This system allows lymphocytes to identify and destroy cells in which viruses or bacteria are hidden and multiplying.

Tuesday, December 10

How the Host Avoids 'Friendly Fire'
John W. Kappler
10:00 a.m. – 11:00 a.m.

Normally these trillions of lymphocytes do not attack their host. To prevent such attacks, lymphocytes bearing receptors that might react with host tissues are selectively destroyed during their development. Cells that escape this screen treat host molecules as invaders, causing serious autoimmune (self-destructive) diseases such juvenile diabetes, rheumatoid arthritis, and lupus erythematosis.

Stalking the Elusive Pathogen
Philippa Marrack
11:30 a.m.– 12:30 p.m.

Some organisms have evolved ways of evading or subverting the body's defenses. The malaria parasite, for example, changes its coat proteins to stay one step ahead of the host's immune cells. Herpes viruses become almost undetectable to lymphocytes. The AIDS virus destroys a subset of T cells that are essential for a successful immune response. Thus the immune system fights off many but not all infections. By learning more about how such pathogens work, new means may be found to thwart them.

vast array of T cells and that most self-reactive ones die in the thymus," says Marrack. "But a few that can self-react sneak through—somewhere between 1 in 1,000 or 1 in 10,000. Somehow the system has to clobber these cells in order to prevent autoimmune disease, while allowing T cells that recognize pathogens to do their job."

Her research now is centered on understanding the complex fail-safe system that holds the remaining self-reactive cells in check. "If you just put antigen on T cells in a culture dish, they divide and grow," says Marrack. "But a few years ago we found that in an intact mouse, the T cells that recognize an antigen divide a few times, and then just die. This was totally unexpected." Pursuing this phenomenon further, Marrack showed that *in vivo*, a T cell that meets its particular antigen immediately puts several new proteins on its surface, including one that triggers an internal self-destruct program called apoptosis. Unless the newly stimulated T cell gets another signal—a yet-unknown confirmation code that counteracts the destruct sequence—it dies.

"We believe that invading pathogens somehow carry with them a signal that counteracts the death flag, and that the signal that rescues them from death is evolutionarily very old," says Marrack. "Even our invertebrate ancestors had receptors that could sense the material of foreign invaders, such as generic bacterial and fungal cell wall components. We believe that mammals use these same generic mechanisms to tell an activating T cell that instead of dying it must continue to divide."

But, one might ask, how does the immune system avoid activating the few self-reactive cells as well as pathogen-directed T cells in the presence of infection? "Now we've come to the edge of the envelope," Marrack answers. "Since the body constantly filters any self-reactive clones that escape the thymus, I suppose it's unlikely that you'd have a self-reactive cell at the same time and place as an infection, but I'm not sure. And there are doubtless other backup mechanisms that we don't know about."

Marrack and Kappler intend to pursue these and other questions about the immune system for the rest of their careers. Their children are now grown, but all those dinner table conversations about T cell recognition of MHC-antigen complexes and other esoteric scientific subjects seem to have rubbed off: Jim is a first-year graduate student in neurobiology at Rockefeller University in New York City, and Katy is a junior at Brown, deciding between a career in science or politics.

After talking to Kappler and Marrack, it becomes abundantly clear that these sociable people definitely do not fit the popular caricature of shy or unimaginative scientists. "Your whole day is spent interacting with people in your own lab, and in other labs," says Marrack. "Making and maintaining successful partnerships is a major part of your work."

Student interns from the Washington, D.C., metropolitan area worked with Institute staff in developing curricular materials and a World Wide Web site for the 1996 Holiday Lectures. From left to right: Ben deBivort, Joe Train, Jason Carroll.

Marrack and Kappler will speak to high school students on their scientific partnership, their work, immunology, and the scientific process on December 9 and 10 at 10:00 a.m. from the Howard Hughes Medical Institute in Chevy Chase, Maryland.

Howard Hughes Medical Institute Home Page

The area of the HHMI Web site currently under the most intense development involves the HHMI Holiday Lectures on Science *(http://www.hhmi.org/lectures/)*. Visitors to these pages can choose to participate in the 1996 Holiday Lectures on Science, which will be made available through satellite transmission and through cable television. Research summaries of recent investigations by Philippa Marrack and John W. Kappler, presenters of the 1996 lectures, are also available, as are the lectures that were given in 1993, 1994, and 1995. Those who missed the 1995 lectures by Nobel laureate Thomas R. Cech on "The Double Life of RNA" may order a free videotaped copy on line.

For viewing on line and for downloading, the Holiday Lecture area of the HHMI Web site makes available resources and teaching material suitable for classroom reading and discussion for the 1996 lectures on immunology (Table 3). High- and low-bandwidth paths are available. Users capable of viewing the high-bandwidth path will be able to enjoy multimedia resources, such as a virtual laboratory viable through the Shockwave plug-in for Netscape Navigator and Microsoft Internet Explorer. Interesting and important links to general science and genetics information Web sites are also available. These range from Access Excellence, which offers a resource center and bulletin board area, to Virtual Fly Lab, a dry laboratory to test the rules of genetic inheritance.

Table 3

Student and Teacher Advisers for Holiday Lectures Resource Guide

Teacher Advisers

Judy Brown
Columbus Center for Marine Biotechnology
on leave from Montgomery County Public Schools

Melanie Fields
Sidwell Friends School
Washington, D.C.

Toby Horn
Thomas Jefferson High School for Science and Technology
Fairfax County, Virginia

Thelma Newman
Quince Orchard High School
Montgomery County, Maryland

Jonetta Russell
Montgomery Blair High School
Montgomery County, Maryland

Gloria Seelman
Office of Science Education
National Institutes of Health

Project Adviser

Julie Graf
Executive Director, Hughes Initiative
University of Colorado, Boulder

Student Interns

Joe Train, *multimedia review and production*
1996 graduate of Thomas Jefferson High School for Science and Technology
Fairfax County, Virginia
freshman, University of Virginia

Ben deBivort, *virtual laboratory development*
junior, Walt Whitman High School
Montgomery County, Maryland

Jason Carroll, *Web site development*
1996 graduate of Sidwell Friends School
Washington, D.C.
freshman, Harvard University

A Teacher Resource Group consulted with Institute staff and Washington area students in developing a resource guide to accompany the 1996 Holiday Lectures (l–r : Institute Vice President Joseph G. Perpich, teacher Toby Horn, student Joe Train, and teacher Judy Brown).

Table 4

Washington Metropolitan Area High School Students Attending the Howard Hughes Medical Institute Holiday Lectures on Science, December 18 and 19, 1995

MARYLAND

Montgomery County

Academy of the Holy Cross
Lauren MacWilliams
Christine Roddy

Albert Einstein High School
Brendan Fife
Timothy Fife

Barrie School
Joe Lee

Bethesda-Chevy Chase High School
Chenxi Dong
Gabor Fenyes
Yimin Li
James Walters

Charles E. Smith Jewish Day School
Karen Pressman
Joel Sandler
Vida Yazdi

Chelsea School
David Fishman
Peter Martel
Stephen Wells

Connelly School of the Holy Child
Emily Sama Martin
Kim McArthur

Damascus High School
Andrea Baines
Karen Hague
Michelle Mendoza

Gaithersburg High School
Kean Ching
Sachin Duggal
Nicole Hankin

Hebrew Academy of Greater Washington
Yoni Levine
Ilan Prager
Margaret Stein

Heights School
John Lee
John Yi

John F. Kennedy High School
Judy Klang
Charkeeta Nelson
Maketa Patterson

Landon School
Alex Boni-Saenz
Olivier Kamanda
Arvin Vohra

Montgomery Blair High School
Elana Berger
Carmen Holmes
Ali McTague
Elizabeth Stranges

Paint Branch High School
Sonia Jesrani
Wendy Tseng

Richard Montgomery High School
Anna Cross
Sandi Tun

Rockville High School
Martin Dahn
Martine Paul
Muhammad Said

St. Andrew's Episcopal School
Vaughn Gray
Becca Ohle
Gemma Smith

Seneca Valley High School
Rachna Arora
Jungwook (Tina) Ryu
Julius Wilder

Sherwood High School
Ramya Banninthaya
James Regeimbal
Christopher Trask

Springbrook High School
Funminiyi Ajayi
Kafui Dzirasa
Katherine Hober

Stone Ridge School of the Sacred Heart
Catie DeLuca
Keri Smolka

Thomas Edison High School of Technology
Elizabeth Grimes
Lilly Huang
Veronica Villalobos

Thomas S. Wootton High School
Matt Donnellan
Emily Van Degrift

Walter Johnson High School
Chris Drury
April Franks
Robin Kessel

Watkins Mill High School
Nykia Ashmeade
Rahul Pawar
Danielle Sanders

Wheaton High School
Gisela Fajner
John Karaian
Thomas Williams

Winston Churchill High School
Jennifer Cabrera
Andrew Kin

Yeshiva of Greater Washington
Leona Berkovich
Melanie Gellman
Chaya Twerski

Prince George's County

Central High School
Michael Grant
Amanda Scott

Crossland High School
Gia Little
Charles Pickard

DeMatha High School
Gerry Boyle
Sean Burke

DuVal High School
Sheila Agyeman
Lisa Saunders

Eleanor Roosevelt High School
Mya Fisher
March Wood

Fairmont Heights High School
Melinda Beale
Omarr Oliver

Forestville High School
Charles Mackey
Keon Vasudevan

Frederick Douglass High School
Yvonne Ballard
Jernee Elliott

Friendly High School
Heather Liverpool
Tina Williams

Gwynn Park High School
Taryn Barber
Arrykka Harrison

High Point High School
Leonora Darlington
Bala Kodukula

Laurel High School
Yusef Buchanan

Oxon Hill High School
Ahmed Steadman
Deidre Washington

Queen Anne School
Angela Holland
Catherine Toppin

Table 4 (cont'd)

Washington Metropolitan Area High School Students Attending the Howard Hughes Medical Institute Holiday Lectures on Science, December 18 and 19, 1995

St. Vincent Palotti High School
Theresa Clark
Tina Khair

Surrattsville High School
Taneeka Strickland

DISTRICT OF COLUMBIA

Anacostia Senior High School
Kenyona Price

Archbishop Carroll High School
Jennifer Johnson
Clayton Mitchell III

Bell Multicultural Senior High School
Amine Ben Adada
Katia Zelaya

Duke Ellington School of the Arts
Maya Orr
Jennifer Robertson

Eastern Senior High School
Ivonna Smith

Edmund Burke School
Kyle Serrette

Eleanor Roosevelt Senior High School
Robin Griffin
Nicole Hawkins

Georgetown Visitation Preparatory School
Lisa Moyer
Kate O'Reilly

Maret School
Rachel Kline
Sarah Olmstead

McKinley Senior High School
Dawn Medley
Joseph Sweatmon

St. Albans School
Nikhil Garg
Jamie Platts

St. Anselm's Abbey School
Sean R. Brennan
Danilo S. Jayson

Sidwell Friends School
Eric Edelson
Ankur Kumar

Woodrow Wilson Senior High School
Asmara Ghebremichael
Khalil Maalouf

VIRGINIA

City of Alexandria

Bishop Ireton High School
Sallie Fox
Michael Pasquale

T.C. Williams High School
Travis Barton
Meredith Haines

Arlington County

Bishop Denis J. O'Connell High School
Jennifer Chuppe
Rhacquel Munsayac (12/18 only)
Janice Siguitan (12/19 only)

Fairfax County

Annandale High School
Matthew Floyd
Adrian Porter

Centreville High School
Scott Heffner
Jennifer Rodriguez

Chantilly High School
Samina Raja
Virginia Song

Episcopal High School
Marcy Behnam
Kirsten Burton

Fairfax High School
Matthew Dombroski
Bree Gipstein

Hayfield Secondary School
Lauren Gaudreault
Sima Tamaddon

Herndon High School
Wei Wei Yen
Jennifer Zaborsky

James Madison High School
Anoushka Afonso
Andrea Young

Lake Braddock Secondary School
Brian Hacker
Rosemarie Liu

Langley High School
Jen Amaral
Gene Chien

Madeira School
Premal Dharia

McLean High School
Myrvet Cocoli
Diane Fritz

Mount Vernon High School
Christine Brophy
Kevin Noble

Oakton High School
David Paik
Jennifer Skene

Potomac School
Ann Johnson
Shelby Smith

Robert E. Lee High School
Shruti Chandra
John Perrine

South Lakes High School
Amanda Britt
Justin McLaughlin-Williams

Thomas A. Edison High School
Nick Jones
Anouesh Sayah

Thomas Jefferson High School for Science and Technology
Ian Hagemann
Catherine Malmberg
Baninder Taneja

W. T. Woodson High School
Kyle Jensen
Rachel White

West Potomac High School
Brian Schaffter
Sabina Younis

West Springfield High School
Riz Ahmed
Jane Yoo

Washington, D.C., Metropolitan Area Precollege Science Education Grants

Table 5

Institutes Offering Student Research in HHMI's Summer Research Fellowship Program and the Student and Teacher Intern Program at the National Institutes of Health

NCI	National Cancer Institute
NEI	National Eye Institute
NHLBI	National Heart, Lung, and Blood Institute
NIAID	National Institute of Allergy and Infectious Diseases
NIAMS	National Institute of Arthritis and Musculoskeletal and Skin Diseases
NICHD	National Institute of Child Health and Human Development
NIDR	National Institute of Dental Research
NIDDK	National Institute of Diabetes and Digestive and Kidney Diseases
NIMH	National Institute of Mental Health
NINDS	National Institute of Neurological Disorders and Stroke
NCHGR	National Center for Human Genome Research
DCRT	Division of Computer Research and Technology

Howard Hughes Medical Institute Summer Research Fellowship Program at the National Institutes of Health

For decades science educators have known that the laboratory serves several crucial functions in the student's intellectual development. Although time and budget constraints may limit laboratory work, sophisticated laboratory experiences are becoming routinely available at the secondary school level for both students and teachers. Moreover, summer programs increasingly enable students to "do science" side by side with working scientists. These programs are exceptional opportunities for exceptional individuals—from the students who enroll, to the scientists who commit themselves and their laboratories to providing vital learning environments for young minds.

Norman Tyler Sobel's bequest of slightly more than $100,000 to the United States government in 1988 provided the seed money for a summer research program in the intramural laboratories at the National Institutes of Health. Initiated as the Sobel Summer Scholars Program, it was an NIH initiative to draw young people into biomedical research, nurture their enthusiasm during training, and propel them into productive careers in scientific research or administration.

In the first summer of the program, 21 students chosen from 127 applicants entered NIH laboratories. Another 21 were accepted in 1989. The following year the Howard Hughes Medical Institute awarded a five-year grant of $360,000 to the Foundation for Advanced Education in the Sciences at NIH to continue the summer research program. In 1995 HHMI provided an additional $400,000 to extend the program for four more years.

Since 1990 the Institute funding has provided research opportunities for up to 40 students each year. The program enables selected students who participate during or immediately after high school to return to the NIH campus after one or more years in college.

Program Elements

Each year 167 secondary schools in the Washington metropolitan area are invited to distribute summer research program applications. Science resource teachers from each high school nominate up to two students who have completed their junior or senior year. Fellowship recipients are selected by a committee of senior NIH scientists on the basis of their grades, SAT scores, teacher recommendations, and involvement in science-related activities. The program is competitive, with one in five applications accepted. Nearly one-half of the students are from Montgomery County, Maryland, and the rest are from Washington, D.C., and nearby Maryland and Virginia. Accepted fellows are assigned research mentors, who help to place them in laboratory projects suited to their interests and abilities. The projects range across the scientific disciplines represented

at NIH, including biological, physical, computational, and behavioral sciences.

The 10-week intensive summer research experience is not limited to a laboratory assignment. Weekly student research presentations and occasional social gatherings encourage students to interact as a group while developing an affiliation with their laboratory. Participants are also invited to present their findings at Poster Day, held each summer. High school students receive a stipend of $2,000, and those returning from college receive $2,500.

Involvement in the program beyond high school encourages students to remain in scientific training during college, when those with an interest in science often turn to other pursuits. It is hoped that two or three summers at NIH will confirm their interest in science, increase their knowledge of how research is done, fire enthusiasm for its intellectual rewards, and encourage them to go on to medical or graduate school.

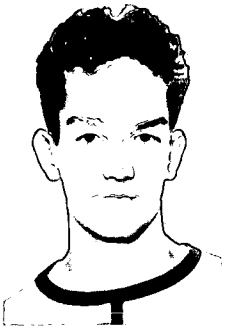
Getting a Jump on a Scientific Career

As is evidenced in the following student profiles, many summer fellows decided early in their lives that they wanted to pursue a career in medicine or biomedical research, some as early as elementary school. In a 1995 survey of 85 current and previous HHMI summer fellows, 63, or nearly 75 percent, were majoring or planning to major in science in college. An additional nine had chosen engineering as an academic major. Over 40 percent planned to pursue medical school, and 33 percent had career plans that involved graduate work in science.

Some of the fellows return for a second or third summer after graduating from high school and going on to college. They could not benefit from the continuity of their research experience were it not for the scientist preceptors who welcome the fellows into their laboratories year after year. Not only do the NIH scientists gain a valuable extra set of hands, but they themselves are stimulated as mentors and infused with new ideas and approaches. For some students, the laboratory becomes a second home and a place to test their analytical and social skills. This all comes together at Poster Day, when students from 33 states, the District of Columbia, and countries worldwide display their summer-long research projects for the NIH community.

Besides the valuable experience that the internship provides in terms of skills and knowledge, it also gives students a sense of the culture and organization of science. This is valuable for the young person making an educational and career decision. Some fellows thrive on the intensity and collegiality of the laboratory; others are still making up their minds. In any event, each student gains some knowledge of self in the process.

Profiles of the 1996 interns are presented below. They are a diverse, talented, responsible, and enthusiastic group of students whom the Institute is pleased to support as they make critical decisions about their futures.



Dana Ackerly
St. Albans School
Years in Program: 1
Preceptor:
Dr. Alan Wolffe
Laboratory of Molecular Embryology
National Institute of Child Health and Human Development

Project Title: Expression of Xenopus Imitation Switch Protein in Recombinant Bacteria

How DNA transcription is initiated is one of "the greatest mysteries facing modern medicine," according to Dana (Clay) Ackerly. During his first summer in an NIH laboratory, Clay set out to unravel part of this mystery: he tried to purify a protein, called imitation switch protein, that is hypothesized to play an important role in activating DNA transcription. Through *in vitro* studies imitation switch protein has been identified as one of four polypeptides that come together to form a complex molecule called nucleosome remodeling factor (NURF). This molecule appears to act directly on nucleosomes.

Nucleosomes are the basic subunits of chromosomal structure. They are made up of DNA wrapped around what looks like a spool of histone proteins. Nucleosomes form repeating units on the proverbial "string" of DNA. By condensing into nucleosomes, billions of DNA base pairs that comprise the genome can be packaged into the nucleus. Yet the nucleosome structure must be "unwound" to enable transcription factors to reach their target sequences to launch transcription. Here's where NURF comes in. It appears to be crucial in generating a nucleosome-free region above DNA promoter sequences. Without NURF, the promoter region might not be accessible to transcription factors because it is coiled into a nucleosome.

Clay's laboratory is eager to learn about the *in vivo* functions of NURF and its constituent polypeptide, imitation switch protein, in Xenopus because chromatin biochemistry is well developed in this organism. More specifically, they want to explore "the hypothesis that imitation switch protein itself does not bind to nucleosomes without the other factors within the NURF complex," said Paul Wade, a postdoctoral fellow who mentored Clay. Clay worked feverishly to purify imitation switch protein with a bacterial expression system, but he was unable to finish the project by summer's end. Dr. Wade plans to pursue the purification of imitation switch protein and eventually NURF.

Clay, a senior at St. Albans School, spent an earlier summer in Ecuador on a public health project for which he trained during the school year. His role was to vaccinate dogs and cats in an area in which rabies was endemic. Clay has aspirations to become a biologist or a medical doctor because, in his words, "I would like some day to be able to do for others what so many people have done for me."

Anoushka Afonso
James Madison High School
Georgetown University
Years in Program: 1
Preceptor:
Dr. Marston Linehan
Surgery Branch
National Cancer Institute

Project Title: Chromosome 13 Loss of Heterozygosity in Prostate Cancer

Prostate cancer is the most common cancer in men, yet precious little is known about which genes are responsible. While much of the spotlight has been focused on chromosome 8, Anoushka Afonso has concentrated her efforts on chromosome 13. It is on this chromosome where Anoushka has identified a region that may be involved in the progression, rather than in the initiation, of prostate cancer.

Many cancers are thought to arise, in part, from deletion of a tumor suppressor gene. Without the gene product to keep cancer at bay, cells become more vulnerable to tumor formation. Suspecting that prostate cancer also may result from deletion of a tumor suppressor gene, Anoushka subjected normal and cancerous prostate tissue from the same patient to a standard test for chromosome deletion—the loss of heterozygosity. This test involves the use of PCR amplification and gel electrophoresis to determine whether cancer cells are missing one of the two normal copies of a DNA segment. Normal cells that are heterozygous for a given DNA segment possess two slightly different copies, one from the mother and one from the father. In cancer cells with loss of heterozygosity, one of the two copies disappears.

Anoushka found loss of heterozygosity in two regions on the long arm of chromosome 13 near the gene for retinoblastoma. This finding is consistent with the possibility that prostate cancer may result from the deletion of a tumor suppressor gene found somewhere within this general area, although the specific location, identity, and function of the gene are not yet known. Moreover, Anoushka determined that in patients with loss of heterozygosity on chromosome 13, 63 percent had advanced prostate cancer, whereas in patients with no loss of heterozygosity, only 27 percent had advanced prostate cancer. "What she found is a highly interesting correlation between loss of heterozygosity and patients with advanced cancer, suggesting that these changes may be involved in the progression of prostate cancer," said Anoushka's preceptor, Dr. Marston Linehan, who plans follow-up studies.

Anoushka is majoring in biology as a pre-med student at Georgetown University. By the time she hopes to receive her degree in medicine, she will be smiling with pride about her earlier research contributions to the genetics of prostate cancer.

Azunna Anyanwu
Benjamin Banneker Academic High School

Harvard University

Years in Program: 1

Preceptor:
Dr. Steve Massaquoi

Human Motor Control Section

National Institute of Neurological Disorders and Stroke

Project Title: Changes in Multi-Joint Coordination After Extended Practice

Learning may have limits, according to research conducted by Azunna Anyanwu. Azunna sought to explore the limits of human motor learning through a task requiring multi-joint coordination. The task at first seemed relatively simple: to trace a simple diagonal line (/). But there was a catch: the subjects could only use two joints—their shoulder and elbow joints. Seated and immobilized at a chest-high table with a felt-tip pen in hand, subjects were asked to make a left to right cross-body extension movement, akin to a tennis backhand, without using their wrist or other joints, except for their shoulder and elbow. And in total darkness, no less!

After three weeks of intensive practice—consisting of about 2,000 trials—the normal subjects were still almost never able to reproduce the diagonal line. What emerged instead were two characteristic patterns of error. One error pattern was the generation of an (S) and the other was the generation of an outwardly bowed arc. Although everyone did improve somewhat, they still were only extremely rarely able to recreate faithfully the diagonal line, as assessed by various measurements of the distance between the template and the curve they produced. Said Azunna's preceptor, Dr. Steve Massaquoi, "This may represent a fundamental limitation in the neural control of multi-joint movements and therefore may shed light on the structure of the brain circuitry involved."

Azunna's skill with computers came in very handy in helping Dr. Massaquoi to refine the experimental setup and to troubleshoot. One computer was used to instruct subjects, while another captured their movements through infrared cameras. Azunna's sense of humor was also critical to maintaining morale among some dispirited and frustrated subjects.

Azunna's findings on normal subjects will be used by Dr. Massaquoi to evaluate a novel computer model of brain coordination of movement. Dr. Massaquoi plans to compare the normal findings with those from patients with cerebellar ataxia. This is a condition of clumsiness and incoordination that afflicts many thousands of people suffering from cerebellar injury or degeneration.

Azunna is a freshman at Harvard University planning to major in computer science and biology. He hopes to become a cardiac surgeon because, in his words, "I have always been fascinated by the human body, its capabilities, uniqueness, and limitations."

Stephanie Bomar
Lake Braddock Secondary School

Loyola College

Years in Program: 1

Preceptor:
Dr. Philip Fox

Clinical Investigations Section

National Institute of Dental Research

Project Title: Salivary Gland Cytokine Expression in Sjogren's Syndrome

Stephanie Bomar's research delved into the immunological basis of Sjogren's syndrome, a debilitating condition that afflicts about two million individuals, 90 percent of whom are women. It is an autoimmune disorder that attacks exocrine glands, which include the salivary glands. Dry mouth, one of the hallmarks of Sjogren's syndrome, occurs as a result of salivary gland dysfunction. Patients are deprived of saliva's normal roles in swallowing and in the enzymatic breakdown of proteins in food.

The purpose of Stephanie's project was twofold: to determine which types of cells found in the salivary gland produce cytokines—small proteins that regulate the immune response—and which types of cytokines they produce. Stephanie microdissected salivary glands from Sjogren's patients in order to separate three cell types: acini cells, ductal cells, and lymphocytes. Acini and ductal cells are epithelial cells. The former produce saliva, and the latter line the cavity through which saliva is released into the mouth. Lymphocytes, which are not normally present in salivary glands, are found in large aggregates in Sjogren's patients.

After dividing cell types, Stephanie extracted their mRNAs, which were reverse-transcribed into DNA. She amplified the DNA by PCR before using labeled oligonucleotide probes to identify DNA encoding seven specific cytokines. What she found was that acini expressed higher quantities, and more types, of cytokine mRNAs than did ductal cells. Acini expressed mRNAs for three types of interleukins (IL-2, IL-6, IL-10), tumor necrosis factor-I, transforming growth factor β, and interferon-K, but not for IL-4. The lymphocytes produced the same complement of cytokine mRNAs. Stephanie concluded that "salivary epithelial cells in Sjogren's syndrome patients are a site of active immunologic activity." Further studies are planned to test the hypothesis that lymphocytes induce the acini to produce cytokines, which ultimately leads to their own demise, according to Dr. Di Sun, a postdoctoral fellow who worked with Stephanie.

Stephanie started her freshman year at Loyola College with the intention of becoming an orthodontist. She was named in high school as a semifinalist for the National Achievement Scholarship Program for Outstanding Negro Students. In her spare time, she enjoys reading and crafts.

Jason Carroll
Sidwell Friends School

Harvard University

Years in Program: 1

Preceptor:
Dr. Julianna Barsony

Laboratory of Cellular Biology and Biochemistry

National Institute of Diabetes and Digestive and Kidney Diseases

Project Title: 3-D Analysis of the Structure and Order of the MMTV-LTR Tandem Repeat in 3134 Cell Nuclei

Silicon Valley may not have discovered the computer skills of Jason Carroll, but Dr. Julianna Barsony certainly has. Dr. Barsony was Jason's preceptor during his summer in the HHMI-supported program. Using his advanced computer programming skills, Jason generated the world's first map of glucocorticoid receptor target genes and captured this extraordinary structure in a movie.

The glucocorticoid receptor (GR) is a cytosolic steroid receptor that, upon binding to a steroid hormone, translocates to the nucleus. There the GR functions as a transcription factor to turn on specific genes. To visualize this extraordinary event in living cells, Jason used a unique reagent developed by Dr. Han Htun of the National Cancer Institute. This reagent is a gene encoding the green fluorescent protein (GFP) from jellyfish annealed to the gene encoding GR. This genetic combination was incorporated into a plasmid vector. When the vector was transfected into a particular mouse adenocarcinoma cell line, a chimeric protein was expressed. Under confocal microscopy, the movement of the fluorescent chimeric protein was tracked with ease.

The advantage of the cell line Jason used was that, in addition to containing hundreds of endogenous GR target genes, each nucleus had a "minichromosome," a tandem array of 200 copies of mouse mammary tumor virus long-terminal repeat (MMTV-LTR). Each MMTV-LTR contains four GR binding sites. With roughly 800 additional binding sites, Jason was able to visualize the binding between the newly fluorescent GRs and their target sites.

Jason collected serial 0.2 micron images from many nuclei. He wrote a computer program that assembled the images and reconstituted the nuclei in 3D. The program was capable of identifying the fluorescent foci on target genes, including the ribbon-like minichromosome. Using fluorescence *in situ* hybridization, Jason confirmed that the bright ribbon he photographed was indeed the minichromosome. The work was of such significance that Jason's name will appear on a publication.

Jason is a freshman at Harvard University. While his major is undecided, he may well find himself caught between the allure of computer science and biology.

Sulene Chi
Thomas S. Wootton High School

Princeton University

Years in Program: 3

Preceptor:
Dr. Adrian Parsegian

Laboratory of Structural Biology

Division of Computer Research and Technology

Project Title: Temperature-Induced Self-Assembly of Biological Macromolecules

Most biologists consider biophysics to be one of the more daunting areas of biomedical research, but not Sulene Chi. She brings to her HHMI-sponsored research in biophysics strong academic grounding in chemistry and physics. During her third summer in the program, Sulene studied how water affects collagen structure.

Collagen is the most abundant protein in humans, making up about one-quarter of all body protein. It is a major component of skin, tendons, and bone. What distinguishes collagen from many other proteins is its ability to form fibers assembled from triple helices—three intertwined polypeptide chains held together by hydrogen bonds. According to Sulene, "What we are trying to prove is that water molecules are important in collagen self-assembly. Right now, no one is paying attention to them."

Sulene studied the interaction between water molecules and the amino acid histidine on the collagen polypeptide. Her hypothesis was that the displacement of water molecules around histidine controls the assembly of collagen triple helices into fibers. By a combination of x-ray diffraction and spectrophotometry, Sulene studied the effects of modifying histidine on the packing of the triple helices.

Sulene is an accomplished violinist, creative writer, and former member of her high school's championship physics and science bowl teams. She is eager to pursue a career in biomedical research because "it combines the logic of experimental design with the unpredictability of living systems."

Nancy Cho
Walt Whitman High School

Harvard University

Years in Program: 3

Preceptor:
Dr. Drew Weissman

Laboratory of Immunoregulation

National Institute of Allergy and Infectious Diseases

Project Title: Role of a Single Infusion of Interleukin-10 in Modulating Cytokines in HIV-1 Infected Individuals

Nancy Cho's third summer studying retroviruses was devoted to a new project that, on the surface, seemed counterintuitive: it was designed to block HIV replication by administering an immunosuppressant. An immunosuppressant? If the hallmark of HIV infection is severe immunosuppression, then why would an immunosuppressant help to treat HIV?

If the immunosuppressant is the cytokine interleukin-10 (IL-10), there is ample justification for its administration to HIV-positive patients. Nancy's laboratory previously demonstrated *in vitro* that IL-10 inhibits the replication of HIV in macrophages and T cells, two of the cell types that HIV infects. This inhibition has been shown to occur via the blockade of pro-inflammatory cytokines, i.e., intercellular messengers that activate T cells. According to Dr. Drew Weissman, a senior postdoctoral fellow who worked closely with Nancy, "HIV is a disease of activation. In order for HIV to grow, you have to activate T cells. Any event that activates T cells leads to an increase in HIV growth."

With the goal of preventing T cell activation, 10 relatively healthy HIV positive patients volunteered to receive a single infusion of IL-10. Their plasma was studied at various points thereafter to determine whether HIV replication was repressed and whether pro-inflammatory cytokines were also repressed. Using a type of quantitative PCR, HIV's single-stranded RNA genome was found to decline precipitously among these patients, with reductions ranging from 70 to 100 percent. Similarly, ELISA assays revealed reductions in three pro-inflammatory interleukins (IL-2, IL-6, and IL-1) and in the cytokine tumor necrosis factor-I. Unfortunately, the reductions were all transitory in these preliminary studies.

Nancy is a junior biochemistry major at Harvard University. She plans to become a doctor, but she is still undecided about whether to seek a Ph.D. as well. She is gravitating toward patient care as a result of her rewarding clinical experiences this past summer at the NIH Clinical Center and at the Massachusetts General Hospital, where she volunteers during the school year. In her spare time, she relishes playing volleyball and teaching piano to disadvantaged children.

Lauren Cochran
Walt Whitman High School

Years in Program: 1

Preceptor:
Dr. Daniel Alkon

Laboratory of Adaptive Systems

National Institute of Neurological Disorders and Stroke

Project Title: Long-Term Learning–Induced Plasticity in Rabbit Purkinje Cells

Learning can be as simple as the blink of an eye. That's what Lauren Cochran discovered during a summer devoted to identifying neural substrates of learning.

Through classical conditioning, rabbits can learn to blink a special eyelid, called a nictitating membrane, solely in response to a simple tone. In an earlier three-day learning trial, the tone repeatedly had been presented immediately before an electrical pulse, which, by itself, elicited the blink as part of the animal's defensive response to a noxious stimulus. The rabbit's later ability to blink merely with the presentation of a tone is described as associative learning.

Lauren's project was designed to extend previous findings of the laboratory showing that Purkinje cells of the cerebellum were more physiologically excitable after three days of conditioning. She sought to determine whether these cerebellar cells still exhibited increased excitability one month after the conditioning trial. The hippocampus has long been considered the foremost brain region involved in learning, but increasing evidence also points to an important role for the cerebellum. According to Dr. Bernard Schreurs, a tenure-track investigator in the laboratory who worked closely with Lauren, "There is much evidence from brain imaging, recording, and ablation studies that implicates the cerebellum in associative learning."

Using a glass electrode, Lauren performed *in vitro* recordings from the rabbit's Purkinje cells located in an anterior region of the cerebellum termed lobule HVI. One month after the learning trial, she found these cells to have lower thresholds before generating a characteristic, local electrical discharge termed a spike. The Purkinje cells from control animals required the delivery of more electrical current to elicit the same spike. From these findings, Lauren concluded that "Lobule HVI of the cerebellum is a locus of both short- and long-term learning–induced plasticity."

The rarefied atmosphere of a laboratory devoted to learning contrasts with some of Lauren's real-world experiences. Lauren participates as a teacher of at-risk children who require enrichment in the Saturday Learning Extension Program sponsored by Howard University. In this program, she teaches reading to groups of 10 elementary students who had been slipping in school. "It is fun and rewarding to reach kids who had almost been given up on," said Lauren. Her other outside interests include dance and playing piano, for which she has received numerous awards.

Kathryn Dewey
Thomas Stone High School

Johns Hopkins University

Years in Program: 1

Preceptor:
Dr. Susan Gottesman

Laboratory of Molecular Biology

National Cancer Institute

Project Title: The Overproduction of the Lon Protease in *Escherichia Coli*

As an environmentally conscious high school student, Kathryn Dewey organized fellow students to clean up the environment. As a budding researcher, Kathryn managed to study one of nature's own "cleaner uppers" in the form of a protease.

Proteases are enzymes that break down proteins. Kathryn strove to refine our understanding of a protease called Lon, one of five ATP-dependent proteases found in the cytoplasm of *E. coli.* Kathryn's laboratory was intrigued by an earlier study establishing that an overproduction of Lon leads to the death of *E. coli* at high temperatures. *E. coli* normally survives at high temperatures—with normal levels of Lon—because of the protective effects of heat shock proteins. But, for reasons that are not understood, heat shock proteins appear unable to work effectively amidst excess concentrations of Lon.

Kathryn Dewey's project was to characterize more carefully what happens when Lon is overexpressed. She had at her disposal a convenient means of calibrating the internal levels of Lon: a plasmid vector which placed the Lon gene under the control of a special promoter. The level of promoter activity could be exquisitely regulated by varying the concentrations of the sugar, arabinose, in the media bathing *E. coli.* High concentrations of arabinose in the media would induce high levels of promoter activity and lead to high expression of Lon, whereas low amounts of arabinose in the media would have the opposite effect. "Kathryn's goal was to look for the survival of *E. coli* containing the vector after varying arabinose concentrations and temperature," said postdoctoral fellow Dr. Laurence Van Melderen, who mentored Kathryn.

What Kathryn found was that the two highest concentrations of arabinose in the media led to the death of *E. coli* at 42° C and 37° C, but not at 32° C. The cells survived under low arabinose concentrations even at the high temperatures. Dr. Van Melderen hypothesized that "Lon is probably degrading heat shock proteins essential for *E. coli's* survival at high temperatures."

Kathryn is a freshman at Johns Hopkins University. She is majoring in biomedical engineering with the goal of becoming a biomedical engineer. True to her professional objective, she says she "enjoys problem solving and thinking things through. I'd prefer to find my own solution rather than using other people's."

Nassim Ebrahimi
Walter Johnson High School

University of Maryland

Years in Program: 1

Preceptor:
Dr. Serge Beaucage

Biological Psychiatry Branch

National Institute of Mental Health

Project Title: The Role of the Glucocorticoid Receptor in Major Affective Disorders: A Mouse Tale

Nassim Ebrahimi was intrigued by research on the role of glucocorticoid receptors in depression. She joined the laboratory of Dr. Serge Beaucage in order to study transgenic mice that had fewer glucocorticoid receptors. These transgenic animals share biochemical and behavioral features of seriously depressed patients, many of whom display high levels of cortisol. Through fewer numbers of glucocorticoid receptors (GR), transgenic mice have a reduced ability to respond to excess levels of the hormone cortisol by downregulating its production.

The transgenic mice contained a foreign gene which encoded—in reverse sequence—part of the GR protein. Consequently, after the gene was transcribed, its incorrect mRNA, which appears to bind to the correct mRNA for GR, was digested by the enzyme ribonuclease. The result was a paucity of receptors.

"Nassim's role was to assist me in setting up the experimental apparatus and paradigm for behavioral experiments to help categorize these transgenic animals," said Dr. Beaucage. Nassim and Dr. Beaucage conducted two behavioral experiments—one to study the startle response and the other to study a behavior known as "fear potentiated startle." In the first experiment, Nassim found the transgenic mice to react more when exposed to an acoustic startle, i.e., a loud noise. The effect was reversed with the administration of desipramine, an antidepressant. The purpose of the second experiment on fear-potentiated startle was to gain insights into the role of a brain region called the amygdala. The animals were trained to fear the turning on of a light because it was repeatedly paired with a small shock. During a later testing phase, Nassim measured the difference in the animals' reaction to a startle noise, with and without a light turned on. The transgenic animals were expected to display a more prominent fear-potentiated startle reaction when the light was turned on, "because these animals are less able to control their reactivity to stress," noted Dr. Beaucage.

Nassim is a freshman at the University of Maryland at College Park. With a major in biochemistry, she is planning to enter pediatrics. Her strong interests include martial arts, dance, soccer, and tutoring.

Kathryn Getek
Lake Braddock Secondary School

Princeton University

Years in Program: 2

Preceptor:
Dr. William Figg

Clinical Pharmacology Branch

National Cancer Institute

Project Title: Detection of Micrometastases in Prostate Cancer Patients

During her second summer at NIH, Kathryn Getek focused on prostate cancer, the leading malignancy in males. Kathryn sought to detect micrometastases in patients with advanced prostate cancer. Micrometastases are tumor cells that have escaped from the primary tumor site, but are too few in number to form an identifiable tumor mass. If unchecked, the micrometastases can establish a foothold in distant tissues and eventually grow into new tumors. By developing a sensitive assay for prostate micrometastases, Kathryn had hoped to provide doctors with an early warning system to help them monitor and treat patients more aggressively.

Under the guidance of Dr. Shannon Dixon, a postdoctoral fellow, Kathryn assayed for the mRNA for prostate-specific antigen (PSA) under the assumption that any circulating cells expressing mRNA for this prostate-specific protein originated in a prostate tumor because normal prostate cells are not present in the circulation. The conventional diagnostic test for prostate cancer detects the PSA protein—not the mRNA from an intact cell—because this protein is released from epithelial cells of the prostate into the blood in normal males and, at higher concentrations, in males with prostate cancer. Thus, detection of this protein is not a sensitive method of finding micrometastases.

Kathryn obtained blood samples from advanced prostate cancer patients and controls, from which she separated out the fraction containing lymphocytes as well as any metastatic prostate cells. She extracted total RNA and applied reverse transcriptase to generate cDNAs. Using PCR, she amplified only the PSA-specific cDNA with a series of primers, i.e., small single-stranded oligonucleotides that hybridize with the cDNA. What she found, however, was that blood samples from both prostate cancer *and* normal controls were positive. Dr. Dixon hopes to refine the assay procedures to eliminate false positives.

Kathryn is a sophomore at Princeton University, where she intends to major in molecular biology. Although she has not yet decided on a career preference, her writing conveys a fierce interest in biomedical research. She has written, "Life is one of the most ingenious mechanisms created.... It is a credit to generations of scientists ... that there will always be investigations that tap deeper into the seemingly limitless pool of knowledge ... It is the art of questioning that makes science great and ... draws me ..."

Julie Goldberg
Montgomery Blair High School

Wesleyan University

Years in Program: 1

Preceptor:
Dr. Sharon Powell

Laboratory of Developmental Biology

National Institute of Dental Research

Project Title: Screening Laminin Peptides for New Neurite Outgrowth Active Sites

Julie Goldberg describes herself as someone who has "caught the disease of human curiosity and cannot stop asking questions." It is no wonder that her scientific attention has been drawn to one of the most fundamental questions in developmental biology: how do newly formed nerve cells grow toward and ultimately form connections with their target cells?

One clue has emerged from the study of laminin, a large glycoprotein found in the extracellular matrix of many tissues. Laminin is a directional growth stimulant. Laminin molecules in the extracellular matrix are like lights on a runway that steer nerve cells to their destination.

Since laminin is such a large molecule—consisting of over 6,000 amino acids arranged on three peptide chains—Julie's preceptor Dr. Sharon Powell wanted to know which portion of the laminin molecule is most important for nerve cell outgrowth. In her research project, Julie subjected cells in culture to over 500 small synthetic peptides representing different, sometimes overlapping, portions of the laminin molecule. Her goal was to determine which peptides elicited the greatest outgrowth. Each synthetic peptide was approximately 12–14 amino acids in length. Julie found that neonatal cerebellar cells were most responsive, in a dose-dependent manner, to about 20 of the 500 synthetic peptides she examined. Further studies are planned to determine whether these 20 peptides have any properties in common, such as composition, charge, or 3-D proximity on the laminin molecule. Once more is known about laminin's growth-promoting regions, laminin holds potential as a therapeutic agent for developmental disorders or for injuries to the nervous system.

Julie is a freshman at Wesleyan University, where she is considering a double major in English and biology. Her appreciation of both fields is captured in a passage she wrote, "Life is a dance with just a few steps known. If those few steps are enough to catch one's breath, imagine the wonder of the entire ... choreographed performance."

Vaughn T. Gray
St. Andrew's Episcopal School

Amherst College

Years in Program: 1

Preceptor:
Dr. Reed Wickner

Laboratory of Biochemical Pharmacology

National Institute of Diabetes and Digestive and Kidney Diseases

Project Title: Non-Mendelian Genetic Elements in Yeast

Studying yeast on the bucolic NIH campus seems far removed from England, where a public health crisis required hundreds of thousands of beef cattle to be slaughtered because of feared contamination with infectious proteins known as prions. But according to Vaughn (Tom) Gray, yeast may hold some answers to the baffling nature of prions and the diseases they cause.

Mad Cow Disease in England and a number of other neurodegenerative diseases (including scrapie, kuru, and Creutzfeldt-Jakob disease) appear to be caused by prions rather than by viruses. A prion protein is an altered form of a normal protein that is "infectious" because it appears to induce the normal protein to "flip," or convert, into a prion shape that causes dysfunction. One prion protein, known as PrP^{sc} and found only in the brains of afflicted animals, may be responsible for all of the mammalian prion diseases. "In essence, a prion is an entirely new type of pathogen," remarked Tom.

Yeast have provided a glorious model in which to study prions, especially because research in mammals is fraught with difficulties, including years-long latency periods after exposure. As single-celled eukaryotic organisms, yeast are a geneticist's delight because their entire genome has been sequenced, they have fewer chromosomes, and yet they have many cellular functions in common with higher eukaryotes. In 1994, Tom's preceptor, Dr. Reed Wickner, discovered a yeast prion termed [URE3]. [URE3] is an altered and inactive form of the protein Ure2. It is distinct from Ure2 insofar as it is resistant to proteases that degrade Ure2. [URE3] also has a number of properties that, taken together, provide evidence of a prion.

In his project, Tom tried to increase prion formation in yeast with a variety of exogenous compounds. Normally, yeast cells containing [URE3] arise infrequently. Tom found that their appearance was boosted when normal yeast cells were incubated with a particular compound. The finding impressed Dr. Wickner, who noted, "No one has ever described a compound that can induce a prion—assuming, of course, that [URE3] is a prion!"

Cautioning against hysteria about British beef, which does not contain contaminated brain tissue, Tom is eating beef (with bread!) at Amherst College, where he is majoring in biology and psychology. He aspires to become a molecular biology researcher.

Raqeeb Haque
Walt Whitman High School

Years in Program: 2

Preceptor:
Ms. Jane Trepel

Medicine Branch

National Cancer Institute

Project Title: Transcriptional and Post-Translational Regulation of the Retinoblastoma Family Member p107

Lovastatin is a drug marketed for its cholesterol-lowering capabilities, but it also holds promise in treating cancer. Raqeeb Haque's research probed lovastatin's ability to arrest the cell cycle and to induce cell death in a variety of cancer cell lines. During his second summer in Ms. Trepel's laboratory, Raqeeb followed up on his earlier finding that lovastatin eliminates in cancer cell lines an intriguing protein called p107. This protein, which is a member of the retinoblastoma family, is thought to be involved in controlling the cell cycle, but exactly how is not yet known. Raqeeb's stated goal for the second summer was to study the effects of lovastatin "to understand the mechanism by which p107 disappears and how p107 is involved in arresting cancer cells."

Using Northern and Western blotting, Raqeeb found that the mechanism by which lovastatin inhibited p107 was different, depending on the cancer cell line. In Ewing's sarcoma cells, p107 was destroyed by proteolysis after it had been translated into protein, a mechanism described as post-translational control. In prostate cancer cells, however, lovastatin worked by transcriptional control. This was first established with Northern analysis by showing reductions in mRNA for p107 after lovastatin treatment. Confirmation of this mechanism was achieved by transfecting prostate cancer cells with a DNA construct carrying a p107 promoter and a reporter gene to monitor levels of gene expression. With this recombinant system, transcription of the gene encoding p107 was still inhibited, verifying that lovastatin's action on prostate cells was by transcriptional repression. Further studies are needed to determine how lovastatin actually achieves such disparate effects on different cancer cell lines.

As a freshman at Harvard, Raqeeb harbors ambitions of becoming a pediatrician. He feels that pediatrics is ideal for combining his love of biology and his love of teaching children. Not only has he taught kindergarteners at Sunday school, but he also has taught children in less conventional settings: while waiting for gels to run, he stole away to another floor at the NIH Clinical Center to run touch football plays with children being treated for cancer. Through the camaraderie of sports, he was able to answer with ease their questions about cancer treatment. Despite his numerous academic and athletic achievements, he most cherishes the time he has spent educating young children.

Andrew House
Frederick High School
Rice University
Years in Program: 1
Preceptor:
Dr. Tohru Kamata
Laboratory of Biochemical Physiology
National Cancer Institute

Project Title: Isolation of Mouse NSP60 cDNA

Through his HHMI-supported summer research project, Andrew House discovered the thrills of mapping a gene. Andrew searched for the locus containing the gene that encodes the protein NSP60. This somewhat ungainly term stands for neural specific protein with a molecular weight of 60 kilodaltons.

NSP60 is not just another protein. It is a highly conserved protein expressed in the peripheral and central nervous system during development, but also at lower concentrations throughout adulthood. Andrew's first step toward finding its genetic locus was to create a cDNA library of the proteins found in the neurons of adult mice. He purified all mRNAs present in these cells and then used reverse transcriptase to create single-stranded cDNAs. With these strands as a template, he synthesized a second strand using DNA polymerase. To create sufficient quantities of the double-stranded cDNAs, he infected *E. coli* with recombinant bacteriophages containing the cDNAs. The task of identifying the cDNA encoding NSP60 from the other cDNAs in the library was made relatively easy: the laboratory already had isolated the gene encoding bovine NSP60. With the expectation of a sequence homology, the laboratory made P^{32}-labeled primers from the bovine gene to aid the screening for the murine gene. This expectation proved to be correct because the labeled primers hybridized to a locus on chromosome 14 of the mouse genome.

The precise role of NSP60 in development or in neurological disorders is unclear, but Dr. Tohru Kamata, Andrew's preceptor, believes the mapping project to be highly important. "The NSP60 locus is in the vicinity of another locus that appears to be responsible for a spontaneous mutation that accounts for a neurological disorder in mice," observed Dr. Kamata.

Andrew is a freshman at Rice University. He plans to major in biology in preparation for a career in medicine. He has attained distinction in a host of leadership positions, including president of the student government and Eagle Scout. Equipped with survival skills and athletic prowess, Andrew encountered few obstacles as a gene hunter.

Andrew Huling
St. Albans School
Harvard University
Years in Program: 3
Preceptor:
Dr. Louis Staudt
Metabolism Branch
National Cancer Institute

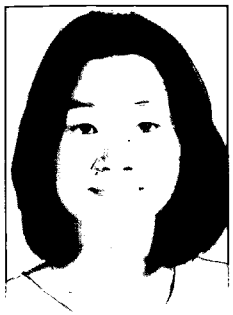
Project Title: Site-Directed Mutagenesis of the BCL-6 POZ Domain

Andrew Huling has devoted three summers to studying the molecular biology of diffuse large-cell lymphoma. This is an aggressive cancer that targets mature B lymphocytes. It is thought to be caused by the overexpression of a regulatory protein known as BCL-6. The laboratory in which Andrew has worked is scrutinizing an important domain of BCL-6: the POZ domain, a 121-amino acid segment found at the amino terminus. Evidence is accumulating for the POZ domain to be critical for BCL-6's function as a transcriptional repressor, i.e., a protein that blocks transcription of a target gene.

"Through studies of the POZ domain, Andrew is investigating the mechanisms underlying transcriptional repression," said Dr. Vicki Seyfert, a postdoctoral fellow who worked closely with Andrew.

Andrew spent his third summer in the program constructing plasmids containing mutated DNA sequences coding for the POZ domain. Through site-directed mutagenesis, many different mutated sequences can be generated with exquisite specificity and then introduced into the BCL-6 protein. Distinct BCL-6 proteins with mutations in the POZ domain then are examined for their ability to repress transcription of a reporter gene in a well-known enzymatic assay system (the CAT assay). In this system, a normal and unaltered POZ domain in BCL-6, for example, causes a quantitative decline in CAT production in a mammalian cell line. By studying mutant BCL-6 proteins, Andrew can help the laboratory identify which of the amino acids in the POZ domain are critical for transcriptional repression, thereby helping to pin down the role of BCL-6 in lymphoma.

A gifted athlete, Andrew has cultivated his skills in both baseball and basketball. Now a sophomore at Harvard University, Andrew plans to pursue a research career with a rich grounding in the molecular determinants of lymphoma.



Masako Irie
Thomas S. Wootton High School

Years in Program: 1

Preceptor:
Dr. Gordon Hager
Laboratory of Molecular Virology
National Cancer Institute

Project Title: Direct Visualization of Steroid Receptor Binding in Living Cells

Masako Irie was a witness to live-action molecular biology. Through her summer research project she was able to visualize a steroid receptor binding directly to DNA. The receptor was the glucocorticoid receptor, which after binding in the cytoplasm to a ligand (e.g., dexamethasone) translocates to the nucleus where it functions as a transcription factor: the receptor binds to target genes, thereby turning them on.

The novel system which Masako studied was pioneered by her mentor in the laboratory, postdoctoral fellow Dr. Han Htun. Dr. Htun and his collaborators took advantage of a naturally fluorescent protein found in jellyfish called green fluorescent protein (GFP). They reasoned that this protein could be fused with cellular proteins of interest to track their whereabouts in cells under fluorescence microscopy—almost like radar. To follow the trajectory of the newly fluorescent glucocorticoid receptor, they annealed the gene encoding GFP with that for the glucocorticoid receptor (GR) and ligated them into a plasmid vector. Once inside cultured mouse mammary epithelial cells, the genes on the plasmid were transcribed into chimeric proteins (GFP-GR) that are naturally fluorescent. Upon induction with dexamethasone, Dr. Htun and his collaborators were capable of visualizing the movement of these fluorescent proteins right into the nucleus, where they appeared to bind to target DNA. Mouse mammary epithelial cells were selected because they contain hundreds of copies of the DNA target sequences onto which the glucocorticoid receptor binds. Dr. Htun inferred that binding had occurred because he observed intense foci of fluorescence inside the nucleus. "To ensure that this interpretation was correct, we predicted that with a mutated binding site, GR would not be able to bind to DNA, and the fluorescent foci would be eliminated," said Dr. Htun.

Masako's role was to master a technique called site-directed mutagenesis to create a mutation in the region of the GR gene encoding the protein's DNA-binding domain. She sequenced the mutant protein to verify the placement of the mutation in one of the two zinc finger domains (a section of the protein whose 3D configuration lends itself to DNA binding). When this mutant protein was expressed together with GFP, the new chimeric protein was incapable of binding to DNA, affirming Dr. Htun's prediction.

Masako is a senior at Thomas S. Wootton High School, with many awards for her scholarship and athletic ability. Her hobbies include tennis, piano, backpacking, and chorus.

Cindy Kin
Winston Churchill High School
Harvard University

Years in Program: 1

Preceptor:
Dr. John Brady
Laboratory of Molecular Biology
National Cancer Institute

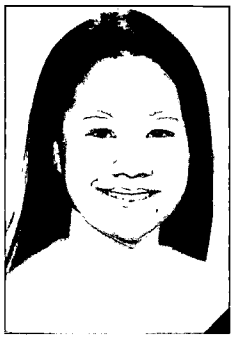
Project Title: Over-Expression and Purification of TRX, a Tax-Binding Protein

Adult T cell leukemia is caused by the human retrovirus HTLV-1 (human T cell leukemia virus-1), a virus endemic to Japan and the Caribbean. Cindy Kin's summer research project focused on the molecular mechanisms of how HTLV-1 transforms normal T cells into leukemic cells. One important line of research has centered on the HTLV-1 protein called Tax. When Tax alone is added to the media bathing fibroblasts, these cells lose contact inhibition, an early indicator of cell transformation. Unlike other transforming agents, however, Tax does not bind directly to DNA. Therefore, researchers have sought to identify T cell proteins that bind to Tax to initiate transformation.

In the past year, a team of researchers from Cindy's laboratory identified and characterized a Tax-binding protein normally present in T cells. They named the protein TRX, which stands for "Tax reactive protein X." They speculated that Tax binding to TRX somehow induces transformation, but how? A key insight was gained when TRX, independent of Tax, was found to bind to other cellular proteins involved in the cell cycle. Alterations in the regulation of the cell cycle is one prominent mechanism of malignant transformation. "Finding that TRX binds to cell cycle proteins ... led to the hypothesis that Tax may have a bridge to the cell cycle machinery through its binding to TRX," said Alidad Mireskandari, the doctoral candidate who worked most closely with Cindy.

To prove this hypothesis, large quantities of TRX were required for studies of its interaction with Tax. It was Cindy Kin's responsibility to insert the TRX gene into a plasmid vector that could replicate autonomously once it entered *E. coli*. The copious amounts of TRX produced could later be purified and used in a variety of experiments. While Cindy succeeded at the demanding task of transfecting *E. coli*, the overexpression of TRX was toxic to the cells. After this problem has been solved, other members of the laboratory will continue the project.

Cindy is no stranger to retrovirology. The summer before her senior year of high school, she held an internship at the Uniformed Services University for the Health Sciences, where she worked on a recombinant vaccine to prevent HIV infection. She is currently a freshman at Harvard University with the goal of becoming a physician.



Anne Lee
Hayfield Secondary School

Massachusetts Institute of Technology

Years in Program: 2

Preceptor:
Dr. Carl Wu

Laboratory of Biochemistry

National Cancer Institute

Project Title: Biochemical Analysis of a Temperature-Sensitive Mutation in the DNA Binding Domain of Heat Shock Transcription Factor

When exposed to high temperatures, organisms possess protective mechanisms to help ensure survival. Anne Lee has become intrigued by the properties of a master switch that turns on critical genes in times of heat stress. The master switch is Heat Shock Transcription Factor (HSF), a protein that binds to the promoter sequences of the heat shock inducible genes. The heat shock gene products exhibit a multiplicity of life-saving functions, such as sustaining protein folding and preventing protein aggregation during heat stress.

For the second consecutive summer, Anne joined the laboratory of Dr. Carl Wu to investigate the heat shock response in *Drosophila melanogaster.* Dr. Wu's laboratory previously isolated a temperature-sensitive mutant that displayed a single amino-acid substitution (valine→methionine) in its DNA-binding domain, a region containing 130 amino acids near the protein's N terminus. This single mutation abolishes the ability of HSF to respond to heat stress.

To find out why, Anne studied the mutated HSF's structural stability and binding affinity to DNA. She expressed the wild-type and mutant DNA binding domains in bacteria and purified the recombinant proteins by column chromatography. Using purified protein, she measured the binding affinities under normal and high temperatures by fluorescence spectroscopy. Because of the presence of tyrosine and tryptophan residues in the DNA binding domain, the normal HSF emits a strong fluorescence signal whose intensity is decreased upon binding to DNA. The mutant HSF binds more weakly to DNA at high temperatures, and this may be measurable by a smaller decrease in fluorescence intensity. "Anne's analysis will help us to understand the physical basis for the conditional mutation in HSF and to illuminate the function of this essential transcription factor which is conserved across the entire spectrum of eukaryotes," said Dr. Wu.

Anne is a sophomore at MIT, where she is majoring in biology. Her ambition is to obtain a Ph.D. in molecular biology in order to conduct research. An avid sportswoman, she plays lacrosse for MIT and holds a green belt in Tae Kwon Do.

Brian Lee
Centennial High School

Messiah College

Years in Program: 1

Preceptor:
Dr. Tito Fojo

Medicine Branch

National Cancer Institute

Project Title: Developing a FISH Assay for Detecting Rearrangements Involving Multidrug Resistance Gene MDR-1

In his summer research project, Brian Lee tackled one of the most devastating reasons for failure of chemotherapy: drug resistance. When cancer cells are resistant to drug therapy, medications are no longer effective and tumor growth becomes unchecked. One of the major types of resistance occurs when the cancer cells actively pump out the chemotherapeutic agent. This is accomplished by a cell surface glycoprotein that is encoded by the multidrug resistance gene, MDR-1. The gene product sits on the cell surface and effectively transports the drug molecules out of the cell. MDR-1 is actively expressed in a wide variety of cancer cell types—cancers of the lymphatic system (leukemia, lymphoma, and multiple myeloma) and breast, bladder, brain, and cervical cancer, among others.

Once the genetic controls over MDR-1 are more fully understood, oncologists will be in a far better position to overcome drug resistance. Brian took a step in that direction by applying fluorescence *in situ* hybridization to cancer cell lines that already had become resistant to Adriamycin and taxol, two anticancer drugs. "Using an MDR-1 probe, and two flanking probes about 0.5 megabase away, this technique can show whether rearrangements have occurred," said Brian. Rearrangements might be responsible for placing the MDR-1 gene under the control of a more active promoter sequence, thereby increasing expression of the gene.

Brian developed his keen interest in science as early as the fourth grade, when he participated in a program at the National Aquarium in Baltimore. Brian became hooked the minute he began testing water chemistry, studying marine life at a local beach, and learning about ecology of aquatic animals. His favorite activity of the program—which he still vividly recalls—was the thrill of working with small sharks three to four feet in length.

Brian plays the cello and is an avid soccer player. He was part of a team of the Appalachian Search, Rescue, and Explorer Group known as "Call-out Qualified." This team is the only high school group on the East Coast that searches overnight for missing persons in the mountains and woods of several states, including Maryland. Brian is currently a freshman at Messiah College, where he intends to major in biology. He has an unwavering ambition to become a doctor.

Marian Lee
Winston Churchill High School

Harvard University

Years in Program: 2

Preceptor:
Dr. Carolyn Bondy

Developmental Endocrinology Branch

National Institute of Child Health and Human Development

Project Title: Analysis of Placental Growth in the IGF-II Knockout Mouse

Why do so many embryos die before birth? Marian Lee's research may provide some clues, based on her studies of dwarfism and its relationship to insulin-like growth factor II (IGF-II). Marian analyzed placental growth in knockout mice lacking expression of the gene for IGF-II. The function of this growth factor was largely unknown until previous research in her laboratory revealed IGF-II to be highly expressed in the normal placenta. Other research had found that mice either heterozygous or homozygous for a deletion of the IGF-II gene displayed dwarfism. The animals' dwarfism was even evident *in utero,* an apparent consequence of what was hypothesized to be a placental defect. Taken together, these earlier findings suggested that IGF-II's role was to support a properly functioning placenta.

Marian examined the placenta supporting embryos heterozygous for a deletion in the IGF-II allele. The mothers were wild-type, but their genotype had no bearing on their offsprings' dwarfism, according to earlier investigations that established the paternal genotype to be determinative. After confirming the genotype of the embryos, Marian examined embryonic genotype in relation to several parameters of placental growth. Her preliminary results suggested that, in comparison to wild-type embryos, the deletion leads to significant reductions in placental size and number of DNA-synthesizing cells. She also found a reduction in the expression of cyclin B1, one of the proteins regulating the cell cycle. Finally she found an increase in the cyclin-dependent kinase inhibitor, p27. These results reveal IGF-II to have widespread effects on placental development. Their impact extends well beyond dwarfism, which is somewhat rare. Said Marian's preceptor, Dr. Carolyn Bondy, "If the placenta is small or insufficient, pregnancy may be jeopardized....We do not usually know the cause. This research gives us something to look for and potentially something to treat."

Marian Lee is a graduate of Winston Churchill High School, where she distinguished herself as editor-in-chief of the school's literary arts magazine, *Erewhon.* This magazine was rated among the top ten scholastic magazines by the National Scholastic Press Association. Marian is a talented musician, athlete, and debater. She is currently a sophomore at Harvard University, where she is planning a double major in history and government.

Ariel Levine
Charles E. Smith Jewish Day School

Brandeis University

Years in Program: 1

Preceptor:
Dr. Bibhuti Mishra

Clinical Gene Therapy Branch

National Center for Human Genome Research

Project Title: Localization of a Human Uromodulin Receptor

Through her research at NIH, Ariel Levine learned a cardinal lesson of molecular biology: the clue to the function of a protein may emerge from understanding its receptor and localizing the receptor's genetic address to a specific chromosomal region.

Ariel was interested in helping her preceptor, Dr. Bibhuti Mishra, to determine the function of the kidney protein, uromodulin. This protein was identified as early as 1953 as the most abundant protein in urine. But its function still remains an enigma. In his earlier research, Dr. Mishra purified, identified, and eventually cloned the receptor for uromodulin, termed HUR (human uromodulin receptor). Ariel's first task was to express the cloned gene to verify that it indeed encoded the receptor. She transfected *E. coli* with a plasmid containing the HUR clone and demonstrated by Western blotting that the expressed protein was HUR because it could bind to labeled uromodulin.

The next major task was to localize the HUR gene to its normal chromosomal address. According to Dr. Mishra's earlier research, the HUR gene appeared to map to a important region on the short arm of chromosome 3 that is often missing—either through chromosomal breakage or translocation—in many human cancers, including lung, breast, and abdomen. Ariel sought to confirm the location of the HUR gene in this region. She first needed to demonstrate that the coding regions of the HUR gene could be found in fragments of the human genome corresponding to the short arm of chromosome 3. These fragments, which were available from the Human Genome Project, were selected as templates for PCR amplification. She synthesized oligonucleotides complementary to a short segment at each end of the cloned HUR gene to determine if they were capable of acting as primers to amplify the intervening sequence of genomic DNA template. This method essentially confirmed that the cloned HUR gene matched sequences of genomic DNA already known to span the fragile region of chromosome 3. Whenever a gene maps to a region missing in cancer cells, a tumor suppressor role for the gene is suspected. Ariel's help in pinpointing the location for the HUR gene suggested that "it might normally function as a tumor suppressor gene ... and uromodulin might function to prevent cancers of the kidney," speculated Dr. Mishra.

Ariel is a freshman at Brandeis University. Since the age of eight, she has wanted to be a biomedical researcher.

Jeffrey Levsky
Hebrew Academy of Greater Washington

Northwestern University

Years in Program: 2

Preceptor:
Dr. Ashok Kulkarni

Gene Targeting Research and Core Facility

National Institute of Dental Research

Project Title: Analysis of the Dentition of TGF-β1 Knockout Mouse

Jeffrey Levsky has committed two summers to the analysis of a tantalizingly complex molecule known as transforming growth factor-β1 (TGF-β1). This molecule is a growth factor that plays an important regulatory role in development and inflammation. Jeff's project during his second summer was to elucidate the function of TGF-β1 in dental development through studies of TGF-β1 knockout mice.

TGF-β1 knockout mice were painstakingly created four years ago by Jeff's preceptor, Dr. Ashok Kulkarni. They are lacking TGF-β1 because the gene has been inactivated through homologous recombination. These knockouts generally die 2–3 weeks after birth because of an excessive inflammatory response. When Jeff sectioned the animals' teeth to examine their morphology, he found the molars to be grossly abnormal. They were lacking enamel and dentin, the two uppermost layers of tissue that envelop the pulp. Jeff concluded that TGF-β1 appears to be crucial to normal tooth development, but he was unsure about whether the disruption was a *direct* or an *indirect* result of the absence of TGF-β1. Since the absence of TGF-β1 upregulates the expression of immune mediators, it could have been the immune mediators that caused tooth degradation rather than the absence of TGF-β1 *per se.* To distinguish between these possibilities, Jeff attempted to compare the teeth from the TGF-β1 knockouts with teeth from knockouts grown in organ culture (without inflammatory agents), and with teeth from so-called double knockouts. The double knockouts were deficient in two genes: TGF-β1 and the gene encoding the protein β2-microglobulin. The absence of the latter results in a diminished immune response because it is responsible for the expression of histocompatibility antigens. Since Jeff was not able to complete the project over the summer, Dr. Kulkarni is planning to continue with these experiments. "Jeff's research is very important because TGF-β1 may prove to be very useful as a therapeutic agent in clinical dentistry," said Dr. Kulkarni.

Jeff is a junior at Northwestern University. His research is serving as a springboard to a career in medicine or biotechnology.

Randy Longman
Charles E. Smith Jewish Day School

Yale University

Years in Program: 1

Preceptor:
Dr. Caroline Philpott

Cell Biology and Metabolism Branch

National Institute of Child Health and Human Development

Project Title: Genes Involved in the Response to Iron Toxicity

Randy Longman investigated iron toxicity in yeast as a model for a human disease called hemochromatosis. This autosomal recessive condition of excess iron accumulation is the most common inherited disease among Northern Europeans. Although hemochromatosis is easily treated, it is difficult to diagnose because its symptoms mimic those of more common conditions, such as alcoholism, diabetes, and heart disease.

Randy's preceptor, Dr. Caroline Philpott, is a Clinical Associate and physician who was drawn to single-cell, yet eukaryotic, yeast because of the ease of performing genetic manipulations and because of their homology to higher eukaryotic cells. Research on hemochromatosis in mammalian cell lines was stymied by the difficulty of performing genetic manipulations. The laboratory in which Randy and Dr. Philpott worked had discovered a mutant yeast strain that could thrive despite excess iron uptake. The gene, termed $AFT1^{UP}$, encodes a transcription factor that constantly turned on other genes, enabling yeast to take in iron at levels normally toxic to yeast. Randy said that the purpose of his project was "to understand how the mutant yeast cell is dealing with excessive iron. What are the cellular responses to iron intoxication?" In short, he wanted to uncover other yeast genes whose products could overcome the iron excess either by detoxifying it, sequestering it, or by repairing iron-mediated damage.

Randy's strategy was to expose yeast to UV radiation in order to create random mutations, with the expectation that one of the mutations would be in a gene involved in the response to iron toxicity. More specifically, he sought to identify a mutation that, in the presence of a plasmid containing the $AFT1^{UP}$ mutant gene, would impair the yeast's ability to handle excess iron. According to Dr. Philpott, "The new mutation would implicate another gene involved in handling iron toxicity."

Randy was able to identify a yeast strain, termed C18, which he confirmed as having a single gene mutation. He found that the C18 strain grew normally until it was transfected with a plasmid carrying the $AFT1^{UP}$ mutant gene, at which point the strain died. He attempted to clone the mutant gene, using a yeast genomic library, but was unsuccessful. Dr. Philpott was eager to proceed with the project after Randy's departure.

Randy is a freshman at Yale University. He plans to pursue a career in medicine. He maintains strong interests in mathematics and soccer, for which he has received numerous awards.

Lauren MacWilliams
Academy of the Holy Cross
Duke University
Years in Program: 1
Preceptor:
Dr. Susan Gentleman
Laboratory of Retinal Cell and Molecular Biology
National Eye Institute

Project Title: A Comparison of the Effects of Cyclic AMP Analogues on Apoptosis and Protein Kinase A Subunit Expression in Y-79 Retinoblastoma Cells

Lauren MacWilliams studied the effects of a potential anticancer drug on retinoblastoma cells. Retinoblastoma is a rare, sometimes fatal, tumor of childhood originating in retinal cells of the eye. Lauren investigated the drug, 8-chloro–cyclic AMP. This drug is an analogue of cyclic AMP, a ubiquitous second messenger inside the cell involved in transducing extracellular signals into cellular processes, including cell division and metabolism.

In earlier studies, 8-chloro–cyclic AMP inhibited the growth of breast cancer cells *in vitro*. It also lowered expression of a subunit—termed RI—of protein kinase A, a phosphorylating enzyme that is activated upon binding with cyclic AMP. How 8-chloro–cyclic AMP lowered RI expression is unknown, but it is believed to be through some kind of post-translational mechanism. The purpose of Lauren's project was to extend previous findings to retinoblastoma cells. Retinoblastoma cells always express copious amounts of the RI subunit, whereas normal retinal cells express RI only early in development. She determined quantitatively whether RI subunit expression also was lowered in retinoblastoma cells treated with 8-chloro–cyclic AMP.

Lauren treated retinoblastoma cells with and without 8-chloro–cyclic AMP, after which she subjected the cells to Western blotting to separate RI from other cellular proteins. She then was able to quantitate the level of RI expression, using a chemiluminescent detection system. This involved coupling the enzyme alkaline phosphatase to antibodies that detected RI. When a special substrate is added, alkaline phosphatase catalyzes a reaction that emits light. The amount of emitted light can be quantitated. Lauren found that 8-chloro–cyclic AMP reduced RI expression to less than 10 percent of its initial level. Other studies in the laboratory showed that 8-chloro–cyclic AMP induced retinoblastoma cells to die. Dr. Susan Gentleman, Lauren's preceptor, said, "8-chloro–cyclic AMP has potential as an adjunct to treatment of a variety of tumor types in which RI subunit expression is enhanced, such as retinoblastoma, breast cancer and small cell lung cancer as long as there is a selective means of delivering it to tumor cells."

Lauren is a freshman at Duke University and plans to major in biomedical engineering. Her ultimate goal is to become a physician. She holds strong interests in debating, public speaking, and volunteer work.

Jennifer Meuchel
Maurice J. McDonough High School
Duke University
Years in Program: 2
Preceptor:
Dr. Marjorie Guroff
Laboratory of Tumor Cell Biology
National Cancer Institute

Project Title: Adenovirus-SIV Recombinants As Vaccine Vehicles in Rhesus Macaques

Jennifer Meuchel knows that the search for a vaccine against HIV often begins in a promising animal model. Her research on rhesus macaques infected with a genetically similar retrovirus, simian immunodeficiency virus (SIV), has been an eye-opening experience in vaccine development.

The approach taken by Jennifer's preceptor, Dr. Marjorie Guroff, was to create a recombinant vaccine, using a mutant adenovirus that can replicate in macaques. Adenoviruses are DNA viruses that normally infect the upper respiratory tract of humans, but not of monkeys. The mutant adenovirus offered a convenient vector for carrying selected viral genes into the macaque host. The envelope gene of SIV was chosen for insertion into the mutant adenovirus because expression of this foreign gene's protein product on the surface of infected host cells was expected to stimulate the formation of host antibodies (as well as cellular and mucosal immunity). By challenging the macaque with live SIV after several immunizations, researchers could test the efficacy of the vaccine in protecting against SIV infection.

After the animals had been injected with the recombinant vaccine, Jennifer's role was to assay for viral shedding in macaque stool samples both before and after SIV challenge. Viral shedding, according to Dr. Guroff, "is a measure of how well the adenovirus is replicating. In order for the envelope gene to be expressed, the adenovirus has to actually replicate." Unfortunately, the PCR assay, which amplified a portion of the adenovirus gene for which primers were readily available, proved problematic. Jennifer and her co-workers worked diligently to refine the assay.

Jennifer is a sophomore at Duke University majoring in biomedical and electrical engineering, with the goal of becoming a doctor. She has been interested in dance since she was three, and for many years she has taught ballet, tap, jazz, and acrobatics. Participation in several national dance competitions prepared her for the vicissitudes of research. "I never came home empty-handed or unsatisfied," she said. "Competing taught me discipline, dedication, and determination."

Amanda Mortl
Bethesda–Chevy Chase High School

Rice University

Years in Program: 1

Preceptor:
Dr. Tito Fojo

Medicine Branch

National Cancer Institute

Project Title: Bcl-2 Expression in the NCI Drug Screen Cell Lines

Amanda Mortl's summer research has led to an appreciation of the potentially broader applications of the anti-cancer drug taxol. This valuable drug already is being used to treat ovarian cancer and advanced breast cancer, but its efficacy against other cancers has not been fully studied. Amanda investigated taxol's effects on an oncogenic protein known as Bcl-2 in almost 60 cancer cell lines that make up NCI's Cancer Drug Screen. Bcl-2 protects cells from apoptosis, or programmed cell death. Earlier research determined that taxol works to *promote* apoptosis in cancer cells by inhibiting Bcl-2 (through its phosphorylation). Using quantitative immunoblot, Amanda first extended earlier research by finding Bcl-2 to be present in most of the cancer cell lines she studied. Amanda then found taxol to be successful at helping to phosphorylate Bcl-2 in most of the cancer cell lines, suggesting that it has more widespread anti-tumor effects than previously known.

At Rice University, Amanda is planning a career as a teacher, a field to which she brings great versatility. Besides biology, she has maintained an interest in anthropology and archaeology. In several years, she expects to participate in an archaeological dig in Botswana, a country in Southern Africa. The invitation to join the dig arose from earlier research she conducted as a high school junior at the Carnegie Institution of Washington. Her research on the age of barbed bone points—a primitive type of harpoon—revealed them to be about 30,000 years old, and thus one of the oldest sets of tools yet discovered in this region.

Each year at Bethesda–Chevy Chase High School, Amanda held leadership positions, culminating in her senior year with the presidency of the Student Government Association. She was chosen to teach leadership skills in a summer program for younger students. The experience of teaching, rather than practicing, leadership had a profound effect on her decision to become a teacher because, in her words, "Teaching leadership is about teaching life skills that everyone needs, like communication, self-awareness, mass communication, and diversity."

Jamalah Munir
Oxon Hill High School

Brown University

Years in Program: 3

Preceptor:
Dr. W. Jay Ramsey

Clinical Gene Therapy Branch

National Center for Human Genome Research

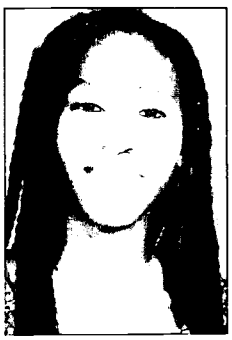
Project Title: Adenovirus Vector Cloning Using DNA-Protein Complexes

Jamalah Munir worked on a project to improve the efficiency of creating vectors for use in human gene therapy. Gene therapy, a means of introducing genes into defective cells, is heralded as the most important new approach to treating a myriad of diseases. "Gene therapy can be used to correct an inherited defect, to reverse an acquired defect, or to program a cell for a new property," observed Jamalah.

Many current gene therapy protocols are reliant on a cumbersome *in vitro* method of introducing therapeutic genes into plasmid vectors that, in turn, can be introduced into patients' cells in order to express the gene of interest. To prepare these recombinant vectors, cell lines are co-transfected with a "shuttle" plasmid containing the therapeutic gene (i.e., the transgene) and another plasmid carrying viral DNA. Through homologous recombination of shared sequences, the transgene from the shuttle plasmid can become incorporated into the viral DNA to form a recombinant viral vector. "Unfortunately, homologous recombination is a very low-frequency event, occurring about 0.001 percent of the time. We needed a more efficient way of transferring the transgene into the viral vector," said James Higginbotham, a doctoral candidate in the laboratory.

Jamalah concentrated her energies on refining a cloning system for a commonly used viral vector, adenovirus type 5. This is a double-stranded linear DNA virus that has a unique structure to facilitate its infectivity: a DNA-protein complex at each terminus. She first isolated the DNA-protein complexes in a biologically active form and confirmed her isolation by performing protease digestion and gel electrophoresis. Then she again isolated the DNA-protein complexes, this time applying restriction enzymes to create "sticky" ends onto which she could directly clone the transgene. This straightforward method avoided the need for homologous recombination, thereby improving efficiency of producing recombinant vectors. "It no longer takes two Ph.D.'s two weeks to isolate the DNA-protein complexes in a cloning form," said Dr. Ramsey.

Jamalah is a junior biology major at Brown University. While she plans to become a doctor, she remains undecided about whether to pursue clinical care or research. She finds herself "amazed by the fact that all of a person's characteristics can be found on pieces of DNA so small that they cannot be seen by the human eye."



Enyi Nwaneri
Eleanor Roosevelt High School

Yale University

Years in Program: 1

Preceptor:
Dr. Edward Ginns

Clinical Neuroscience Branch

National Institute of Mental Health

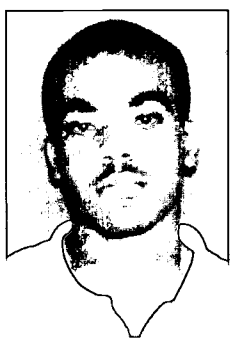
Project Title: The Search for a Possible Bipolar Affective Disorder Gene on Chromosome 4 in the Old Order Amish

Enyi Nwaneri spent her summer attempting to pinpoint chromosomal regions that contain genes involved in bipolar affective disorder. This disorder, which affects at least 0.6–2 percent of the population, is highly heritable. If one identical twin has the disorder, the likelihood is 85–90 percent that the other twin is affected. Its hallmark is recurrent episodes of mania and depression. The manic episode can be punctuated by decreased sleep, elevated mood, rapid speech, and hyperactive behavior.

The Old Order Amish are considered to be an excellent population in which to study bipolar affective disorder. They keep careful records, remain in their community, and lack access to alcohol and illegal drugs. The latter point is especially important because the symptoms of substance abuse can mimic those of bipolar affective disorder, thereby leading to misclassification of cases. Since there is no biological test for this condition, its diagnosis relies solely on behavioral criteria.

Enyi's project was to help verify earlier published findings that the short arm of chromosome 4 contained a vulnerability locus for bipolar affective disorder. "We are hoping to localize the genes that underlie this vulnerability ... As few as 3 and as many as 10 vulnerability loci may be involved," said Dr. Robert Philibert, a Medical Staff Fellow who worked closely with Enyi. With the goal of finding DNA regions that segregate with the disorder, Enyi used microsatellite markers that map to the short arm of chromosome 4. Microsatellite markers are repetitive DNA sequences—in this case dinucleotide repeats of base pairs cytosine and adenine—that are usually in noncoding regions. Each marker is potentially adjacent to a coding region that, once amplified by PCR and sequenced, hopefully contains some kind of alteration, such as a mutation, that is found only in those with the disorder.

Enyi is a freshman at Yale University who aspires to become a doctor. She performed research at the U.S. Department of Agriculture and NASA before entering the NIH laboratory. Her hobbies include the 3 "R's"—reading, writing, and running.



Larry Overton II
Benjamin Banneker High School

George Washington University

Years in Program: 3

Preceptor:
Dr. Eric Green

Genome Technology Branch

National Center for Human Genome Research

Project Title: Human Genome Sequencing

Larry Overton has served two consecutive summers with the Sequencing Core Facility, a cutting-edge facility available to the 420-person staff of the National Center for Human Genome Research. The facility is equipped with state-of-the-art sequencing machines capable of reading nucleotide sequences of samples containing 500–6,000 base pairs. The facility handles about 200 DNA samples on a given day.

Once a fragment was received, Larry performed the necessary steps to generate within hours a colorful computer printout of the exact sequence. In the process, he mastered the use of two critical pieces of equipment. The first—called a catalyst or robotic lab station—was used to amplify the fragment with PCR and to incorporate into the DNA extension products either 5'-dye–labeled primers or 3'-dye–labeled dideoxynucleotides. The mixture of fluorescently labeled products is then run on an automated fluorescent sequencer machine, which detects each of four fluorescent dyes to identify the corresponding A, G, C, and T extension reactions. "My goal is to produce sequencing data that can be used to characterize genes and detect mutations," said Larry.

The implications have hardly escaped his keen interest. He pointed out that the diagnosis of Huntington's disease hinges on the identification of a gene with 40 or more trinucleotide repeats of the sequence CAG. The greater the number of trinucleotide repeats, the more severely affected is the patient. According to Ms. Christiane Robbins, lab manager of the core facility, "Larry definitely learned the intricacies of the machines and the medical significance of the results."

A sophomore at George Washington University and an avid sportsman, Larry plans to become a pediatrician and to open his own practice.

Margaret Parker
National Cathedral School

Swarthmore College

Years in Program: 2

Preceptor:
Dr. Edward Ginns

Clinical Neuroscience Branch

National Institute of Mental Health

Project Title: Characterization of Glycosylation in Carbohydrate-Deficient Glycoprotein Syndrome

Carbohydrate-deficient glycoprotein syndrome (CDGS) is a rare and tragic metabolic disorder that fascinated Margaret Parker during her second summer as a student intern. The underlying problem in CDGS is a defect in the complex synthetic pathway that generates glycoproteins (carbohydrates linked to proteins). Patients cannot properly make the carbohydrates that attach to one amino acid—asparagine—on the protein backbone. The synthesis of asparagine-linked glycoproteins entails about 200 steps, 30 of which are enzymatically driven. The defect in CDGS can occur in any one of these steps, meaning that CDGS is likely a heterogeneous group of defects. Yet its clinical manifestations fall into four distinct categories, all of which are characterized by developmental delays, failure to thrive, and unusual facial features.

Margaret Parker was asked to help characterize a three-year-old child whose symptoms did not fit in any of the known clinical categories. The child had profound, rather than mild, developmental delays; severe, rather than mild, seizures; and yet robust health—a far cry from most CDGS children, who are frail and diminutive. Nevertheless, the child was positive on the hallmark diagnostic test for CDGS: a glycoprotein in her blood called transferrin showed the characteristic CDGS pattern on an isoelectric focusing gel.

Under the guidance of senior staff fellow Dr. Donna Krasnewich, Margaret sought to characterize more fully the nature of the glycoprotein defect in this case. After culturing fibroblasts, she found a defect in the uptake of radioactively labeled mannose, a monosaccharide building block of oligosaccharides. With other biochemical tests, she discovered a preponderance of high mannose species, implying a deficiency in the early stages of glycoprotein synthesis. Nevertheless, these findings were similar to those for other CDGS patients. "Margaret set out to biochemically characterize the asparagine-linked glycosylation in an unusual CDGS patient.... She did not uncover the reason why this child was so extraordinary, yet she did confirm the diagnosis and showed the fibroblasts to carry the defect," observed Dr. Krasnewich.

Margaret is a freshman at Swarthmore College. She has not yet decided on a given profession, but she has shown remarkable research acumen. Her hobbies include cross-country running, environmental awareness, rock climbing, singing, and drama.

Maria Pletneva
Montgomery Blair High School

University of Maryland

Years in Program: 1

Preceptor:
Dr. Kim Green

Laboratory of Infectious Diseases

National Institute of Allergy and Infectious Diseases

Project Title: Expression of a Hawaii Human Calicivirus Capsid Protein in Mammalian Cells

Maria Pletneva came to the United States from Russia in 1991 without speaking any English. Five years later, she has mastered not only English but also the complex languages of molecular biology and virology.

Maria's research concerns caliciviruses, a family of viruses that attack the gastrointestinal tract, causing gastroenteritis. While fairly benign in the United States, they are deadly in Third World countries, where they cause an estimated 5 million deaths annually in children under age five. Given the sheer magnitude of the viruses' reach, Maria hopes her research eventually will lead to a vaccine for caliciviruses.

Maria succeeded in demonstrating that the capsid protein of the Hawaii strain of caliciviruses can be expressed in several mammalian cell lines. She inserted the capsid gene into a plasmid specially treated to penetrate mammalian cells that earlier had been infected with a recombinant vaccinia virus. A foreign promoter engineered into the attenuated vaccinia virus helped to enhance expression of the capsid gene. Successful expression of the capsid protein on the surface of mammalian cells is important for eventual vaccine development because the protein could act as an immunogen, eliciting antibody formation *in vivo*.

Maria's parents are both scientists, formerly affiliated with a biochemistry institute in Siberia before emigrating to Maryland, where her father was able to continue his research at NIH. During her four years at Montgomery Blair High School, Maria distinguished herself as a member of engineering and chemistry teams that successfully competed in county- and statewide competitions.

Maria is currently in the honors program at the University of Maryland. She is majoring in biochemistry and molecular and cell biology in preparation for a degree in medicine or a joint M.D./Ph.D. degree. In contrast to other areas of research, she says, "Biomedical research is the best area to pursue because it is more closely associated with the actual problems and disorders of patients, while still focused on investigation."

Anousheh Sayah
Thomas A. Edison High School
University of Virginia
Years in Program: 2
Preceptor:
Dr. Thea Kalebic
Laboratory of Molecular Oncology
National Cancer Institute

Project Title: Expression of Mutated IGF Type 1 Receptor on Rhabdomyosarcoma Cells

Gene therapy holds potential as a treatment for a childhood cancer known as rhabdomyosarcoma, according to research by Anousheh Sayah. Anousheh worked closely with preceptor Dr. Thea Kalebic, a visiting scientist from Croatia, to pioneer a new approach to treating this relatively rare tumor of muscle cells. Although most cases of rhabdomyosarcoma can be treated successfully with conventional chemotherapy, about 20 percent are beset by an aggressive, metastatic tumor that is often fatal.

Rhabdomyosarcoma growth and proliferation is partially reliant on insulin-like growth factor–1 (IGF-1). IGF-1 is an autocrine growth factor, produced and secreted by the same cells that need it for growth. Its ability to stimulate growth depends on cell surface expression of IGF-1 receptors. In other words, the rhabdomyosarcoma cells express receptors for the very growth factor they generate.

Dr. Kalebic's earlier research demonstrated that antibody binding to IGF-1 receptors *in vivo* interfered with IGF-1 binding, thereby suppressing growth of rhabdomyosarcoma. Building on this concept, she and Anousheh transfected a rhabdomyosarcoma cell line with a plasmid containing a mutated gene encoding the IGF-1 receptor. The mutation, introduced by site-directed mutagenesis, destroyed the capacity of the intracellular portion of the receptor to function as a kinase (i.e., to phosphorylate tyrosine residues after stimulation with IGF-1). Phosphorylation of the IGF-1 receptor itself is the first step in signal transduction to the nucleus. The phosphorylated receptor acts, in turn, as a kinase enzyme to phosphorylate other substrates (transducing proteins) in the pathway. "By introducing a mutated receptor that binds to the ligand but has no kinase activity, we hoped to interfere with signal transduction and thereby suppress the actions of IGF-1," noted Dr. Kalebic. Using Western blotting, Anousheh found a reduction in phosphorylation levels of IGF-1 receptors and transducing proteins in cultured cells expressing the mutated receptor, as compared with wild-type cells. This study may lead to new gene therapy approaches to rhabdomyosarcoma.

As a freshman at the University of Virginia, Anousheh plans to major in biology. She reflects, "I am striving to gradually build my knowledge and experiences now, so that when I enter the laboratory as a scientist, I can be a significant contributor to society."

Brian Schulman
Hammond High School
Years in Program: 1
Preceptor:
Dr. Charles Vinson
Laboratory of Biochemistry
National Cancer Institute

Project Title: Construction of Mammalian Vector to Inactivate the Ras Oncogene

Brian Schulman loves to build new molecules. One of the new molecules Brian is helping to build has the potential to arrest transformation of normal cells into cancer cells.

The laboratory Brian joined is refining techniques for the expression of a unique molecule that is an inactive version of the transcription factor AP-1, which plays an important role in transforming cells into cancer cells. When AP-1 binds to DNA, normal cells in culture lose contact inhibition, one of the cardinal steps in transformation. By understanding how AP-1 is normally assembled, Brian's laboratory was able to design a dysfunctional version of AP-1 that can no longer bind to DNA to initiate transformation.

AP-1 is a heterodimer made from two proteins—Jun and Fos. These two proteins normally dimerize in a manner that allows each of their basic N-terminus regions to bind to DNA, an acid. The laboratory has patented a variant of Fos called A-Fos, because it has an acidic, instead of a basic, N-terminus region. When A-Fos comes into contact with Jun, "the basic amino acids of Jun that normally would have bound to DNA now interact with the acidic region of A-Fos. The newly formed heterodimer cannot bind to DNA," noted Dr. Charles Vinson, Brian's preceptor. To generate A-Fos, separate oligonucleotide sequences that encode different components of the protein are inserted into a plasmid vector that is incorporated into a mammalian cell line. The cell line is also transfected with a plasmid containing the *ras* gene. Ras encodes a protein kinase that activates Jun to stimulate formation of AP-1. This second plasmid alone is sufficient to transform the mammalian cells, but when introduced into the cells along with the other plasmid encoding A-Fos, cell transformation is almost, but not completely, prevented. Brian and other members of the laboratory are working on ways to improve this complex recombinant system in order to completely stop cell transformation.

Brian is a senior at Hammond High School, where he is an active member of both the math team and the team that represents the school on the competitive television program "It's Academic." He enjoys daily practice sessions and unwinds by playing basketball, his favorite sport.

Siddhartha Shukla
Washington-Lee High School
Yale University
Years in Program: 1
Preceptor:
Dr. Michael Iadarola
Neurobiology and Anesthesiology Branch
National Institute of Dental Research

Project Title: A Spinal Cord Circuit for Bilateral Activation of p-CREB vs. Unilateral Activation of c-Fos

For Siddhartha Shukla, scientific discovery is truly about the unexpected. During his first summer in the laboratory, he serendipitously found an anatomical pathway in rats that may help to explain a curious, yet distressing, problem among chronic pain patients: pain can spread from the injured side of the body to the unaffected side. Siddhartha noted that the findings begin to answer the question, "How can you get a bilateral response from unilateral input?"

Through immunocytochemical labeling techniques, Siddhartha started the project by exploring anatomical pathways that carry pain information from the site of injury to the spinal cord, where nociceptive (pain-carrying) fibers terminate and form synapses with second-order spinal neurons. Previous research had established that unilateral injury to the rat hindpaw results in an elevation in second-order spinal neurons of transcription factor c-Fos, which upregulates gene expression—on the side of injury, but not on the *other* side of the spinal cord. What Siddhartha found by examining another transcription factor was that upregulation of gene expression also appears to occur bilaterally, and this happens very soon after the injury.

Siddhartha first induced inflammation in one of the rat's hind limbs and then double-labeled the spinal cord with antibodies to calcitonin gene-related peptide (CGRP) and phosphorylated-CREB (p-CREB). CGRP is one of several peptide neurotransmitters found in pain fibers coming from the periphery, while p-CREB is a nuclear transcription factor that controls expression of a variety of genes. The finding that p-CREB–containing spinal cord neurons were labeled bilaterally after injury to one side surprised preceptor Dr. Michael Iadarola, who already has planned the next series of experiments. He plans to examine whether CGRP-containing afferent fibers form synapses with second-order p-CREB containing spinal neurons in an intriguing area of the spinal cord around the central canal. Siddhartha's research had revealed this to be an area of convergence for CGRP-containing primary afferents from both sides of the spinal cord.

Siddhartha is currently a freshman at Yale University, where he expects to build on his knowledge of neurobiology and to refine his talents in vocal music, debating, and rowing.

Manish Tripathi
Montgomery Blair High School
Stanford University
Years in Program: 3
Preceptor:
Dr. Joan Schwartz
Clinical Neuroscience Branch
National Institute of Neurological Disorders and Stroke

Project Title: An Analysis of Somatostatin As a Trophic Factor in the Cerebellum, Cortex, and Striatum of Mice

Somatostatin is a peptide that has captured the interest of Manish Tripathi for three consecutive summers, all in the laboratory of Dr. Joan Schwartz. During this past summer Manish sought to identify whether somatostatin release by astrocytes plays any physiological role in adult mice. Normally, somatostatin is only produced by astrocytes in the cerebellum until two weeks after birth. Astrocytes are support cells in the brain that, in contrast to neurons, do not conduct action potentials. It is well accepted from *in vitro* studies that somatostatin release by astrocytes acts as a trophic factor during development. This means that somatostatin induces immature neurons to send out neurites, tentacle-like projections that are destined to become either dendrites or axons. Manish's project, according to Dr. Schwartz, "was to determine whether astrocytes' somatostatin has a role in adults or whether its role is exclusively limited to early in development."

Manish began by studying transgenic mice whose astrocytes continually produce somatostatin throughout life and in all areas of the brain, not just in the cerebellum. The reason is that the transgene places the somatostatin gene under the control of a promoter sequence that is always active in driving expression of an astrocyte-specific protein (glial fibrillary acidic protein).

Manish spent most of the summer refining an ELISA assay for measuring minuscule concentrations of somatostatin in the cerebellum, cortex, and striatum of transgenic and normal mice. Baseline studies were needed before attempting to explain the serendipitous finding that female transgenic mice had enhanced locomotor activity. Manish had planned to study how different pharmacological agents affect somatostatin levels and locomotor behavior in transgenics vs. normals, but there was insufficient time. Dr. Schwartz is expected to follow up on Manish's preliminary studies of the impact of cysteamine, which temporarily depletes somatostatin, and of an anti-estrogen, which appears to indirectly reduce somatostatin levels.

Manish is a junior at Stanford University. With a joint major in economics and biology, he hopes to obtain M.D. and M.B.A. degrees. He envisions hospital administration or managing a biotechnology company, ambitions not surprising for someone with such broad interests. He serves as a senator on Stanford's campus council, and he tutors elementary students from disadvantaged backgrounds.

Gilbert Tyan
Winston Churchill High School

Massachusetts Institute of Technology

Years in Program: 1

Preceptor:
Dr. Jonathan Ashwell

Laboratory of Immune Cell Biology

National Cancer Institute

Project Title: PI3-Kinase Is Required for IL-2 Production Following T Cell Receptor Activation

Gilbert Tyan chose to study a novel pathway of T cell activation. When T-lymphocytes (T cells) are activated by a foreign antigen, they produce the cytokine interleukin-2 (IL-2), which, upon its release controls proliferation of other T cells as part of an orchestrated campaign to destroy the antigen. There are two known pathways that convey the signal from the T cell receptor to the nucleus in order to upregulate expression of the gene for IL-2. Gilbert investigated a newly discovered third pathway for signal transduction leading to IL-2 production.

Recent studies have pointed to an important role for a particular protein kinase known as phosphatidylinositol 3-kinase (PI3-kinase). This kinase was named for its substrate, phosphatidylinositol. PI3-kinase is an enzyme that adds a phosphate group to phosphatidylinositol, a phospholipid which is an integral part of the cell membrane. One product of the reaction is PI-3,4-diphosphate. It is this product (and related reaction products) that accumulate when T cell receptors are activated.

Gilbert probed the importance of PI3-kinase in signal transduction by inhibiting it with a compound called wortmannin. This compound is a fungal metabolite that binds to PI3-kinase, thereby preventing the phosphorylation of phosphatidylinositol. Using a bioassay, Gilbert demonstrated that after treatment with wortmannin, the production of IL-2 is greatly reduced. The bioassay employed an IL-2-responsive cell line, in which Gilbert measured the incorporation of radioactively labeled thymidine after adding the supernatant from the activated T cells treated with wortmannin. In a separate, but related, experiment, IL-2 promoter activity was shown to be diminished after inhibiting PI3-kinase. Dr. Astrid Eder, a visiting fellow who mentored Gilbert, said that, "he found that PI3-kinase is involved in the production of IL-2 by activated T cells." The other elements of the pathway remain an active area of research by the laboratory.

Gilbert is a freshman at MIT. He hopes to become a biomedical engineer. He thoughtfully describes himself "as a hands-on type of person [who] enjoys lab work.... I am particularly attracted to the interdisciplinary areas involving biomedical sciences and engineering, such as the study of ... artificial organs, computer simulation of biological phenomena, and development of prosthetics to help others cope with their disabilities. Nothing would be more wonderful than to change people's lives for the better."

Li-Ming Ueng
Walter Johnson High School

University of Pennsylvania

Years in Program: 1

Preceptor:
Dr. Yves Pommier

Laboratory of Molecular Pharmacology

National Cancer Institute

Project Title: The Interaction of Camptothecin with Damaged DNA

In her research project, Li-Ming Ueng investigated the cytotoxic properties of camptothecin, a promising anti-cancer drug. Camptothecin and its analogues are an exciting new class of anti-cancer agents under development. They target an enzyme normally present in eukaryotic cells, topoisomerase I. This enzyme induces temporary breaks in one strand to ready the DNA for vital functions, including transcription, replication, and repair. After creating the temporary break, topoisomerase I re-ligates—or recloses—the broken strand to return it back to normal. In other words, topoisomerase I has two functions.

Camptothecin is a topoisomerase I–inhibitor: it prevents the re-ligation of DNA strands, the second function of topoisomerase I. When strand breakage is permanent, rather than temporary, the cell eventually dies. Cancer cells are considered more vulnerable to camptothecin's deadly effects than are normal cells because rapidly dividing cells place higher demands on topoisomerase I.

Li-Ming examined the conditions under which camptothecin worked most effectively. In a cell-free system, she combined a synthetic double-stranded oligonucleotide and topoisomerase I, with and without camptothecin. She found camptothecin to be most effective at creating permanent cleavages when she introduced a nick into a strand in a position immediately opposite to a topoisomerase I–binding site on the other strand. According to Dr. Philippe Pourquier, a postdoc who worked closely with Li-Ming in the laboratory, "These results suggest that camptothecin should be used in conjunction with other anti-cancer drugs that produce DNA damage."

At the University of Pennsylvania, Li-Ming is planning to major in biology with the expectation of becoming a medical researcher. The research possibilities are limitless for someone who sees herself as having "developed a great interest in biomedical engineering over the years because of my desire to understand how our genetic processes work. Without this knowledge, I would always feel that there is a mystery to be solved."

Jose Vargas
Colonel Zadok Magruder High School

Loyola College

Years in Program: 2

Preceptor:
Dr. Nancy McCartney-Francis

Cellular Immunology Section

National Institute of Dental Research

Project Title: Phenotypic and Functional Properties of Inflammatory Cells in Transforming Growth Factor β1 Knockout Mice

Jose Vargas can speak to the sublime wisdom of studying the abnormal to shed light on the normal. He has spent two consecutive summers examining transforming growth factor β1 (TGF-β1) knockout mice. These mice present a golden opportunity to study the normal function of TGF-β1 because they lack the gene that encodes this particular protein. TGF-β1 is a multi-functional protein that regulates inflammatory and immune function in ways not completely understood.

TGF-β1 knockout mice die within 2–3 weeks of birth. Their organs are infiltrated with all types of immune cells, in spite of the absence of viral or bacterial infection. The knockouts die from complications of a massive immune cell infiltration. Jose has sought to characterize the nature of the immune response in order to understand the normal regulatory roles of TGF-β1.

During his second summer in Dr. Nancy McCartney-Francis' laboratory, Jose concentrated on refining two sophisticated laboratory techniques for studying the immune cells of TGF-β1 knockout mice—immunofluorescent staining of intracellular cytokines for flow cytometric analysis and a new technique for detecting multiple cytokines. With the former, Jose identified cytokine-containing immune cells in various organs of knockout and wild-type mice. Preliminary data suggested that the spleen and peritoneal cavity of knockouts contain a higher percentage of cells producing the cytokine tumor necrosis factor. He then isolated RNA from the mice and used the assay to identify a broad range of cytokine RNA species and compare expression levels with the wild-type mice. Although Jose did not have time to complete the analyses, the preliminary data showed increased levels of interleukin-1 and interleukin-6 in spleen, lung, heart, and liver of the knockout mice. Dr. McCartney-Francis is eager to continue with Jose's project because "We now have the means to characterize the inflammatory cells in these mice and can begin to ask mechanistic questions about the inflammatory process that ultimately kills these mice. Jose did the hard part by working out the assay systems—now we get to do the fun stuff!"

It is hard to believe that Jose left the Dominican Republic about five years ago. He went through Magruder High School with academic distinction. Since boyhood Jose has dreamed of becoming a doctor. That dream is closer to reality, now that Jose is a premedical student at Loyola College, where he is a sophomore majoring in biology.

Anil Vedula
Thomas S. Wootton High School

Years in Program: 1

Preceptor:
Dr. Daniel Kastner

Arthritis and Rheumatism Branch

National Institute of Arthritis and Musculoskeletal and Skin Diseases

Project Title: Mutational Analysis of Putative Disease Genes in Familial Mediterranean Fever

Anil Vedula has caught the "fever" of a gene hunter. He is part of a laboratory in hot pursuit of the gene for familial Mediterranean fever (FMF), an autosomal recessive disorder affecting 20,000 people worldwide, mostly Sephardic Jews, Arabs, Armenians, and Turks. The disorder is characterized by recurrent episodes of abdominal pain, fever, and inflammation of joints and other tissues. Its fatality rate from kidney failure has declined dramatically as a result of the introduction in the last two decades of colchicine as the treatment of choice.

Several years ago Anil's preceptor, Dr. Daniel Kastner, collected blood samples from affected families in Israel. Their white blood cells were immortalized into lymphoblastic cell lines for long-term study. Dr. Kastner's laboratory over the course of seven years has painstakingly performed linkage analysis and other genetic studies to localize the putative gene to a region on the short arm of chromosome 16.

When Anil entered the laboratory, he was asked to perform a mutational analysis of a cDNA segment of 5,000 base pairs that was considered likely to contain the gene for FMF. After sequencing 2,000 of the base pairs, Anil found two polymorphisms. Unfortunately, neither polymorphism was significant in relation to FMF. The remainder of the segment—which has yet to be fully sequenced—continues to hold potential, according to Dr. Michael Centola, a postdoctoral fellow in the laboratory who took Anil under his wing. Dr. Centola found that Anil had "helped in a very real sense to revitalize the lab. As a group we have been able to share our knowledge and watch that knowledge take hold in an individual. That, in turn, has motivated us to continue with some very difficult work."

At Wootton High School, Anil finds the rigors of mathematics and physics competitions so rewarding that he plans to major in both fields in college. Yet he also is intrigued by medicine and medical research, so much so that he would like to attend medical school. His experiences with medical research—which include a previous summer at NIH studying medications that release nitric oxide for potential treatment of angina and other disorders—have made an enduring impression. Anil admits to having "gained such a wealth of knowledge and intense passion for research that it is now in my blood."

Chandra Westergaard
Governor Thomas Johnson High School
Western Maryland College
Years in Program: 1
Preceptors:
Dr. Nancy Colburn and Dr. Jian-Jian Li
Laboratory of Viral Carcinogenesis
National Cancer Institute

Project Title: Transactivation and Transrepression of Transcription Factor AP-1 by Multiple Tumor Promoters and Anti-Promoters

How do tumor promoters and anti-promoters work? This is the intriguing question addressed by Chandra Westergaard in her summer research project. Chandra studied the action of several known tumor promoters and anti-promoters on transcription factor AP-1. This transcription factor has been shown to be involved in transforming normal cells into cancer cells.

Chandra used an elegant assay system to determine the impact on AP-1 activity of three tumor promoters—epidermal growth factor (EGF), tumor necrosis factor (TNF-I) and tetradecanoylphorbol acetate (TPA). She also tested two anti-promoters—retinoic acid and curcumin. The assay used a mouse epidermal cell line stably transfected with a DNA construct containing a collagenase promoter with an AP-1 binding site upstream of the luciferase gene from fireflies. This system sensitively assays for AP-1 activity because AP-1 binding to the promoter upregulates expression of luciferase, a reporter gene whose product can be readily detected. Luciferase catalyzes a reaction that produces bioluminescence: the greater the amount of luciferase produced, the stronger the luminescence as measured by a luminometer. In other words, the transfected epidermal cells provide a means of measuring the degree of AP-1 activity. "Using this cell line, almost any compound can be quickly screened to see if it induces or inhibits AP-1 activity," according to Chandra.

Chandra found AP-1 activity to be induced by TPA, EGF, and, to a lesser extent, by TNF-I. Retinoic acid (vitamin A) and curcumin, a derivative of the spice turmeric, inhibited the induction of AP-1 activity when cells were also treated with TPA and EGF, but not with TNF-I. Chandra's preceptor, Dr. Jian-Jian Li, observed, "These results indicate that AP-1 is an important link between gene regulation and cell transformation, and that anti-promoting compounds targeting AP-1 are promising candidates for prevention of carcinogenesis."

As a freshman at Western Maryland College, Chandra is majoring in chemistry in preparation for a career in research and development.

Stefan Zimmerman
Oakland Mills High School
Boston University
Years in Program: 1
Preceptor:
Dr. Warren Leonard
Laboratory of Cellular and Molecular Biology
National Heart, Lung and Blood Institute

Project Title: Signaling Through the Interleukin-2 Receptor

The proliferation of T-lymphocytes is a critical component of the immune system's attack on a foreign antigen. One signal for T-lymphocytes to proliferate comes from a cytokine, or intercellular messenger, called interleukin-2 (IL-2). When IL-2 is released by other immune cells, it acts on T-lymphocytes through the IL-2 receptor to induce proliferation. Stefan Zimmerman devoted his summer to the study of one of the subunits of the IL-2 receptor.

The IL-2 receptor consists of three polypeptide subunits, one of which is the β subunit. When IL-2 binds to the IL-2 receptor, the β subunit is thought to associate with a tyrosine kinase (JAK1) inside the cell. The interaction appears to be pivotal, for it results in the phosphorylation of the IL-2 receptor, a key first step in a signaling pathway that ultimately leads to proliferation of the T-lymphocytes.

To examine the impact on signal transduction of different regions of the β subunit, Stefan's laboratory created two types of mutant receptor: one was missing a region rich in the amino-acid serine (the S region) and the other was missing a region rich in acidic amino-acid residues (the A region). Together, these two regions constitute two-thirds of the β subunit. The mutants were created by targeted deletions in the cDNA encoding the β subunit, each of which was then transfected into a cell line. Using immunoprecipitation and Western blotting, Stefan found that, after administration of IL-2, neither mutant receptor could interact with the tyrosine kinase. According to a postdoc in the lab, Dr. Thi-Sao Migone, "What Stefan learned was an approach to study the function of a receptor by looking at different domains and trying to correlate them with a signaling function. Both the A and S regions of the J subunit appear to be implicated as important in an association with JAK1."

Stefan is currently a freshman at Boston University. With the ambition of becoming a physician, he is majoring in biology. His extracurricular interests include basketball, cross-country running, and public service for the homeless.

Montgomery County Public Schools Student and Teacher Intern Program at the National Institutes of Health

The Student and Teacher Intern Program was initiated as a pilot project in 1990 by the Montgomery County Public Schools (MCPS). During the past six years, the Howard Hughes Medical Institute has committed over $1.3 million to its support. Selected students work at NIH laboratories full time in the summer and part time during the school year. Teachers participate in week-long summer science institutes and, in some cases, summer research opportunities in NIH laboratories before taking their new found knowledge back to their classrooms in the fall. The project was designed to encourage educational advancement in science and increase opportunities for motivated high school students to perform hands-on scientific research under the direction of experienced mentors. In addition, science teachers are given the opportunity to experience laboratory research and to bring that experience back to their classrooms.

The program consists of student and teacher activities, some of which are combined. For example, this past summer, 5 teachers and 13 students were selected to participate in a two-week molecular biology course taught at Thomas S. Wootton High School in Rockville, followed by six weeks of research in an NIH laboratory. During the school year, students attend their home high school in the morning before heading to NIH for the afternoon, averaging 16 hours per week of laboratory time. Teachers meet periodically throughout the school year to share experiences, compare notes on a classroom activity developed cooperatively over the summer, and learn additional research techniques.

Now in its second year, the Instrumentation in Chemistry Program, a two-week intensive course in spectrophotometry, aims to provide teachers with advanced training in analytical instrumentation. The course is described further below.

In the NIH laboratories, both the student and teacher interns learn to define a scientific problem and state a testable hypothesis. They learn how to participate in the design and implementation of appropriate experimental approaches, to analyze experimental data, to draw and discuss conclusions, and to present their scientific work in a coherent and systematic manner. On a personal level, they see what scientists are like and learn how to function effectively in a research community.

Students have an opportunity to present their findings at the annual NIH Poster Day. And each spring the Institute hosts a dinner symposium at which students present a summary of their research to their preceptors, parents, and invited guests, which include school board members and science teachers.

In 1995 a Student Academy of Science was established with three goals in mind: to stimulate student interest in careers in biomedical and other research through extracurricular activities; to provide peer

mentors for students who wish to improve their academic performance; and to assist students as they prepare applications for internships and other career exploration programs. Academy chapters were conducted at 8 high schools and 2 middle schools in the 1995–1996 academic year. Members visited the National Medical Museum at NIH, laboratories at George Washington University, Howard University, the Armed Forces Institute of Pathology, and NIH, the National Audubon Society, and the National Zoo. In addition, they heard guest speakers, and had access to the NIH EdNet, a computer-assisted bulletin board service. Club sponsors included many teacher interns who had been in the program previously.

Teachers are provided with the opportunity to expand their science training and take part in professional development activities. Alix Pratt, a veteran of the program, was selected for the National Science Teachers Association Outstanding Science Teacher Award in 1995. Her application included descriptions of her internship experiences. Another teacher intern, Paula Rowe, received a fellow award from the National Society for Experiential Education for 1994–1996. The award provides Rowe with training opportunities, conference participation, and a grant for use in experiential programs for students, which Rowe applied to the purchase of software, a telephone line, and a printer that allowed students to communicate with research partners.

Instrumentation II: Chemistry with Calculator-Based Laboratories

"Calculator-based laboratories" are the rage among Montgomery County high school science teachers. Teachers are flocking to the HHMI-supported course, "Instrumentation II: Chemistry with Calculator Based Laboratories." Who would have imagined that such an unwieldy title could generate such enthusiasm? This new one-week course for chemistry and science teachers is taught by fellow science teachers, Julianna

Julianna Pax, course instructor and teacher at Walt Whitman High School, works with Carol Gregory, a teacher at Quince Orchard High School, in a popular "calculator-based" chemistry laboratory course offered during the summer of 1996.

Don Osmon, Wheaton High School, instructor Jean Maloney of Watkins Mill High School, and Mary Kay Bates, Quince Orchard High School, enhance their knowledge of the use of calculators, spectrophotometers, gas-liquid chromatographs, and other tools for use in their high school classes.

Pax of Walt Whitman High School and Jean Maloney of Watkins Mill High School. They jointly developed the course after the technology caught the imagination of Maloney, who has a master's degree in Educational Technology.

The course is designed to introduce teachers to the tantalizing possibilities of calculator-based laboratories. It trains teachers to use 15 distinct laboratory experiments through lectures and hands-on experience. According to Pax, "This course is about teachers upgrading their training, contacting other teachers, and getting ideas for the classroom." At the end of the course, teachers may borrow spectrophotometers, gas-liquid chromatographs, and computer-based laboratory devices for use in their classrooms (Table 6).

Simple, accurate, versatile, and inexpensive. These are the compelling reasons to use calculator-based laboratories, or CBLs, in a myriad of chemistry experiments. The fundamentals of chemistry, Boyle's law, Beer's law, and Hess's law, are no longer relegated to textbook exercises. CBLs consist of three separate yet interconnected devices: a probe, an interface, and a graphing calculator. With these three pieces of equipment, students can measure, collect, display, graph, and analyze a battery of data. Different probes can be used to measure such physical properties as temperature, pH, pressure, color, and voltage. The interface device handles a multiplicity of probes and converts their output into useful data which it feeds into the graphing calculator. This last device is the linchpin, for it offers the ability to manipulate, analyze, and graph data. Best of all, this calculator, a Texas Instrument-82 Graphing Calculator, is used by each student in Montgomery County who takes algebra. With all students owning or renting a graphing calculator, budget-conscious science teachers

need only worry about purchasing enough probes and interfaces for several work stations. A laboratory manual offers 35 ready-to-use experiments and is published by Vernier Software, the manufacturer of the probes and interfaces.

To enhance the format even further, there is also an accompanying graphical analysis software program for an IBM or Macintosh computer. The software program enables students to visualize and further manipulate the data stored in the graphing calculator. The software is capable of curve fitting, integration, interpolation, and other types of manipulations. A simple example illustrates the power of CBLs and the related software program.

Boyle's law, a mainstay of introductory chemistry, expresses the mathematical relationship between pressure and volume of a gas at constant temperature. Simply put, the relationship is an inverse one: the higher the pressure, the smaller the volume. This relationship comes alive with a CBL. A pressure probe is hooked up to a large syringe full of

Table 6

Instrumentation II: Chemistry with Calculator-Based Laboratory

Instructors: Dr. Julianna Pax and Jean Maloney

June 24–28, 1996

Teachers

Mary Kay Bates
Quince Orchard High School

Kathleen Bettinger
Poolesville High School

Kathy Blair
Herbert Hoover Middle School

Carol Gregory
Quince Orchard High School

Gerald Link
Quince Orchard High School

Sally McAneny
Gaithersburg High School

Donald Osmun
Wheaton High School

Elena Pisciotta
Montgomery Blair High School

Cathy Reams
Walt Whitman High School

Jennifer Russell
Bethesda-Chevy Chase High School

Rosemary Shaw
Walt Whitman High School

Beverly Stross
Richard Montgomery High School

Sharon Walton
Watkins Mill High School

August 19–23, 1996

Teachers

Lesli Adler
Thomas S. Wootton High School

Fred Basgier
Seneca Valley High School

Ellen Brinsko
Paint Branch High School

Dewey Brown
Wheaton High School

Mavis Burdett
Thomas S. Wootton High School

Christina Canham
Thomas S. Wootton High School

Steve Christiansen
Colonel Zadok Magruder High School

Susan Feldhuhn
Springbrook High School

Karen Furr
Thomas Edison High School of Technology

Daniel Gabel
Gaithersburg Middle School

Gregg Gochnour
Rockville High School

Christine Grant
Quince Orchard High School

Emily Hauber
Watkins Mill High School

Jeffrey Hodos
Richard Montgomery High School

Maria Lynch
Gaithersburg High School

Judith Parsons
Thomas S. Wootton High School

Judith Price
Watkins Mill High School

Denise Smith
Springbrook High School

Virginia Trulio
Walt Whitman High School

Anna VonArx
John F. Kennedy High School

air. The student manually presses on the syringe's plunger in an incremental manner to control the volume of air inside the syringe. The incremental changes in pressure are sensed by the pressure probe, which relays the pressure readings to the interface device. This device, in turn, converts and relays the readings to the graphical calculator. The two-inch screen on the face of the calculator can instantaneously plot the relationship between pressure and volume. Because the calculator's screen is so small, the graph is hard to resolve. Here's where Vernier's "Graphical Analysis" software shines: the software imports the data from the graphing calculator, labels the axes, and displays the graph on a large and colorful computer screen. The plot of pressure vs. volume shows a distinct and smooth curve, thereby graphically depicting Boyle's law. "This is awesome. My students will eat this up!" says Beverly Stross, a course participant who teaches honors chemistry at Richard Montgomery High School.

Kirsten Barnes, a student at Seneca Valley High School, and instructor Lesli Adler, of Thomas S. Wootton High School, learn to integrate computers and molecular biology as they explore the world of proteins, RNA, and DNA.

Stross is not alone in her excitement. Her lab partner in the course, Jennifer Russell of Bethesda–Chevy Chase High School, anticipates "rave reviews from my students." Russell plans to add at least 10 new laboratories to her chemistry courses as a direct result of her participation in the course. She is especially eager to use CBLs to teach acid-base titration and colorimetry. Colorimeters use sensitive probes to measure emitted light in order to identify the concentration of a known solute in aqueous solution. "Colorimeters are not as sophisticated as spectrophotometers, which are needed for Advanced Placement courses, but they work fine in introductory classes," notes Pax, one of the course instructors.

The CBLs have such ease of translation into the classroom that middle school teachers also attended the course. Helen Quave of Wood Middle School and Cathy Blair of Hoover Middle School wanted to participate because no one had been trained to use the CBLs already in their schools. The teachers emerged from the course energized and ready to train other teachers in their department. What especially thrilled Quave was, "this kind of equipment

"This kind of equipment is so easy to use that it will move kids beyond data collection and force them into analysis. We can now move kids into the thinking realm."

–Helen Quave

is so easy to use that it will move kids beyond data collection and force them into analysis. We can now move kids into the thinking realm."

An invited lecturer offered an insider's perspective on chemistry resources on the Internet. Larry Dusold, an FDA chemist who has written about the Internet and developed FDA's World Wide Web site, gave course participants a guided tour: he showed them how to access an updated periodic table and standard reference texts like the *Handbook of Chemistry and Physics*, and how to download software featuring 3-D models of chemical compounds. By the end of course, even veteran instructor Jean Maloney was overwhelmed "by the awareness, fascination, excitement, and appreciation of the teachers who participated."

Introductory Molecular Biology

A molecular biology course can even be fun during a power failure. In total darkness, someone quips, "We're being down-regulated!"

Humor and camaraderie punctuated the 1996 summer introductory course in molecular biology. Power failures, thunderstorms, and other acts of nature could not have diminished the excitement of this one-and-a-half–week course taught for the second straight year by science teachers Judith Price of Watkins Mill High School and Lesli Adler of Thomas S. Wootton High School. Their HHMI-supported course was designed to acquaint high school teachers and students with molecular biology in order to prepare them for a research experience in an NIH laboratory. After the course, the teachers in the group entered an NIH laboratory to work on a summer project, while the students stayed at NIH beyond the summer and throughout the school year (Table 7). According to course instructor Judith Price, who has taught high school science for more than 20 years, "Our overall objective was to get students and teachers out of the school mindset and into the research mindset ... This course is a perfect transition to an NIH laboratory."

The course is a blend of six laboratory exercises, two lecture-demonstrations from NIH scientists, and unforgettable experiences to familiarize students with the content, vocabulary, and techniques of molecular biology. The course systematically covers the mainstays of molecular biology, proteins, RNA, and DNA, and their interrelationships. Most importantly, the participants "learn to think independently, act assertively, and become ready for the process of doing research," said Ms. Adler, a 15-year veteran of Montgomery County Public Schools. In addition to participating in a year of independent research supported by HHMI in the early 1990s, Adler joined an NIH laboratory for the summer following the 1996 course. Her major goal was to develop a high school laboratory exercise with polymerase chain reaction (PCR).

PCR is a versatile biochemical technique for amplifying DNA fragments. It was the focus of a lecture-demonstration by Visiting Research Fellow Neale Weitzman of the

National Institute of Diabetes and Digestive and Kidney Diseases. Weitzman provided a vivid picture of how PCR works and how it can be used in a stunning variety of applications. In meticulous detail, he described the three crucial steps of PCR: denaturing into single-stranded DNA the fragment that is to be amplified; annealing, or attaching, primer segments to each piece of single-stranded DNA; and generating from the primer sequence a newly synthesized strand of DNA that is complementary to the original single-stranded fragment. The last step, primer extension, requires the presence of two raw materials: deoxynucleotides and an enzyme that polymerizes each successive deoxynucleotide to the primer sequence. When this three-step process is repeated, in what is termed a "cycle," up to a billion copies of the original DNA fragment can be created. According to Weitzman, "PCR is very much like a Xerox machine. With 20 cycles of PCR you can get 1,000,000 copies of your DNA for use in sequencing, cloning, or other applications ... That is the magic of PCR." Course participants learned the value of PCR in the early detection of HIV infection, prenatal disorders, and other conditions whose diagnosis was previously hampered by insufficient amounts of DNA for analysis.

Another laboratory was designed to shed light on enzymes and on an instrument used to measure their concentrations. The laboratory exercise, which was developed at the University of Maryland Department of Zoology, was built around a gripping scenario: a beloved dog was ill with what the veterinarian tentatively diagnosed as a bone disease. To confirm the diagnosis, the veterinarian had to characterize the functional activity of an enzyme, alkaline phosphatase, in the dog's blood. Using an enzyme assay, participants determined if the activity of alkaline phosphatase was diminished. For many of the participants, this was the first exposure to spectrophotometry, a sensitive method that deploys light to detect concentrations of substances in colored solutions. Alkaline phosphatase activity can be monitored through a reaction in which a colorless solution is converted into a yellow-colored solution (with the release of a phosphate group). The concentration of the yellow-colored

Table 7

Summer Workshop in Molecular Biology—June 20–July 2, 1996*
Instructors: Lesli Adler and Judith Price

Teachers

Virginia J. Brown
Winston Churchill High School

Doria Estelle Hillsman
Rockville High School

Shelia Shipmon
Gaithersburg High School

Clare Von Secker
Walt Whitman High School

*See Table 9 for list of students.

(l-r) Shelia Shipman, teacher at Gaithersburg Middle School, Dr. Neale Weitzman of the National Institute of Diabetes and Digestive and Kidney Diseases, and students Hanna Freeman (Rockville High School), Mary Whitman (Thomas S. Wootton High School) and Qian Shen (Walt Whitman High School) discuss Weitzman's lecture on PCR, a biochemical technique for amplifying DNA fragments.

solution, which yields information about the functional activity of alkaline phosphatase, can be inferred from the spectrophotometer readings. Participants learned how the instrument is calibrated and how certain variables, such as pH and time course, influence the outcome of the assay. Kirsten Barnes, a student at Seneca Valley High School, was thrilled with the enzyme assay and the use of the spectrophotometer. She laughingly admits to having been disappointed that the dog's enzyme assay came out normal. Said Barnes, "After all that, the dog didn't even have the disease!"

Other activities exposed students to gel electrophoresis, ELISA (enzyme-linked immunosorbent assay), and immunohistochemistry, a method of using antibodies to visualize proteins inside of cells. Beyond the excitement of new techniques, participants were even given training in the "sociology" of science. For instance, the instructors stressed the importance of communication by having the group simulate journal clubs and poster sessions.

One theme, reinforced by course instructors, was the importance of verifying results. In a laboratory on transformation of *E. coli* with a foreign gene, course participants were required to verify that the foreign gene was actually inserted into the bacterium. They began the experiment by introducing into *E. coli* a plasmid containing a foreign gene for ampicillin resistance. Next, they grew the transformed *E. coli* and controls on an agar medium containing ampicillin. *E. coli* without the plasmid conferring ampicillin resistance would not survive; whereas *E. coli* with the plasmid containing this gene would. Surviving colonies of *E. coli* then were subjected to gel electrophoresis to confirm that the

foreign gene was indeed present. The appearance of thriving colonies alone was considered inadequate proof of colony transformation.

Course participant and biology teacher Virginia Brown of Churchill High School marveled at the lessons learned and experiences gained. "This is an outstanding course that will help me to bring real-life into the classroom. Now I can see science through my students' eyes," she exclaimed.

"Now I can see science through my students' eyes."

–Virginia Brown

Parul Agarwal
Albert Einstein High School

Preceptor:
Krishan K. Arora, Ph.D.
Section on Hormonal Regulation

National Institute of Child Health and Human Development

Mentor:
Krishan K. Arora, Ph.D.

Functional Expression and Characterization of the Mouse Gonadotropin-Releasing Receptor Hormone Bearing a Flag Epitope

Gonadotropin-releasing hormone (GnRH), a hypothalamic decapeptide, binds to its high-affinity receptors on the pituitary gonadotrophs and controls the biosynthesis and secretion of luteinizing hormone (LH) and follicle-stimulating hormone (FSH), and thus plays a central role in reproductive systems. The cloning and sequencing of the GnRH receptor (GnRH-R) has revealed that it has seven transmembrane-spanning helices, thus belonging to the G protein–coupled receptors (GPCRs) superfamily. Desensitization of pituitary gonadotrophs and attenuation of gonadotropin release following continuous exposure to GnRH-R agonists has been reported *in vivo* and *in vitro*, but the molecular basis of this process is unknown. Receptor phosphorylation by a variety of kinases is a well-recognized mechanism for desensitization of agonist-induced responses. The GnRH-R is unique among GPCRs, since it lacks a carboxyl terminal tail, which has been implicated to play an important role in desensitization of other GPCRs. GnRH-R contains several potential phosphorylation sites, but it is not known whether phosphorylation plays a role in the receptor desensitization. In order to carry out these studies, we need a GnRH-R-specific antibody to immunochemically identify the GnRH-R protein. To this end, we have constructed and functionally characterized GnRH-R with a flag epitope that can specifically recognize a commercially available monoclonal antibody. We have modified the mouse GnRH-R cDNA by inserting a 24-nucleotide sequence after the 5′-ATG codon that encodes the DYKDDDDK flag epitope. This modified cDNA encodes a functional GnRH-R in terms of ligand binding, and agonist-induced internalization and inositol phosphate production. This epitope was also introduced at the carboxyl terminal end of the receptor before the stop codon, but the resultant receptor was poorly expressed, as judged by radioligand-binding assay. Presently we are using antibodies to the amino-terminal flag epitope to identify and characterize the GnRH-R protein by techniques that include Western blotting and immunoprecipitation.

Jeremy Chou
Thomas S. Wootton High School

Preceptor:
Albert J. Fornace, M.D.

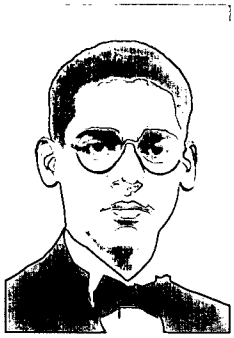
Laboratory of Molecular Pharmacology, National Cancer Institute

Mentor:
France Carrier, Ph.D.

Laboratory of Molecular Pharmacology, National Cancer Institute

The Effect of UV-Induced Cytokines on the Activation of HIV1-LTR

The ability of many viruses to replicate in human cells is under the control not only of viral-encoded proteins, but also of many host-related factors. UV light has been shown to induce transcription and expression of certain viruses. UV irradiation has also been linked to the secretion of cytokines. The purpose of this project is to determine what effect cytokines have on the induction of HIV1-LTR in the Xp-Hiv-Cat cell line. The purpose is also to determine which cytokines are involved, and then to find out which pathway or mechanism they follow. First, we UV-irradiated plates with the Xp-Hiv-Cat cell line growing inside. Half were irradiated and half were not. To all the plates we added antibodies, which were used to trap their respective cytokine to each plate. The cells were then harvested, and a CAT assay was performed. After data analysis, we determined that the TGF-β and IL-β antibodies reduced the induction of the HIV1-LTR. We are still in the process of seeking the mechanism that the cytokines follow to be secreted.



Ansumana Cooper
Rockville High School

Preceptor:
Esther M. Sternberg, M.D.

Clinical Neuroendocrinology Branch, National Institute of Mental Health

Mentors:
Ruth Barrientos and Mariâ Gomez, D.V.M.

Clinical Neuroendocrinology Branch, National Institute of Mental Health

Effects of Neurohormones in Regulating Behavior

The genetically similar Lewis and Fischer pure strains of rat vary from each other only in the amount of CRH produced by their brains and in differences resulting from this. Lewis rats produce low levels of CRH, whereas Fischers produce high levels. In tests involving normal outbred rats, exploratory behavior has been shown to be a response linked to CRH levels. In incorporating these observations, the researcher was attempting to discern whether exploratory behavior would be an effective and clearly observable phenotypic trait to separate Lewis from Fischer and could eventually be used in genetic studies to ascertain whether the offspring of a cross between the two strains was a homozygous Lewis, homozygous Fischer, or a heterozygote. The researcher utilized the open field photobeam system, and through several trials determined under which conditions—consisting mainly of time of day as a test of circadian rhythm—this device would be the most effective for testing exploratory behavior. It was determined that exploratory behavior differed only in the males of each strain, and that circadian rhythm did not maximize the difference in exploratory behavior between the strains. As a result, exploratory behavior will now be used in differentiating between Lewis and Fischer rats, but only in the males. The previous practice of conducting the trials at night will be changed for convenience. A future study will seek to determine why females showed no difference in exploratory behavior. This study could involve an analysis of sex hormones and a repeat of the experiment, using prepubescent animals, as these were parapubescent.

Sam Jahanmir
Quince Orchard High School

Preceptor:
Mark E. Sobel, M.D., Ph.D.

Laboratory of Pathology, National Cancer Institute

Mentor:
Mark E. Sobel, M.D., Ph.D.

Molecular Analysis of the HOXA4 Gene in Breast Cancer

The genes of the homeobox family are regulators of cellular development and differentiation. All homeobox genes contain a highly conserved 183-bp sequence known as the homeobox, which codes for a sequence-specific DNA-binding protein. Homeobox genes may constitute a new class of proto-oncogenes, as their unregulated expression results in unrestrained cell proliferation. To determine if breast cancer is subject to irregularities in homeobox gene expression, HOXA4 was cloned and studied. Analysis of HOXA4 in normal and neoplastic mammary cell lines demonstrated differential patterns of expression and the presence of multiple mRNA transcripts. All known Class I homeobox genes contain, just upstream of the homeodomain, an intron that may be the site of regulatory elements. Using oligonucleotide primers derived from the HOXA4 cDNA sequence, an intron of 546 bp was amplified from human placental DNA by polymerase chain reaction and sequenced. Computer analysis of the human HOXA4 intron revealed a 95 percent homology to that of the murine Hoxa-4 gene, further evidence of the common evolutionary ancestry of all homeobox genes. The proposed homeodomain binding sites reported in experiments with the murine Hoxa-4 intron were found to be conserved in the cloned human intron, suggesting a dependence on an identical autoregulatory mechanism. Further research should elucidate the functional role of HOXA4 in the normal and neoplastic human mammary gland.

Rachel Keller
Gaithersburg High School

Preceptor:
Margaret Altemus, M.D.

Laboratory of Clinical Science, National Institute of Mental Health

Mentor:
Chuang C. Mike Chiueh, Ph.D.

Laboratory of Clinical Science, National Institute of Mental Health

Is Estrogen an Anti-Oxidant?

There have been recent reports that women who use estrogen replacement therapy after menopause are protected against degenerative brain diseases such as Alzheimer's and Parkinson's. The steroid hormone estrogen is produced by the ovaries and passes easily into the brain. How estrogen may exert this protective effect is unknown. One possibility is that estrogen protects the brain against damage from free radicals, which often result in the degeneration of molecules in cellular components. There is evidence that estrogen protects against free radical damage to lipids circulating in the blood. Researchers think this is one reason why premenopausal women are less likely than men to develop heart disease.

To study the effects of estrogen on free radical activity in the brain, we added a range of doses of estrogen to rat brain tissue. The brain samples were incubated with estradiol for varying lengths of time in a water bath at 37° C. Ferrous ammonium sulfate at a concentration of 1 μM was added after the incubation, to stimulate lipid peroxidation in the brain samples, and they were then incubated for two more hours with the iron stimulant. After incubation, the malondialdehyde was separated by chloroform and methanol extraction. A spectrofluorometer was used to measure the relative fluorescent intensities of malondialdehyde products in the brain tissue extracts. For comparison we did the same experiment using other sex steroids: progesterone and DHEA. Incubation for one hour with estradiol at a concentration of 100 μg/ml resulted in a dose-dependent inhibition of lipid peroxidation of 36 percent. Progesterone did not inhibit brain lipid peroxidation as effectively as estradiol. At one-hour of incubation with a progesterone concentration of 1000 μg/ml, lipid peroxidation was only inhibited 19 percent. DHEA had no effect on lipid peroxidation.

One problem with our findings is that the doses of estrogen needed to inhibit free radical formation are higher than the estrogen levels found in the body. A low dose may only have antioxidant effects in a live animal where the cellular processes are functioning.

Ava Onalaja
Montgomery Blair High School

Preceptor:
Jacqueline Crawley, Ph.D.

Section on Behavioral Neuropharmacology, National Institute of Mental Health

Mentor:
Terrence L. Sills, Ph.D.

Section on Behavioral Neuropharmacology, National Institute of Mental Health

Individual Differences in Amphetamine-Stimulated Locomotor Activity and Nucleus Accumbens Dopamine Release

Rats exhibit individual differences in response to drugs of abuse such as cocaine and amphetamine (AMP). Rats that naturally consume high amounts of sugar (High) show a greater locomotor response to acute and repeated administrations of moderate (>1.0 mg/kg) doses of AMP than rats that normally consume low amounts of sugar. Intrinsic variation in nucleus accumbens (Acb) dopamine (DA) function is one potential mechanism underlying the expression of these individual differences. The purpose of the present study was twofold: (1) to determine whether Low and High feeders would exhibit differences in their locomotor response to low doses of AMP; (2) to determine whether Low and High feeders would exhibit differences in AMP-stimulated DA overflow in the Acb. To this end, Low and High feeders were first tested for their locomotor response to three doses of AMP (0.25, 0.5, 1.0 mg/kg, i.p.). Subsequently, Low and High sugar feeders were tested for 0.5 mg/kg AMP-induced DA overflow in the Acb, using *in vivo* microdialysis in combination with HPLC-EC. Results showed that High sugar feeders exhibited higher levels of locomotor activity than Low sugar feeders across all three doses of AMP. High sugar feeders also exhibited higher levels of DA overflow from the Acb following 0.5 mg/kg AMP than Low sugar feeders. Taken together these results indicate that intrinsic differences in Acb-DA function underlie the individual differences in responsiveness to AMP treatments exhibited by Low and High feeders. In light of the fact that Acb-DA function has been implicated in drug addiction and schizophrenia, the present results have important implications for the study of the biological mechanism of these disease states, especially with regard to the issue of vulnerability.

Timothy Owolabi
Colonel Zadok Magruder High School
Preceptor:
Adam B. Glick, Ph.D.
Laboratory of Cellular Carcinogenesis and Tumor Promotion, National Cancer Institute
Mentor:
Adam B. Glick, Ph.D.

The Role of TGF β Receptor in Genomic Stability

Cancer cells exhibit genomic change, such as gene amplification, mutations, and chromosomal rearrangements. TGF-β1, a 25-kDa secreted cellular protein, acts as a potent growth inhibitor for epidermal keratinocytes by binding to specific TGF-β1 surface receptor proteins. We are testing the hypothesis that TGF-β1 plays a role in genomic stability, using an assay that quantitates drug-induced gene amplification as a measure of genomic stability. PALA is a toxic drug that blocks the ability of cells to synthesize nucleotides by blocking an enzyme in the pathway of this synthesis. Cancer cells become resistant to PALA by making extra copies of the gene that encodes this enzyme, while normal cells are unable to undergo gene amplification. Previous studies have shown that cells which do not express TGF-β1 have decreased genomic stability in this assay, and that TGF-β1 can block the formation of PALA-resistant colonies. To test whether a functional TGF-β type II receptor is required for this latter effect, a PALA assay was conducted on human cancer cells with an inactive TGF-β receptor. Results of these experiments show that TGF-β1 has no effect on the formation of PALA-resistant colonies in cells with an inactive TGF-β receptor. To test whether inactivation of the TGF-β receptor leads to genomic instability, we used murine keratinocytes from transgenic mice with a dominant negative TGF-β receptor. Before a PALA assay could be conducted on the keratinocytes, it was necessary to characterize the cells in preparation for a PALA assay. The growth inhibition response to TGF-β1 should be blocked by the dominant negative receptor. Expression of the dominant negative receptor is controlled by a zinc-inducible promoter from the metalothienin gene. To test for blocking of the TGF-β1 response by the dominant negative receptor, a cell proliferation assay was conducted on wildtype and transgenic cells. If the dominant negative receptor is functioning and is zinc inducible, then we expect to see a high level of tritiated thymidine incorporation in transgenic cells with added zinc as compared with the cells without zinc, and absence of TGF-β1-mediated growth inhibition. After several modifications, the results suggested that the receptor may be zinc influenced rather than zinc inducible.

Danielle St. Ulme
Montgomery Blair High School
Preceptor:
Gordon Guroff, Ph.D.
Section on Growth Factors, National Institute of Child Health and Human Development
Mentor:
Hao Jiang, Ph.D.
Section on Growth Factors, National Institute of Child Health and Human Development

High-Affinity Nerve Growth Factor Receptor (trkA) Involved in NGF-Stimulated Calcium Uptake in 3T3 Fibroblast Cells

Many studies have shown that nerve growth factor (NGF) stimulates a small, rapid increase in the intracellular calcium concentration of PC12 cells. However, the mechanism of NGF-mediated calcium uptake is still not well understood, and it appears that calcium is mediated by calcium channels present on the cell surface. The present studies were designed to identify the calcium channels involved in the NGF-induced increase of calcium uptake. We obtained a 3T3 fibroblast clone (3T3-trkA-WT.11) that stably expressed the high-affinity NGF receptor (trkA). Western blotting and immunoprecipitation studies had confirmed the presence of trkA in 3T3 cells. NGF treatment of 3T3-trkA-WT.11 cells stimulated the receptor autophosphorylation, which is one of the characteristics of NGF receptor. Radioactive calcium uptake experiments had shown that NGF could induce calcium uptake in 3T3 cells only when trkA was expressed. However, NGF could not stimulate calcium uptake in regular 3T3 cells, demonstrating that NGF receptor is involved. Different calcium channel blockers were used to identify which one was actually blocking the NGF-stimulated calcium uptake.

Marian Tan
Thomas S. Wootton High School

Preceptor:
Y. Peng Loh, Ph.D.
Laboratory of Developmental Neurobiology, National Institute of Child Health and Human Development

Mentor:
Niamh Cawley, Ph.D.
Laboratory of Developmental Neurobiology, National Institute of Child Health and Human Development

The Purification and Characterization of the Novel Yeast Aspartic Protease 3, a Prohormone-Processing Enzyme

Yeast aspartic protease 3 (YAP3p), a member of the novel subclass of aspartic prohormone processing enzymes, has been purified to apparent homogeneity from the media of a yeast expression system and partially purified from the media of a baculovirus/High 5 cell expression system. The YAP3p expressed in yeast was purified by a combination of ion exchange and gel filtration chromatography and characterized as two hyperglycosylated forms of ~150 kDa and ~90 kDa that were highly active. The baculovirus/High 5 system expressed a ~65 kDa inactive enzyme that was partially purified by a combination of ion exchange and hydrophobic interaction chromatography. The pro-YAP3p that was expressed in the High 5 cells could be activated by incubation at 37° C in an acidic pH, while a time course for the activation of pro-YAP3p generated a linear response. Western blot analysis confirmed a reduction in size of the activated YAP3p corresponding to the removal of the "pro-"region. Additionally, expression of the mature YAP3p in the High 5 cells resulted in an enzyme that could not be activated. These results show that the pro-region is required for the correct folding of the enzyme and that removal of the pro-region by an autocatalytic mechanism is required for activation of the enzyme. It is hoped that in the near future pro-YAP3p from High 5 cells will be purified in quantities sufficient for x-ray crystal structure analysis.

Juanna Tingem
Albert Einstein High School

Preceptor:
Steven Kozlowski, M.D.
Center for Biologics Evaluation and Research, Food and Drug Administration

Mentor:
Steven Kozlowski, M.D.

Immunization of MHC Class I Restricted T Cells with Peptide Antigens Restricted to MHC Class II

Objective: to design a vaccine based on the attachment of a class II peptide antigen to a protein domain that will directly or indirectly bind CD8. This vaccine will allow the binding of a CD8 T cell to a class II–associated peptide antigen. The protein domain binding CD8 will bring the CD8 coreceptor into the T cell receptor antigen complex. The loss of CD4 cells leads to the absence of specific antibodies against protein antigens and weakened cellular responses. CD4 cells can acquire some CD8-like lytic functions *in vivo*. We want to see if CD8 can also acquire CD4 functions by receiving antigens for CD4. This vaccine will be helpful in boosting the immune system, since the loss of CD8 effector cells is not as serious to an individual as the loss of CD4 effectors. This vaccine will also be very helpful for AIDS patients, whose main difficulty is their low CD4 T cell count.

Wendy Tseng
Paint Branch High School

Preceptor:
Wendy C. Weinberg, Ph.D.

Laboratory of Cellular Carcinogenesis and Tumor Promotion, National Cancer Institute

Mentor:
Wendy C. Weinberg, Ph.D.

The Role of the p53 and WAF1 Gene Products in Epidermal Carcinogenesis

The p53 gene is mutated in the majority of human cancers, including skin. We are using mouse epidermis as a model to understand the role of the wildtype protein in preventing tumor growth. Papillomas derived from p53(-/-) keratinocytes grow five times faster than those from p53(+/+) keratinocytes, and have a higher frequency of malignant conversion. p53 can act to enhance transcription of a number of genes, including WAF1, an inhibitor of cyclin-dependent kinases. There is a correlation between p53 gene dosage and expression of WAF1 mRNA in normal, primary epidermal keratinocytes, which may explain the phenotype of p53-null tumors. To explore the role of WAF1 in the keratinocyte, we are using mice with a null mutation in the WAF1 gene for tumor studies, and have established keratinocyte cell lines from these mice. These studies should help clarify whether p53 acts through WAF1 in epidermal growth regulation.

Li-Ming Ueng
Walter Johnson High School

Preceptor:
Yves G. Pommier, M.D., Ph.D.

Laboratory of Molecular Pharmacology, National Cancer Institute

Mentors:
Malini Gupta, Yves Pommier, and Philippe Pourquier

Laboratory of Molecular Pharmacology, National Cancer Institute

The Effects of the Introduction of Damage to DNA to Camptothecin

Abasic sites created in SV40 DNA do not produce a significant enhancement of cleavage with the addition of topoisomerase I (topI) and camptothecin (CPT). Nicks were created in oligonucleotides containing a unique topI cleavage site. Various nicks in the strand produced different results. A nick opposite the cleavage site produces an irreversible topI-linked DNA break. Nicks between other bases may also produce irreversible breaks or suicides, slowly reversible reactions, suppression of the normal cleavage with CPT, or production of a new cleavage site. These data may provide a basis for the use of CPT with DNA-damaging agents in cancer chemotherapy.

Zi-Rong Xu
Albert Einstein High School

Preceptor:
Thomas Hoffman, M.D.
Laboratory of Cell Biology, Center for Biologics Evaluation and Research, Food and Drug Administration

Mentor:
Ennan Guan, M.D., Ph.D.
Laboratory of Cell Biology, Center for Biologics Evaluation and Research, Food and Drug Administration

The Role of Human Notch/TAN-1 Ankyrin Repeats in Interaction of NF-κB Transcription Factors

TAN-1, the human counterpart of the *Drosophila* Notch, was discovered as a t(7;9)(q34.3) translocation in the β T cell receptor in certain T lymphocytic leukemias. Extensive genetic studies of the Notch locus have revealed that Notch plays a central role in regulating events influencing cell fate decisions. The human Notch/TAN-1 gene encodes a transmembrane protein. The extracellular domain contains 36 tandemly arrayed epidermal growth factor (EGF)-like repeats, and the intracellular domain contains six ankyrin repeats. The intracellular six ankyrin repeats of Notch/TAN-1 are similar to those in IκB-like family proteins, including Bcl3, IκBα, PP40, NF-κB1 and NF-κB2. IκB proteins are specific inhibitors of NF-κB/Rel transcription factors. Previous studies have shown that the cytoplasmic portion of human Notch/TAN-1 (TAN-1c) specifically inhibits NF-κB activity and binds the p50 subunit *in vitro*. Its transfection modulates κB-mediated nuclear gene expression. To investigate the role of Notch ankyrin repeats in signaling transcription factor NF-κB, we carried out transfection experiments in NTera-2 cells and electrophoretic mobility shift assays (EMSA). TAN-1c derivatives were cotransfected with p50 and p65 expression vectors and the 6 κB-luciferase reporter gene. The TAN-1c mutant with the N-terminal was able to suppress κB-mediated transactivation, while the N-terminal-deficient TAN-1c mutants failed to suppress κB-mediated transactivation. Interestingly, one mutant containing the first four ankyrin repeats of TAN-1c (but not the mutant containing five or six ankyrin repeats) did partially inhibit κB-mediated transactivation. Recombinant TAN-1c mutants were tested for their ability to inhibit NF-κB binding of the κB site in EMSA. The inhibitory pattern in EMSA resembles that of the transfection experiments. Our data suggest that both the N-terminal and the ankyrin repeats are required for the functional integrity of TAN-1 interaction with κB factors.

Table 8

Montgomery County Public Schools Student and Teacher Intern Program at the National Institutes of Health, Class of 1996

Teachers

Leslie Bennett
Albert Einstein High School
Robert J. Crouch, Ph.D., NICHD

Angelique Bosse
Montgomery Blair Magnet School
John O'Shea, Ph.D., NIAMS

David Goldenson
Albert Einstein High School
Mary Herman, M.D., NIMH

Michelle Lugo
Key Middle School
M. T. Ruda, Ph.D., NIDR

Elena McComas
Colonel Zadok Magruder High School
Jacqueline Crawley, Ph.D., NIMH

Judith Ruppert
Walter Johnson High School
Paul Russell, Ph.D., NEI

Jennifer Russell
Bethesda–Chevy Chase High School
David Goldstein, M.D., Ph.D., NINDS

Cynthia Stouffer
Cabin John Middle School
Larry W. Kwak, Ph.D., NCI

Barney Trams
Eastern Middle School
Anne Schaffner, Ph.D., NINDS

Phuong Vu
Takoma Park Middle School
Esther Sternberg, M.D., NIMH

Students

Parul Agarwal
Albert Einstein High School
Krishan K. Arora, Ph.D., NICHD

Jeremy Chou
Thomas S. Wootton High School
Albert J. Fornace Jr., M.D., NCI

Ansumana Cooper
Rockville High School
Esther M. Sternberg, M.D., NIMH

Sam Jahanmir
Quince Orchard High School
Mark E. Sobel, M.D., Ph.D., NCI

Rachel Keller
Gaithersburg High School
Margaret Altemus, M.D., NIMH

Ava Onalaja
Montgomery Blair High School
Jacqueline Crawley, Ph.D., NIMH

Timothy Owolabi
Colonel Zadok Magruder High School
Adam B. Glick, Ph.D., NCI

Danielle St. Ulme
Montgomery Blair High School
Gordon Guroff, Ph.D., NICHD

Marian Tan
Thomas S. Wootton High School
Y. Peng Loh, Ph.D., NICHD

Juanna Tingem
Albert Einstein High School
Steven Kozlowski, M.D., FDA/CBER

Wendy Tseng
Paint Branch High School
Wendy C. Weinberg, Ph.D., NCI

Li-Ming Ueng
Walter Johnson High School
Yves G. Pommier, M.D., Ph.D., NCI

Zi-Rong Xu
Albert Einstein High School
Thomas Hoffman, Ph.D., FDA/CBER

Table 9

Montgomery County Public Schools Student and Teacher Intern Program at the National Institutes of Health, Class of 1997

Teachers

Lesli Adler
Thomas S. Wootton High School
Ellen Sidransky, M.D., NIMH

Angelique Bosse
Montgomery Blair High School
John O'Shea, M.D., NIAMS

Virginia J. Brown
Winston Churchill High School
Rosemarie Hunziker, Ph.D., NIAID

Karen Chagalis
Rockville High School
Lynn Sorbara, Ph.D., NCI

Helen J. Ghent-Paloucci
Richard Montgomery High School
Pradman Qasba, Ph.D., NCI

Doria Hillsman
Rockville High School
Constance Noguchi, Ph.D., NIDDK

Richard Miller
Seneca Valley High School
Mary Herman, M.D., NIMH

Shelia Shipmon
Gaithersburg High School
Mary Herman, M.D., NIMH

Clair Von Secker
Walt Whitman High School
Esther Sternberg, M.D., NIMH

Students

Kamini Bajaj
Wheaton High School
Yves G. Pommier, M.D., Ph.D., NCI

Kirsten Barnes
Seneca Valley High School
William G. Coleman, Ph.D., NIDDK

Jessica Baxter
John F. Kennedy High School
Thomas Hoffman, Ph.D., FDA/CBER

Rachel Bortnick
Walter Johnson High School
Albert J. Fornace, Jr., M.D., NCI

Semuteh David
John F. Kennedy High School
Krishan K. Arora, Ph.D., NICHD

Hannah Freeman
Rockville High School
M. T. Ruda, Ph.D., NIDR

Abraham Hemmingaard
Damascus High School
Michael Redmond, Ph.D., NEI

Katherine Miller
Walter Johnson High School
Jacqueline Crawley, Ph.D., NIMH

Kamal Pathak
Watkins Mill High School
Irwin J. Kopin, M.D., NINDS

Lisa Marie Pierre
Gaithersburg High School
Wayne Bowen, Ph.D., NIDDK

Jacob Richard
Watkins Mill High School
Christian Gerloff, M.D., NINDS

Qian Shen
Walt Whitman High School
Chuang C. Chiueh, Ph.D., NIMH

Mary Whitman
Thomas S. Wootton High School
Stephen Kozlowski, M.D., FDA/CBER

Regina Wong
Watkins Mill High School
Esther Sternberg, M.D., NIMH

Wendy Wroblewski
Thomas S. Wootton High School
Albert J. Fornace, M.D., NCI

(l-r) Mary Whitman, Kamal Pathok, Jacob Richard, Kamini Bajaj, Wendy Wroblewski, Regina Wong, Rachel Bortnick, Katherine Miller

Montgomery County Public Schools Elementary Science Education

Since the late 1980s, the Montgomery County Public Schools have been engaged in the development and introduction of hands-on activities at the elementary level in a productive partnership with the National Science Foundation and the Howard Hughes Medical Institute. This program includes extensive teacher training in content and current pedagogy, adoption of new curriculum units, and provision of instructional materials for all students.

In 1994 the Howard Hughes Medical Institute joined an ongoing effort of the Montgomery County Public Schools to revise the elementary school science curriculum. The plan began in 1988 with the development of a philosophical framework that adopts four science processes around which grade level objectives can be written: Asking Questions, Communicating, Gathering Data, and Making Sense of Data.

The County developed a curriculum framework and designed model science units, using materials developed nationally through the National Science Foundation (NSF) and the National Academy of Sciences (Table 10). The units were introduced and tested in 1991.

Following two years of extensive field testing and revision, these exemplary science curriculum units are being implemented in all County schools, pre-kindergarten through Grade 5. The units support an experiential, inquiry-based approach to science that addresses the needs of a diverse population and, specifically, those students typically underrepresented in science. The unit materials conform with *Benchmarks for Science Literacy* (American Association for the Advancement of Science, 1993), indicating that the content and processes being taught to Montgomery County elementary school children are consistent with national trends in excellence in science education.

In 1994 HHMI awarded the Montgomery County Public Schools $250,000 over a three-year period for replenishing and replacing the science kits. During the 1994–1995 school year, Institute funds helped implement the revised curriculum in all 123 elementary schools and four special education centers. Since 1994, County and NSF funds have supported teacher training for 2,600 teachers, prekindergarten through 5th grade. The Institute grant also provides partial funding for establishing and training a cadre of lead teacher-trainers. In addition, all participating schools have designated a science liaison who receives additional training, serves as a science coordinator for the school, and advises the principal on science-related issues.

In 1996 the Institute has renewed its investment in this program, making a three-year award of $390,000 for additional teacher training. These funds will be used to train teachers in the 37 remaining elementary schools that have not yet benefited from the program and will provide

for additional training of all teachers for the units just completed.

A newly established Science Materials Center assures that all elementary teachers have the science materials they need for classroom use by providing complete materials sets for each unit. In the first year of the grant more than 4,600 sets of materials were put to use. The number of schools receiving materials sets for three or more units per grade level grew from 39 during the 1994–1995 school year to 90 during the 1995–1996 school year (an increase from 4,600 to more than 5,200 materials sets). Remaining elementary schools will be added next year. When all schools are involved, over 9,000 materials sets will be processed and sent to classes each year.

Feedback from teachers makes it clear that easy access to these materials through the Science Materials Center is as important as the training they receive. The value of high-quality science materials, regularly made available to teachers and supported by sound training, is too often underestimated. In comparison to secondary school science departments, which focus solely on science and usually have a department chair who takes responsibility for ordering quality materials, elementary teachers are responsible for all of the disciplines (science and nonscience) and cannot effectively and efficiently order and maintain quality science materials. By being relieved of this burden, teachers are now able to focus their attention on science instruction. The result has been an increase in the amount and quality of science being taught.

Local Heroes

Three teachers who were involved as leaders in the program received highly coveted awards over the past year. Ellie Shutak, Grade 1 elementary science lead teacher at Wheaton Woods Elementary, was one of ten teachers in the Washington, D.C., area to receive the Agnes Meyer award for outstanding teaching. Two other teachers, Marcia Rehm, elementary science lead teacher at Luxmanor Elementary, and Karen Anastasi Wills, science liaison at Wyngate Elementary, were selected as two of three Maryland finalists in the elementary science division of the Presidential Awards for Excellence in Mathematics and Science Teaching, sponsored by the National Science Foundation.

In addition, the Taylor Elementary Science Materials Center, under the direction of Thomas DuMars, was selected as an exemplary site by the National Science Resources Center and has been visited by representative teams from over 40 school districts across the country. These teams were brought to see the materials center as part of a summer institute for school districts that are beginning systemic reform of science education. DuMars has been asked by the National Science Resources Center to advise groups on the logistics and benefits of large-scale science materials management.

Feedback from teachers makes it clear that easy access to these materials through the Science Materials Center is as important as the training they receive.

Table 10

Examples of Elementary Science Units Distributed to Montgomery County Public Schools by Grade Level

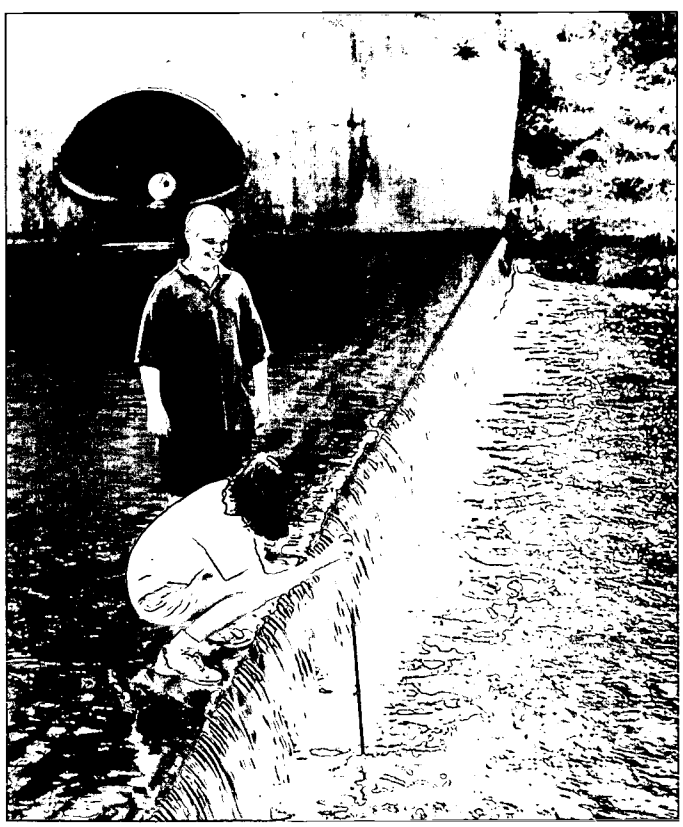
Prekindergarten	**Play It, Weigh It, Say It** Children investigate a variety of changes including pouring together various colors of water, opening and crushing peanuts, and mixing a variety of items and powders with water.
Kindergarten	**Myself and Others** Children look at themselves and their classmates and gather information about characteristics such as height, eye color, skin color, and hand size. As they explore similarities and differences, they use a variety of science thinking and process skills.
First grade	**Rocks, Sand, and Soil** Children investigate a variety of rocks, sand, and soil. They sort and classify rocks, observe soil components, and investigate various sand particles.
Second grade	**Life Cycle of Butterflies** Children observe and record the changes in painted lady butterfly larvae from caterpillar to adult. As they observe the changes, they learn about stages of development and structure of the organisms. Misconceptions they may have held are challenged through observation and discussion.
Third grade	**Plant Growth and Development** Children plant and observe the growth of *Brassica rapa.* Records of growth are kept and used to construct charts and graphs. The students pollinate the flowers with dead bees and harvest the seeds.
Fourth grade	**Earth Materials** Children investigate synthetic rocks and learn techniques for identifying characteristics. These skills and processes are used to investigate a variety of other minerals.
Fifth grade	**Solar Energy** Children investigate sunlight as a heat source. During the unit the children build model houses, monitor temperature, and explore techniques for improving the efficiency of solar collectors.
Sixth grade	**Variables** Children investigate several phenomena by manipulating variables. They construct simple systems, manipulate conditions, and record the results. These data are manipulated and analyzed and used to draw conclusions.

Montgomery County Public Schools and Chesapeake Bay Foundation Collaboration in Environmental Science Education

In August 1993 the Chesapeake Bay Foundation received a three-year, $295,000 grant from the Howard Hughes Medical Institute in support of an environmental and science field education program for Montgomery County Public School students and teachers. The grant also supports a Chesapeake Bay Foundation partnership with the Global Ecology Studies Program at Poolesville Middle/Senior High School. In 1996, the Institute awarded $303,000 to continue the program for an additional three years.

The Foundation's education programs enhance science studies by adding field work to the usual mix of classroom science instruction and laboratory work. Classroom concepts come to life in the field as students collect specimens, perform tests, and use scientific equipment to analyze results. Teachers in the environmental science workshops of the Chesapeake Bay Foundation also learn in the field. Six-day summer workshops for teachers culminate with the development of classroom implementation plans for integrating field work with classroom instruction.

Middle school students collect samples to assess acidity (pH), oxygen content, and other indicators of water quality.



CBF's education program for Montgomery County Public Schools promotes science literacy by

- Exposing participants to science, mathematics, and environmental concepts and skills through hands-on learning techniques
- Practicing scientific research techniques—observation, data collection, data recording, hypothesis testing and critical thinking
- Encouraging interest in science careers through role modeling by CBF staff and outside experts
- Motivating participants to act for positive change by integrating local environmental issues into field studies

CBF field trips rely minimally on educator/teacher lectures. Participants are physically (through hands-on activities) and mentally (through the use of critical-thinking skills) involved in the learning process. They work in small groups and are encouraged to participate in conservation projects during field trips or post-trip classroom projects. Participants are emotionally and

physically connected to the local environment through the field trip experience. While activities may concentrate on a river, stream, or section of the Bay, efforts are made to relate activities to participants' lives and everyday experiences (Tables 11 and 12).

By their actions, CBF's field educators model their own enthusiastic, sincere commitment to the Bay and environmental science education. Participants leave a CBF trip with a sense of empowerment that their actions and newfound knowledge can, and will, have a positive impact on the Bay's water quality and estuarine life.

In the past year 2,257 Montgomery County Public School students, teachers, and other adult participants spent a total of 105 days in CBF field education activities, including 21 days of field trips for high school students; 13 days of trips specifically for Poolesville High School students; and 52 days of field experience for the county's middle school students. The summer workshop attracted 22 Montgomery County Public School teachers.

From City to Saltmarsh: Field Experiences Are the Key to Learning

In the 1995–1996 academic year, Montgomery County students and teachers participated in field experiences at 14 of CBF's 16 education centers. Activities at each of these centers, and each particular field experience, varied according to the geographic locale and the curricular emphasis requested by the participating classroom teacher. In all of the educational experiences, teachers are active partners.

A partnership between the Poolesville Middle/Senior High School and the Chesapeake Bay Foundation, funded in part through the Institute grant, has greatly enhanced the school's field program. The Poolesville Global Ecology Program has scheduled 20 field experiences for the 1996–1997 school year. Several of CBF's education programs will be included in this year's program at the school, so that students new to the Poolesville program can build a comprehensive picture of the Bay watershed. Field trip curricula relate directly to classroom studies and reflect the students' level of expertise.

We All Live Downstream

From July 22–27, 1996, 22 Montgomery County teachers participated in a teacher training workshop, *We All Live Downstream* (Table 13). The five-day workshop is jointly produced by CBF and the Montgomery County Public Schools Outdoor Education Program. The program is not just for science teachers; physical education, art, social science, and English teachers enthusiastically participate. Bernie Sam, supervisor of Montgomery County Public Schools Outdoor Education and one of the trip leaders, firmly believes that teachers outside science bring a different outlook to their learning.

Because they do not have a science background, they require more detailed explanations. This is no more considered a negative than a similar response from a student. Their input is extremely valuable because they come to the program with no preconceptions and their observations signal to instructors potential reactions from students. Furthermore, as Montgomery County increasingly emphasizes interdisciplinary curricula, the interaction of teachers from a variety of disciplines sparks new ideas and partnerships.

The week begins with exploration of the local watershed as teachers test streams in Montgomery County and compare water quality. A trip on the Potomac River led to the Blue Plains sewage treatment plant outside Washington, not exactly a cruise on the tourist boat, the *Dandy*. By midweek the teachers were on the Bay en route to the CBF's education center at Port Isobel. Hands-on activities included

- examining saltmarsh plants and animals
- scraping for organisms in grassbeds
- identifying organisms, using identification guides
- dredging for oysters
- collecting fish specimens for observation in aquarium
- collecting water data
- studying household energy production and conservation, as well as waste disposal
- modeling the shallow nature of the Bay and
- using navigational gear.

In one of the most popular and affecting stops, the group stopped in Tangier Island to talk with local watermen about the health of the Bay and the impact of recent regulations on crabbing.

In a post-trip meeting after the start of the school year, one teacher's enthusiasm for "the single best in-service experience I have had in 20 years of teaching" was echoed by all. The teachers chuckled with delight at a slide show that captured the mud, salt water, and legendary mosquito bites of their days on the Bay, but they also recounted the lasting personal and professional impact of the trip. Each described an "action project" undertaken back at school; one teacher has started a service club for local watershed exploration and protection. Mr. Sam, of MCPS, says that he has seen the positive results of CBF teacher workshops over the past three years of HHMI funding. During outdoor education at the Smith Environmental Education Center, the teachers have emphasized watershed issues with the kids and they "know what they're talking about."

The task of Bay restoration is increasingly becoming a matter of helping people to "think globally

"...the single best in-service experience I have had in 20 years of teaching."

–A participant

and act locally," in the words of Rene Dubos. CBF is placing ever greater emphasis on informing, motivating, and equipping students and teachers to do just that, through an outdoor education program that enhances classroom work and encourages environmental community service projects that allow students to apply the science they learn to the world around them.

Table 11

Urban Field Programs of the Chesapeake Bay Foundation

Baltimore Harbor Education Center and Potomac River Education Program

- study urban impact
- collect water data using chemical test kits, secchi disk, salinity, and dissolved oxygen meters
- trawl for fish and assess them as indicators of water quality
- examine fish for signs of toxics impact
- collect, identify, and examine plankton under a microscope
- use bottom sampler to examine sediments
- use sediment samples and dissolved oxygen meter to examine effects of anoxia (lack of oxygen) in water column
- use navigational gear on boat
- test water near sewage treatment plants and compare with samples from other locations

Clagett Farm Education Center

- define and discuss the concept of watershed
- examine amount and condition of run-off from various land use practices
- collect and examine soil samples
- collect and test ground water samples using chemical test kits
- observe sustainable agricultural practices
- for multi-day trips involving workboats, activities as described above

Table 12

Field Programs of the Chesapeake Bay Foundation's Saltmarsh Education Centers

Karen Noonan Education Center, Fox Island Education Center, Port Isobel Island Education Center, and Smith Island Education Program

- examine saltmarsh plants and animals
- scrape for organisms in grassbeds
- identify organisms using identification guides
- dredge for oysters
- collect fish specimens for observation in aquarium
- collect water data as described above
- study the Bay's unique heritage through interactions with local watermen and cultural experts
- study household energy production and conservation, as well as waste disposal

Maryland Canoe Rig Program, Maryland Streams Restoration Program, and Virginia Canoe Rig Program

- conduct macroinvertebrate surveys
- examine macroinvertebrate morphology and how it relates to organism's function
- collect water quality data using chemical test kits
- collect and identify specimens and use them to help assess water quality
- engage in conservation projects, where appropriate

Meredith Creek Estuarine Education Center

- perform water quality testing as described above
- seine for fish specimens and study fish habitats and morphology
- examine predator/prey relationships and identify food webs
- examine tidal fresh wetland plant and animal species
- examine marsh mud (detritus) and learn about its role in food web

Skipjack Education Program

- collect biological sampling of fish, oysters, and plankton
- compare species diversity with total species number
- perform water quality testing
- demonstrate filtering capacity of oysters
- model shallow nature of the Bay
- use navigational gear

Southern Bay Mobile Education Center

- perform water quality testing as described above
- use navigational tools and engage in map work
- collect specimens for examination using a trawl net
- observe land uses and their potential effects on water quality
- contrast urban, suburban, and natural areas and study the effects of industry on the environment

Virginia Watershed Education Program

- examine how land use affects water quality through visits to local farms and activities that trace the effects of land use on local waterways
- incorporate the expertise of outside experts from local Soil and Water Districts, the Soil Conservation Department, and 4-H Extension Agents
- collect water quality data using chemical test kits
- examine macroinvertebrate and fish specimens
- encourage student observation of birds and mammals along the water

Table 13

We All Live Downstream, July 1996
Montgomery County Public School Teacher Participants

Elaine Allnutt	Julius West Middle School
Gretchen Autry	Forest Oak Middle School
Ann Bedford	Dept. of Academic Programs, MCPS
Nancy Deprey	John T. Baker Middle School
Patricia Diehl	Carl Sandburg Learning Center
Barbara Dietsch	Cabin John Middle School
Jacquelyn Fujiwara	Julius West Middle School
Margaret Gwin	Forest Oak Middle School
Margy Hall	Gaithersburg Middle School
Susanna Horner	Lathrop E. Smith Environmental Education Center
Douglas Jacoby	John T. Baker Middle School
Pamela Kucsan	Neelsville Middle School
Roxann Luttner	Robert Frost Middle School
Daniel McCabe	Thomas W. Pyle Middle School
Meryl Moran	White Oak Middle School
Stefanie Parizer	John T. Baker Middle School
Katherine Partlow	Julius West Middle School
Jean Phillips	Forest Oak Middle School
Phoebe Smith	Diamond Elementary School
Bill Sutton	John T. Baker Middle School
Deborah Symons	Cabin John Middle School
Frank Wilkinson	Roberto W. Clemente Middle School

Montgomery County Public Schools and Audubon Naturalist Society Collaboration in Environmental Science Education

In 1996, the Institute awarded the Audubon Naturalist Society a three-year grant of $37,000 for GREEN LABS, a program that provides teachers with in-service training and credit for attending workshops consisting of 15 hours of classroom and field activity. The program emphasizes multidisciplinary and multicultural approaches to environmental science education with methods for introducing science in English, mathematics, art, and history classes. Audubon Naturalist Society is one of 11 independent Audubons in the eastern United States. It is regional, serving the Washington, D.C., metropolitan area and has 10,000 members and a staff of 30. It provides environmental education programs to K–12, postsecondary, and adult populations.

GREEN LABS–Montgomery is the focus of the Institute's grant to the Audubon Naturalist Society, having already been successfully introduced in the Washington, D.C., public schools. The GREEN LABS–Montgomery instructional plan was developed in accordance with the new National Academy Standards for Science Education and in compliance with the Maryland Environmental Education Bylaw, which requires that by 1999 elementary school teachers complete 12 credits in coursework related to science and 12 credits in math. The concept behind GREEN LABS is that it provides teachers with access to low-cost models for integrating science and math into their curriculum. The program focuses on K–8 teachers who have little or no formal training in applied math and science. Workshops provide teachers with access to community expertise and resources for low-cost environmental and science education.

Four modules will be developed. Each consists of classroom activities and field trips. Three units will be adapted from GREEN LABS–Washington:

Water and Watersheds—units of measurement, water cycles, watersheds, aquatic and stream quality, calibration and maintenance of meters, stream gauging, sand motion, soil acidity, and stream insects.

Weather and Urban Air Quality—chemistry, pollution measurement, pH and acid precipitation, fronts and clouds, wind force and velocity, hurricanes, and weather maps and measurements.

Urban Neighborhoods—surveying, map reading, archaeology, topographical mapping, and natural history.

After the first year of the GREEN LABS–Montgomery program, an extensive evaluation will be conducted to review the instructional strategies and program conformance with Montgomery County Public Schools goals. In subsequent years, an advisory panel will meet twice yearly to update and improve the written materials and workshop design.

Edison Career Center Middle School Biotechnology Summer Focus Program: *Fun With DNA*, July 1996

Two questions are asked of students entering the Edison Career Center's program, *Fun with DNA:*

1. Most scientists are:
   A. Men
   B. Women
   C. Equally distributed by gender in all fields of science.
2. What best describes the role you would see yourself taking if you were selected as a member of a team conducting scientific research?
   A. Observer
   B. Gathers/assembles equipment
   C. Program equipment
   D. Data recorder
   E. Decision maker/data evaluator

The change in student responses to these survey questions between days one and fifteen tell a lot about whether the goals of the summer laboratory course are being met. Responses indicate that during the intensive biotechnology focus program, middle school girls expand their perceptions of scientists and explore their own scientific abilities through laboratory work and field trips. Intensive laboratory experiences using sophisticated equipment in a supportive environment help build confidence and enthusiasm at a time in a girl's development when attitudes about science and one's own abilities dramatically change. The program intentionally targets girls in grades 6 through 8, a critical time for intervention to slow the decline in the number of women entering science. The program is not a one-shot deal. If the students are stimulated by this state-of-the-art, hands-on experience in biotechnology, they can plan to enroll in higher-level science programs or the biotechnology program in their junior and senior years of high school.

Fun with DNA was designed by Judy Brown, former instructor in the

Vinh Tong (l) and Johane Francois check cell growth during a laboratory of *Fun With DNA* at the Thomas Edison High School of Technology in Wheaton, Maryland.

biotechnology program at the Center and now an education consultant, and is made possible by an annual grant from the Howard Hughes Medical Institute. So far, the Institute has awarded $69,000 to the Center. The summer of 1996 was the program's third year.

The 25 students enrolled in the summer focus program were selected from approximately 85 applicants. Middle school guidance counselors and science and mathematics teachers publicized the program and recommended students. Information was sent to each middle school PTSA newsletter. Final selection was based on student essays on science topics that interest them most.

The classroom work, laboratory experiments, and field trips are geared toward realizing the program's goals and objectives

- to increase participant selection of elective high school science courses
- to provide participants with peer support network
- to encourage students to work together in problem solving
- to expose participants to a variety of science career options
- to introduce participants to successful role models
- to provide study groups for specific enrichment opportunities

The girls worked in cooperative laboratory groups using the "3-P model": *problem posing* in the classroom, *problem solving* in the laboratory, and *peer persuasion* in the classroom. The instructional units and lab exercises begin with confidence-building exercises, broadening student perceptions of scientists to include women and minorities and introducing the work approach of scientists, experimental design, and the scientific method. Within a few days, the girls are deftly using biotechnicians' tools to grow cells and test effects of chemicals on growth rates, differentiating between normal and cancer cells, and using classroom computers for graphics and journal-keeping.

"It was a joy to see them evolve as science students."

–Jeff Laws

One of the program's strengths is the use of ordinary materials, many available at the grocery store, to explore and test complex scientific concepts. The laboratory supply list includes lemon juice, onions, applesauce, coffee filters, and milk as well as pipettes, agarose gel, and centrifuge tubes.

This year, Jeff Laws, of the Biotechnology Department of Thomas Edison High School of Technology, led the class (Table 14). He was assisted by co-teachers and volunteers, most of whom were former students in the program. One co-teacher, a former student, asserted, "Everything I know about biotechnology, I learned here. It has really helped now that I am taking biology courses in school. And the interaction with the younger girls is great!" Another former student volunteering this year said, "As a student we used all types of lab equipment. It was really neat to do all these 10th-grade things when I wasn't in 10th grade yet!"

Formal, ongoing program evaluation includes

- quantitative evaluation—profiles of the incoming participants (test scores, grades, level of completed math/science courses) for comparison to follow-up profiles after program participation;

- qualitative evaluation—measuring participants' opinions and attitudes toward science and math, weekly participant feedback on programs; and
- outside evaluation—effectiveness of teaching strategies and program design.

After teaching his first *Fun with DNA* session in the summer of 1996, Jeff Laws laughingly recalled that being the only male in the classroom of female co-teachers, aides, and students was a "unique" situation. He echoed the observations made by everyone involved with the class over the last three years, "It was challenging but I enjoyed working with these students. They were motivated and always interested in what went on in the classroom.

Table 14

Fun with DNA, 1996 Class Roster

Students	School/Grade 1996–1997
Tracy L. Aksamit	Rockville High School, 9th grade
Lauren C. Carey	Montgomery Blair High School, 9th grade
Rachel P. Carlson	Takoma Park Middle School, 8th grade
Radhika Chandrasekaran	Gaithersburg Middle School, 8th grade
Zosia A. Czerska	John F. Kennedy High School, 9th grade
Sabrina A. DeConti	Damascus High School, 9th grade
Princess L. Dula	William H. Farquhar Middle School, 7th grade
Karla Flores	John T. Baker Middle School, 7th grade
Johane Francois	Springbrook High School, 9th grade
Alison J. Frichtl	Albert Einstein High School, 9th grade
Rupali Goel	Gaithersburg Middle School, 8th grade
Julia T. Golden	Ridgeview Middle School, 8th grade
Susan C. Goldhar	White Oak Middle School, 8th grade
Farah L. Lawal	Takoma Park Middle School, 7th grade
Waymee Lwin	Albert Einstein High School, 9th grade
Ebony M. McMillian	Takoma Park Middle School, 8th grade
Anetra E. Moore	Gaithersburg Middle School 7th grade
Sruthi Pandipati	Cabin John Middle School, 8th grade
Anna Pazos	Rockville High School, 9th grade
Joelle N. Price	Springbrook High School, 9th grade
Ellen H. Teng	Ridgeview Middle School, 8th grade
Teresa H. Tien	Ridgeview Middle School, 8th grade
Vinh Tong	Quince Orchard High School, 9th grade
Jennifer D. Wallen	Redland Middle School, 8th grade
Lindsey C. Weber	John T. Baker Middle School, 8th grade

Contacts for Howard Hughes Medical Institute Precollege Science Education Initiatives in the Washington, D.C., Metropolitan Area

Howard Hughes Medical Institute Summer Research Fellowship Program at the National Institutes of Health

Michael Gottesman, M.D., Deputy
Director for Intramural Research
National Institutes of Health
Building 1, Room 114
Bethesda, MD 20892
phone: 301-496-1921
fax: 301-402-0450
mgottesman@nih.gov

Lois Kochanski, Executive Director
Foundation for Advanced Education in the Sciences
Box 101, One Cloister Court
Bethesda, MD 20814-1460
phone: 301-496-7975
fax: 301-402-0174
kochanski@faes.od.nih.gov

Montgomery County Public Schools and Audubon Naturalist Society Collaboration in Elementary Science Education

Dr. Jane Netting Huff
Education Director
Audubon Naturalist Society
8940 Jones Mill Road
Chevy Chase, MD 20815
phone: 301-652-9188
fax: 301-951-7179

William McDonald
Elementary Science Coordinator
Montgomery County Public Schools
850 Hungerford Drive
Rockville, MD 20850-1747
phone: 301-279-3423
fax: 301-279-3153
bill_mcdonald@fc.mcps.k12.md.us

Montgomery County Public Schools and Chesapeake Bay Foundation Collaboration in Elementary Science Education

Kathleen A. Bettinger
Resource Teacher
Global Ecology Studies Program
Poolesville High School
17501 Willard Road
Poolesville, MD 20837
phone: 301-972-7916
fax: 301-972-7943

Don Baugh
Vice President for Education
Chesapeake Bay Foundation
162 Prince George Street
Annapolis, MD 21401
phone: 410-268-8816
fax: 410-268-6687
cbf@ari.net

Montgomery County Public Schools Elementary Science Education

Gerald F. Consuegra, Ph.D.
Coordinator,
Secondary Science Education
Montgomery County Public Schools
850 Hungerford Drive
Rockville, MD 20850-1747
phone: 301-279-3398
fax: 301-279-3153
gerry_consuegra@fc.mcps.k12.md.us

William McDonald
Elementary Science Coordinator
Montgomery County Public Schools
850 Hungerford Drive
Rockville, MD 20850-1747
phone: 301-279-3423
fax: 301-279-3153
bill_mcdonald@fc.mcps.k12.md.us

Montgomery County Public Schools Student and Teacher Intern Program at the National Institutes of Health

Gerald R. Consuegra, Ph.D.
Coordinator,
Secondary Science Education
Montgomery County Public Schools
850 Hungerford Drive
Rockville, MD 20850-1747
phone: 301-279-3398
fax: 301-279-3153
gerry_consuegra@fc.mcps.k12.md.us

Sandy Shmookler, Assistant to the Superintendent for Resource and Internship Development
Montgomery County Public Schools
Room 149
850 Hungerford Drive
Rockville, MD 20850-1747
phone: 301-279-3432
fax: 301-279-3428
sandra_shmookler@fc.mcps.kla.md.us

Bruce Fuchs, Ph.D., Acting Director
Office of Science Education
National Institutes of Health
Room 5H01
6100 Executive Boulevard
Bethesda, MD 20892
phone: 301-402-2469
fax: 301-402-3034

Gloria Seelman, Office of Education
National Institutes of Health
Room 5H01
6100 Executive Boulevard
Bethesda, MD 20892
phone: 301-496-0608
fax: 301-402-3034
gq5@cu.nih.gov

Thomas Edison High School of Technology Summer Biotechnology Focus Program

Sandy Shmookler, Assistant to the Superintendent for Resource and Internship Development
Montgomery County Public Schools
Room 149
850 Hungerford Drive
Rockville, MD 20850-1747
phone: 301-279-3432
fax: 301-279-3428
sandra_shmookler@fc.mcps.kla.md.us

Jeffrey Laws
Science Resource Teacher
Thomas Edison High School of Technology
Montgomery County Public Schools
12501 Dalewood Drive
Wheaton, MD 20906
phone: 301-929-2186
fax: 301-929-2177
jlaws@umd5.umd.edu

Regional Awards in the Washington, D.C., and Baltimore Areas Under the National Grants Program

Regional Awards in the Washington, D.C., and Baltimore Areas Under the National Grants Program

In 1987 the Institute launched a grants program to strengthen science education and encourage talented young people to pursue research and teaching careers. The grants, which also support biomedical research abroad and research resources at U.S. medical schools, fund a wide range of institutions, including colleges and universities, medical schools, research institutes, science museums, and elementary and secondary schools. Several institutions in the Washington, D.C., and Baltimore areas have successfully competed through proposals to offer science education activities for prekindergarten through college.

Precollege Science Education

The Institute's precollege science education program aims to improve general scientific literacy through support of hands-on and inquiry-based science education programs at the elementary and secondary school levels. Grants are awarded to science museums and biomedical research institutions to support precollege programs for students and their families, for teachers, and for curriculum development.

Through a precollege science education initiative for science museums, approximately $10.5 million in five-year grants was awarded in 1992 and 1993 to 51 children's and youth museums, natural history museums, science and technology centers, aquaria, botanical gardens, and zoos (Table 15). With a major focus on elementary school children, this initiative complements the outreach activities funded by the Institute through the undergraduate science education program, primarily directed to secondary schools and teachers.

In June 1994 the Institute awarded a total of $10,325,000 in five-year grants to 42 institutions through its precollege science education initiative for biomedical research institutions (Table 16). Through this program initiative, medical schools, academic health centers, and research institutions provide hands-on research experience and science education for precollege students and teachers.

- In the program's first three years, over 210,000 students, 10,500 teachers, and 56,000 adults (family) participated in Institute-funded program activities across the nation. Many of these programs are directed to girls and to students historically underrepresented in the sciences.
- Nearly half of the students involved were very young—prekindergarten to third grade—confirming the Institute's commitment to provide opportunities to explore science at the earliest elementary school levels. An additional 25 percent of the children were in grades 4 and 5.

Under the Institute's precollege science education initiatives, awards are based on national competitions. Institutions are invited to submit proposals in response to a specific program announcement. In making the awards, the Institute relies on the recommendations of external and internal review panels. Awards made under these programs to institutions in the Washington, D.C., and Baltimore areas are listed below.

Table 15

Awards to Regional Institutions Under the Howard Hughes Medical Institute Precollege Science Education Initiative for Science Museums, 1992–1993

Program Director
Joe Harber
Project Director
Department of Education
Irvine Natural Science Center
8400 Greenspring Avenue
Stevenson, MD 21153
phone: (410) 484-2413
fax: (410) 484-5910
joeyharber@aol.com

The **Irvine Natural Science Center** is a natural history museum in Stevenson, Maryland. In 1993 the Institute awarded the Science Center $125,000 to support Natural Connections, a program that trains volunteers to work with small groups of inner-city elementary school children in outdoor science activities focusing on the characteristics and ecology of plants and animals. The activities are selected from the Outdoor Biology Instructional Strategies (OBIS) curriculum. With teenage volunteers from high school science classes as leaders, sessions for 3rd graders are held six times each year in school yards and local neighborhoods. During the summer, six weekly sessions for 8–10-year-olds are offered at recreation centers with the help of adults recruited from the local community. It is anticipated that 620 volunteers and 2,040 children from 20 pairs of schools and 10 recreation centers will have participated by the fifth year of the project.

Program Director
Sylvia M. James
Director of Education Programs
National Aquarium in Baltimore
Pier 3, 501 East Pratt Street
Baltimore, MD 21202
phone: (410) 576-3875
fax: (410) 659-0116
sjames@aqua.org

In 1993 the Institute awarded the **National Aquarium in Baltimore** $125,000 to provide support to the Baltimore public school system in implementing STARS (**S**cience: **T**hinking, **A**pplication, and **R**esearch **S**kills), a new science curriculum designed to meet the needs of urban children. The Aquarium will provide elementary school teachers with workshops, field experiences, and kits containing support materials. Enrichment classes are provided for 2nd- to 5th-grade students of the new curriculum. Grade 2 teachers study vertebrate and invertebrate structure, classification, and adaptation for survival. Hands-on sessions with live animals and artifacts reinforce lectures and observation sessions in the Aquarium. Grade 5 teachers study the natural and human history of the Chesapeake Bay through lectures, observations, and hands-on activities.

Program Director
Judy M. Manning, Ph.D.
Director, Science Outreach
NOAHS Center
National Zoological Park Department of Animal Health
3001 Connecticut Avenue, N.W.
Washington, DC 20008
phone: (202) 673-4689
fax: (202) 673-4733
nzpnc004@sivm.si.edu

In 1993 the Institute awarded the **National Zoological Park** $125,000 to conduct a multilevel science education program that targets minority populations in five Washington, D.C., area schools. The program focuses on 4th, 5th, and 6th grades, involving a total of 3,600 students. The activities include (1) Scientist in the Schools, an interactive lecture series, (2) workshops to develop multisensory activities for students as a complement to on-site visits, (3) class visits to zoo laboratories and participation with scientists in theme-related activities, (4) development of computer-assisted learning on zoo-based conservation biology with equipment and software placed in selected schools, and (5) teacher-selected student participation in five-week summer enrichment programs at the Zoo. The overall aim of the program is to foster a positive attitude toward science and scientists by providing alternate models, relevant experiences, and interesting activities.

Table 16

Awards to Regional Institutions Under the Howard Hughes Medical Institute Precollege Science Education Initiative for Biomedical Research Institutions, 1994

Program Director
Ines L. Cifuentes, Ph.D.
CASE Program Director
Carnegie Institution of Washington
1530 P Street, N.W.
Washington, DC 20005
phone: (202) 387-8103
fax: (202) 387-8092
icifuentes@science.pst.ciw.edu

The **Carnegie Institution of Washington** is an independent research institution in Washington, D.C. In 1994 HHMI awarded the Carnegie Institution $200,000 to support the First Light Science School, a neighborhood Saturday school focusing on interactive science and serving inner-city children in grades 3–6. Through a National Science Foundation award, the Carnegie Institution has established the Carnegie Academy for Science Education (CASE) to train K–6th-grade teachers in the District of Columbia public schools in science and mathematics. The First Light Science School serves as a laboratory and testing site for teaching interactive science to elementary school children. The Institute award supplements the National Science Foundation grant by providing funds for supplies, teacher stipends, computer equipment, and assessment activities.

Program Director
Jack G. Chirikjian, Ph.D.
Professor
Department of Biochemistry and Molecular Biology
Georgetown University Medical Center
3900 Reservoir Road, N.W.
Washington, DC 20007
phone: (202) 687-2160
fax: (202) 687-2232

In 1994 the Institute awarded **Georgetown University** $175,000 for Biotechnology Collaborative Research and Education (BIOCORE) Partnerships, a teacher training and outreach program in the Washington metropolitan area. The primary objective is to meet the need for biotechnology training for precollege teachers and to provide them with the necessary skills to incorporate biotechnology into the current science curriculum. A total of 20 teachers will be selected to participate in the project during the five-year period. They will be trained in workshops, followed by a summer experience in a research laboratory. Medical Center faculty will be recruited and selected on the basis of their willingness and commitment to contribute time, expertise, and laboratory resources to the program.

Program Director
Dwight L. Lassiter
Director, Dunbar/Hopkins Health Partnership
Johns Hopkins University School of Medicine
Johns Hopkins University Hospital
129 School of Medicine Administration Building
720 Rutland Avenue
Baltimore, MD 21205-4196
phone: (410) 955-1567
fax: (410) 955-4367

In 1994 the Institute awarded the **Johns Hopkins University School of Medicine** $175,000 for the "SEA" bound Academy, a partnership between the School of Medicine and the Dunbar Project. It aims to improve science and computer science education in six schools of inner-city Baltimore, grades 3 to 12, and to increase students' and parents' interest in science. The project has four components: (1) a Saturday Science Academy; (2) a Science Summer Scholars Academy to ease the transition from elementary to middle school and from middle to high school; (3) a Parent Academy to establish a network of parents who are both knowledgeable and involved in the project's science and technology efforts; and (4) program assessment.

Undergraduate Biological Sciences Education

The Institute's Undergraduate Biological Sciences Education Program has awarded $335 million since 1988 to strengthen life sciences education at 220 public and private colleges and universities. A primary objective is to attract and prepare students, including women and underrepresented minorities, for careers in science and science teaching. The Institute's undergraduate program is intended to enrich educational opportunities for science majors and enhance the general scientific literacy of students who major in nonscience subjects.

- Since 1988 the program has supported research by over 25,000 undergraduates. Of these, 56 percent are women and 27 percent are from underrepresented minorities.
- Faculty member appointments have totaled 239. The Institute has also supported the development or revision of over 4,800 courses covering 30 fields of biology and other disciplines.
- Grants have been used to develop science programs at elementary, middle, and high schools, particularly those in urban and rural areas. Almost 63,000 precollege students and 18,400 teachers have benefited from these outreach efforts. Of the students, 56 percent are women and 52 percent are from underrepresented minorities. Of the teachers, 58 percent are women and 20 percent are from underrepresented minorities.

Awards to institutions in the greater Washington, D.C., and Baltimore areas are listed in Table 17.

Table 17

Awards to Regional Institutions Under the Institute's Undergraduate Biological Sciences Education Program, 1992–1996

Program Director
Benedict T. DeCicco, Ph.D.
Professor
Department of Biology
Catholic University of America
Washington, DC 20064
phone: (202) 319-5269
fax: (202) 319-5721
decicco@cua.edu

Catholic University of America is a private doctoral institution in Washington, D.C. In 1994 the Institute awarded the University $1,200,000 to support (1) enhancements in the undergraduate teaching laboratories, to include renovation of the introductory biology laboratory and a facility used for science outreach to Washington, D.C.–area students, instrumentation for courses in biochemistry, cell and molecular biology, physiology, and other disciplines, and creation of an undergraduate computer laboratory; (2) summer research in faculty laboratories for students, with opportunities to present research at scientific meetings; and (3) enhancement of an existing outreach program to provide science footlockers with curricular materials and supplies to Washington, D.C., public schools.

Program Director
Joseph H. Neale, Ph.D.
Professor and Chair of Biology
427 Reiss Science Building
Georgetown University
37th and O Streets, N.W.
Washington, DC 20057
phone: (202) 687-5574
fax: (202) 687-5662
neale@guvm.georgetown.edu

Georgetown University is a private research institution in Washington, D.C. In 1992 the Institute awarded the University $1,000,000 to support (1) laboratory and curriculum development, to include new undergraduate concentrations in neurobiology and developmental biology and experiments and exercises involving computer analysis and microscopy in such disciplines as biochemistry, cell biology, genetics, and physiology; (2) a four-year research "track" for undergraduates, including women and underrepresented minorities, to provide stipends for summer experiences in University and medical school laboratories, enrollment in research-oriented courses, opportunities to present research, and other activities; and (3) outreach in the sciences to teachers and students in Washington, D.C., high schools, particularly those with significant minority enrollments.

Program Director
Clarence M. Lee, Ph.D.
Professor of Biology and Dean, College of Arts and Sciences
Locke Hall, Room 101
Howard University
2441 Sixth Street, N.W.
Washington, DC 20059
phone: (202) 806-6700
fax: (202) 806-4562

Howard University is a private, historically black research institution in Washington, D.C. The Institute awarded the University grants of $900,000 in 1988 and $1,800,000 in 1994 for combined total funding of $2,700,000 through the undergraduate program, with a supplement of $180,000 from another source. The 1994 grant supports a program that will include motivational and enrichment activities for underrepresented minority students in elementary through high school from the Washington, D.C., metropolitan area, such as academic preparation and counseling, and summer workshops in the biological sciences for elementary and junior high school teachers.

Program Director
Dr. Gary K. Ostrander
Associate Dean for Research
College of Arts and Sciences
Johns Hopkins University
222B Mergenthaler Hall
34 North Charles Street
Baltimore, MD 21218
phone: (410) 516-8215
fax: (410) 516-6017
gofish@jhu.edu

Johns Hopkins University is a private research institution in Baltimore, Maryland. The Institute awarded the University grants of $1,000,000 in 1989 and $1,800,000 in 1994, for a combined total of $2,800,000 through the undergraduate program. The 1994 grant supports (1) equipment acquisitions and renovations for undergraduate laboratory courses in such areas as biophysics, chemistry, genetics, and neurophysiology to provide hands-on laboratory experiences, expanded training in scientific concepts and research techniques, and increased biological examples in physical science courses; (2) stipends and other support for Johns Hopkins University undergraduates to conduct independent summer research; and (3) outreach activities, including opportunities for students from Baltimore-area historically black institutions to participate in biomedical research in the University's laboratories.

Program Director
Kathleen C. Blits, Ph.D.
Tutor
St. John's College
P.O. Box 2800
Annapolis, MD 21404
(410) 267-9197
(410) 263-4828 (fax)
k_blitz@sjca.edu

St. John's College is a private baccalaureate institution in Annapolis, Maryland. In 1996 the Institute awarded the College $1,000,000 to support (1) renovations and equipment for teaching laboratories, including a core molecular biology laboratory and a plant tissue culture facility, that will also be used for student-faculty research; (2) professional enrichment opportunities during the summer for faculty members to develop scientific knowledge and skills and to integrate that knowledge into the curriculum; (3) a partnership with a local Annapolis middle school with significant enrollments of underrepresented minority students, to include development of a curriculum in mathematics and science, teacher training, materials development, and assessment and dissemination of the new approach; and (4) off-campus summer research opportunities for College students at research-intensive institutions including the Johns Hopkins University School of Medicine and the National Institutes of Health.

Program Director
William J. Higgins, Ph.D.
Associate Professor of Zoology and
Associate Dean, College of Life Sciences
1212 Symons Hall
University of Maryland College Park
College Park, MD 20742
phone: (301) 405-2908
fax: (301) 314-9358
higgins@zool.umd.edu

University of Maryland College Park is a public research institution. In 1992 the Institute awarded the University $1,300,000 to support (1) development and implementation of upper-division laboratory courses in biochemistry, cell biology, genetics, and neurophysiology, to emphasize hands-on experimentation and encourage student research; (2) acquisition of teaching equipment for the new laboratories; and (3) summer and academic-year research experiences for students, including those from groups underrepresented in the sciences, to follow participation in the research-oriented laboratory courses.

Program Director (1996 Award)

Carol A Rouzer, Ph.D.
Associate Professor
Chemistry Department
Western Maryland College
2 College Hill
Westminster, MD 21157-4390
phone (410) 857-2492
fax:: (410) 857-2729
crouzer@nsl.wmc.car.md.us

Program Director (1993 Award)

G. Samuel Alspach Jr., Ph.D.
Chair and Professor of Biology
Department of Biology
Western Maryland College
2 College Hill
Westminster, MD 21157-4390
phone (410) 857-2403
fax: (410) 857-2729
salspach@nsl.wmc.car.md.us

Western Maryland College is a private liberal arts institution in Westminster, Maryland. In 1993 the Institute awarded the College $500,000 in support of (1) updated and enhanced laboratory instrumentation for undergraduate courses in molecular modeling and cell biology, and other courses in biology and biochemistry; (2) an expanded outreach program engaging Baltimore-area high school students and teachers in studies of the biology of the Chesapeake Bay, using the bay as a science laboratory; and (3) broadening opportunities for student laboratory experiences through on- and off-campus collaborations, to include student stipends, housing, and travel to present research results.

In 1996 the College received a grant of $700,000, making a total of $1,200,000. The 1996 grant supports (1) acquisition of microscopes for biology laboratories, renovations for student research facilities, and laboratory setups for emeritus scientists; (2) outreach to include curriculum and pedagogical development for middle school science teachers in Prince George's County, Maryland, and computers and microscopes for the schools; (3) an institute for emeritus scientists to mentor student researchers; and (4) undergraduate research conducted by teams of students at various educational levels.

Since 1988, the Institute has provided about $95 million in fellowship support to 1,400 students and physician-scientists who have shown strong promise of becoming tomorrow's leading biomedical researchers. Additional graduate education support has been provided through research resources grants to research and educational organizations such as the Cold Spring Harbor Laboratory and the Marine Biological Laboratory at Woods Hole. The Institute makes a special effort to encourage women and underrepresented minorities to apply to its three fellowship programs:

- **Predoctoral Fellowships in Biological Sciences** are awarded for up to five years of full-time study toward the Ph.D. or Sc.D. degree in specified biological disciplines. The Institute currently supports more than 350 predoctoral fellows at $10 million annually. Women have received 42 percent of the predoctoral fellowships since 1988; underrepresented minorities have received 12 percent.
- **Research Training Fellowships for Medical Students** go to students enrolled in U.S. medical schools, primarily for one year of full-time research. Fellows may apply for a second year of research support, and they may also compete for continued fellowship support for up to two years while they complete their M.D. studies. Presently, 100 fellows receive Institute support at $2.7 million annually. Women have received 36 percent of the initial research year fellowships since 1989; underrepresented minorities have received 11 percent.
- **Postdoctoral Research Fellowships for Physicians** provide support for three years of full-time research. Currently 88 postdoctoral fellows are receiving Institute support at $6.5 million annually. Women have received 21 percent of these fellowships since 1990; underrepresented minorities have received 4 percent.

Eleven predoctoral fellows are studying at the Catholic University of America, Georgetown University, Johns Hopkins University, and the University of Maryland College Park. One medical student fellow is participating in a year of research at Georgetown University and one at Johns Hopkins University. In addition, three medical student fellows are being supported while completing their medical degree at Johns Hopkins University. Three physician postdoctoral fellows are at the National Institutes of Health (Table 18).

Table 18

Awards to Regional Institutions for Fellows Supported Under the Howard Hughes Medical Institute Graduate Science Education Program, 1995–1996

Predoctoral Fellowships in Biological Sciences

Catholic University of America

Fellowship Officer:
John E. Lynch, Ph.D.
Associate Academic Vice President for Graduate Studies
phone: (202) 319-5247
fax: (202) 319-3199
e-mail: lynch@cua.edu

Emmanuel Jerry Green
Cell and Molecular Biology Department

Georgetown University

Fellowship Officer:
Mary E. Schmiedel
Assistant Director, Office of Sponsored Programs
phone: (202) 687-3911
fax: (202) 687-4555
e-mail: schmiedm@gunet.georgetown.edu

Alexander Jude Adduci
Pathology Department

Johns Hopkins University

Fellowship Officer:
Milton Thomas Cole, Ph.D.
Homewood Research Administrator
phone: (410) 516-8668
fax: (410) 516-7775
e-mail: mtc@jhuspo.ca.jhu. edu

Carlos D. Aizenman-Stern
Neuroscience Department
Research Mentor, David J. Linden, Ph.D.
Synaptic plasticity

Pamela Lynn Bradley
Biochemistry, Cellular and Molecular Biology Program

Josh David Lauring
Biochemistry, Cellular and Molecular Biology Program
Research Mentor, Mark Steven Schlissel, M.D., Ph.D., Department of Molecular Biology and Genetics
Transcriptional regulation of the recombination activating genes, RAG-1 and RAG-2, during lymphocyte development

Brian Christopher Lewis
Human Genetics Program
Research Mentor, Chi V.Dang, M.D., Ph.D., Department of Medicine
Characterization of cbl1, a novel growth-related gene

Karen Etta Miller
Biochemistry, Cellular and Molecular Biology Program
Research Mentor, Janice E. Clements, Ph.D., Department of Molecular Biology and Genetics
Cloning the visna virus receptor

Laura Rusché
Biochemistry, Cellular and Molecular Biology Program
Research Mentor, Barbara Sollner-Webb, Ph.D., Department of Biological Chemistry
RNA editing in kinetoplastids: the mechanism and protein cofactors

Kimberly Michelle Taylor
Department of Biophysics
Research Mentor, Peter L. Privalov, Ph.D.
Energetic basis of the structure of multidomain and dimeric proteins

Paul Dylan Wes
Biochemistry, Cellular and Molecular Biology Program
Research Mentor, Craig Montell, Ph.D., Department of Biological Chemistry
Calcium signaling: lessons from Drosophila *vision*

University of Maryland College Park

Fellowship Officer:
William Hodos, Ph.D.
Associate Dean and Director Graduate Fellowship Office
phone: (301) 405-4206
fax: (301) 314-9305
e-mail: hodos@bss3.umd.edu

Christina Lynn Burch
Department of Zoology
Research Mentor, Lin Chao, Ph.D.
Beneficial and deleterious mutations to test Fisher's geometric model of mutation

Research Training Fellowships for Medical Students

Georgetown University

Fellowship Officer:
James F. Burris, M.D.
Associate Dean for Research Operations
phone: (202) 687-2585
fax: (202) 687-7007

Year of Research
Adam Robert Burkey
Research Mentor, Luc Jasmin, M.D., Ph.D.
Neurosurgery Department
Functional anatomy of cortical pain inhibition

Johns Hopkins University

Fellowship Officer:
H. Franklin Herlong, M.D.
Associate Dean for Student Affairs, School of Medicine
phone: (410) 955-3416
fax: (410) 955-0544

Year of Research
Amer Samdani
Research Mentors, Ted Dawson, M.D., Ph.D., and Valina Dawson, Ph.D.
Neurology Department
Nitric oxide mediates potentiation of neurotoxicity by neurotrophins

Completion of Medical Studies
Tuan Tuong Lam
Michael E. Matos
Kimberly Moore

Postdoctoral Research Fellowships for Physicians

National Institutes of Health

Fellowship Officer:
Carole Hackett
Grants Program Manager
Foundation for Advanced Education in the Sciences
phone: (301) 496-8063
fax: (301) 480-5319

Eric Charles Holland, M.D., Ph.D.
Research Mentor, Harold Varmus, M.D.
National Cancer Institute
Transgenic mouse models for glioblastoma

Robert S. Sikorski, M.D., Ph.D.
Research Mentor, Harold Varmus, M.D.
National Cancer Institute
p16 *mutations in melanoma, and development of software tools to analyze complex genetic changes in human cancer*

Joseph Michael Vinetz, M.D.
Research Mentors, David Kaslow, M.D., and Louis H. Miller, M.D.
National Institute of Allergy and Infectious Diseases
The chitinase of Plasmodium: *a stage-specific mosquito invasion factor and transmission-blocking vaccine candidate for malaria.*

Participants

Table 19

Students Participating in the Washington, D.C., Metropolitan Area Precollege Science Education Initiatives of the Howard Hughes Medical Institute, 1995–1996

Ackerly, Dana, St. Albans School
Afonso, Anoushka, James Madison High School
Agarwal, Parul, Albert Einstein High School
Agyeman, Sheila, DuVal High School
Ahmed, Rizwan, West Springfield High School
Ajayi, Funminiyi, Springbrook High School
Aksamit, Tracy L., Rockville High School
Amaral, Jen, Langley High School
Anyanwu, Azunna, Benjamin Banneker High School
Arora, Rachna, Seneca Valley High School
Ashmeade, Nykia, Watkins Mill High School
Baines, Andrea, Damascus High School
Bajaj, Kamini, Wheaton High School
Ballard, Yvonne, Frederick Douglass High School
Banninthaya, Ramya, Sherwood High School
Barber, Taryn, Gwynn Park High School
Barnes, Kirsten, Seneca Valley High School
Barton, Travis, T. C. Williams High School
Baxter, Jessica, John F. Kennedy High School
Beale, Melinda, Fairmont Heights High School
Behnam, Marcelina, Episcopal High School
Ben Adada, Amine, Bell Multicultural High School
Berger, Elana, Montgomery Blair High School
Berkovich, Leona, Yeshiva of Greater Washington
Bomar, Stephanie, Lake Braddock Secondary School
Boni-Saenz, Alex, Landon School
Bortnick, Rachel, Walter Johnson High School
Boyle, Gerry, DeMatha High School
Brennan, Sean R., St. Anselm's Abbey School
Britt, Amanda, South Lakes High School
Brophy, Christine, Mount Vernon High School
Buchanan, Yusef, Laurel High School
Burke, Sean, DeMatha High School
Burton, Kirsten, Episcopal High School
Cabrera, Jennifer, Winston Churchill High School
Carroll, Jason, Sidwell Friends School
Carey, Lauren C., Montgomery Blair High School
Carlson, Rachel P., Takoma Park Middle School
Chandra, Shruti, Robert E. Lee High School
Chandrasekaran, Radhika, Gaithersburg High School
Chi, Sulene, Thomas S. Wootton High School
Chien, Gene, Langley High School
Ching, Kean, Gaithersburg High School
Cho, Nancy, Walt Whitman High School
Chou, Jeremy, Thomas S. Wootton High School
Chuppe, Jennifer, Bishop Denis J. O'Connell High School
Clark, Theresa, St. Vincent Palotti High School
Cochran, Lauren, Walt Whitman High School
Cocoli, Myrvet, McLean High School
Cooper, Ansumana, Rockville High School
Cross, Anna, Richard Montgomery High School
Czerska, Zosia A., John F. Kennedy High School
Dahn, Martin, Rockville High School
Darlington, Leonora, High Point High School
David, Semuteh, John F. Kennedy High School
DeConti, Sabrina A., Damascus High School
DeLuca, Catie, Stone Ridge School of the Sacred Heart
Dewey, Kathryn, Thomas Stone High School
Dharia, Premal, Madeira School
Dombrowski, Matthew, Fairfax High School
Donellan, Matt, Thomas S. Wootton High School
Dong, Chenxi, Bethesda-Chevy Chase High School
Drury, Chris, Walter Johnson High School
Duggal, Sachin, Gaithersburg High School
Dzirasa, Kafui, Springbrook High School
Dula, Princess L., William H. Farquhar Middle School
Ebrahimi, Nassim, Walter Johnson High School
Edelson, Eric, Sidwell Friends School
Elliott, Jernee, Frederick Douglass High School
Fajner, Gisela, Wheaton High School
Fenyes, Gabor, Bethesda-Chevy Chase High School
Fife, Brendan, Albert Einstein High School
Fife, Timothy, Albert Einstein High School
Fisher, Mya, Eleanor Roosevelt High School
Fishman, David, Chelsea School
Flores, Karla, John T. Baker Middle School
Floyd, Matthew, Annandale High School
Fox, Sallie, Bishop Ireton High School
Francois, Johane, Springbrook High School
Franks, April, Walter Johnson High School
Freeman, Hannah, Rockville High School
Frichtl, Alison J., Albert Einstein High School
Fritz, Diane, McLean High School
Garg, Nikhil, St. Albans School
Gaudreault, Lauren, Hayfield Secondary School
Gellman, Melanie, Yeshiva of Greater Washington
Getek, Kathryn, Lake Braddock Secondary School
Ghebremichael, Asmara, Woodrow Wilson Senior High School
Gipstein, Bree, Fairfax High School
Goel, Rupali, Gaithersburg Middle School
Goldberg, Julie, Montgomery Blair High School
Golden, Julia T., Ridgeview Middle School
Goldhar, Susan C., White Oak Middle School
Grant, Michael, Central High School
Gray, Vaughn T., St. Andrew's Episcopal School
Griffin, Robin, Eleanor Roosevelt Senior High School

Grimes, Elizabeth, Thomas Edison High School of Technology
Hacker, Brian, Lake Braddock Secondary School
Hagemann, Ian, Thomas Jefferson High School for Science and Technology
Hague, Karen, Damascus High School
Haines, Meredith, T. C. Williams High School
Hankin, Nicole, Gaithersburg High School
Haque, Raqeeb, Walt Whitman High School
Harrison, Arrykka, Gwynn Park High School
Hawkins, Nicole, Eleanor Roosevelt Senior High School
Heffner, Scott, Centreville High School
Hemmingaard, Abraham, Damascus High School
Hober, Katherine, Springbrook High School
Holland, Angela, Queen Anne School
Holmes, Carmen, Montgomery Blair High School
House, Andrew, Frederick High School
Huang, Lilly, Thomas Edison High School of Technology
Huling, Andrew, St. Albans School
Irie, Masako, Thomas S. Wootton High School
Jahanmir, Sam, Quince Orchard High School
Jayson, Daniel S., St. Anselm's Abbey School
Jensen, Kyle, W. T. Woodson High School
Jesrani, Sonia, Paint Branch High School.
Johnson, Ann, Potomac School
Johnson, Jennifer, Archbishop Carroll High School
Jones, Nicholas, Thomas A. Edison High School
Kamanda, Olivier, Landon School
Karaian, John, Wheaton High School
Keller, Rachel, Gaithersburg High School
Kessel, Robin, Walter Johnson High School
Khair, Tina, St. Vincent Palotti High School
Kin, Andrew, Winston Churchill High School
Kin, Cindy, Winston Churchill High School
Klang, Judy, John F. Kennedy High School
Kline, Rachel, Maret School
Kodukula, Bala, High Point High School
Kumar, Ankur, Sidwell Friends School
Lawal, Farah L., Takoma Park Middle School
Lee, Anne, Hayfield Secondary School
Lee, Brian, Centennial High School
Lee, Joe, Barrie School
Lee, John, Heights School
Lee, Marian, Winston Churchill High School
Levine, Ariel, Charles E. Smith Jewish Day School
Levine, Yoni, Hebrew Academy of Greater Washington
Levsky, Jeffrey, Hebrew Academy of Greater Washington
Li, Yimin, Bethesda-Chevy Chase High School
Little, Gia, Crossland High School
Liu, Rosemarie, Lake Braddock Secondary School
Liverpool, Heather, Friendly High School
Longman, Randy, Charles E. Smith Jewish Day School
Lwin, Waymee, Albert Einstein High School
Maalouf, Khalil, Woodrow Wilson Senior High School
Mackey, Charles, Forestville High School
MacWilliams, Lauren, Academy of the Holy Cross
Malmberg, Catherine, Thomas Jefferson High School for Science and Technology
Martel, Peter, Chelsea School
Martin, Emily Sama, Connelly School of the Holy Child
McArthur, Kim, Connelly School of the Holy Child
McLaughlin-Williams, Justin, South Lakes High School
McMillian, Ebony M., Takoma Park Middle School
McTague, Ali, Montgomery Blair High School
Medley, Dawn, McKinley Senior High School
Mendoza, Michelle, Damascus High School
Meuchel, Jennifer, Maurice J. McDonough High School
Miller, Katherine, Walter Johnson High School
Mitchell, Clayton III, Archbishop Carroll High School
Moore, Anetra E., Gaithersburg High School
Mortl, Amanda, Bethesda-Chevy Chase High School
Moyer, Lisa, Georgetown Visitation Preparatory School
Munir, Jamalah, Oxon Hill High School
Munsayac, Rhacquel, Bishop Denis J. O'Connell High School
Nelson, Charkeeta, John F. Kennedy High School
Noble, Kevin, Mount Vernon High School
Nwaneri, Enyi, Eleanor Roosevelt High School
Ohle, Becca, St. Andrew's Episcopal School
Oliver, Omarr, Fairmont Heights High School
Olmstead, Sarah, Maret School
Onalaja, Ava, Montgomery Blair High School
O'Reilly, Kate, Georgetown Visitation Preparatory School
Orr, Maya, Duke Ellington School of the Arts
Overton, Larry II, Benjamin Banneker High School
Owolabi, Timothy, Colonel Zadok Magruder High School
Paik, David Sunghan, Oakton High School
Pandipati, Sruthi, Cabin John Middle School
Parker, Margaret, National Cathedral School
Pasquale, Michael, Bishop Ireton High School
Pathak, Kamal, Watkins Mill High School
Patterson, Maketa, John F. Kennedy High School
Paul, Martine, Rockville High School
Pawar, Rahul, Watkins Mill High School
Pazos, Anna, Rockville High School
Perrine, John, Robert E. Lee High School
Pickard, Charles II, Crossland High School
Pierre, Lisa Marie, Gaithersburg High School
Platts, Jamie, St. Albans School
Pletneva, Maria, Montgomery Blair High School
Porter, Adrian, Annandale High School
Prager, Ilan, Hebrew Academy of Washington
Pressman, Karen, Charles E. Smith Jewish Day School
Price, Joelle N., Springbrook High School
Price, Kenyona, Anacostia Senior High School
Raja, Samina, Chantilly High School
Regeimbal, James, Sherwood High School
Richard, Jacob, Watkins Mill High School

Robertson, Jennifer, Duke Ellington School of the Arts
Roddy, Christine, Academy of the Holy Cross
Rodriguez, Jennifer, Centreville High School
Ryu, Jungwook, Seneca Valley High School
Said, Muhammad, Rockville High School
St. Ulme, Danielle, Montgomery Blair High School
Sanders, Danielle, Watkins Mill High School
Sandler, Joel, Charles E. Smith Jewish Day School
Saunders, Lisa, DuVal High School
Sayah, Anousheh, Thomas A. Edison High School for Science and Technology
Schaffter, Brian, West Potomac High School
Schulman, Brian, Hammond High School
Scott, Amanda, Central High School
Serrette, Kyle, Edmund Burke School
Shen, Qian, Walt Whitman High School
Shukla, Siddhartha, Washington-Lee High School
Siguitan, Janice, Bishop Denis J. O'Connell High School
Skene, Jennifer, Oakton High School
Smith, Gemma, St. Andrew's Episcopal School
Smith, Ivonna, Eastern High School
Smith, Shelby, Potomac School
Smolka, Keri, Stone Ridge School of the Sacred Heart
Song, Virginia, Chantilly High School,
Steadman, Ahmed, Oxon Hill High School
Stein, Margaret, Hebrew Academy of Greater Washington
Stranges, Elizabeth, Montgomery Blair High School
Strickland, Taneeka, Surrattsville High School
Sweatmon, Joseph, McKinley Senior High School
Tamaddon, Sima, Hayfield Secondary School
Tan, Marian, Thomas S. Wootton High School
Taneja, Baninder, Thomas Jefferson High School for Science and Technology
Teng, Ellen H., Ridgeview Middle School
Tien, Teresa H., Ridgeview Middle School
Tingem, Juanna, Albert Einstein High School
Tong, Vinh, Quince Orchard High School
Toppin, Catherine, Queen Anne School
Trask, Christopher, Sherwood High School
Tripathi, Manish, Montgomery Blair High School
Tseng, Wendy, Paint Branch High School
Tun, Sandi, Richard Montgomery High School
Twerski, Chaya, Yeshiva of Greater Washington
Tyan, Gilbert, Winston Churchill High School
Ueng, Li-Ming, Walter Johnson High School
Van Degrift, Emily, Thomas S. Wootton High School
Vargas, Jose, Colonel Zadok Magruder High School
Vasudevan, Keno, Forestville High School
Vedula, Anil, Thomas S. Wootton High School
Villalobos, Veronica, Thomas Edison High School for Technology
Vohra, Arvin, Landon School
Wallen, Jennifer D., Redland Middle School
Walters, James, Bethesda-Chevy Chase High School
Washington, Deidre, Oxon Hill High School
Weber, Lindsey C., John T. Baker Middle School
Wells, Stephen, Chelsea School
Westergaard, Chandra, Governor Thomas Johnson High School
White, Rachel, W. T. Woodson High School
Whitman, Mary, Thomas S. Wootton High School
Wilder, Julius, Seneca Valley High School
Williams, Thomas, Wheaton High School
Williams, Tina, Friendly High School
Wong, Regina, Watkins Mill High School
Wood, March, Eleanor Roosevelt High School
Wroblewski, Wendy, Thomas S. Wootton High School
Xu, Zi-Rong, Albert Einstein High School
Yazdi, Vida, Charles E. Smith Jewish Day School
Yen, Wei Wei, Herndon High School
Yi, John, Heights School
Yoo, Jane, West Springfield High School
Young, Andrea, James Madison High School
Younis, Sabina, West Potomac High School
Zaborsky, Jennifer, Herndon High School
Zelaya, Katia, Bell Multicultural Senior High School
Zimmerman, Stefan, Oakland Mills High School

Table 20

Teachers Participating in the Washington, D.C., Metropolitan Area Precollege Science Education Initiatives of the Howard Hughes Medical Institute, 1995–1996

Adler, Lesli, Thomas S. Wootton High School
Allnutt, Elaine, Julius West Middle School
Ashbert, Ann, Colonel E. Brooke Lee Middle School
Autry, Gretchen, Forest Oak Middle School
Basgier, Fred, Seneca Valley High School
Bates, Mary Kay, Quince Orchard High School
Bauer, Janet, Richard Montgomery High School
Bedford, Ann, Montgomery County Public Schools
Behrens, Rosemary, Springbrook High School
Bennett, Leslie, Albert Einstein High School
Bettinger, Kathleen, Poolesville High School
Blair, Kathy, Herbert Hoover Middle School
Bosse, Angelique, Montgomery Blair Magnet School
Brinsko, Ellen, Paint Branch High School
Brown, Dewey, Wheaton High School
Brown, Virginia J., Winston Churchill High School
Burdett, Mavis, Thomas S. Wootton High School
Canham, Christina, Thomas S. Wootton High School
Carey, Nancy, Colonel E. Brooke Lee Middle School
Chagalis, Karen, Rockville High School
Chisser, Jackie, Gaithersburg Middle School
Christiansen, Steve, Colonel Zadok Magruder High School
Cross, Mary, Sherwood High School
Davis, Marie, Sligo Middle School
Deprey, Nancy, John T. Baker Middle School
Diehl, Patricia, Carl Sandburg Learning Center
Dietsch, Barbara, Cabin John Middle School
Faust, Ernest, Sherwood High School
Feldhuhn, Susan, Springbrook High School
Freiland, Bernard, Sherwood High School
Fujiwara, Jacquelyn, Julius West Middle School
Furr, Karen, Thomas Edison High School of Technology
Gabel, Daniel, Gaithersburg Middle School
Garms, Signe, Walt Whitman High School
Ghent-Paloucci, Helen J., Richard Montgomery High School
Gochnour, Gregg, Rockville High School
Goldenson, David, Albert Einstein High School
Goudy, Juanita, Sligo Middle School
Grant, Christine, Quince Orchard High School
Greenwood, P., Gaithersburg Middle School
Gregory, Carol, Quince Orchard High School
Gwin, Margaret, Forest Oak Middle School
Hall, Margy, Gaithersburg Middle School
Hashmon, Molly, Wood Middle School
Hauber, Emily, Watkins Mill High School
Hepner, Susan, Roberto W. Clemente Middle School
Hillsman, Doria Estelle, Rockville High School
Hodos, Jeffrey, Richard Montgomery High School
Horner, Susanna, Lothrop E. Smith Environmental Education Center
Hudson, John, Rockville High School
Jacoby, Douglas, John T. Baker Middle School
Keiser, Galen, John F. Kennedy High School
Kucsan, Pamela, Neelsville Middle School
Lamaze, Catherine, Quince Orchard High School
Lee, Brenda, Gaithersburg Middle School
Link, Gerald, Quince Orchard High School
Lock, John, Roberto W. Clemente Middle School
Lugo, Michelle, Key Middle School
Luttner, Roxann, Robert Frost Middle School
Lynch, Maria, Gaithersburg High School
Malker, Edgar, Rockville High School
Maloney, Jean, Watkins Mill High School
Marker, Jeff, Quince Orchard Middle School
Marstiller, Julie, Chevy Chase Elementary School
McAneny, Sally, Gaithersburg High School
McCabe, Daniel, Thomas W. Pyle Middle School
McComas, Elena, Colonel Zadok Magruder High School
Miller, Richard, Seneca Valley High School
Monine, Carole, Gaithersburg Middle School
Moran, Meryl, White Oak Middle School
Morris, Dave, Gaithersburg Middle School
Niedbalski, Linda, Walt Whitman High School
O'Connor, Courtney, White Oak Middle School
Osmun, Donald, Wheaton High School
Palkovic, Ivan, Colonel Zadok Magruder High School
Palmer, Feliciz Williams, Gaithersburg Middle School
Paper, Susanne, Gaithersburg Middle School
Parizer, Stefanie, John T. Baker Middle School
Parsons, Judith, Thomas S. Wootton High School
Partlow, Katherine, Julius West Middle School
Patterson, Ina, Gaithersburg Middle School
Pax, Julie, Walt Whitman High School
Phillips, Jean, Forest Oak Middle School
Pisciotta, Elena, Montgomery Blair High School
Powell, Helen, Sligo Middle School
Price, Judith, Watkins Mill High School
Quave, Helen, Wood Middle School
Reams, Cathy, Walt Whitman High School
Reilly, Michelle, Eastern Middle School
Richards, Pat, Sligo Middle School
Ruppert, Judith, Walter Johnson High School
Russell, Jennifer, Bethesda-Chevy Chase High School
Sanderson, Keith, Thomas S. Wootton High School
Schulz, Cynthia, Eastern Middle School
Shaw, Rosemary, Walt Whitman High School
Shellabarger, Kathy, Gaithersburg Middle School

Shipmon, Shelia, Gaithersburg High School
Slatniske, Gregory, Gaithersburg Middle School
Smiley, Martin, Gaithersburg Middle School
Smith, Denise, Springbrook High School
Smith, Phoebe, Diamond Elementary School
Stouffer, Cynthia, Cabin John Middle School
Stross, Beverly, Richard Montgomery High School
Sutton, Bill, John T. Baker Middle School
Swimpson, Inge, Gaithersburg Middle School
Sykes, Theresa, White Oak Middle School
Symons, Deborah, Cabin John Middle School
Thomesson, Clarissa, Gaithersburg Middle School
Tiso, Kathy, Rosa Parks Middle School
Townsend, Traci, Gaithersburg High School
Trams, Barney, Eastern Middle School
Tredwell, Diane, Chevy Chase Elementary School
Trulio, Virginia, Walt Whitman High School
Urband, Jackie, Quince Orchard Middle School
VonArx, Anna, John F. Kennedy High School
Von Secker, Clair, Walt Whitman High School
Vu, Phuong, Takoma Park Middle School
Walker, Thomas, Gaithersburg Middle School
Walton, Sharon, Watkins Mill High School
Wang, Mei, Montgomery Blair High School
Wilkinson, Frank, Roberto W. Clemente Middle School
Williams, Marilyn, Paint Branch High School
Wise, Judith, Watkins Mill High School

Table 21

Preceptors Participating in the Howard Hughes Medical Institute Student and Teacher Intern Program (1995–1996) and the Summer Research Fellowship Program (1996) at the National Institutes of Health

Alkon, Daniel, M.D., Laboratory of Adaptive Systems, National Institute of Neurological Disorders and Stroke

Altemus, Margaret, M.D., Laboratory of Clinical Science, National Institute of Mental Health

Arora, Krishnan K., Ph.D., Section on Hormonal Regulation, Endocrinology and Reproduction Research Branch, National Institute of Child Health and Human Development

Ashwell, Jonathan, M.D., Laboratory of Immune Cell Biology, National Cancer Institute

Barsony, Julianna, M.D., Ph.D., Laboratory of Cell Biology and Genetics, National Institute of Diabetes and Digestive and Kidney Diseases

Beaucage, Serge, Ph.D., Biological Psychiatry Branch, National Institute of Mental Health

Bondy, Carolyn, M.D., Developmental Endocrinology Branch, National Institute of Child Health and Human Development

Brady, John, Ph.D., Laboratory of Molecular Biology, National Cancer Institute

Colburn, Nancy, Ph.D., Laboratory of Viral Carcinogenesis, National Cancer Institute

Crawley, Jacqueline, Ph.D., Section on Behavioral Neuropharmacology, Experimental Therapeutics Branch, National Institute of Mental Health

Figg, William, Pharm.D., Clinical Pharmacology Branch, National Cancer Institute

Fojo, Tito, Medicine Branch, National Cancer Institute

Fornace, Albert J. Jr., M.D., Laboratory of Molecular Pharmacology, Division of Cancer Treatment, National Cancer Institute

Fox, Philip, D.D.S., Clinical Investigations Section, National Institute of Dental Research

Gentleman, Susan, Ph.D., Laboratory of Retinal Cell and Molecular Biology, National Eye Institute

Ginns, Edward, M.D., Ph.D., Section on Molecular Neurogenetics, Clinical Neuroscience Branch, National Institute of Mental Health

Glick, Adam B., Ph.D., Laboratory of Cellular Carcinogenesis and Tumor Promotion, Division of Cancer Biology, National Cancer Institute

Gottesman, Susan, Ph.D., Laboratory of Molecular Biology, National Cancer Institute

Green, Eric, M.D., Ph.D., Genome Technology Branch, National Center for Human Genome Research

Green, Kim, Ph.D., Laboratory of Infectious Diseases, National Institute of Allergy and Infectious Diseases

Guroff, Gordon, Ph.D., Section on Growth Factors, National Institute of Child Health and Human Development

Guroff, Marjorie, Ph.D., Laboratory of Tumor Cell Biology, Division of Cancer Treatment, National Cancer Institute

Hager, Gordon, Ph.D., Section on Hormone Action and Oncogenesis, Laboratory of Molecular Virology, National Cancer Institute

Herman, Mary, M.D., Neuropathy–Clinical Brain Disorders Branch, National Institute of Mental Health

Hoffman, Thomas, M.D., Laboratory of Cell Biology, Center for Biologics Evaluation and Research, Food and Drug Administration

Hunziker, Rosemarie, Ph.D., Transgenic Mouse Facility, National Institute of Allergy and Infectious Diseases

Iadorola, Michael, Ph.D., Neurobiology and Anesthesiology Branch, National Institute of Dental Research

Kalebic, Thea, M.D., Ph.D., Laboratory of Molecular Oncology, National Cancer Institute

Kamata, Tohru, Ph.D., Laboratory of Biochemical Physiology, National Cancer Institute

Kastner, Daniel, M.D., Ph.D., Arthritis and Rheumatism Branch, National Institute of Arthritis and Musculoskeletal and Skin Diseases

Kozlowski, Steven, M.D., Laboratory of Molecular and Developmental Immunology, Division of Monoclonal Antibodies, Center for Biologics Evaluation and Research, Food and Drug Administration

Kulkarni, Ashok, Ph.D., Gene Targeting Research and Core Facility, National Institute of Dental Research

Leonard, Warren, M.D., Laboratory of Cell and Molecular Biology, National Heart, Lung, and Blood Institute

Li, Jian-Jian, Ph.D., Laboratory of Viral Carcinogens, National Cancer Institute

Linehan, Marston, M.D., Surgery Branch, National Cancer Institute

Loh, Y. Peng, Ph.D., Laboratory of Developmental Neurobiology, National Institute of Child Health and Human Development

Massaquoi, Steve, M.D., Human Motor Control Section, National Institute of Neurological Disorders and Stroke

McCartney-Francis, Nancy, Ph.D., Cellular Immunology Section, National Institute of Dental Research

Mishra, Bibhuti, M.D., Clinical Gene Therapy Branch, National Center for Human Genome Research

Noguchi, Constance, Ph.D., Laboratory of Chemical Biology, National Institute of Diabetes and Digestive and Kidney Diseases

O'Shea, John, M.D., Lymphocyte Cell Biology Section, Arthritis and Rheumatism Branch, National Institute of Arthritis and Musculoskeletal and Skin Diseases

Parsegian, Adrian, M.D., Laboratory of Structural Biology, Division of Computer Research and Technology

Philpott, Caroline, M.D., Cell Biology and Metabolism Branch, National Institute of Child Health and Human Development

Pommier, Yves, M.D., Ph.D., Laboratory of Molecular Pharmacology, Division of Cancer Treatment, National Cancer Institute

Powell, Sharon, Ph.D., Laboratory of Developmental Biology, National Institute of Dental Research

Qasba, Pradman, Ph.D., Laboratory of Mathematical Biology, National Cancer Institute

Ramsey, W. Jay, Ph.D., Clinical Gene Therapy Branch, National Center for Human Genome Research

Schwartz, Joan P., Ph.D., Clinical Neuroscience Branch, National Institute of Neurological Disorders and Stroke

Sidransky, Ellen, M.D., Clinical Neuroscience Branch, National Institute of Mental Health

Sobel, Mark E., M.D., Ph.D., Laboratory of Pathology, National Cancer Institute

Sorbara, Lynn, Ph.D., Biology–Laboratory of Pharmacology, National Cancer Institute

Staudt, Louis, M.D., Ph.D., Metabolism Branch, Division of Cancer Biology, Diagnosis, and Centers, National Cancer Institute

Sternberg, Esther M., M.D., Clinical Neuroendocrinology Branch, National Institute of Mental Health

Trepel, Jane, Medicine Branch, National Cancer Institute

Vinson, Charles, Ph.D., Laboratory of Biochemistry, National Cancer Institute

Weinberg, Wendy C., Ph.D., Laboratory of Cellular Carcinogenesis and Tumor Promotion, Division of Cancer Etiology, National Cancer Institute

Weissman, Drew, M.D., Ph.D., Laboratory of Immunoregulation, National Institute of Allergy and Infectious Diseases

Wickner, Reed, M.D., Laboratory of Biochemical Pharmacology, National Institute of Diabetes and Digestive and Kidney Diseases

Wolffe, Alan, Ph.D., Laboratory of Molecular Embryology, National Institute of Child Health and Human Development

Wu, Carl, Ph.D., Laboratory of Biochemistry, Developmental Biochemistry Section, National Cancer Institute

Table 22

Schools Participating in the Howard Hughes Medical Institute Washington, D.C., Metropolitan Area Precollege Science Education Initiatives, 1995–1996

Academy of the Holy Cross, Montgomery County, Maryland
Albert Einstein High School, Montgomery County, Maryland
Anacostia Senior High School, Washington, D.C.
Annandale High School, Fairfax County, Virginia
Archbishop Carroll High School, Washington, D.C.
Barrie School, Montgomery County, Maryland
Bell Multicultural Senior High School, Washington, D.C.
Benjamin Banneker Academic High School, Washington, D.C.
Bethesda-Chevy Chase High School, Montgomery County, Maryland
Bishop Denis J. O'Connell High School, Arlington, Virginia
Bishop Ireton High School, Alexandria, Virginia
Cabin John Middle School, Montgomery County, Maryland
Carl Sandburg Learning Center, Montgomery County, Maryland
Centennial High School, Howard County, Maryland
Central High School, Prince George's County, Maryland
Centreville High School, Fairfax County, Virginia
Chantilly High School, Fairfax County, Virginia
Charles E. Smith Jewish Day School, Montgomery County, Maryland
Chelsea School, Montgomery County, Maryland
Colonel Zadok Magruder High School, Montgomery County, Maryland
Connelly School of the Holy Child, Montgomery County, Maryland
Crossland High School, Montgomery County, Maryland
Damascus High School Montgomery County, Maryland
DeMatha Catholic High School, Prince George's County, Maryland
Diamond Elementary School, Montgomery County, Maryland
Duke Ellington School of the Arts, Washington, D.C.
DuVal High School, Prince George's County, Maryland
Eastern Middle School, Montgomery County, Maryland
Eastern Senior High School, Washington, D.C.
Edmund Burke School, Washington, D.C.
Eleanor Roosevelt High School, Prince George's County, Maryland
Episcopal High School, Alexandria, Virginia
Fairfax High School, Fairfax County, Virginia
Fairmont Heights High School, Prince George's County, Maryland
Forest Oak Middle School, Montgomery County, Maryland
Forestville High School, Prince George's County, Maryland
Frederick Douglass High School, Prince George's County, Maryland
Frederick High School, Frederick, Maryland
Friendly High School, Prince George's County, Maryland
Gaithersburg Middle/High School, Montgomery County, Maryland
Georgetown Visitation Preparatory School, Washington, D.C.
Governor Thomas Johnson High School, Frederick, Maryland
Gwynn Park School, Prince George's County, Maryland
Hammond High School, Howard County, Maryland
Hayfield Secondary School, Fairfax County, Virginia
Hebrew Academy of Greater Washington, Montgomery County, Maryland
Heights School, Montgomery County, Maryland
Herndon High School, Fairfax County, Virginia
High Point High School, Prince George's County, Maryland
James Madison High School, Fairfax County, Virginia
John F. Kennedy High School, Montgomery County, Maryland
John T. Baker Middle School, Montgomery County, Maryland
Julius West Middle School, Montgomery County, Maryland
Key Middle School, Montgomery County, Maryland
Lake Braddock Secondary School, Fairfax County, Virginia
Landon School, Montgomery County, Maryland
Langley High School, Fairfax, Virginia
Lathrop E. Smith Environmental Center, Montgomery County, Maryland
Madeira School, Fairfax, Virginia
Maret School, Washington, D.C.
Maurice J. McDonough High School, Baltimore, Maryland
McKinley Senior High School, Washington, D.C.
McLean High School, Fairfax, Virginia
Montgomery Blair Magnet School, Montgomery County, Maryland
National Cathedral School, Washington, D.C.
Neelsville Middle School, Mongomery County, Maryland
Oakland Mills High School, Montgomery County, Maryland
Oakton High School, Fairfax, Virginia
Oxon Hill High School, Prince George's County, Maryland
Paint Branch High School, Montgomery County, Maryland
Potomac School, Fairfax County, Virginia
Queen Anne School, Prince George's County, Maryland
Quince Orchard High School, Montgomery County, Maryland
Redland Middle School, Montgomery County, Maryland
Richard Montgomery High School, Montgomery County, Maryland
Ridgeview Middle School, Montgomery County, Maryland
Robert E. Lee High School, Montgomery County, Maryland
Robert Frost Middle School, Montgomery County, Maryland
Roberto W. Clemente Middle School, Montgomery County, Maryland
Rockville High School, Montgomery County, Maryland
St. Albans School, Washington, D.C.
St. Andrew's Episcopal School, Montgomery County, Maryland
St. Anselm's Abbey School, Washington, D.C.
St. Vincent Palotti High School, Prince George's County, Maryland
Seneca Valley High School, Montgomery County, Maryland
Sherwood High School, Montgomery County, Maryland
Sidwell Friends School, Washington, D.C.
South Lakes High School, Fairfax, Virginia
Springbrook High School, Montgomery County, Maryland
Stone Ridge School of the Sacred Heart, Montgomery County, Maryland
Surattsville High School, Prince George's County, Maryland
Takoma Park Middle School, Montgomery County, Maryland
T. C. Williams High School, Alexandria, Virginia
Thomas A. Edison High School, Fairfax, Virginia
Thomas Edison High School of Technology, Montgomery County, Maryland

Thomas Jefferson High School for Science and Technology, Fairfax County, Virginia
Thomas Stone High School, Waldorf, Maryland
Thomas S. Wootton High School, Montgomery County, Maryland
Thomas W. Pyle Middle School, Montgomery County, Maryland
Walt Whitman High School, Montgomery County, Maryland
Walter Johnson High School, Montgomery County, Maryland
Washington-Lee High School, Arlington, Virginia
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Howard Hughes Medical Institute
Office of Grants and Special Programs
4000 Jones Bridge Road
Chevy Chase, MD 20815-6789
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