



DORIS DUKE  
CHARITABLE FOUNDATION

# Medical Research Program BULLETIN

october 2004

## Program Director's Update

Once again, we are pleased to update the community on our programs. Now entering our seventh year, the Medical Research Program (MRP) has funded more than 172 grants totaling a commitment of over \$120 million to support and strengthen clinical research. Despite the challenges faced by clinical investigators, the opportunities for them to make a difference are unprecedented. This Bulletin highlights some of the work of our grantees who are making a difference.

This past year, two grant competitions were launched — the 2004 Distinguished Clinical Scientist Award competition and the second Clinical Interfaces Award Program competition — and we renewed the Doris Duke Clinical Research Fellowship (CRF) Program for another three years. Training and mentoring of junior clinical investigators continues to be a major part of both our U.S.-based programs and our international AIDS grants.

A few recent activities are worth noting. First, following the advice of our Scientific Advisory Council and other experts, the scope of the current Distinguished Clinical Scientist Award competition has been expanded beyond our original four disease areas — cardiovascular diseases, blood disorders, AIDS, and cancer — so that physician-scientists working in any area of translational clinical research can be nominated. Second, a new intellectual property policy (described in a following story) was developed for 10 grants awarded in 2003 to support development of low-cost AIDS diagnostics for use in the developing world. And finally, because we support open access publishing, we are making a small grant to the Public Library of Science which will enable our grantees to receive a 100% discount on publication charges for articles published in Public Library of Science journals for the next two years.

We appreciate being part of the clinical research community, and we thank our Scientific Advisory Council members and the many other experts who have provided advice throughout the year. •

Elaine K. Gallin, Ph.D.



Don Ganem and Joe DeRisi (Clinical Interfaces Award grantees) with Elaine Gallin at the March 2004 Doris Duke Clinical Scientist Meeting in Cold Spring Harbor, New York.

## DDCF Summary

The mission of the Doris Duke Charitable Foundation is to improve the quality of people's lives through grants supporting the performing arts, wildlife conservation, medical research, and the prevention of child maltreatment, and through preservation of the cultural and environmental legacy of Doris Duke's properties.

In addition to the Medical Research Program, the foundation awards grants in three other program areas:

- The Arts Program, which supports performing artists in the creation and public performance of their work;
- The Environment Program, which seeks to preserve wildlife in the U.S., both flora and fauna, by supporting efforts to complete the nation's wildlife conservation system; and
- The Child Abuse Prevention Program, which seeks to protect children from abuse and neglect in order to promote their healthy development.

The Foundation also oversees three properties that were owned by Doris Duke and are now open to the public — Duke Farms in Hillsborough, New Jersey; Shangri La in Honolulu, Hawaii; and Rough Point in Newport, Rhode Island.

### Staff of MRP

Elaine K. Gallin, Ph.D., Program Director  
Jessica Fanzo, Ph.D., Program Officer  
Latasha Jackson, M.S., Program Assistant

For more information about the foundation, visit [www.ddcf.org](http://www.ddcf.org).

# DISTINGUISHED CLINICAL SCIENTIST AWARD

## DIANNA MILEWICZ

### Combining Genetics and Cardiology to Prevent Aortic Aneurysms



**D**istinguished Clinical Scientist 2001 awardee Dianna Milewicz enjoys the career satisfaction of knowing that her work has helped save lives. Dr. Milewicz studies the genetic basis of aortic aneurysms (weakenings of the primary artery exiting the heart) that are a prelude to catastrophic failure and sudden death, accounting for approximately 20,000 deaths in the U.S. annually. Her work has yielded clues to its underlying cause and has raised awareness of the condition and its tendency to run in families. Today, many affected relatives are now being identified while they are still healthy, and can have their aneurysms repaired through surgery.

A native Texan, Dr. Milewicz was bitten by the research bug early and pursued projects in the lab during summers in high school. Having decided on a career in biomedical research, she gives credit to a series of knowledgeable mentors for sound advice and for pointing her in the right direction. After undergraduate studies at Rice University, Dr. Milewicz went on to earn an M.D. and Ph.D. from University of Texas Southwestern Medical School, where her thesis work with Dr. Richard G. Anderson centered on cholesterol trafficking within and between cells.

#### A Fellowship in Clinical Genetics Led to a Clinical Research Career

After an internal medicine residency and a short foray into cardiology, Dr. Milewicz began a fellowship in clinical genetics at the University of Washington, working with Dr. Peter Byers. Drs. Milewicz and Byers set out to determine the molecular

defect underlying Marfan syndrome. The disease is inherited as an autosomal dominant with characteristic skeletal and ocular features (Abraham Lincoln is thought to have had Marfan syndrome). While the visible manifestations are not life threatening, Marfan patients also have an aortic weakness. With age, the aorta progressively enlarges, and left untreated, it can tear or rupture (dissect), with a mortality rate within 48 hours of 90%. Fortunately, their visible skeletal features make Marfan patients relatively easy for clinicians to identify, and their expanded aortas can be surgically repaired with a Dacron graft. Twenty-year follow-up studies of those patients indicate that after surgery, they have a near-normal life expectancy.

Dr. Milewicz's work identified mutations in the gene fibrillin 1 (FBN1), which encodes a major component of extracellular microfibrils, as responsible for Marfan syndrome. After establishing her own lab at the University of Texas Health Sciences Center in Houston, Dr. Milewicz's group showed that a similar disease, congenital contractural arachnoidactyly, is caused by mutations in a related gene, fibrillin 2 (FBN2).

#### Focusing on Genes Responsible for Non-Marfan Cases of Aortic Dissection

Marfan syndrome accounts for only a small fraction of aortic aneurysm cases. What's worse, a developing aortic aneurysm is asymptomatic — in the absence of the characteristic Marfan external features, there is often no way to know who is at risk, until the patient, often in the prime of life, dies suddenly and an autopsy reveals the cause. With DDCF support, Dr. Milewicz has examined the family histories of aortic dissection patients, and has shown that 20% of cases have an affected relative, suggesting a genetic cause. In order to identify the genes responsible, her group is focusing on two candidate loci, that together account for more than 40% of inherited cases. But the search is

complicated by variable penetrance and expression; that is, not all who inherit the mutation have the disease, and the severity of disease and age of onset vary as well. Cases may be missed — with fewer families opting for autopsies, victims whose first and only symptom is sudden demise may have their deaths misattributed to fatal myocardial infarction (heart attack). Despite these difficulties, the work continues.

Recent high-profile articles about aortic aneurysm in the *Wall Street Journal* and *Washington Post* have greatly increased public awareness so that lives can be saved through preventive surgery. Dr. Milewicz is often contacted directly by patients asking for advice. With her efforts and those of others working in the field, many tragic deaths associated with aortic dissection may be averted in future generations. •

#### Distinguished Clinical Scientist Award

Since 1999, the Distinguished Clinical Scientist Award (DCSA) has recognized and supported the achievements and promise of outstanding mid-career physician-scientists working in four disease areas: AIDS, cancer, cardiovascular diseases, and sickle cell anemia and other blood disorders. Each awardee receives up to \$1.5 million to be used over five to seven years.

The 2004 competition has been open to physician-scientists working in any area of Translational Clinical Research. Nominations were received from 48 different institutions. It is expected that up to 4 grants will be awarded in December of 2004. A DCSA competition will not be held in 2005.

# DISTINGUISHED CLINICAL SCIENTIST AWARD

## DANIEL HABER

At the Forefront of Cancer Genetics



As a scientist-clinician specializing in cancer genetics, 2002 Distinguished Clinical Scientist awardee Daniel Haber works in the brave new world of genetic testing — identifying cancer susceptibility genes and genetic markers of drug response to cancer.

After undergraduate studies at the Massachusetts Institute of Technology (MIT), Dr. Haber earned his M.D. and Ph.D. degrees from Stanford University, where his research with Dr. Robert Schimke focused on the role of gene amplification in resistance to chemotherapy drugs. He then continued his medical training with an internship and residency at Massachusetts General Hospital (MGH), before taking a medical oncology fellowship at the Dana-Farber Cancer Institute, and finally, returning to MIT for postdoctoral work on the genetics of Wilms tumor, a pediatric kidney cancer.

### Focusing on Breast Cancer Genetics

Over the last decade, the genetics of breast cancer have been Dr. Haber's major focus. Research on human breast cancer genetics is in many respects a success story — work by Dr. Mary-Claire King and others showing mutations in the BRCA1 and BRCA2 genes are major risk factors in inherited predisposition to breast cancer has led to routine testing for women with a family history of breast and ovarian cancer. It has also led to the development of a procedure called prophylactic oophorectomy (removal of the ovaries) in women carrying these mutations, which effectively reduces the risk of ovarian or breast cancer. But the story is incomplete; many families

with inherited breast cancer do not carry BRCA mutations. This might be explained by the existence of a number of “low-penetrance” genes, which in combination may predispose to disease.

### Discovering the CHK2 Gene

Dr. Haber's group set out to identify new breast cancer risk genes, looking specifically at genes already known to function in maintaining genomic integrity and DNA repair. Remarkably, because these genes and their functions are conserved throughout a wide variety of species, Dr. Haber's group was the first to identify a candidate gene — CHK2 — in yeast cells, that is mutated in some families with a history of cancer. This gene regulates the function of two breast cancer genes: BRCA1 and p53. Subsequent work by Michael Stratton and others has shown that a specific mutation in the CHK2 gene (called 1100delC) is found at a frequency of 1% in the general population, but in as many as 5% of breast cancer families. Having the 1100delC mutation carries a 2–5 fold increase in risk of developing breast cancer. Because CHK2 is a low-penetrance gene, conferring only a modest increase in cancer risk, conveying clear and accurate information to patients is more difficult than for the BRCA genes. Developing and adhering to clear and ethical guidelines for patient privacy, disclosure and counseling are another goal of Dr. Haber's work, which is assisted by three full-time genetic counselors.

### A Single Genetic Marker Determines the Clinical Responsiveness of Lung Cancer to Iressa.

Most recently, Dr. Haber's group has uncovered the genetic basis for the response of lung cancers to the “smart drug” Iressa. Iressa belongs to a new class of anticancer agents, called tyrosine kinase inhibitors (TKI), modeled after the drug Gleevec, which induce a dramatic remission in patients with chronic myeloid leukemia. Iressa targets the epidermal growth factor receptor (EGFR), a molecule on the surface of many cancer cells which

signals the cells to grow. While clinical trials using Iressa to treat other cancers have generally yielded disappointing results, 10% of patients with non-small cell lung cancer (NSCLC) show remarkable clinical responses to Iressa.

Dr. Haber's research has demonstrated that virtually all patients with NSCLC who respond to Iressa have tumors with specific mutations in the EGFR gene. The mutations activate the EGFR gene, increasing the growth signals that it delivers to the cancer cells and, in particular, allowing the cancer cells to escape from death signals that would otherwise compromise their growth. However, the very same mutations in the EGFR gene also make the cancer cells extraordinarily responsive to Iressa. Together with his colleague Dr. Jeff Settleman, Dr. Haber's group showed that Iressa sensitivity results from the fact that cancer cells with these mutations have become dependent or “addicted” to the EGFR signal, and Iressa blocks this signal. These findings make it possible to predict which cases of NSCLC are likely to respond to Iressa and which cases are not responsive to the drug and should continue to receive intensive chemotherapy.

With our increasingly sophisticated understanding of the molecular basis of disease, future studies are likely to yield more such cases in which tumors can be genetically-typed for their drug sensitivity. Whether patients are “typed” for a number of different genes that identify an increased risk for developing a particular cancer, or whether tumors are screened for specific genetic alterations that are used to guide therapy, Dr. Haber's work is a model case for the future of cancer genetics. •

### Farewell

We would like to say farewell to and thank Sylvie Le Blancq, Ph.D., the Program Officer of MRP for the past 4 years.

# CLINICAL INTERFACES AWARD PROGRAM

**DON GANEM**

**JOSEPH DERISI**

**HOMER A. BOUSHEY**

**Searching for New Pathogens  
in Human Health and Disease**

The Clinical Interfaces Award Program was created to support multidisciplinary research teams that apply novel approaches to solving clinical problems. Don Ganem, Joseph DeRisi and Homer Boushey's collaborative DDCF-funded project, aimed at discovering new infectious agents through application of cutting-edge gene chip technology, embodies this approach.

## The Team

Don Ganem, M.D. is a renowned expert in infectious diseases, specifically the biology of human viral pathogens. He has worked extensively on how the viruses of hepatitis B and Kaposi's sarcoma cause their respective diseases. With his clinical training and expertise in virology, Dr. Ganem, like many others, suspects that viruses might underlie diseases whose origins are currently obscure. The search for these agents, however, has been hampered by current methodology, which tends to be non-systematic and time-consuming.

Enter Joseph DeRisi, Ph.D., a colleague of Dr. Ganem's at the Mission Bay campus of the University of California at San Francisco (UCSF). Dr. DeRisi is a pioneer in the field of bioinformatics and the design of microscopic arrays of defined DNA sequences for high-throughput genetic analyses.

Homer Boushey, M.D., a pulmonologist and Chief of the Asthma Clinical Research Center and Division of Allergy and Immunology at UCSF, also joined the team because of his interest in the role of viral respiratory infections in asthma and other chronic lung diseases of unknown etiology.

## The Technology

First articulated in discussions between Dr. DeRisi and one of his postdoctoral fellows, David Wang, who had done a stint in Dr. Ganem's lab, the idea is to bring the power of bioinformatics to bear upon the search for new viruses in settings and diseases carefully chosen to enhance the probability of a "hit." They designed a chip-based reagent — in essence, a microscope slide — containing sequences from every fully sequenced viral genome available in public databases. They validated the use of the chip using virus specimens grown in the Ganem lab, as well as with some clinical specimens provided by Dr. Boushey.

The chip was ready for further testing in January 2003, fortuitously just before the Asian outbreak of the contagious and potentially fatal respiratory disease SARS (severe acute respiratory syndrome). The UCSF team obtained clinical and labora-

tory samples from the Centers for Disease Control, and was among the first to sequence the DNA of the virus responsible for the disease, a novel member of the coronavirus family known as SARS CoV. These successes validated the strategy.

## Linking Viral Pathogens to Diseases

Now the team is addressing its next challenge: identifying new viruses associated with respiratory infections. An estimated 20–40% of common cold cases are caused by unknown agents, making this a prime area for potential discovery of new viruses. Because clinical samples are relatively painless to obtain, the problem is easily studied, and might result in new therapeutic targets to treat respiratory infections.

With the support of the Doris Duke Charitable Foundation, they also plan to look for new viruses in diseases for which a viral cause is at present unproven but suspected, including chronic lung and liver diseases such as asthma, primary biliary cirrhosis and idiopathic interstitial pneumonias. With the power of the latest technologies at their disposal, their work has remarkable potential to open new avenues of investigation for every disease they choose to target. •

## Clinical Interfaces Award Program

Established in 2003, the Clinical Interfaces Award Program (CIAP) is designed to encourage outstanding researchers from all scientific disciplines to collaborate and undertake innovative and novel clinical research to address important clinical problems. CIAP aims to catalyze clinical breakthroughs by supporting new collaborations and by strengthening existing ones. In 2003, one full award and five planning grants were awarded, and in June 2004, the Medical Research Program announced a new call for proposals for the Clinical Interfaces Award Program.

We expect to award up to three CIAP grants of up to \$2.25 million each for five years in the fall of 2005. The deadline for pre-proposals is November 2, 2004. For more information, visit our website at [www.ddcf.org/mrp/ciap](http://www.ddcf.org/mrp/ciap).

## Advisory Panel for 2004 Clinical Interfaces Award Program

Kenneth R. Chien, M.D., Ph.D., Chair

David Altshuler, M.D., Ph.D.

Don Ganem, M.D.

David Ginsburg, M.D.

Michael J. Kahana, Ph.D.

Robert Langer, Ph.D.

Bernard Lo, M.D.

Stephen S. Morse, Ph.D.

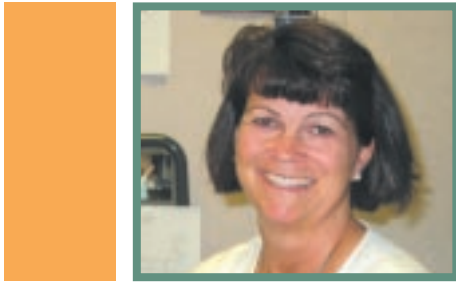
Philip M. Murphy, M.D.

Charles Sawyers, M.D.

# CLINICAL SCIENTIST DEVELOPMENT AWARD

## CAROLYN C. HOPPE

Understanding Sickle Cell Anemia,  
One Child at a Time



Carolyn Hoppe, M.D., recipient of a DDCF Clinical Scientist Development Award in 2000, is combining her clinical knowledge with modern techniques of genetic analysis to better understand why children with sickle cell anemia are vulnerable to disabling strokes.

### Sickle Cell Anemia

Although the discovery of the molecular cause of sickle cell disease (a point mutation in the hemoglobin gene) was an early milestone of modern molecular medicine, existing treatments for sickle cell disease are less than ideal.

Stroke is a particular threat to the long-term welfare of children with sickle cell disease, affecting up to 30% of these patients. Being able to identify at-risk patients would enable close monitoring for possible stroke. In addition, these patients would be ideal candidates for preventive therapy.

### The “Candidate Gene” Approach

In a pilot project for identifying stroke risk factors in sickle disease, Dr. Hoppe and her collaborators at Children’s Hospital Oakland took advantage of existing pre-transplant typing of patients,

to see if human leukocyte antigen (HLA) variants were a factor in stroke risk. Indeed, certain HLA variants were associated with increased risk of small-vessel strokes. These encouraging results led Dr. Hoppe to undertake a larger-scale study of a more representative group of sickle cell patients. This work, funded by the DDCF, uses a “candidate gene” approach, focusing on genes already known to play a role in blood vessel disease or inflammation. Many of the genes being typed have been previously implicated in the pathogenesis of atherosclerosis and coronary artery disease.

Typing 65 genes in 230 patients is no trivial undertaking, and a high-tech collaboration between Dr. Hoppe and scientists at Roche Molecular Systems made analysis of the clinical samples technically possible. The results are promising, showing associations between specific genes, (including the interleukin 4 receptor (IL4R), tumor necrosis factor (TNF), the low-density lipoprotein receptor) and risk of either large- or small-vessel stroke. For example, a patient with particular variants of IL4R and TNF carries a 5.5-fold greater risk than a patient carrying neither of these.

**This work will help establish a profile that can identify patients vulnerable to stroke; in addition, the identity and nature of the predisposing variants are clues to the underlying mechanisms, and offer potential targets for therapy.**

### Combining Clinical Care with Research

Dr. Hoppe’s successes are motivated by her overriding concern for the welfare of her patients. Her early training was in epidemiology at the University of California, Los Angeles. Wishing to work more directly to advance patient health, she went on to medical school and residency, specializing in hematology/oncology. Dr. Hoppe credits strong mentorship at Children’s Hospital Oakland as key in prompting and supporting her initial move into clinical research. •

### Clinical Scientist Development Award

Established in 1998, the Clinical Scientist Development Award (CSDA) has supported junior physician-scientists and research fellows as they begin their independent clinical research careers. The CSDA award has provided \$100,000 each year for up to five years to junior faculty members and \$65,000 each year to research fellows working in the following four disease areas: cardiovascular disease, cancer, AIDS, and blood disorders. Fellows receiving CSDA grants are expected to transition to faculty-level grants within two years of receiving their grant. No new CSDA awards were made in 2003 and 2004.

## Consortium Publication Delineates Problems with Oversight of Human Subject Research

Members of the **Consortium to Examine Clinical Research Ethics**, funded by DDCF since 2000, recently outlined 15 problems with the oversight system to protect human subjects. These problems were categorized into organizational problems, operational problems, and performance-assessment problems. The authors concluded that none of the proposed reforms addresses all 15 problems, and recommended the following reforms to the system: (1) establish a single federal office with regulatory authority over

all human subject research; (2) create a permanent advisory committee; (3) mandate single-time review for multi-site research protocols; (4) increase the funding for oversight activities; and (5) develop standards to assess the performance of the oversight system.

(Emanuel, E.J., Wood, A., Fleischman, A., Bowen, A., Getz, K., Grady, C., Levine, C., Hammerschmidt, D., Faden, R., Eckenwiler, L., Muse, C.T., Sugarman, J. (2004) *Oversight of Human Participants Research: Identifying Problems to Evaluate Reform Proposals*. *Ann Intern Med*. 141:282-291).

# INTERNATIONAL AIDS PROJECTS

The Medical Research Program continues to support clinical research and the related capacity-building activities needed to determine how to best treat and care for HIV/AIDS patients in low-resource regions. Our major activities this past year have focused on the development of low-cost diagnostics for AIDS care and treatment, support for a small grants program directed and administrated by African scientists, and a grant to help fund a research center in rural Uganda.

## AIDS Care Research in Africa: Initiative Supports Junior Researchers

Together with the Rockefeller Foundation, DDCF has supported a small grants program for AIDS Care Research in Africa (ACRiA) to fund young African investigators. The primary goal of the program is to help build the local research capacity so that Africans can determine how to best care for and treat their AIDS patients. ACRiA is directed by Dr. Peter Mugenyi from the Joint Clinical Research Center, Kampala, Uganda, Dr. Elly Katibira from Makerere Medical School, Kampala, Uganda, and Dr. Brooks Jackson from the Johns Hopkins University School of Medicine. ACRiA is administered at the Joint Clinical Research Center in Kampala.

Now entering its second year, ACRiA has completed several open competitions soliciting research proposals from junior investigators working on AIDS care and treatment throughout Africa. Proposals are reviewed by an expert panel made up primarily of African researchers. For many of the applicants, their ACRiA grant is the first research proposal they have written.

To date, ACRiA has committed over \$300,000 to provide up to two years of funding (ranging from \$10,000 to \$65,000) to support 8 projects. The scope of the research supported by ACRiA broadly falls under the category of AIDS care and treatment, and includes work on malaria and tuberculosis as they affect AIDS patients. The current grantees are:

- Lucy Matu, M.D., Kenya
- Joshua Kimani, M.D., Kenya
- Raveen Parboosing, M.D., South Africa
- Neil Martinson, M.D., South Africa
- Doreen Anna Sophia Mloka, B.Sc. Microbiology (Hons), Tanzania
- Samuel Biraro, M.D., Uganda
- Hakim Sendagire, M.D., Uganda
- Joseph Rujumba, S.S., Uganda

## Rakai Health Sciences Program Builds a Laboratory in Rural Uganda

For the last 17 years, the Rakai Health Sciences Program has conducted clinical research and provided medical services to a rural population in the Rakai District of southwestern Uganda. This program, which has collected some of the earliest epidemiologic data on the AIDS epidemic in Africa, is a collaboration between the Uganda Virus Research Institute of the Ministry of Health and researchers at Makerere, Columbia and Johns Hopkins Universities. The program's considerable achievements have been made in spite of limited infrastructure.

With assistance from the DDCF, the National Institutes of Health, and the Gates Foundation (plus loans from Johns Hopkins and Columbia Universities) the Rakai Program is completing the construction of a new building for clinical and laboratory uses, data management, and administration. The new facility, which is expected to open in February 2005, will be among the most advanced in rural Africa and will allow for an expanded research and training program, and provision of care.

As part of our commitment to build local capacity, DDCF funds also support training stipends for African researchers working on Rakai Program projects. With the provision of antiretroviral therapy (ART), made possible by the Presidential Emergency Program for AIDS Relief, the researchers at the Rakai Health Sciences Center anticipate that 200–400 HIV-positive persons will be placed on therapy in the coming year.

These patients will come predominantly from the Rakai Community Cohort Study, which conducts annual surveillance in a population of 12,000 adults from 50 different rural communities. Studies are being planned to track the effectiveness of implementing point-of-care ART in a rural setting, and to determine the impact of ART on HIV incidence, risk behaviors, emergence of resistant virus, and the sociodemographic effects of ART. •

From left, Godfrey Kigozi, Heena Brahmhatt, Noah Kiwanuka, David Serwadda, Fred Nalugoda, and other Rakai staff



The New Rakai Facility



# ADDRESSING A CRITICAL NEED IN THE FIGHT AGAINST AIDS

## Developing Simple, Low-Cost Diagnostics

Decreases in the price of antiretroviral therapy (ART) and the infusion of much-needed funds from a variety of sources including the Global Fund to Fight AIDS, Tuberculosis, and Malaria and the President's Emergency Program for AIDS Relief have made it possible to begin to roll out ART to treat the millions of AIDS patients in sub-Saharan Africa and other low-resource areas. To effectively treat AIDS patients with ART, their immune status and viral load need to be measured periodically along with other measurements that detect drug toxicity. While these tests are available, they are too costly and often too complex to be used in local settings in economically disadvantaged countries (EDCs).

Developing simple, low-cost diagnostics for AIDS care and treatment and ensuring their access and use in low-resource regions will be difficult, but the need is too great to ignore.

Thus in late 2002, DDCF responded to this vital need by launching a grant competition as part of its Innovation in Clinical Research Award Program to support the development of point-of-care diagnostic and therapeutic monitoring tools needed to care for and treat AIDS patients in low-resource areas. A panel of experts<sup>1</sup> in AIDS care and treatment, biotechnology and the development of diagnostics helped us identify 10 research teams that received two-year grants of up to \$200,000.

All 10 teams, are working on projects which minimize sample volume and processing steps, and eliminate reliance on large, expensive and hard-to-service equipment.

However, their approaches range widely from refining and simplifying conventional methods, to creating and or testing new technologies, such as nanoparticle probes and immunosensors. Some of these new or refined assays are ready for field testing, while others are in the early stages of development.

<sup>1</sup> Gunnel Biberfeld, M.D., Ph.D. (Karolinska Institute and Swedish Institute for Infectious Disease Control), Michel Canavaggio, M.D., M.B.A. (Baxter R&D Europe), Richard Decker (World Health Organization), Roger Y. Dodd, Ph.D. (American Red Cross), Gregg Gonsalves (Gay Men's Health Crisis), Indira Hewlett, Ph.D. (Center for Biologics Evaluation and Research, FDA), Gregory R. Reyes, M.D., Ph.D. (Schering-Plough Research Institute), Eric S. Rosenberg, M.D. (Massachusetts General Hospital and Harvard Medical School, AIDS Research Center), Gaby Vercauteren, Ph.D. (World Health Organization)

The following are abstracts from three of the ten grants awarded.

To obtain a complete list of grants visit our website at [www.ddcf.org](http://www.ddcf.org).

**P. Robert Beatty, Ph.D.  
and Eva Harris, Ph.D.**

### **ImmunoSensor for HIV Infections**

Drs. Beatty and Harris from the University of California at Berkeley are adapting a tiny biochip (ImmunoSensor), which employs microelectronics, immobilized DNA probes, and magnetic beads to develop a device to measure HIV-specific antibodies, HIV RNA, and HIV viral antigens in a single small blood sample.

**Alan L. Landay, Ph.D.,  
Suzanne M. Crowe, M.D.,  
and Tom N. Denny, M.Sc.**  
**Novel and Improved Manual  
Low-Cost CD4 Tests**

Dr. Landay (Rush University Medical Center) and colleagues from Australia are developing a robust, point-of-care, semi-quantitative manual assay to monitor CD4+ T cell numbers by utilizing special, high-affinity anti-CD4 antibodies in an adapted immunoassay.

**Neil T. Constantine, Ph.D.,  
Janet M. Barletta, Ph.D.,  
and Maja Sommerfelt, Ph.D.**

### **A Portable, Visually -Read, Amplification-Boosted Test to Monitor HIV Viral Load**

A team of investigators from the University of Maryland School of Medicine, led by Dr. Constantine, are exploiting an "amplification" strategy to detect low levels of HIV viral protein. They have already demonstrated that this strategy, which uses a magnetic bead support and an antigen/antibody colorimetric reaction can lower the detection limit of HIV viral load (*American Journal of Clinical Pathology*, July, 2004). DDCF funds are supporting their efforts to develop a portable, battery-operated monitoring system to use in low-resource settings.

## Modifying Our Intellectual Property Strategy

To ensure the new technologies and tests that may result from these grants will be available and accessible in EDCs the Foundation modified its intellectual property policy. The new policy requires the institutions receiving these awards to agree to assign the Foundation a non-exclusive, royalty-free, paid-up, irrevocable license to any patents filed in EDCs resulting from these grants. This license enables the Foundation to sublicense (after a standstill period) the right to make, use, import and sell the products within EDCs. The Foundation's license would only be executed if access to these products at low-cost in EDC's were threatened. We are very pleased that all the institutions awarded grants in this competition not only share our goal for this program, but have agreed to our new intellectual property policy.

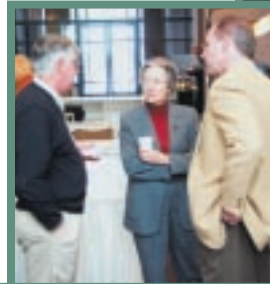
# Doris Duke Clinical Scientist Meeting

In late March 2004, over 130 Doris Duke clinical scientists congregated on the unexpectedly snowy campus of the Cold Spring Harbor Laboratory to attend the fourth Doris Duke Clinical Scientist meeting. After the welcoming introduction by DDCF president Joan E. Spero on the first evening, attendees spent the next two days presenting their research at platform and poster sessions and participated in forums and discussion groups on the benefits of academic-pharmaceutical partnerships, conflicts of interest in clinical research, and balancing career and family.

Scientific sessions began with remarks by the Medical Research Program's Scientific Advisory Council chair Dr. David G. Nathan, President Emeritus of the Dana Farber Cancer Institute, followed by presentations by the 2002 Distinguished Clinical Scientist Award winners. Interjected among these sessions was the keynote address by Dr. Joseph Goldstein, Chairman of Molecular Genetics at the University of Texas Southwestern Medical Center and winner of the 1985 Nobel Prize in Physiology. Dr. Goldstein counseled young clinical investigators to be boldly curious with their scientific questions. He also spoke of the benefit and importance of collaborations. The second day culminated with an animated discussion led by Dr. Steven Straus, Director of the National Center for Complementary and Alternative Medicine at the NIH, on the NIH road map for supporting clinical research. The last evening ended with a performance by the New Jazz Composers Octet, a grant recipient of the Foundation's Performing Arts Program. •



David Nathan and Joseph Goldstein



**Top to bottom:**  
Foundation President, Joan Spero, chats with Laurence Demers and Michael Ackerman; Charis Eng, Olufunmilayo Olopade, William Hahn, and Dan Haber chat at the poster session.

## Scientific Advisory Council

Thanks to our Council members for their advice and help throughout the year:

David G. Nathan, M.D., Chair  
Max D. Cooper, M.D.  
Raphael Dolin, M.D.  
Helen H. Hobbs, M.D.  
Mary-Claire King, Ph.D.  
Arthur W. Nienhuis, M.D.  
Michael J. Welsh, M.D.  
Jean D. Wilson, M.D.

Special thanks to Karen H. Antman, M.D., Robert M. Califf, M.D. and Judith L. Swain, M.D., who ended their tenure this year.



**DORIS DUKE**  
CHARITABLE FOUNDATION

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## medical research program bulletin

Newsletter contributors: Charlotte Wang, Ph.D. and Jason Harlow