A Center for the Epidemic
TAKING ON D.C.’S AIDS CRISIS
From the Editors

As this issue of Medicine + Health went to press, a number of important changes took place at the GW Medical Center.

Last May, the University’s Board of Trustees asked the administration to conduct a strategic review of the Medical Center’s vision, strategy, and structural relationship with the GW Hospital and the GW Medical Faculty Associates. Given that the existing relationship between the three separate entities has been in place for more than 10 years; there are new changes and challenges in the nation’s health care system; and there is greater competition for research funds, the Board hopes that the multi-phase review, being conducted by an experienced consulting firm, will continue to raise the Medical Center’s academic stature and position it for the greatest level of success in the decades ahead.

As part of this process, John “Skip” Williams, M.D. ’79, Ed.D. ’96, M.P.H., senior vice provost and vice president for Health Affairs, decided to take a year-long sabbatical. In addition, Jim Scott, M.D., recently announced that he will step down from his position as dean of the School of Medicine and Health Sciences (SMHS) and return to his full-time faculty position. We extend our deepest gratitude to both Williams and Scott for their guidance, leadership, and generous support for this magazine.

Until a permanent dean is appointed, University Provost Steven Lerman, Ph.D., appointed Jeffrey Akman, M.D. ‘81, the Leon M. Yochelson Professor and chair of the Department of Psychiatry and Behavioral Sciences, as interim dean of SMHS and vice provost for Health Affairs. Akman also will assume the roles and responsibilities of the vice president for Health Affairs. In addition, the provost appointed Vincent Chiappinelli, Ph.D., the Ralph E. Loewy Professor and chair of the Department of Pharmacology and Physiology, as interim associate dean and associate vice provost for Health Affairs. More can be read about the Medical Center review and interim leadership at www.gwumc.edu.

In the meantime, Lynn Goldman, M.D., M.P.H., the new dean of the School of Public Health and Health Services, is moving the school forward with an ambitious agenda (see page 16). Jean Johnson, Ph.D., F.A.A.N., has also assumed her new role as the founding dean of GW’s School of Nursing (see page 7), with significant plans to expand our nursing programs.

Finally, as you’ll read elsewhere in Medicine + Health, an extraordinary amount of new research is taking place across the campus, from an NIH-sponsored center for HIV/AIDS investigations, to advances in our understanding of cardiac problems and cancer cells, to the search for a treatment for children who suffer from a deadly genetic disease.

We hope you will find these stories as interesting as we do and trust that you’ll contact us with your views and ideas.
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Redefining Normal
RISK FOR MISCARRIAGE GREATER IN WOMEN WITH SUBCLINICAL THYROID DISEASE

Throughout his 20-year career studying thyroid disease and pregnancy, Alex Stagnaro-Green, M.D., M.H.P.E., senior associate dean for Medical Education at the School of Medicine and Health Sciences, has found that “normal” is not so easy to define. Although the normal level of thyroid hormone in non-pregnant women is already a relatively narrow range, Stagnaro-Green recently confirmed that these numbers might need to be tightened even further during pregnancy.

“In the last two decades, we have learned that an underactive thyroid, or hypothyroidism, is associated with an increased risk of miscarriage, an increased risk for preterm delivery, and a decreased IQ in the unborn child,” he explains. “Now, the question is: Does an even slightly lower thyroid function still put a woman and her developing child at risk?”

To find out, Stagnaro-Green and his colleagues from the University of Illinois-Chicago and two hospitals in Italy measured the thyroid stimulating hormone (TSH) level in more than 4,000 pregnant women. TSH is a hormone that is released when the thyroid's function becomes too low. Because recent studies suggested that the normal TSH may be no higher than 2.5 milli-international units per liter (mIU/L) in pregnant women — as opposed to the accepted 5.0 mIU/L upper limit for non-pregnant women — Stagnaro-Green and his colleagues compared the pregnancy outcomes in women who had TSH levels below 2.5 mIU/L with those whose TSH was between 2.5 and 5.0 mIU/L.

Although the team found no differences in the preterm delivery rate, the difference in miscarriage rates was startling: It was 3.6 percent in the women with a TSH of less than 2.5 mIU/L versus 6.1 percent in the others.

“This study is the first to demonstrate that the upper half of the accepted normal range on thyroid function tests is associated with a 69 percent increase in miscarriage,” says Stagnaro-Green. “This leads us to think that all pregnant women should be screened for thyroid function and treated for any abnormalities.”

Bridging Science and Medicine
CHILDREN’S NATIONAL MEDICAL CENTER AND GW PARTNER ON $20-MILLION AWARD TO CONVERT BASIC SCIENCE TO CLINICAL CARE

In recent years, significant insights have advanced our understanding of such fundamental human health issues as the human genome, cancer cell behavior, and brain function. But, as many researchers know, the challenge lies in translating those insights into clinical applications that improve patient health.

Increasing the momentum of, and nationwide capacity for, this crucial translational research is the focus of a prestigious, nationwide awards program funded by the National Institutes of Health. And as a recent recipient of the program’s five-year, $20-million Clinical and Translational Science Award (CTSA), a collaboration between the School of Medicine and Health Sciences, the School of Public Health and Health Services, and partner institution Children’s National Medical Center will be a key part of that effort.

“Our vision for the CTSA is the same as other CTSA institutions in the country,” says Jill Joseph, M.D., Ph.D., principal investigator of the CTSA and director of the Clinical and Translational Science Institute at Children’s National. “It is to do everything we can to ensure that there is that movement from basic discovery to improvements in human health.”

The GW/Children’s National partnership joins the CTSA coalition of 55 leading health institutions nationwide, but is the first award recipient to...
focus specifically on how scientific breakthroughs from the laboratory bench can be brought more quickly and efficiently to children’s health care.

The partnership will explore avenues for translational research among childhood diseases including cancer, birth defects, developmental disabilities, and asthma; diseases that persist into adulthood, most notably congenital heart disease, cystic fibrosis, and muscular dystrophy; and diseases of adulthood that begin in childhood, such as hypertension, type 2 diabetes, and obesity.

“We’ve been talking about everything,” explains Joseph, “from methods to improve vaccinations for diseases of poverty, to intervention programs that help terminally ill adolescents communicate their wishes regarding their end-of-life care, to creating opportunities to develop the high-performance computing capabilities necessary to support the advanced imaging needs of modern health care.”

According to co-principal investigator Peter Hotez, M.D., Ph.D., GW Distinguished Research Professor and chair of the Department of Microbiology, Immunology, and Tropical Medicine, “There have been a lot of genomics and proteomic activities at both institutions, and this award will help move those spheres of research into clinically applied methods and technologies.”

Chief among the goals of the grant will be the health needs of the District of Columbia population. “We want to create strong linkages with the Washington, D.C., community to better understand and address their needs,” says Joseph. “Childhood asthma, for example, is exceptionally common in the District. Families in the area, and across the country, have already benefited from what we’ve learned about better clinical treatments. . . . We look forward to even greater breakthroughs bolstered by potential collaborations with consortium institutions.”

The grant also is expected to expand the pool of young investigators engaged in translational research. “Expanding our translational research and development activities within the different components at both GW and Children’s National will provide new education opportunities for young investigators,” says Hotez.

Those education opportunities will include the region’s first Master of Science degree in Clinical and Translational Research, as well as a Graduate Certificate in Clinical and Translational Research, based in the School of Medicine and Health Sciences.

Joseph Bocchino, Ed.D., M.B.A., chair of the Department of Clinical Research and Leadership, will serve as the director of the new programs, which are geared toward Ph.D.s, M.D.s, and others working in basic or clinical research who want to broaden their skills. “Traditional research programs train people in a deep, but narrow scope of interest,” he explains. The strategy of these new programs is to help people develop a broader base of experience across the continuum, from basic science, to clinical research, to matters of health policy.

GW and Children’s National hope that this multifaceted approach will put a new focus on pediatric translational research not only during the grant period, but long into the future.

Battling Global Infectious Diseases

When the AIDS epidemic first emerged in the early 1980s, the median length of survival for an individual diagnosed with the disease was just 26 weeks, recalled Anthony S. Fauci, M.D., director of the National Institute of Allergy and Infectious Diseases. But today, according to Fauci, a newly infected 20-year-old might live an additional 52 years, thanks to the development of more than 30 anti-retroviral drugs. “There are very few examples in biomedical research and the application of therapeutics that are as impressive as this,” he said.

Fauci made these and other compelling observations about the state of global infectious diseases at an event to celebrate the 10th anniversary of the School of Medicine and Health Sciences’ Department of Microbiology, Immunology, and Tropical Medicine.

During his lecture, Fauci called upon the global health care community to mobilize and use the same research model it employed against AIDS to combat the world’s three other most devastating and widespread diseases that affect millions of people: tuberculosis, malaria, and neglected tropical diseases. “We live in a global community,” he said, and the health of that community “is critical to everything from our security to our economy.”
Sidawy Named New Chair of Surgery

Following a nationwide search for a new chair of the Department of Surgery, the School of Medicine and Health Sciences found the person for whom it was looking close to home with the appointment of vascular surgeon Anton N. Sidawy, M.D., M.P.H., to the position. Sidawy, who has held academic appointments in GW's Department of Surgery, joins the school after having served as the chief of surgical services at the Veterans Affairs Medical Center in Washington, D.C., since 1996.

Sidawy brings to the GW Medical Center a distinguished career. He completed a fellowship in vascular surgery at the former Boston University Hospital (now Boston Medical Center). His work has been published in more than 100 peer-reviewed articles, and he has authored or co-authored more than 40 chapters and abstracts. He holds or has held leadership positions in local, regional, and national organizations, including serving as the current president of the Society for Vascular Surgery and on the Board of Governors of the American College of Surgeons from 2001 to 2007. Currently, Sidawy serves as the editor-in-chief of the Journal of Vascular Surgery, the premier journal in the specialty, and on the editorial boards of Annals of Vascular Surgery, Vascular, and Perspectives in Vascular Surgery and Endovascular Therapy.

“We may be studying one very specific compound and one very specific type of cancer,” says Sidawy, “but I have always been confident that the results of our work will have much broader implications.”

Breathing Easier
Susan Ceryak Receives R21 Grant to Uncover Mysteries of Respiratory Carcinogen

It is a pervasive environmental and occupational hazard used in numerous industrial processes and commonly found in dyes, paints, car exhaust, and cigarette smoke. Erin Brockovich made it famous, and the Environmental Protection Agency (EPA) condemns it. Numerous in vitro studies have made clear that hexavalent chromium (Cr (VI)) is a compound that, when inhaled, initiates tissue inflammation, cell death, and eventually lung cancer. But no one has quite yet figured out how.

Through a two-year, $275,000 R21 grant from the National Institutes of Health, a team of researchers led by Susan Ceryak, Ph.D., associate research professor in the Department of Pharmacology and Physiology, will study exactly what happens from the time a cell is exposed to Cr (VI) particulates to the time a tumor develops.

The GW team, which includes Stephanie Constant, Ph.D.; Steven Patierno, Ph.D.; and Arnold Schwartz, M.D., Ph.D., will use a new mouse model that displays chronic lung tissue inflammatory responses and a form of Cr (VI) that is environmentally and occupationally relevant, mimicking human exposure to particulate chromate compounds more closely than ever before. As a result, they hope to show the steps of chromate-induced carcinogenesis and to confirm the link between tissue inflammation and carcinogenesis.

The investigators also expect their research to result in key pharmacological benefits by identifying molecular targets for potential interventional and preventive therapy. “We may be studying one very specific compound and one very specific type of cancer,” says Ceryak, “but I have always been confident that the results of our work will have much broader implications.”

“I have been associated academically with GW for 25 years, and I have always been impressed with the high quality of surgical work being performed at this institution,” says Sidawy. “I am very fortunate to be given the opportunity to lead this department to the next level.”
GW Doctor Receives Top Psychiatry Honor

Amir Afkhami, M.D. ’03, Ph.D., has witnessed the devastation of war in regions of Iraq and Afghanistan. He has seen cities destroyed, citizens and humanitarian workers injured, and helicopters downed on his very same flight path.

But most concerning to Afkhami, who is assistant professor of Psychiatry and Behavioral Sciences in the School of Medicine and Health Sciences (SMHS) and of Global Health in the School of Public Health and Health Services, isn’t anything visible. For him, the mental wreckage of warzones is more than just collateral damage.

“Very few other issues can be addressed from a medical perspective for a population if you do not first address the underlying psychological and psychiatric impact of conflict,” he believes.

This philosophy — and the reputable career he has made from it — recently earned him the recognition of “Psychiatrist of the Year” by the Washington Psychiatric Society (WPS).

“Dr. Afkhami had the profound insight that stabilization of health and especially mental health services is a crucial element of rebuilding societies that have been severely damaged, by war and terrorism,” said Robert W. Keisling, former president of WPS. “For his creativity, clinical wisdom, and commitment to fostering psychiatric services as an instrument of peace, the WPS is proud to honor Dr. Amir Afkhami.”

As an advisor to the U.S. Department of State, the U.S. Army, and the Iraqi Ministry of Health, Afkhami guides efforts to rebuild the mental health infrastructure in Iraq and Afghanistan — regions whose mental health systems are deeply antiquated, if not absent altogether. Working with clerics and faith healers in Iraq, Afkhami has helped to shift the nation’s view of psychiatric disorders from morally wrong to medically significant. His mantras of cultural competency and respect have shaped a generation of military personnel, whom he briefs prior to deployment.

Afkhami’s reputation as a global policy authority — he was instrumental in the Iraqi Health Initiative and influential in the U.S. State Department’s targeted development plans for Iraq, which included mental health thanks to his memo — earned him the recent election to the prestigious Council on Foreign Relations, where his presence as a doctor is extremely rare.

“Psychiatry and mental health have, in general, been neglected in global health,” Afkhami explained. “I hope to use my presence on the Council to raise awareness on ways to enhance psychiatric care, expand our knowledge on the extent of the problem globally, and to suggest ways in which we can bring about measurable change.”

Afkhami earned his M.D. at SMHS, while simultaneously pursuing a Ph.D. in the History of Medicine in the Middle East at Yale University. “GW put me in a unique position to bring together these two seemingly disparate fields,” he says. “Had GW not been supportive, I wouldn’t be where I am today.”

An Environment for Science

Perry Appointed Chair of Environmental and Occupational Health at SPHHS

For nearly two decades, Melissa J. Perry, Sc.D., M.H.S., has championed the cause of health and safety for farmers and agricultural workers, publishing extensively her research on environmental and occupational hazards, such as excess rates of cancer in those exposed to toxic chemicals. As the new professor and chair of the Department of Environmental and Occupational Health at the School of Public Health and Health Services, she will bring that zeal for environmental science research to the school’s leadership team, beginning in January 2011.

“Dr. Perry has been a leader in researching the health effects of agricultural work and exposure to pesticides, including cutting-edge research on endocrine effects of pesticide exposures on women’s hormonal cycles and male fertility,” says Lynn Goldman, M.D., M.P.H., dean of the School of Public Health and Health Services.

Perry brings a distinguished list of credentials to her new position at GW. She earned a Sc.D. from the Johns Hopkins University and has served on the faculty of the Harvard School of Public Health for more than a decade, most recently as associate professor of Occupational Epidemiology in the Department of Environmental Health.
Paving the Way for a Smooth Continuum of Care
Survivorship and Patient Navigation Grants Help GW Cancer Institute
Plot the Course from Diagnosis to Life After Cancer Treatment

When tourists visiting Washington, D.C., lose their way, they consult a map or a friendly local. But when new cancer patients get lost within the labyrinth of health care systems, treatment options, and appointments, their solution is not so obvious. Without a map or a guide, navigating cancer care, as well as life after successful treatment, can become nearly as traumatic as the cancer itself.

But two major grants promise to help the GW Cancer Institute (GWCI) create a road map to guide patients along both the local and national routes from diagnosis to post-cancer care.

The American Cancer Society (ACS) and GWCI recently received a $4.25-million grant from the Centers for Disease Control and Prevention (CDC) to establish a National Cancer Survivorship Resource Center, allowing ACS and GWCI to collaboratively guide national progress toward improved health outcomes for cancer survivors. The partners will develop a strategic plan for enhancing nationwide surveillance of cancer survivors.

“Collaboration is critical to address the needs of more than 12 million cancer survivors in the United States,” says Steven Patierno, Ph.D., executive director of GWCI. “The GW Cancer Institute and the American Cancer Society are taking a major step toward developing and implementing a cancer survivorship strategy that will improve cancer survivor care and quality of life through the new center.”

Over the next five years, GWCI and ACS will assess current survivorship initiatives, identify gaps in cancer survivorship, and support collaborations with cancer coalitions and national, state, and community-based organizations to set the course for cancer care and survivorship programs in the future.

On the local level, GWCI is already one step ahead. Having recently received a $2.4-million grant from the D.C. Cancer Consortium, the institute will establish and coordinate the Citywide Patient Navigation Network (CPNN). Through a system of patient navigators and community sites, the network will serve as a seamless and cohesive framework for cancer care coordination across the entire city.

“This grant allows us to both deepen and widen citywide efforts in cancer care coordination,” says Patierno, noting that CPNN will be an expansion of GWCI’s existing navigation network — which resulted from the institute’s five-year Patient Navigation Research Program demonstrating the effectiveness of patient navigation.

Through CPNN, D.C. residents will receive assisted access to appropriate screening services. Should a suspicious result be found or a cancer diagnosis be made, the network will further guide patients through timely and coordinated treatment following the standard of care. Finally, navigators will monitor patients throughout the cancer continuum, connecting them with appropriate support services all the way into the post-treatment survivorship period. This comprehensive aid is anticipated to improve health outcomes, particularly among populations suffering from cancer care disparities.

Research Finds Extra Pounds Lighten the Wallet

A report by Avi Dor, Ph.D., professor of Health Policy in the School of Public Health and Health Services, calculated the startlingly high individual costs of obesity to Americans. The report, “A Heavy Burden: The Individual Costs of Being Overweight and Obese in the United States,” measures indirect costs such as lost productivity, and direct costs including obesity-related medical expenditures, to estimate the price tag of obesity at the individual level.

Dor and co-authors Christine Ferguson, J.D., Casey Langwith, and Ellen Tan concluded that the yearly individual cost of being obese is $4,879 and $2,646 for women and men, respectively, and adding the value of lost life to these annual costs produces even more dramatic results: $8,365 and $6,518 annually for women and men, respectively. The findings reveal that the areas where costs are highest for women are job-related costs, including lost wages, absenteeism, and disability.

Dor notes that these estimates, while staggering, may even underestimate the total individual costs of obesity. “Existing literature provides information on health- and work-related costs, but with the exception of fuel costs, no published academic research offers insight into consumer-related costs, such as clothing, air travel, automobile size, or furniture,” he says. “Anecdotal evidence suggests that these costs could be significant.”
In the coming years, the U.S. is expected to face a national shortage of nurses twice as large as any experienced since the mid-1960s. Many experts believe the need for more nurses will intensify as baby boomers enter their golden years, and as health care reform allows millions of additional Americans to access primary care services. Moreover, many women and men in the current nursing workforce are also reaching retirement age.

GW, which has educated nurses for more than a century, recently took a significant step to help address this serious issue in the nation’s health care system. At its May 2010 meeting, the GW Board of Trustees voted to move the former Department of Nursing Education out of the School of Medicine and Health Sciences and establish a new School of Nursing (SON).

“We are thrilled to launch the School of Nursing, which will give our programs the national recognition they need and deserve to reach their full potential,” says Dean Jean Johnson, Ph.D., F.A.A.N., who was selected as one of the school’s founding administrators, along with Ellen Dawson, Ph.D., A.N.P., a new senior associate dean at the school. The act of establishing a new school “demonstrates that the University believes nursing education is important to its future. This is a big step forward for us, one that brings with it the potential to recruit more outstanding faculty and students, and improve our rankings,” Johnson explains.

Nursing education at GW reached this point, says Johnson, largely thanks to the team she built after her leave of absence in 2002, when she served as a Robert Wood Johnson Foundation Scholar-in-Residence. The team, including Dawson, who was serving as chair of the Department of Nursing Education, recruited a highly motivated faculty that created outstanding education programs, including the Master of Science in Nursing (M.S.N.) degree, the Doctor of Nursing Practice (D.N.P.) program, and the second degree Bachelor of Science in Nursing (B.S.N.) — a program whose relevance was reflected in a fivefold increase in applications in its first year alone. All three nursing programs have been accredited for the maximum term by the Commission on Collegiate Nursing Education.

Most recently, the Department of Nursing Education established a learning laboratory for policy activism through a Robert Wood Johnson Foundation grant to improve the quality of health care. In addition, Johnson and Dawson have fostered a nationally recognized partnership with the National Committee for Quality Assurance, making GW’s M.S.N. program the only one in the country with a focus on quality improvement.

“In a short period of time we’ve generated a sizable amount of research grant activity,” notes Johnson. “That’s important in academic health. We don’t just educate, we also add new knowledge.”

For Johnson and Dawson, the development of SON is a green light for continued growth. Chief among their priorities are expanding the B.S.N. and the Nurse Practitioner programs, which will help increase the nursing workforce.

“As the founding dean of the school, I hold a lot of responsibility,” Johnson admits. “But,” she quickly adds, “everyone in the school shares that sense of responsibility; it’s a big part of why we’ve been so successful.”

Establishing a Higher Level of Care

GW MEDICAL CENTER LAUNCHES SCHOOL OF NURSING

PHOTOGRAPHY BY DANIEL OTFINOWSKI
The District of Columbia Developmental Center for AIDS Research

A Center for the Epidemic
Sitting in his office along Pennsylvania Avenue, Alan E. Greenberg, M.D. ’82, M.P.H., radiates an air of excitement. Greenberg, professor and chair of the Department of Epidemiology and Biostatistics at the School of Public Health and Health Services (SPHHS), recently learned that the National Institutes of Health (NIH) has selected the group he leads — a partnership of Washington, D.C., institutions — to establish the District of Columbia Developmental Center for AIDS Research (D.C. D-CFAR). This designation marks the University's first-ever NIH Center grant and instantly vaults his consortium into a network of the 21 most elite HIV/AIDS research organizations in the United States.

News of the grant could not have come sooner. By all accounts, the nation's capital is in the grip of an epidemic. Washington, D.C. has an HIV/AIDS prevalence of more than three percent among adults, the highest infection rate in the country and more than three times the Centers for Disease Control and Prevention's threshold for a severe epidemic. African-American residents account for 57 percent of D.C.'s population, but they total 81 percent of all new HIV cases and approximately 86 percent of people living with AIDS. The challenges confronting African-American women in the District are still more daunting: They represent 90 percent of all new female HIV cases and 93 percent of women living with the disease.

NIH founded the Center for Aids Research (CFAR) program in 1988 with the goal of providing administrative and shared research support to academic institutions that conduct the best investigations involving HIV/AIDS. NIH currently supports 17 full CFARs and four developmental centers. The program emphasizes interdisciplinary collaboration, especially between basic, clinical, and behavioral investigators, to achieve translational research in which findings from the laboratory are brought to the clinic and community and vice versa. It also stresses creating opportunities for early stage and minority investigators and research on prevention and behavioral change.

The five-year D-CFAR designation, with funding totaling $3.75 million, brings together GW's SPHHS, School of Medicine and Health Sciences (SMHS), and Columbian College of Arts and Sciences, Children's National Medical Center, Georgetown University, Howard University, and the Veterans Affairs Medical Center (VA). “What the D.C. D-CFAR can do in Washington, D.C., is create a community of scientists who can conduct the highest level of research on this disease,” explains Greenberg.

Many would say that Greenberg had excellent preparation to make the D.C. D-CFAR a success. He earned his medical degree from GW’s School of Medicine and Health Sciences in 1982 and his M.P.H. from the Harvard School of Public Health in 1999, and then served for two decades as a U.S. Public Health Service Commissioned Corps Officer at the Centers for Disease Control and Prevention (CDC). He ultimately rose to head the center’s HIV Epidemiology Branch, where he supervised research studies in 28 states and nine countries in Africa and Asia. Greenberg also has
co-authored more than 100 articles and book chapters on the epidemiology and prevention of HIV/AIDS and related diseases in the U.S. and Africa. Among his numerous other appointments, he is a principal investigator of the Public Health-Academic Partnership with the D.C. Department of Health; clinical research site leader for the D.C. site of the NIH-funded HIV Prevention Trials Network; chair of the Global Work Group on the Advisory Committee to the director at the CDC; and a voluntary HIV/AIDS physician at the D.C. Veterans Affairs Medical Center.

“**This is an important chance** for all of us to have a major impact on an epidemic that is harming so many people in our nation’s capital.”

With GW serving as the administrative home of the D.C. D-CFAR and Greenberg as the principal investigator, this partnership will provide the infrastructure to facilitate collaboration, data sharing, and enhanced research opportunities among the entities. The center will be led by an executive committee and five coordinating bodies, or “cores” — administrative; developmental; clinical; basic science; and behavioral science, prevention, and biostatistics.

“Our main deficiency in HIV/AIDS research in Washington is in basic science. That’s the area we’re focusing on,” explains Michael Bukrinsky, M.D., Ph.D., professor and vice chair for research at SMHS’ Department of Microbiology, Immunology, and Tropical Medicine, director of the developmental core, and interim director of the basic science core. The region has a talented pool of clinical and public health researchers, Bukrinsky explains, but “there are very few HIV/AIDS researchers doing basic science work. This is an area we need to develop in order to support the other research studies. The only way to accomplish that is to attract new people, especially young investigators.”

Earning such a prestigious research classification was no small task for Greenberg and his colleagues. Successful applicants need to have a significant level of funded research already in place, as well as a demonstrated commitment to HIV/AIDS care. To meet that standard, Greenberg and D.C. D-CFAR co-director Gary Simon, M.D., Ph.D., who is also the director of the Division of Infectious Diseases and vice chair of the Department of Medicine at SMHS, decided to pool resources from across Washington. “Our vision was that by getting people together from institutions throughout the city, we could assemble a successful D-CFAR,” explains Greenberg. At the time the application process began, GW might not have met those criteria on its own. By creating a proposal that included all the major HIV/AIDS research institutions in the city, however, the application exceeded all benchmarks.

“The HIV/AIDS community in the nation’s capital is allied and deeply committed,” says Greenberg. “The idea is to transfer this positive energy into increasing the quantity and quality of research.”

Each of the institutions in the D.C. D-CFAR has a robust HIV/AIDS care and treatment program and boasts active, federally funded researchers. Together, they bring strengths to the center that are simultaneously diverse and complementary. The VA and Children’s National have distinct patient populations. Children’s National is actively involved in adolescent and pediatric HIV trials networks. Fred Gordin, M.D., chief of Infectious Diseases at the VA and professor of Medicine at GW, leads HIV/tuberculosis studies and the local component of the Community Programs for Clinical Research on AIDS, a community-based clinical trials network. Georgetown University is home to the Women’s Interagency HIV Study, and Howard University is a critical partner for its own HIV/AIDS research initiatives and for the recruitment and training of minority scientists. GW, in addition to having strong epidemiology, surveillance, behavioral, and biostatistics resources, is home to Simon and his team’s clinical, patient-based work that uses antiretrovirals and antiretroviral regimens.

Greenberg notes that the developmental designation is a one-time, nonrenewable probationary step. After that five-year period is over, centers may apply for full CFAR status. The new D.C. D-CFAR, he says, will be judged on the collective success of the participating institutions in conducting outstanding HIV/AIDS research that will influence the field and, they hope, lead to better prevention and treatment in the future. “If the research and financial contributions are strong, and we do the things necessary to demonstrate that we took this opportunity and made the most of it, I’m confident that we can make the transition to a full CFAR,” says Greenberg. “This is something we can all be proud of because it gives us the chance to have a major impact on an epidemic that is harming so many people in our nation’s capital.”
A Smart Investment
COMMUNITY HEALTH CENTERS OFFER ANSWERS TO CONCERNS SPARKED BY NEW HEALTH CARE LAW

By Anna Miller

Leighton Ku, Ph.D., M.P.H., professor and director of the Center for Health Policy Research in the Department of Health Policy at the School of Public Health and Health Services, doesn’t try to quell the political and ideological discord ignited by the passage of health care reform. “Unfortunately, empirical information does very little when people have strong ideological beliefs,” he maintains.

But above the din, two key questions have emerged that Ku feels quite comfortable answering: Will the United States have the primary care capacity to serve the newly insured? And can we contain the growing costs of health care? These issues, he and his colleagues have found, are largely addressed within the health care bill itself.

“The $11 billion in additional grant money for non-profit community health centers included in the health care reform bill will both bolster the capacity of the nation’s primary care system and reduce the long-term growth in health care costs,” the team concluded in a report released June 30, 2010, by the Geiger Gibson/RCHN Community Health Foundation Research Collaborative at GW’s School of Public Health and Health Services.

According to the report, the expansion of community health centers (local, non-profit, community-governed health care providers that offer comprehensive primary and preventive care in medically underserved communities) will increase the number of patients receiving primary care by at least 18 million by the end of the decade, effectively doubling the number of people served.

Not only will the law create more sites and bigger venues, the report says, but it also will shift the patient demographic from uninsured to insured. Because 32 million more people are expected to be insured by 2019, health centers — which accept patients regardless of ability to pay — will absorb fewer uncompensated health care costs, thus increasing their capacity to serve. “These two forces, additional grant funding on one hand, more insurance coverage on the other, act synergistically to enable health centers to grow very rapidly,” says Ku, who is an expert in health care financing and budgets.

Community health centers are lauded for their team-based approach to care. As opposed to private practices, the centers thrive on a diversity of professions, with nurse practitioners, physician assistants, and community health workers all helping to deliver care. “This is a more efficient way to deal with the scarcity of primary care physicians, without risking quality,” says Ku. “This is the kind of team-based care that primary care needs to adopt in the future.”

In addition to helping millions of people receive primary care, the expansion of community health centers will save the country billions of dollars. According to the analysis, the investment will reduce total national medical costs by more than $180 billion over the next 10 years, including more than $50 billion in federal Medicaid expenditures, and more than $30 billion in state Medicaid expenditures. Even after controlling for differences including insurance status, health, gender, and age, the annual savings from community health centers totaled as much as $1,100 per person.

Although the exact savings are subject to variability, the findings are supported by prior research demonstrating that community health centers improve the quality of care and reduce the need for more expensive treatment. Even more important, the predictions are likely underestimates. If future appropriations are approved, medical costs may be reduced by as much as $300 billion over the next 10 years.

“We have been running community health centers since the 1960s,” says Ku. “Our government has supported this system on a bipartisan basis for decades, and this proven system of care will continue to make a difference in the future.”
Making the Right Connections

GW's New Institute for Neuroscience Explores the Mystery of Mental Illness

Seated with his colleagues at a conference table, Anthony-Samuel LaMantia, Ph.D., founding director of the new George Washington Institute for Neuroscience (GWIN), intuitively used his hands when describing a stage in brain development.

His fingers articulated pinching, shifting, and stretching motions around his head to mime a dynamic series of cell migrations between the developing face and brain that occur roughly halfway through embryonic development in a mouse.

“The brain is sending out a set of cellular ambassadors to instruct the periphery on how to develop so it’s ready for the brain and the brain is ready for it,” later explains LaMantia, an internationally renowned neuroscientist who came to GW’s School of Medicine and Health Sciences (SMHS) in 2010 from the University of North Carolina School of Medicine. “The idea that this is a target for disorders should be something everybody embraces. We have known for years that patients with a variety of behavioral disorders, including autism and schizophrenia, also have mild to severe facial anomalies that are thought to arise during development.”

GWIN was established with the aim of revealing many such “targets” for mental illness through a focused, multidisciplinary approach. LaMantia has assembled two dozen researchers from across GW and partner institution Children’s National Medical Center with a wide range of neuroscience backgrounds to take on collaborative projects, including the basic science of brain development, its clinical relevance, and others. Specialist Norman Lee, Ph.D., professor of Pharmacology and Physiology, for example, draws from his research on gene networks and pathways relating to behavior, while Sally Moody, Ph.D., professor of Anatomy and Regenerative Biology, provides insights into genes involved in neural tube and craniofacial birth defects.

Researcher Molly Huntsman, Ph.D., principal investigator at the Center for Neuroscience Research at Children’s National, provides insight from her work on the development of inhibitory neurons in neural circuits. Vittorio Gallo, Ph.D., the Wolf-Pack Chair of Neuroscience and director of the Center for Neuroscience Research at Children’s National, contributes his experience exploring neural progenitor development and injury responses in the immature and adult brain.

By synergizing all this expertise, GWIN seeks to understand mental illness from a holistic perspective, including the molecular, cellular, and behavioral elements. “Putting together these labs will make a whole that is much bigger than the sum of its parts,” Gallo predicts.

The institute’s multi-front approach reflects a growing philosophy in neuroscience: By finding common ground, formerly disparate labs from various fields can collaborate and jointly delve deeper into heritable, genetic disorders that disrupt brain function, and, therefore, behavior. New ideas are in demand, as the true cause of mental illnesses remains a mystery. Disorders like autism, fragile X syndrome, pediatric epilepsy, perinatal brain injury, and attention deficit hyperactivity disorder (ADHD) remain largely unsolved, but their symptoms demonstrate that complex behaviors, when disrupted, have a big impact on the quality of life. “That’s what we’re ultimately trying to shed light on,” LaMantia emphasizes.

GWIN’s translational approach to neuroscience research puts a focus on the developing brain. While the institute will not exclusively focus on children, its work will be caged in the
DISCONNECT
understanding that the onset of neurological diseases comes much earlier in life than scientists have previously believed. One disorder of keen interest to GWIN is DiGeorge syndrome, a disease with wide-ranging signs and symptoms caused by a deletion of one copy of a small subset of the normal complement of genes on chromosome 22. Those who lack this network of genes often suffer physical malformations and various types of mental illness, showing that the missing genes are vital during early stages of development. Numerous mental symptoms arise: 50 to 60 percent of children with DiGeorge syndrome suffer a psychotic break in late adolescence, 30 to 40 percent are diagnosed with an autistic spectrum condition, 30 to 40 percent are diagnosed with ADHD, and roughly 10 percent are diagnosed as intellectually disabled.

LaMantia suspects that a person’s unique genetic makeup, such as a missing set of genes — along with distinct environmental factors — plays into the behavioral outcomes of the disease. Further complicating matters is the possibility of a mutation altering brain development at several points throughout its orchestration. “It’s a nightmare thinking about this in terms of therapeutic interventions. Where do you fix it?” he asks.

CORTICAL CONNECTIVITY

Discernible behavioral symptoms of psychiatric illnesses ultimately arise from disrupted electrical connections between nerve cells, much as palpable chest pains are elicited by a clogged coronary artery. The detective work needed to understand the cause of, say, schizophrenia demands a nuts-and-bolts, neurobiological understanding of the disease. “It’s clear that there is a neurogenetic component,” observes Gallo, “but how does the genetic component become expressed, manifested, and translated into abnormal cellular structures?” Once a specific gene or set of genes is identified, Gallo says, the next step will be to understand how those irregular genes generate abnormal proteins, and how those proteins, in turn, generate aberrant nerve cell connections and functions.

Nerve cell interaction, or connectivity, is a key component in understanding how complex behaviors are disrupted in mental disorders, according to LaMantia. “My guess is that for all of these
diseases,” he says, “some aspect of the basic rules of connectivity is broken.”

In fact, LaMantia and many other neuroscientists now believe that most, if not all, behavioral and psychiatric diseases — including autism, ADHD, bipolar disorder, and schizophrenia — are part of a broad class of diseases referred to as “disorders of cortical connectivity.” All these disorders arise from the improper development of the cerebral cortex, particularly regions of the frontal cortex, which occupies the most anterior part of the brain. LaMantia describes this region as “the heavy lifter” because it’s the throne of executive functions that include memory, selective attention, social interaction, language, learning, and cognition.

Deciphering the link between the improper wiring of the frontal cortex (and the associated behavioral consequences) and a genetic source would be a huge step toward understanding psychiatric disease. A key goal of GW-IN will be to define and assign specific functions to genes and sort out how they work together to control various aspects of cortical circuits’ wiring. “We have to understand how normal development occurs,” explains Gallo, “because it is the disruption of these pathways and their interactions that is modified in neuropsychiatric disorders.”

LaMantia likens the business of gaining a molecular understanding of neural development to that of cancer biology research 20 years ago, when it delved into signaling pathways that regulate cell proliferation, apoptosis, and migration motility. “In the isolated instance of each of these detailed molecular experimental paradigms, you’re not necessarily identifying the target for therapy,” he says, “but rather looking at a piece and understanding how it goes slightly awry.” The subsequent step, he adds, would be to see what happens when they adjust this piece therapeutically and apply it to the brain.

ARRIVING LATE TO THE PARTY

Despite the neurodevelopmental hypothesis of mental illness that began to take hold in the late 1980s, this paradigm shift hasn’t translated into effective medicine for many people with mental disorders. Overall, progress in reducing the morbidity and mortality of psychiatric diseases has been slow in comparison to that of cancer and cardiovascular disease. When speaking at GW-IN’s inaugural seminar series in mid-September 2010, Thomas Insel, M.D., the director of the National Institute of Mental Health and a friend of LaMantia’s, described existing treatment options as “not so good.”

Insel conveyed that the challenges of diagnosing and treating mental illness are based on its lack of reliable biomarkers, the essential tools of objective diagnosis, making it one of the few areas of medicine that still relies on skills of observation. Since the cause of most mental disorders remains largely unknown, so, too, is a psychiatric patient’s response to treatment. And cure and vaccine are terms that still seem to have no place in the lexicon of treating mental disorders.

These disadvantages have snowballed to make mental illness the largest source of disability of all medical disorders in the United States. Ninety percent of all suicides are due to mental illness, a total that surpasses the yearly death toll from homicides and AIDS, and the fiscal toll of mental illness is around $300 billion per year.

When LaMantia considers the Herculean task that lies ahead of neuroscience, he thinks again of cancer. Oncology’s identification of targets for chemotherapy is based on the understanding that the ways in which cells divide, move, and die are expressions of transformation and malignancy.

Similarly, LaMantia sees the need to understand neuronal circuitry in terms of neurons themselves and how their processes grow. He wants to grasp how neurons initially become specified to be what they are and — importantly — how they construct synapses to wire up with other neurons.

GW-IN already employs strong scientists recognized for probing neuronal precursor specification and early patterning in morphogenesis, the stage when cells acquire the potential to blossom into a mature neuron. LaMantia intends to complement this effort by bolstering research that focuses on the next step in neuronal development: synapse building.

As a neuron differentiates, it puts out processes and makes connections with other neurons. LaMantia thinks this step is a crucial component in the origins of frontal cortex disorders. “We all believe that there are neurogenic proliferation and migration deficits in these disorders,” he says. “But where the rubber really meets the road is when they don’t wire up properly.”

Nerve cell interaction, or connectivity, is a key component in understanding how complex behaviors are disrupted in mental disorders, according to LaMantia.
You won’t find Lynn Goldman, M.D., M.P.H., stuck in a rut. The self-proclaimed adventurer has blazed an indomitable and vibrant career path, serving in such positions as pediatrician, epidemiologist, professor, investigator, and government appointee. Countless people and places have reaped the benefits of her broad work in environmental health practice and chemical regulatory policy — efforts that were recently recognized with a prestigious award from the Heinz Family Foundation.

Goldman has a simple explanation for a career that is as varied as it is venerated: “I like new challenges,” she says. “I haven’t done the same type of thing my whole life because I like to make an impact in a lot of ways.”

In August 2010, Goldman took on her newest challenge when she was appointed as the third dean of GW’s School of Public Health and Health Services (SPHHS). The school — which boasts seven departments, has one of the fastest-growing research portfolios of any school of public health in the nation, and is developing plans for a new state-of-the-art building — has an exhilarating trajectory of change that keeps pace with Goldman’s own.

“One of the exciting things about SPHHS is that it’s still growing and developing,” she says. “I am excited to build upon the good work that has been done so far, most recently under the leadership of my colleague, Josef Reum, who served with such distinction and passion as interim dean for the last two years. It’s part of what convinced me to come here.” Reum, Ph.D., is a professor of Health Policy and of Health Services Management and Leadership at the school and now serves as senior associate dean.

In Goldman, GW has found exactly what it needed: a dynamic individual who could bring multifaceted experience to the post. “With her breadth of experience in the fields of children's environmental health, public health practice, and chemical regulatory policy, as well as her distinguished career in government, Lynn Goldman is ideally suited to lead our rapidly emerging School of Public Health and Health Services,” said GW President Steven Knapp, in announcing Goldman’s appointment.

Goldman launched her public health career in 1981, when the general belief was that low-level exposure to environmental contaminants wasn’t harmful. Residents of now-infamous Love Canal in Niagara Falls, N.Y., for example, were told by government officials that the nearby hazardous waste site would not induce any adverse health effects. But during a research fellowship at Children’s Hospital and Research Center in Oakland, Calif. — where she investigated the health impacts of toxic chemical exposure on children living near Love Canal — Goldman contributed to early findings linking birth and growth problems to the site itself.

The results, which later became the subject of international attention and controversy, shifted both general beliefs about public health and the scope of Goldman’s career. She decided to dedicate herself to fighting for the underdog. “When public health issues affect small groups of people, rather than the general public, those groups can be marginalized,” she explains. “In the U.S., our biggest challenges are the inequities in health status.”

Goldman followed that experience with a position as an epidemiologist at California’s state health department, where she found she had a strong interest in children’s health. There, she established a blood-lead surveillance system, laying the groundwork for California’s childhood lead poisoning prevention program.

In 1993, President Bill Clinton appointed Goldman to serve as assistant administrator for the Environmental Protection Agency’s (EPA’s) Office of Chemical Safety and Pollution Prevention, where she guided the agency’s expansion of “right to know” laws under the Toxics Release Inventory program and overhauled the nation’s pesticide laws. Later, she helped advance the Food Quality Protection Act of 1996, the first law explicitly requiring measures to protect children from lead poisoning and pesticides.

Goldman joined the faculty at the Johns Hopkins Bloomberg School of Public Health in 1999 with the
primary intention of pursuing her own research. While leading investigations on children’s health and emergency response, however, she discovered a passion for academics. So when it came time for the next step in her career, Goldman found that GW — a university with a strong reputation for policy work — was an ideal fit. “Here at GW, and in the nation’s capital, you can play a very powerful role in policymaking,” she says.

In her new post as dean, Goldman will use her passion for public health, education, and policy-shaping to guide her decisions. She hopes to build upon SPHHS’ rising research portfolio in areas such as HIV/AIDS, environmental health, and health policy. Fostering strong relationships and collaborations between departments and with federal and international organizations is another goal.

In addition, Goldman will oversee another significant change at SPHHS: the development of a new building (see below). The sustainably designed research and educational facility will, for the first time, provide a central home for SPHHS, facilitating greater collaboration among faculty, students, and staff. “The new building is a vital part of the school’s future,” she emphasizes. “The physical space will give us an identity and make it possible for us to become an even greater, more influential institution in the decades to come.”

Key to that identity, says Goldman, is blazing a continuous path of learning and imbuing wisdom in future generations. “We need to teach the skills that will enable our students to acquire more knowledge over time,” she says. “Learning is a lifetime experience.”

Healthy Home Design

SCHOOL OF PUBLIC HEALTH AND HEALTH SERVICES MAKES PLANS FOR NEW BUILDING

At the conclusion of its May 2010 meeting, The George Washington University’s Board of Trustees unanimously endorsed one of the Medical Center’s most important strategic priorities: construction of a new building to house the School of Public Health and Health Services (SPHHS). The new building will, for the first time in the 13-year history of SPHHS, serve as a consolidated home for most of the school’s faculty, students, and staff.

The technically advanced facility, scheduled to be completed in the summer of 2014, will provide a central location for research in public health, facilitating and enhancing synergies among SPHHS’ seven diverse departments. The building will also serve as an essential convening place for collaboration among SPHHS, government agencies, and international public health organizations.

The new structure will be built on land that is currently occupied by GW’s Warwick Building at the intersection of 24th and K streets on Washington Circle. The building will feature 115,000 square feet of state-of-the-art classroom facilities, research labs, departmental and office space, and conference rooms, at a cost of $75 million.

Current plans call for the building to be constructed with a range of “green” materials and sustainable features. The facility is targeting a Silver rating under the Leadership in Energy and Environmental Design (LEED) Green Building Rating System of the U.S. Green Building Council.

Lynn Goldman, M.D., M.P.H, the new dean of SPHHS, said the first-ever home for the seven departments, students, faculty, and staff is a vital part of the school’s future. “This new building will enable GW’s School of Public Health and Health Services to move to the next level of excellence in our education and research programs. It’s hard to think of anything more important to the school’s long-term future and its ability to grow and attract the best faculty and students in public health. I’m very excited to be a part of the project,” she said.

The University expects to begin removing the Warwick Building and start construction on the new SPHHS building in the spring of 2012.

—By Michael Chapman
ub-Saharan Africa bears 24 percent of the world’s disease burden, but has just three percent of its health workforce. Training — and retaining — physicians on the continent has been an ongoing challenge. Impoverished health systems, the world’s highest prevalence of HIV/AIDS, and the constant lure of emigration take heavy tolls on the graduates of the 160 medical schools in sub-Saharan Africa.

Recently, the National Institutes of Health (NIH) tapped the School of Public Health and Health Services to serve as the coordinating center of its Medical Education Partnership Initiative (MEPI), a $12.5-million, five-year project to increase medical education capacity at 12 participating medical schools in sub-Saharan Africa. Researchers Fitzhugh Mullan, M.D., Murdock Head Professor of Medicine and Health Policy, and Seble Frehywot, M.D., M.H.S.A., assistant professor of Health Policy and of Global Health, will serve as principal investigators on the project. They will assist medical schools from 12 countries in enhancing the quantity, quality, and retention of their graduates.

MEPI emerged from the 2008 reauthorization of the U.S. President’s Emergency Plan for AIDS Relief (PEPFAR), which included a mandate to train 140,000 new health workers in Africa over five years. Through the initiative, the NIH seeks to expand medical education and build health care capacity to combat HIV/AIDS, while also creating a workforce that can address other local health problems across the spectrum of diseases.

“It is vital that we develop medical and research capacity in sub-Saharan Africa so that advances can be quickly adapted for local use,” said NIH Director Francis Collins, M.D., Ph.D., when announcing MEPI. “This program will not only strengthen medical education to produce much-needed caregivers, but will also generate well-trained researchers.”

GW will work with the participating medical schools to establish baseline assets and needs. “We want to get a sense of how their educational engines function in terms of the training they offer, numbers of people trained, and where their graduates practice,” explains Mullan.

Following the initial assessments, GW and its local partner, the African Center for Global Health and Social Transformation, led by Francis Omaswa, M.D., will develop technical support plans that address the specific needs of each school. GW will link the schools to resources and expertise to enhance their basic and clinical science teaching.

Communication is an essential aspect of the project. GW will establish an electronic platform to support information sharing, mutual curricular projects, and data collection between the participants. In addition to regular site visits to each school, the GW team will coordinate an annual symposium for the participants.

Despite the challenges presented by the scale of the project, Mullan and Frehywot recognize the enormous potential MEPI offers for both analysis and contribution. “Assisting these institutions is a rare opportunity to conduct educational service and, if we succeed, impact the medical education systems of an entire continent,” Mullan says.
When Tim Russert, the longtime moderator of Meet the Press, died in the offices of WRC-TV in Washington, D.C., he did not succumb to a “massive heart attack,” as some reports suggested. Instead, he died of a sudden arrhythmia — sometimes called “sudden cardiac death” — when his heart’s electrical pulse lost sync and went haywire.

An autopsy found that a piece of plaque had broken free in one of Russert’s arteries, lodging in a blood vessel that feeds the heart. That section of Russert’s heart lost oxygen. This ischemia, in turn, induced ventricular fibrillation — uncontrolled twitching of the muscle fibers in the lower chambers of the heart. Instead of pumping blood, Russert’s heart went into useless spasms. The 58-year-old died within minutes.

“Instead of following the main pacemaker of the heart, the cells that receive only partial oxygen start screaming ‘there’s something wrong here,’” says cardiac physiologist Narine Sarvazyan, Ph.D. “This message, whatever it is, interferes with the heart’s normal electrical pattern. The heart goes into fibrillation, and the outcome is usually deadly.”

According to the American Heart Association (AHA), some 300,000 Americans receive emergency treatment each year owing to sudden cardiac arrest. Yet scientists don’t fully understand how ischemia causes fibrillation — the cellular message that “something’s wrong” with the heart.

“We would like to understand why when someone has a heart attack, some people — like Tim Russert — immediately have lethal arrhythmia, and some people don’t,” says Matthew Kay, D.Sc., P.E., an assistant professor in GW’s School of Engineering and Applied Science who works closely with Sarvazyan. “That’s the big question.”

That question has prompted Sarvazyan, an associate professor in GW’s Department of Pharmacology and Physiology, and her interdisciplinary team to launch a series of projects to understand heart arrhythmias at a deep level. Their projects span the range of molecular, cellular, tissue-based, whole-organ, and animal studies. In addition, Sarvazyan’s team has begun research that could one day lead to a “Band-Aid” for the heart — patches of stem cell-derived cardiac tissue engrafted onto damaged areas.

The scary thing about sudden cardiac attacks is that they can just come out of nowhere,” says Luke Swift, a Ph.D. student co-mentored by Sarvazyan and Kay. Swift attaches a still-beating rat heart to a tiny spigot and dips the heart into a small, clear plastic box attached to a lab stand. Air is bubbling into the liquid-filled

A rat heart injected with voltage-sensitive dye is bathed in green light to show electrically active cells.
box, and tangled wires snake from the apparatus to equipment that takes images of the heart with two cameras: one recording electrical activity, a second capturing metabolic action.

This imaging system, being developed by Kay, will provide crucial data about where and when low-oxygen conditions in the heart trigger arrhythmias. In particular, the cameras will pinpoint “hot spots” where irregular rhythms originate. In patients with certain types of arrhythmias, cardiologists can zap, or “ablate,” these hot spots with a spark of electricity to the area. At The George Washington University Hospital, specialists regularly perform such procedures, says Marco Mercader, M.D., a clinical electrophysiologist who collaborates with Sarvazyan and Kay. Mercader says the ablation procedure successfully resolves arrhythmias in about 70 percent of patients, but with the benefit of better imaging, those figures could be better still.

With the rat heart prepared, Ph.D. student Huda Asfour consults three computer screens in a corner of the cramped experiment room. An electrical engineer, Asfour writes computer code that processes the heart images for closer scrutiny. As Swift dips two metal leads into the bubbling heart box, the monitors blink to life, displaying a trace of the heart’s electrical activity. The rhythm is erratic at first, then settles into the familiar spike-and-line pattern of a normal heartbeat.

Asfour positions a camera about a foot in front of the heart, then bathes the heart in green light. She explains that the light excites a voltage-sensitive dye — Swift injected it into the heart earlier — that fluoresces as cells become electrically active. The dye allows the camera to record the precise patterns of electrical activity swirling through the heart.

Swift tightens a small suture around the coronary artery at the top of the heart, choking off oxygen. The team wants to see how this localized ischemia impacts the heart’s normal electrical rhythm. A second camera records the fluorescent intensity of a naturally occurring compound called NADH. The compound glows with increasing intensity as the tissue is starved of oxygen. Swift switches off the overhead light and the room glows green. “Now this looks like science,” Swift says, smiling.

The room gets crowded and activity picks up as Kay and a Ph.D. student enter. The ECG rhythm has changed; it is double spiking. The heart is contracting twice rapidly, a condition that may complicate data analysis. Kay and Swift fiddle with the tubes and wires poking into the heart box. Kay suggests warming the heart. The ECG rhythm settles momentarily, then reverts. “It’s double spiking again,” Asfour says.

When the rhythm stabilizes, Asfour runs the cameras. She starts them with a click, and data from the devices flows into the computer. In just a few seconds, the data run is over. Minutes later, Asfour runs the cameras a second time. She’s unsure if the data will be clean enough to work with — the double spikes have returned.

“The studies are technically challenging,” Kay says, adding that the team did retrieve useful data from the experiment, even though things didn’t go according to plan. “Usually about half the time we’re successful at collecting the data we need to answer our questions.”

And so, in fits and starts, science moves ahead. Days later, Kay discusses the heart imaging experiments, studies for which he and Sarvazyan have received a new five-year grant from the National Institutes of Health. While inducing ischemia in the rat heart, the metabolic imaging camera pinpoints small areas screaming for oxygen. That data is then overlaid on images of electrical flow around the heart. Together, the two data sets reveal where and when the ischemic regions trigger arrhythmia. So far, the studies have shown that premature beats — a type of arrhythmia — often begin at the boundary of the ischemic regions.

It’s a Tuesday afternoon, and Sarvazyan has gathered her team for a meeting. Assistant Research Professor Zaruhi Karabekian, Ph.D., presents the latest experiments in Sarvazyan’s second project, the effort to design Band-Aids for the heart. Worldwide, in a series of human trials, researchers are attempting to repair heart damage using stem cells derived from the patients’ own
blood and bone marrow. But these studies have shown only transient benefits, and Sarvazyan says one reason is that the injected cells fail to engraft in the damaged heart.

Ultimately, Sarvazyan believes patches of heart cells grown from either embryonic stem cells or adult cells returned to the embryonic state could be designed to permanently stitch themselves into the heart. In a step toward that goal, the team has engineered a new type of stem cells to produce surplus sticky proteins on their surface. These two sticky proteins, called N-cadherin and connexin-43, help bind patches of the new heart cells to the existing tissue. Whereas N-cadherin aids the cells’ connections, connexin-43 helps them fire together, a discovery the team made three years ago.

Next, a student who spent her summer in the lab before heading to medical school at GW, Sana Idrees, presents the results of her experiments. She’s been working with Karabekian on another aspect of the heart Band-Aid project: reducing the immune system profile of newly grown heart cells, a project for which Karabekian recently received an AHA grant. Every cell in the body carries a passport, Sarvazyan explains, called the major histocompatibility complex (MHC). If a cell has the wrong passport — meaning the cell has been transplanted — the immune system will attack it as a foreigner. In ongoing clinical trials of various types of stem cells for heart repair, researchers are finding that after several weeks, all evidence of the implanted cells has disappeared. The implanted cells don’t engraft in the heart, where they could provide a long-term boost of pumping power. To make viable heart grafts that don’t suffer this fate, the team hopes to squelch production of MHC. Cells without an MHC passport will, in essence, be invisible to the immune system. Such a step could be key to developing a viable heart therapy, says Sarvazyan. “We really need to … understand how to implant these heart stem cells in a way that is durable, so the cells stick,” she adds.

The field of cardiac stem cell therapy is nascent, according to Sarvazyan, similar to where bone marrow transplantation for leukemia was decades ago. “We really need to go back to the blackboard and understand the basics of cellular activity” before cell transplants can be improved to help heart patients, she says. If a pending NIH grant is funded, it would provide Sarvazyan the means to scale up the heart-patch experiments in live animals, to see if her team can make tissue patches that engraft properly in the heart and conduct electrical signals.

Of course, there are no guarantees that those experiments, if funded, would work. And so Sarvazyan takes the long view, as any basic scientist must. She knows that the human health applications of her work are years, if not decades, off. The cardiac physiologist is moved by the same desire that drives every other scientist: the quest to understand, to accumulate knowledge, to explain some corner of the universe.

Not that it’s easy. “I tell my students when they come into the lab that out of 10 experiments, maybe only one will work,” she says. “You have to have enough drive and feel enough inspiration from those successes to push you through to the next set.”
n the fifth floor of Children's National Medical Center, in the southeast corner of a large lab, is a cubby with a desk, a computer, two bike helmets, and three phones. From this understated workspace, Eric Hoffman, Ph.D., directs one of the world’s largest centers for the study of genetic disorders — the Center for Genetic Medicine Research.

Hoffman, a family man who spends most of his free time outdoors, dislikes doors or walls in his workspace. He thinks academic medicine is too “silied,” and believes that more openness means more collaboration. He explains his science by using metaphors of Slinkys, Tinker Toys, and cookbook recipes. He laughs a lot. It’s not yet 11 a.m., and Hoffman has already advised on a grant application, spoken with members of his lab, and interviewed a prospective nurse. Now, he is explaining a new treatment possibility for Duchenne muscular dystrophy, the disease that best defines his research and that lies closest to his heart.

Children's National serves as the home of two GW School of Medicine and Health Sciences (SMHS) departments: Pediatrics and Integrative Systems Biology, which Hoffman chairs. Hoffman, who is also a professor of Pediatrics at SMHS, landed at Children's National 10 years ago, after a long stint at University of Pittsburgh School of Medicine and several years of teaching and postdoctoral work at Children's Hospital Boston and Harvard Medical School. He has been awarded fellowships from the Howard Hughes Medical Institute, the Muscular Dystrophy Association, and the American Heart Association. Now, he runs a lab that covers thousands of square feet and spans two floors, staffed by 35 faculty members and 200 researchers.

Duchenne is a muscle-wasting disease that strikes one in every 3,500 children, mostly boys. It is an X-linked recessive trait — carried on the X-chromosome and more commonly expressed in males — but, like dwarfism, occurs spontaneously more often than it is passed down. Typically, children with the disease develop normally for their first few years, and then begin to have trouble climbing stairs, getting up from the ground, or breaking into a run. Most are in wheelchairs by their teens, and as the disease progresses, eventually require respirators to breathe. The majority die in their 20s or 30s from heart failure. There is no cure.

Hoffman is one of the leading researchers working on a new treatment option for Duchenne called exon skipping. He has high hopes for the therapy, but worries that existing regulatory rules and overwhelming cost will slow efforts to get the drug approved and made widely available to patients.

“The real tragedy is if something works that can help these patients, and we can’t deliver it,” he says.

Hoffman’s interest in muscular dystrophy can be traced back to his postdoctoral days at Harvard, when he first began manipulating the genes of fruit flies, changing their eye color and turning their wings backward. He spent long hours in the lab and often took the flies home with him. One Thanksgiving, he stationed a jar of fruit flies beside his plate during the meal to be sure the flies weren’t having “inappropriate sex,” which might compromise his research. “Of course,” he recalls, “there’s only so long that you can turn their eyes [different] colors and their wings backward before you start to ask the question: How is this helping humanity?”

So he shifted his focus. Using what he’d learned
manipulating genes, he turned his attention to human genomes. Soon after, his Harvard research team, led by Louis Kunkel, Ph.D., became the first to identify and clone the gene responsible for muscular dystrophy: the DMD gene.

It was 1986, and little was known about the disease at the molecular level. But suddenly, characteristics of muscular dystrophy that had baffled researchers began to make sense. Most genes have about 30,000 DNA units. The DMD gene, they found, had more than two million, making it the largest known human gene. Its sheer size made it more prone to spontaneous mutations, which explained why the disease was so common. And, researchers discovered, it coded for a protein critical to muscle function. They named the protein dystrophin.

The job of dystrophin is to reinforce the walls of muscle cells, which are long and tubelike, and which constantly stretch apart and slam together as people move. The dystrophin protein gets plastered along the muscle walls, providing the strength and support needed during muscle contraction. But mutations can cause the gene translation process to go haywire.

Genes are divided into exons and introns. Exons code for protein; introns, also known as “junk” DNA, are the stuff in between, and unnecessary for protein production. During gene translation, the 79 exons that make up a normal dystrophin gene are spliced from the gene’s introns and pieced together like a puzzle into messenger RNA (mRNA), which then translates into the dystrophin protein. When the exons are appropriately assembled, they form a reading frame in which each three-letter section of mRNA translates into one amino acid.

The structure of this frame is enormously important. If any part of any of these 79 exons is damaged or deleted through a mutation, then the message can get scrambled. This can prevent the mRNA from being assembled in a readable form, resulting in a nonfunctional dystrophin protein. Hence, Duchenne. “If you’re missing it, you start blowing holes in your plasma membrane,” Hoffman says. “And that’s the first key finding to diagnose a patient with Duchenne. You might actually see enormous amounts of muscle guts in their blood.”

Exon skipping drugs, a form of antisense compound that interact with nucleic acids to modify gene expression, are sometimes described as “molecular patches.” They seal and repair the damaged fragments of the mRNA. “What the exon skipping drugs do, in lay terms, is go into the genetic molecule, trim the ends around that deleted area, and splice them back together. And then the message makes sense again,” says Valerie Cwik, M.D., research and medical director for the Muscular Dystrophy Association. Exon skipping would not cure Duchenne, but researchers believe it could substantially reduce symptoms, by remodeling a Duchenne patient’s mRNA.

In 2000, two Washington lobbyists, Joel and Dana Wood, had a disturbing meeting with their son’s preschool teacher. “She was being overly emotional about our need to get him checked out,” Joel Wood recalls. “She’d taught hundreds of students and had never seen a child at the age of three who struggled to get up the stairs as much as James did.” They took him to Hoffman’s lab for a dystrophin identifier test. Within a week, they had the full diagnosis: Duchenne muscular dystrophy. James was missing exons 44 through 52.

“It’s a devastating diagnosis when it’s your child,” Joel Wood says. “And I think anyone faced with that pretty much takes an inventory of their resources and figures out what they can do.” Research for the disease was grossly underfunded, the couple discovered, and what little funding did exist was divided among three government agencies.

Only months earlier, Hoffman had transferred from the University of Pittsburgh to Children’s National in Washington, D.C., where he felt he would be better positioned to advocate for federal support. His initial goal,
cloning the first Duchenne gene, had been realized, but he continued to feel a strong obligation to deliver something to patients and their families. “I am quite focused on bringing therapeutics to these patients,” he says, “These kids and their families are my bosses.”

As it turned out, Duchenne was getting only five percent of the amount of federal funding that cystic fibrosis received, Hoffman recalls: “It was dismal, and nothing was being translated to the patients.” Hoffman and the Woods mobilized their efforts. They worked with members of Congress to pass the MD CARE-Act (Muscular Dystrophy Community Assistance, Research, and Education Act), which mandated that the government devote more attention and capital to muscular dystrophy. They led a lobbying effort to secure $60 million from the Department of Defense. The Woods launched the Foundation to Eradicate Duchenne, which has raised more than $10 million.

“The scientific world was alien to me before my son’s diagnosis, and I think the political world was just as mystifying to Eric,” Joel Wood says. “But he has very sophisticated political skills. He has an amazing ability to speak in plain English and make things understandable.”

In the lab and in the clinic, studies are advancing, thanks in part to what Hoffman and the Woods accomplished on Capitol Hill. After studies on Duchenne mouse models and human cells indicated that exon skipping drugs could activate dystrophin production, Hoffman’s lab scaled up its research to study dogs with the disease. Duchenne in dogs is swift and fierce. The dogs usually get sick and die within six months. The dogs in the study had a point mutation in exon 7 of their dystrophin gene. After roughly six months of treatment with exon skipping drugs, the dogs began producing dystrophin again, at about 20 percent of normal levels in all skeletal muscles. And by every criterion studied — walking, running, eating, and drooling — the dogs’ muscle movement improved.

Results have also been promising in humans. Early-phase trials showed that the drugs appear to trigger dystrophin production in human skeletal muscles with no serious side effects. In another still-unpublished but public trial, 19 boys were treated for 12 weeks with varying doses of exon skipping drugs. Responses were varied, but in one case, nearly 50 percent of muscle fibers tested positive for some dystrophin after treatment. “It’s the first time anybody’s been able to get appreciable amounts of dystrophin back into the muscle,” Hoffman says.

Some are more cautious. While most skeletal muscles responded well to the drug, delivery to the heart has been less effective, Cwik says. But Hoffman hopes to see future research confirm that higher doses can fix that problem.

Exon skipping research is pushing regulatory agencies to consider questions that may soon apply to other areas of personalized medicine as well. Each drug, for example, needs to be tailored to the exact spot on the gene where the mutation occurs. “You need different drugs for different patients with an already rare disorder,” Hoffman says. To avoid sending each drug variation through a lengthy approval process, researchers are working instead to get the drug approved as a class.

The cost is also daunting. Developing the drug to treat three dogs cost nearly $1 million.

“I am quite focused on bringing therapeutics to these patients. These kids and their families are my bosses.”

But after 25 years of research, Hoffman says, DMD experts are finally building a good “racehorse. . . . It’s certainly the best place it’s ever been,” he says. “There’s a lot more rationale and knowledge going into this, and a much more coordinated international effort.”

In the meantime, Wood is hoping to get his son, now 13 and recovering from a broken femur, treated with exon skipping drugs as soon as possible. “I have great confidence that this has no significant side effects,” he says. “The alternative is a disease that’s got a 100 percent mortality rate.”

For now, the Wood family has to wait out the research and the regulatory process. “It’s a very tough thing, especially when your kid is suffering,” Wood says. “I know we’re going to get there. What I don’t know is whether it will come in time for my son.”
The southeast African country of Mozambique has endured a tumultuous past. Battered by civil war until 1992, the nation now faces an enemy just as fierce: HIV/AIDS. Though modest in size — about half the size of Alaska — the country has the fourth-largest number of people living with HIV in the world. Approximately 1.8 million citizens, or nearly 16 percent of the country, are infected, and thousands are born with the virus each year.

Far away, in a quiet laboratory in GW Medical Center’s Ross Hall, Jeanne Jordan, Ph.D., professor of Epidemiology in the School of Public Health and Health Services, seems removed from this crisis. But since witnessing the epidemic last year during a visit to Mozambique, the researcher has been determined to have an impact.

Jordan’s inspiration stems from a meeting with Ilesh Jani, M.D., Ph.D., director of Mozambique’s National Institute of Health. In recent years, the institute has focused on the country’s youngest HIV/AIDS patients by launching an Early Infant Diagnosis plan in 2007 to identify HIV-positive babies and treat them as soon as possible. Under the plan, rural health center staffers are trained to collect dried blood spots for HIV diagnosis. With large-scale infant diagnosis under way, the challenge now facing the institute is timing. Under the current diagnostic method, dried blood spots are shipped from village health clinics to provincial labs, and then to one of two central reference laboratories in the country for testing. By the time the results get back to the local clinics, two months or more may have elapsed. For the families, who may hear the results even later due to Mozambique’s poor communications infrastructure, that wait is too long.

Jordan and Jani’s meeting, however, sparked an exciting idea. “We thought it would be really effective to decentralize the process so that provincial labs could do the testing rather than having to send it off to some place that might be hundreds of miles away,” Jordan recalls. By performing tests closer to the point of care, workers could shorten the time between identifying HIV-positive infants and getting those infants into treatment. This, they thought, was something that could dramatically improve outcomes and save young lives.

But there was a reason no one had tried it before: Provincial labs in Mozambique are rarely more sophisticated than a single room with a sink, refrigerator, and microscope. Provincial testing “couldn’t be done with the current process used in the central reference lab because of the cost of the equipment, the highly complex technology, and the training needed,” Jordan explains. But she saw a potential way to circumvent that challenge, and, since her return to the United States, has been evaluating virtually instrument-free HIV detection tests for use in even the most basic labs.

Diagnosing newborns with HIV poses a unique challenge. Unlike adults, who are tested for the presence of HIV antibodies, infants must be tested for HIV genetic material itself. Because maternal IgG antibodies cross the placental
The internationally accepted diagnostic approach for infant HIV testing is twofold. First, technicians extract nucleic acid from a dried blood spot. Next, they conduct amplification tests of the extracted material for HIV-1. Highly trained technicians, specialized equipment, and extensive protocols are required for both steps, so an instrument-free methodology must address them in tandem.

Jordan identified HandyLab, a Michigan-based company that was developing reagents that could be put on an automated extraction instrument. Interested in translating HandyLab’s techniques into a manual approach, Jordan worked with the company to develop an extraction method that would require only the use of a magnet, heating block, and pipettes.

BioHelix Corporation, a Massachusetts-based startup, was a prime candidate for the second step in the process. The company had been working on a nucleic acid amplification test using a disposable cassette-based method. Its approach, too, required only simple devices. “You could essentially even use a car battery or solar panel as your power source for the heating block that is needed for the isothermal amplification step,” Jordan notes.

Though these approaches differ from the standard protocols, Jordan hopes that they will be just as effective in detecting HIV in infants. So far, results are promising: The methods have “very good correlation and a very good level of sensitivity,” she says. Because most samples she has accessed are subtype B cases from the United States, Jordan is partnering with two labs specializing in international work to better diagnose different HIV subtypes, including subtype C, which is the most common type in Mozambique.

The next step will be translating this lab work into the field. Jordan has partnered with the Elizabeth Glaser Pediatric AIDS Foundation (EGPAF), the Association of Public Health Laboratories (APHL), and Jani to submit a proposal to Grand Challenges Canada (a not-for-profit organization dedicated to improving health in developing countries). The proposal, if accepted, will provide comprehensive training, protocols, and quality measures for provincial lab technologists in two laboratories in Mozambique. Meanwhile, EGPAF, which supports the national HIV program in four local provinces, will enroll infants in nearby clinics for implementation research. The project will evaluate — in a true-to-life setting — how the instrument-free approaches compare to the current detection methods.

“We’re excited to bring Dr. Jordan’s work to the field, where it has the real potential to save many lives,” says Nicholas Hellmann, M.D., EGPAF’s executive vice president of medical and scientific affairs. “For us, time is of the essence for identifying and treating HIV-positive infants. Working in local settings with relatively low-tech solutions is often the key to scaling up treatment for the most vulnerable populations.”

Jordan is eager to see how these methods can improve the health landscape in Mozambique. In the meantime, she’s looking even farther ahead. She’s identified two companies — Micronics, in Redmond, Wash., and Wave 80 Biosciences, in San Francisco — that are developing true point-of-care diagnostic tools. The goal is to produce a small instrument activated by a limited power source that would combine the extraction and amplification steps into one, giving results directly from blood or dried blood spots. It may be a year or more before testing can begin, but the possibilities are promising.

“We hope to move the testing from the provincial labs to local clinics and maternity hospitals,” says Jordan, “where nurses and midwives could do the testing at the true point of care.”
Whether it’s the Gulf oil spill, the obesity epidemic, lead in children’s toys, or the outbreak of the H1N1 virus, major public health issues regularly capture newspaper headlines and the public’s attention. But for years, education in public health was reserved exclusively for graduate students. Today, however, it is one of the five most rapidly growing college majors, according to The Chronicle of Higher Education.

In 2003, the Institute of Medicine (IOM) of the National Academies recommended that all undergraduates have access to a public health education. In 2006, the Association of Schools of Public Health (ASPH) agreed that undergraduate public health training was necessary to develop an educated citizenry. And in 2009, the Association of American Colleges and Universities (AACU) found the field so timely that it dedicated an issue of its journal to undergraduate public health.

Even the federal government has hopped on board. The U.S. Department of Health and Human Services recently proclaimed support for undergraduate education in public health through progressive recommendations in Healthy People 2020, a set of science-based objectives for promoting disease prevention and health in this decade.

No one is more knowledgeable about the rapid rise of undergraduate education in public health — or has had a greater impact on it — than Richard Riegelman, M.D., Ph.D., M.P.H., the founding dean of GW’s School of Public Health and Health Services and professor of Epidemiology and Biostatistics. As co-chair of the Healthy People Curriculum Task Force, a chief voice of AACU’s Educated Citizen and Public Health Initiative, a leader in ASPH’s Undergraduate Public Health Learning Outcomes Project, and co-author of the foundational curriculum for undergraduate education in public health,
“We also have a commitment to teaching at GW — we don’t have to pull teeth to get people to teach undergraduate courses. We have people who love it, so everybody who teaches undergraduates here does it because they want to.”

Riegelman is recognized as one of the movement’s key driving forces.

Why is it important to offer undergraduate public health education?
The undergraduate public health degree does much more than prepare students to get a job in public health. Rather, it’s about teaching them how to understand public health issues, whether they become clinicians, lawyers, or business people. The goal is to prepare students to understand the world around them, the thinking process, the evidence process of public health. What we [the AACU] want to build is “the educated citizen,” someone who can incorporate public health concepts into his or her decision-making processes.

Why has undergraduate education in public health grown so rapidly?
This is a student-driven movement. When I talk to people around the country about getting started, I tell them, “Put on a good global health course or a good public health course and the students will do the rest,” because the students will enroll, and they’ll want more. At GW, we have to turn away students in the introductory courses, and that’s been the case for many, many institutions. For students, this field of study is inherently relevant and important to our society, so it’s not a hard sell.

How will the Healthy People 2020 goals affect undergraduate public health education?
There are two key objectives that will impact undergraduate public health education. The first is to increase the number of four-year colleges that offer undergraduate majors or minors. The second is to increase the number of two-year colleges that offer basic public health courses, as well as job-related certificates and associate degrees. Through those objectives we hope to achieve as much as a 40 percent increase in the number of both four-year and two-year colleges and universities.

Why are these goals significant?
At last count, only about 16 percent of colleges and universities offered public health majors or minors. We hope that the Healthy People 2020 goals will enable public health to be seen as an important part of any higher education curriculum. We hope that people will eventually see that Public Health 101, Epidemiology 101, and Global Health 101 are just as important as Economics 101, Psychology 101, and Political Science 101. The mentality should be, “Of course this is a part of undergraduate education.”

What are you doing to help implement these goals?
I have been working a lot on making things easier for the faculty, since one of the major challenges with the movement is recruiting and preparing them to teach undergraduate public health. When the faculty are provided with course frameworks, learning objectives, and help on how to get the classes approved, they can receive the support they need to get this discipline to become part of their institution’s curriculum and academic culture.

What is GW’s role in the undergraduate public health movement?
GW’s undergraduate public health program has been recognized as a national model. This is because, I think, we have had a reasonably clear goal of what we want to do. Our strategy is to create a generalist program, with a lot of broad foundations, integrated courses, and synthesis. The bottom line is that we are creating something that is different from what is done at the graduate level, which tends to be more discipline-based. The undergraduate programs focus on the breadth of the field, while the graduate programs focus on its depth. This is an approach that is catching on nationally.

We also have a commitment to teaching at GW — we don’t have to pull teeth to get faculty to teach undergraduate courses. We have people who love it, so everybody who teaches undergraduates here does it because they want to.

How has the movement changed from when you first began advocating for undergraduate programs in public health?
It’s great to be involved in a project where I can really see changes being made. It’s very reinforcing to see the kind of progress being made and the kind of enthusiasm from students. You push uphill, but once you achieve acceptance from 4,000 four-year colleges, 1,100 community colleges, and even the federal government, all acknowledging that this is a good idea, it’s a different story; a different dynamic. It’s no longer an uphill fight. Now it’s about guidance on how this whole thing should be run.
Sunburns can lead to cancer. Colitis can lead to cancer. Hepatitis B and C can lead to cancer. Persistent infection and inflammation may lead to cancer. Lead a perfectly healthy life, and you might get cancer nonetheless. Any number of factors trigger the disease, depending on your genes and the molecular cascades they set in motion in your body. In some people, a factor may prompt a gene that sets off cascade A, which causes a normal cell to turn cancerous. In others, a variation of that gene may trigger cascade B, which kills a cancerous cell before it can spread. Master control genes direct these cascades, thereby determining the path taken.

One such master controller, a gene encoding a protein called MTA1 (metastasis-associated protein 1), has been found lurking in breast, ovarian, prostate, and other tumors. At GW's School of Medicine and Health Sciences, a small army of scientists recently gathered to tackle the MTA1 family of proteins. They're out to expose how and why it flips the switch to a cancerous outcome, and what molecular middlemen it employs to do its dirty work. The team is led by Rakesh Kumar, Ph.D., professor and the Catharine Birch and William McCormick Endowed Chair of the Department of Biochemistry and Molecular Biology. As co-author of the 2008 book NR [nuclear receptor] Coregulators and Human Diseases, Kumar predicted that “Coregulator ‘master genes’ are poised to pay big future dividends to the field of medicine.” Now he and the bright young minds he’s recruited to his lab are betting their careers on it.

At top, the hepatitis B virus increases MTA1 levels in liver cells. Below, MTA1 increases in irradiated cancer cells, helping them repair DNA damage.

A FORMIDABLE LINEUP
Amanda Lyon, a 26-year-old Ph.D. student at GW, joined the MTA1 team in January 2010. She’s researching the presumed connection between hepatitis B, MTA1, and cancer. Recent studies suggest that bits of the hepatitis B virus interact with the MTA1 molecule, and since MTA1 is associated with cancer, Lyon will try to connect the dots. She’s running experiments to learn how MTA1 helps the virus activate molecular pathways that turn normal cells cancerous. In a similar vein, her lab-mate, postdoctoral fellow Suresh Pakala, is investigating whether infections trigger MTA-mediated cancer pathways. After a recent report by Kumar and his colleagues on how MTA1 orchestrates a type of breast cancer not caused by heritable mutations, GW’s
MTA1 team is looking into whether inflammation triggers MTA1 to do so.

Deep questions posed by the MTA1 team are intended to get at the heart of why inflammation, diseases, and stress are often associated with a risk for cancer. “These are the questions in the back of everyone’s mind,” says Lyon. Every Monday, she and the team gather to share insights and trade secrets. In the process of exposing MTA1’s inner ring, they are turning this gene into the poster child for an emerging field of cancer research on master control genes, or coregulators, that govern a myriad of molecular cascades.

“This MTA1 program will give coregulators national visibility and give focus to a field that is developing in basic research,” says Bert O’Malley, Kumar’s colleague and a longtime coregulator expert at Baylor College of Medicine in Houston, Texas. “Frankly, right now this is one of the hottest fields in fundamental and translational cancer research.”

MTA1: CALLING THE SHOTS

Like CEOs in a corporation, coregulators run the show; they determine which molecular pathways are turned on or off by interfering with genes that act like managers, which in turn guide a staff of genes below them. These genes encode proteins that eventually direct cell growth, division, metabolism, and other functions. When researchers first became cognizant of coregulators about 15 years ago, O’Malley says, they were thought to simply smooth out transcription (the process in which DNA becomes RNA, before RNA is made into protein). “But in time we began to find many more of these than we had expected. And the big surprise is that they turned out to be a type of ‘master gene.’” He adds, “Now, we know these are big-picture molecules in the cell, which is why they’ve been so frequently co-opted by diseases.” In other words, it is more efficient to kidnap a master control gene than to manipulate dozens of individual genes farther down on the chain of command.

Of some 375 coregulators discovered since 1995, more than half have been linked with maladies, such as mental retardation, inflammatory disorders, heart and reproductive abnormalities, and cancer. And MTA1 has some unique properties. Unlike other coregulators, it can either activate or stifle a molecular pathway. Whereas some coregulators act like stop signs, unable to signal “go,” MTA1 flashes like a traffic light. Understanding what makes MTA1 signal “stop” or “go” is the subject of intense research among the scientists in Kumar’s lab.

In 2001, Kumar and his colleagues turned heads with a paper in Nature Cell Biology, proposing a novel process by which MTA1 participates in hormone-independent breast cancer, a type resistant to standard therapies. They suggested that MTA1 dictates which gene cascades activate by remodeling the shape of chromatin, the material in which genes are embedded. When chromatin is in one shape, certain DNA sequences are transcribed into RNA, which is translated into a protein that triggers a cascade. But when chromatin takes on another shape, that DNA sequence is blocked and can no longer be transcribed. The report proposed a basic model for how MTA1 manipulates pathways by remodeling chromatin, but the fine details remain elusive. That’s where Sujit Nair, Ph.D., comes in.

Nair was struck by the wonders of chromatin remodeling back in 2004 as a postdoctoral fellow in Kumar’s laboratory at MD Anderson Cancer Center in Houston. Now he’s come to GW to join the MTA1 team and work as an assistant research professor in the Department of Biochemistry and Molecular Biology. He’s focusing on MTA1 and chromatin remodeling, and the effect that these rearrangements have on genes downstream.

HUNTING FOR A CURE

Because MTA1 has stuck its fingers into so many crannies, blocking the molecule with a drug might have unintended consequences. That’s one of the reasons MTA1 research is so important, says Jeyanthy Eswaran, Ph.D., assistant research professor and director of the McCormick Genomics and Proteomic Center at GW. Eswaran, who is the most recent recruit to the Kumar lab, says pinpointing genes involved in the many cancer-causing cascades that MTA1 halts or launches might inspire drug developers. She plans to explore the genes and proteins that are expressed in human cancer patients bearing high levels of MTA1. If one or more of these proteins is higher or lower than usual when MTA1 is turned up, it could provide a promising target for a cancer drug. “There haven’t been any radical new drugs for a while, so we are looking for new targets with unique qualities,” she explains. “MTA1 could very well be the critical player.”

Last year, the team stumbled on another MTA1 function likely to pique the interest of drug developers. When cancer patients undergo radiation therapy, the goal is to slow cancer by damaging the DNA in cancerous cells. But cancer fights back by turning up the cells’ DNA repair pathways, mitigating damage caused by the treatments. MTA1 may govern at least one pathway that comes to the aid of cancer cells. Therefore, drugs modifying MTA1 might make DNA-damaging therapy more effective.

“Collectively, I know we’ll make progress,” Eswaran adds. “All of us hope to see our projects lead to the clinic, where the patients are. That’s the bottom line.”

Drugs modifying MTA1 might make DNA-damaging therapy more effective for cancer patients in the future.
GW Chair of Surgery Joseph Giordano Closes Academic Career

After training generations of young surgeons and setting the standard for GW surgical residency as head of the program for more than 18 years, Joseph Giordano, M.D., chair of GW’s Department of Surgery, announced his retirement in June, bringing to a close a distinguished 42-year academic career.

During Giordano’s tenure at the Medical Center, the department emphasized inpatient and outpatient care, technical skills, and research training to produce clinically talented surgeons who have high academic potential. Giordano also was instrumental in establishing GW Hospital as a Level I trauma center, which treats nearly 70,000 patients each year.

But it was his role as head of the trauma team that treated President Ronald Reagan, along with Press Secretary James Brady, Secret Service Agent Tim McCarthy, and D.C. police officer Thomas Delahanty, following John Hinckley’s 1981 assassination attempt that thrust Giordano into the national spotlight.

Giordano discovered a bullet was lodged just inches from the president’s heart, inserted a chest tube, and brought his blood pressure back to normal. The president was famously quoted remarking to the surgeons, “I hope you’re all Republicans!” To which Giordano replied, “Today, Mr. President, we’re all Republicans.”

Far from taking it easy in his retirement, Giordano will devote his time to his work with Partner for Surgery, a non-profit organization that provides surgical care in remote Guatemalan communities.

Plack Selected as Interim Head of Health Sciences

Margaret Plack, P.T., Ed.D., chair of the Department of Health Care Sciences and founder and director of the Doctor in Physical Therapy program at the School of Medicine and Health Sciences, was appointed to serve as the interim senior associate dean for Health Sciences. Plack fills the position most recently held by Jean Johnson, Ph.D., F.A.A.N., who became the inaugural dean of GW’s new School of Nursing.

Plack has 25 years of experience in both academics and clinical practice, and specializes in physical therapy for children with developmental disabilities.

Parkin Receives Public Health Award

The Association of Schools of Public Health (ASPH) recently selected Rebecca Parkin, Ph.D., M.P.H., former associate dean for Research and Public Health Practice and professor of Environmental and Occupational Health and of Epidemiology and Biostatistics in GW’s School of Public Health and Health Services, to receive its 2010 ASPH/Pfizer Faculty Award for Excellence in Academic Public Health Practice.

Parkin, who recently retired after 12 years of service at SPHHS, was honored for her renowned practice-oriented scholarship and service in environmental epidemiology and risk science.

GW Surgical Team Brings Cardiac Care to Rural Honduras

A team of health professionals from The Richard B. and Lynne V. Cheney Cardiovascular Institute at GW Medical Center recently participated in a medical mission to rural Honduras. Cindy Tracy, M.D., associate director, Division of Cardiology at the Medical Center, along with cardiology fellow Monica Mukherjee, M.D., and technicians from GW’s Cardiac Catheterization lab provided desperately needed cardiac devices, such as pacemakers and defibrillators, to an underserved population. They also performed surgical procedures on 19 patients suffering from life-threatening heart disease.
1950s

**GEORGE F. SNELL, M.D. ’58**, a retired physician in Kaysville, Utah, was honored as Kaysville’s Unsung Hero in July 2010 for his dedication to the area’s medical community.

1970s

**JUD KNOX, M.H.A. ’72**, chief executive officer of York Hospital, was selected as chair of the Maine Hospital Association Board of Directors in June 2010.

**MAS G. MASSOUMI, M.D., G.M.E. ’73**, an orthopedic surgeon, became a lifetime member of the American Society for Surgery of the Hand in October 2010. He also was a guest lecturer at the 11th Triennial Congress of the International Federation of Societies for Surgery of the Hand, held in Seoul, South Korea, in November 2010.

**OMEGA C. LOGAN SILVA, M.D., G.M.E. ’75, M.A.C.P.,** was awarded the Foremother Award of the National Research Center for Women and Families in May 2010.

1980s

**DAVID B. DOMAN, M.D., G.M.E. ’81**, clinical professor of Medicine at The George Washington University, was appointed to the editorial board of the peer-reviewed journal *Gastroenterology* and *Hepatology*.

**RICARDO EUSEBIO, M.D. ’81, F.A.C.S.,** was appointed associate administrator of medical services for Guam Memorial Hospital Authority.

**HOWARD ZUCKER, M.D. ’82, J.D., L.L.M.,** an anesthesiologist and pediatrician, volunteered in Sacre Coeur Hospital in Milot, Haiti, for a week in April 2010 following the devastating earthquake that struck the nation.

**DAVID P. SNEIEZK, M.D., G.M.E. ’83**, director of the Advanced Integrative Rehabilitation and Pain Center in Washington, D.C., joined a medical relief mission in Haiti for nine days in May 2010.

1990s

**ERICH P. JUNGER, B.S. ’87, PH.D.,** a U.S. Customs and Border Protection scientist, was featured in April in the Investigation Discovery Channel series *Solved: Extreme Forensics*, for his role in aiding the Warren County Sheriff’s Office in solving the murder of a Virginia man.

**PHILEMON BAILEY, B.S. ’92, M.D.,** a board-certified emergency physician with Sussex Emergency Associates at Beebe Medical Center in Lewes, Del., received the EMS Physician of the Year award.

**DAYNA L. WOLFE, M.D. ’95**, a neuromodulation senior clinical research specialist and clinical advisor with Medtronic, Inc., the lead physician with the Minnesota State Medical Review Team, and a consultant to the Minnesota Department of Human Services’ Health Policy Unit, was appointed in March 2010 to the State Rehabilitation Council in Minnesota.

2000s

**JOHN TROTTER II, M.D. ’02**, was appointed as chief medical officer of XYTOS, Inc., a Nevada-based biomedical technologies company, in May 2010.

**JASKARAN BOPARAI, B.S. ’08**, was appointed clinical project manager at ACR Image Metrix, an imaging contract research organization, in July 2010.

**CINDY LENTINO, M.S. ’09**, was referenced in numerous publications, including *Men’s Health*, *Shape*, and *Medical News Today*, for her study “Dog-walking is Associated with a Favorable Risk Profile in Middle-age,” originally published in the journal *Medicine and Science in Sports and Exercise*, May 2010. Lentino presented her findings at the American College of Sports Medicine’s annual meeting June 1–5, 2010, in Baltimore, Md.

In Memoriam

**Bernard Bouscarel, Ph.D., D.Sc.,** professor of Biochemistry and Molecular Biology and of Medicine, director of the Digestive Diseases Center, director of the Molecular Medicine program, and chair of the Basic Science faculty, died on May 30, 2010, at age 53. Bouscarel, known as “the Frenchman” on campus, decorated even the d nastiest of Gastroenterology lectures with his accented speech. But he offered much more to those around him than European charm. A renowned scientist, an admired professor, and an adoring husband and father, Bouscarel was a wealth of wisdom, generosity, humor, and graciousness.

He had been a member of the GW Medical Center community since 1988, conducted leading research in liver disease and anticancer agents and their side effects, and published more than 60 articles in some of the most prestigious journals in the field. Bouscarel was a mentor to numerous students and the husband of Susan Ceryak, Ph.D., associate research professor of Pharmacology and Physiology at GW.

**Stanley Greenspan, M.D., Ph.D.,** clinical professor of Psychiatry and Behavioral Sciences, died April 27, 2010, of complications from a stroke. He was 68. The author of numerous books on child behavior, including *The Challenging Child, First Feelings, The Essential Partnership*, and *Playground Politics*, Greenspan is most remembered for his “Floortime” method of addressing the social and emotional deficits of children with autism.

**ALUMNI**

**BRUCE BENNETT, M.D. ’38**

**THOMAS M. DAVIS JR., M.D. ’52**

**CARL J. HOFFMAN, M.D. ’45**

**CARL MACCARTEE JR., M.D., G.M.E. ’72**

**HAROLD ELLIS RHAME JR., M.D. ’50**
“Your residency teaches you how to practice medicine, but it doesn’t teach you how to build the system. My fellowship at GW taught me how to build the system,” he says, citing training in hospital administration, finance, management, economics, public health, and health policy, among other disciplines.

Mulligan’s public health training complemented his fellowship by teaching him how to “think on the right scale.” “If you don’t have public health training, your thinking is usually too small in terms of medical development.”

Mulligan’s public health training, he says, complemented his fellowship by teaching him how to “think on the right scale” in a multifaceted field. “If you don’t have public health training, your thinking is usually too small in terms of medical development,” he says.

In 2003, Mulligan joined a team from GW who helped to establish Emergency Medicine residencies in Iran, Chile, and India; start a paramedic training school in Oman; begin an emergency nursing training school in Kuwait; and implement ambulance and disaster training in the United Arab Emirates.

Mulligan moved to the Netherlands in 2006 to help create one of the nation’s first emergency medicine residencies at Erasmus University in Rotterdam. He has since helped develop a similar program at UMC Utrecht, another of the country’s eight medical schools. Over the last 10 years, Mulligan has initiated and participated in international emergency medicine development programs in more than two dozen countries and assisted in establishing training schools for paramedics, relief agencies for underserved areas, disaster medicine and preparation programs, and hospital trauma development systems in more than 20 countries.

Among other international leadership roles in emergency medicine, Mulligan currently acts as co-director of the Emergency Medicine Residency at UMC Utrecht and clinical assistant professor in the Department of Emergency Medicine at the University of Maryland School of Medicine.

“The things that are killing health care systems around the world are emergency problems related to non-communicable diseases such as cardiovascular disease, strokes, cancer, and trauma, yet most of the world doesn’t have the capacity to handle them,” says Mulligan. “So, to me, helping countries develop systems for emergency care is the way I can make the greatest public health impact.”

**Terrence Mulligan**

**BUILDING EMERGENCY MEDICINE SYSTEMS AROUND THE WORLD**

Accident-prone travelers take note: “If you get hit by a moped in a country like the Netherlands, you will most likely be taken care of by a first-year doctor — one who has not had any specialized training in emergency medicine,” says Terrence Mulligan, D.O., M.P.H. ’03. “Outside of the United States, a fully developed emergency medicine system is hard to find, even in otherwise well-developed countries.”

Though few ever stop to consider it, an emergency medicine system is dizzyingly complex. From ambulance networks, to emergency room administration, to specialty training, the system involves many interacting components that must be built in the countries where they are lacking.

Thanks to GW — where he simultaneously achieved an M.P.H. and became the Medical Center’s first International Emergency Medicine Fellow — Mulligan is helping to create these systems, one country at a time.
Making an Impact
FROM COMMUNITY TRAINING TO COLON CANCER RESEARCH, GW STUDENT INITIATIVES WORK TOWARD A HEALTHIER WORLD

SARAH DIAMOND, M.P.H. CANDIDATE 2012, GLOBAL HEALTH
A school of public health seems an unlikely home for a chapter of Engineers Without Borders (EWB), an organization promoting sustainable engineering projects in developing countries. But for Sarah Diamond, a second-year M.P.H. candidate in the School of Public Health and Health Services (SPHHS), the two are a perfect fit.

“Many of the engineering projects taking place around the world have substantial public health implications,” argues Diamond, president of EWB, the only chapter based in a public health school.

“For the past 10 months, Diamond has been developing a community health manual for a project in El Salvador, where engineers are building a new water system. “The engineers design and construct this great system, but if the community has never had water piped before, they need to learn how to use it,” she says.

For someone with such zeal for public health, Diamond is a relative newcomer to the field. While pursuing her master’s degree in flute performance at Ohio University, Diamond fell under the influence of friends pursuing fields such as international development. “There was a whole world out there that I had no idea about,” recalls the classically trained musician. “I spent hours a day in a tiny room practicing my flute. What difference was I making?”

To get a sense of what she was missing, Diamond volunteered on a public health mission to Ecuador and fell in love with the experience. “I came back from that trip thinking, ‘Music isn’t the career for me. What am I going to do now?’” she explains.

Diamond was soon swept into a whirlwind of experiences that began during a stint as an AmeriCorps volunteer and ended in Washington, D.C., where she is now studying in the Global Health program.

“I believe you go after what’s important to you,” explains Diamond. “And that’s exactly what I’m doing.”

CARRIE HOUSE, PH.D. CANDIDATE 2011, MOLECULAR MEDICINE
For Carrie House, a fifth-year doctoral candidate in the School of Medicine and Health Sciences’ Molecular Medicine program, basic science represents an irresistible lure to uncover the mechanisms lurking behind disease.

Under the guidance of Norman Lee, Ph.D., professor of Pharmacology and Physiology, House is exploring the role that voltage-activated sodium channels play in colon cancer. By employing a variety of pharmacological tools, she is evaluating how changes in the cells give them an oncogenic advantage.

“This project is so fitting for molecular medicine,” says House. The research corresponds neatly with the program’s three tracks: molecular and cellular oncology, neuroscience, and pharmacology.

The project, which has served as the center of House’s professional life for nearly four years, grew out of a sequencing study in Lee’s lab involving mutations in voltage-activated sodium channels — channels already implicated in breast, prostate, and lung cancers.

House has managed to use her study requirements to advance not only her education, but also the project itself, successfully parlaying a writing grant assignment into funds for her research. “I figured, if I have to write a grant proposal, I may as well submit it,” she recalls. “I thought it was a good idea.” Clearly, the PhRMA Foundation thought so, too, and awarded House a $40,000 grant over two years.
The inaugural class of GW’s Bachelor of Science in Nursing students has a lot to celebrate. At a traditional pinning ceremony on Dec. 6, 2010, members of the class commemorated both the completion of their program and their passage into a health care workforce that needs their skills now more than ever. Though they began their studies in the School of Medicine and Health Sciences’ Department of Nursing Education, they graduated as alumni of the newly established GW School of Nursing.