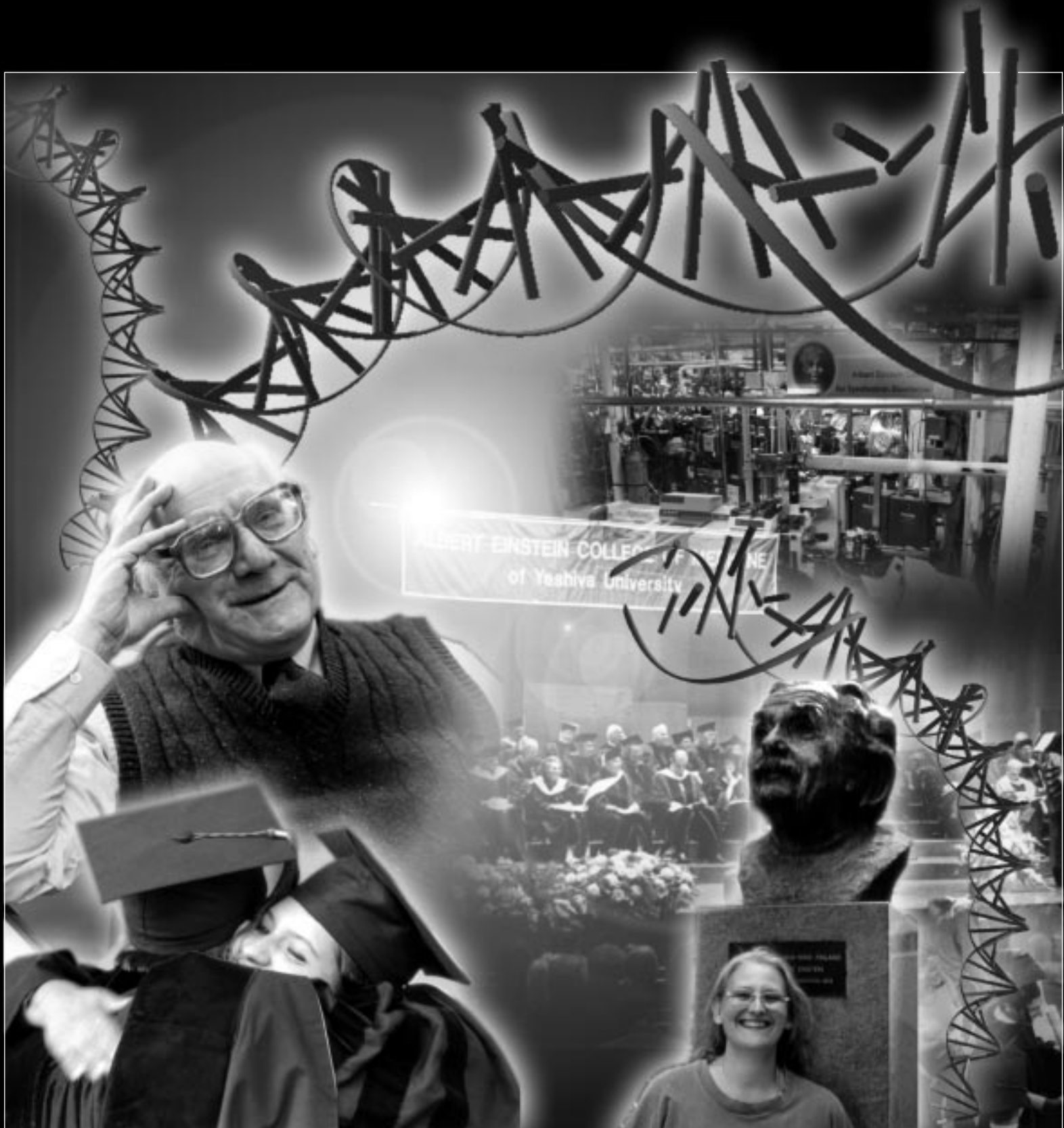


# EINSTEIN



# NewsReel

## NEW CO-CHAIRS FOR ANATOMY & STRUCTURAL BIOLOGY

Drs. John Condeelis and Robert Singer have been named co-chairs of the Department of Anatomy & Structural Biology. They had been serving jointly in an interim capacity since last year, when Dr. Peter Satir stepped down as chair, following a quarter-century in that position.

“Both of these talented researchers have been active members of the Einstein community, serving in leadership positions in the Division of



DR. CONDEELIS

Research,” said Dr. Dominick P. Purpura, The Marilyn and Stanley M. Katz Dean. “They bring diverse, yet complementary experiences with high technology to their new roles that will no doubt strengthen our role in imaging research, as well as offer useful resources to the entire Einstein faculty.”

After receiving his Ph.D. in biology from SUNY-Albany, and completing a postdoctoral fellowship in cell biology at Harvard, Condeelis joined Einstein as assistant professor of anatomy in 1977. Appointed professor in 1987, he currently serves as scientific director of the medical school’s Analytic Imaging Facility. “Modern research will be technology driven and through our common vision, we hope that the department of anatomy and structural biology can spearhead the further development of innovative technology at Einstein,” Condeelis said. He is also director of the Cancer Center’s Motility and Invasion Program. His particular research interests are the differentiation between normal cells and tumor cells and macrophages based on signaling pathways from tyrosine-kinase receptors to the action cytoskeleton in carcinoma cells, macrophages and endothelial cells. By studying how these pathways distinguish and regulate motility in these cell types, Condeelis is gaining

insight into the role of cellular chemotaxis in tumor metastasis and angiogenesis.

Singer received his doctorate in developmental biology from Brandeis University, after which he served as a research associate in molecular biology at the Massachusetts Institute of Technology and as a visiting scientist in cell biology at the Weizmann Institute of Science in Israel. He was recruited to Einstein in 1996 from the University of Massachusetts Medical School, where he was a professor of cell biology, molecular genetics and microbiology. He holds joint appointments as professor of anatomy & structural biology, and of cell biology and is director of the Institute for Molecular Medicine at the College.

“Our strong base in technology is the seed for our goal of making the development of innovative technology a priority,” said Singer, who holds 10 patents for his development of imaging techniques based on *in situ* hybridization. “And serving jointly, which is fitting with the collaborative emphasis here at Einstein, will allow each of us to stay connected and continue with research collaborations, while also tending to administrative necessities.”

Singer’s research interests are the visualization of RNA from the site of its birth to its ultimate biologic destiny in the cytoplasm where it makes proteins at specific locations. Using uniquely developed imaging techniques based on *in situ* hybridization,



DR. SINGER

he looks at specific nucleic acid sequences within individual cells. The tracking of single RNA molecules enables comparisons between normal and cancer cells. The Singer Lab has developed techniques for visualizing RNA movement in living cells and is using them to study “intracellular motors” that connect with and drive the RNA. ■



THE GRUSS MAGNETIC RESONANCE RESEARCH CENTER

## NEW IMAGING CENTER ON CAMPUS

This past spring saw the opening of one of the nation’s most technologically advanced research centers for magnetic resonance spectroscopy. And that opening occurred here on the Einstein campus, with the dedication of the medical school’s new Gruss Magnetic Resonance Research Center. The Gruss center houses the most advanced magnets ever developed for medical research: a 4.0 Tesla magnet for use in human studies and a 9.4 Tesla magnet for use in animal studies.

The three-story, 18,900 square-foot center is the only facility in the metropolitan area, and one of only six in the world, to use such sophisticated high-field magnets to provide imagery of the human body and its cellular components with precision and detail that is simply not possible with conventional MRI’s. Its strategic location on the Einstein campus—it abuts the Chanin Institute for Cancer Research and the Mazer Building (the future site of the Price Center for Genetic and Translational Medicine) and is close to Weiler Hospital and the medical school’s General Clinical Research Center—provides easy access for patients participating in clinical investigations involving magnetic resonance technology.

“Magnetic resonance enables researchers to open a biochemical window on the human body and allows scientists to study entities as small and static as protein or as large and active as the human brain,” explained Dr. Hoby Hetherington, director of the Gruss Center and professor of radiology and of physiology and biophysics. “We can now

actually visualize the brain in action and determine how certain compounds affect the brain and other parts of the body. We can measure nerve loss and damage to assess how well a body organ is functioning and how glucose is metabolized. This technology allows us to develop new techniques for diagnosing different diseases, and, ultimately, because of what we learn we can design effective new therapies as well as optimize existing ones.”

The Gruss Center was made possible thanks to a gift from an Einstein alumna, Dr. Evelyn Gruss Lipper, Class of ’71, a pediatrician and director of child development at New York Hospital-Weill Cornell Medical Center. The Center is named in memory of Dr. Lipper’s parents, Caroline and Joseph S. Gruss. ■

## SYMPOSIUM HONORS DR. RUTH GOTTESMAN

On Tuesday, June 4th, nearly 500 people gathered in Robbins Auditorium for a symposium, held in celebration of the illustrious career of Dr. Ruth Gottesman, founding director of the Fisher Landau Center for the Treatment of Learning Disabilities and professor emerita of pediatrics.

The symposium, titled “How we Teach Reading: What Works,” focused on a subject central to Gottesman’s many professional contributions. Dean Purpura and Dr. Herbert J. Cohen, director of the Children’s Evaluation and Rehabilitation Center, provided welcoming and introductory remarks.

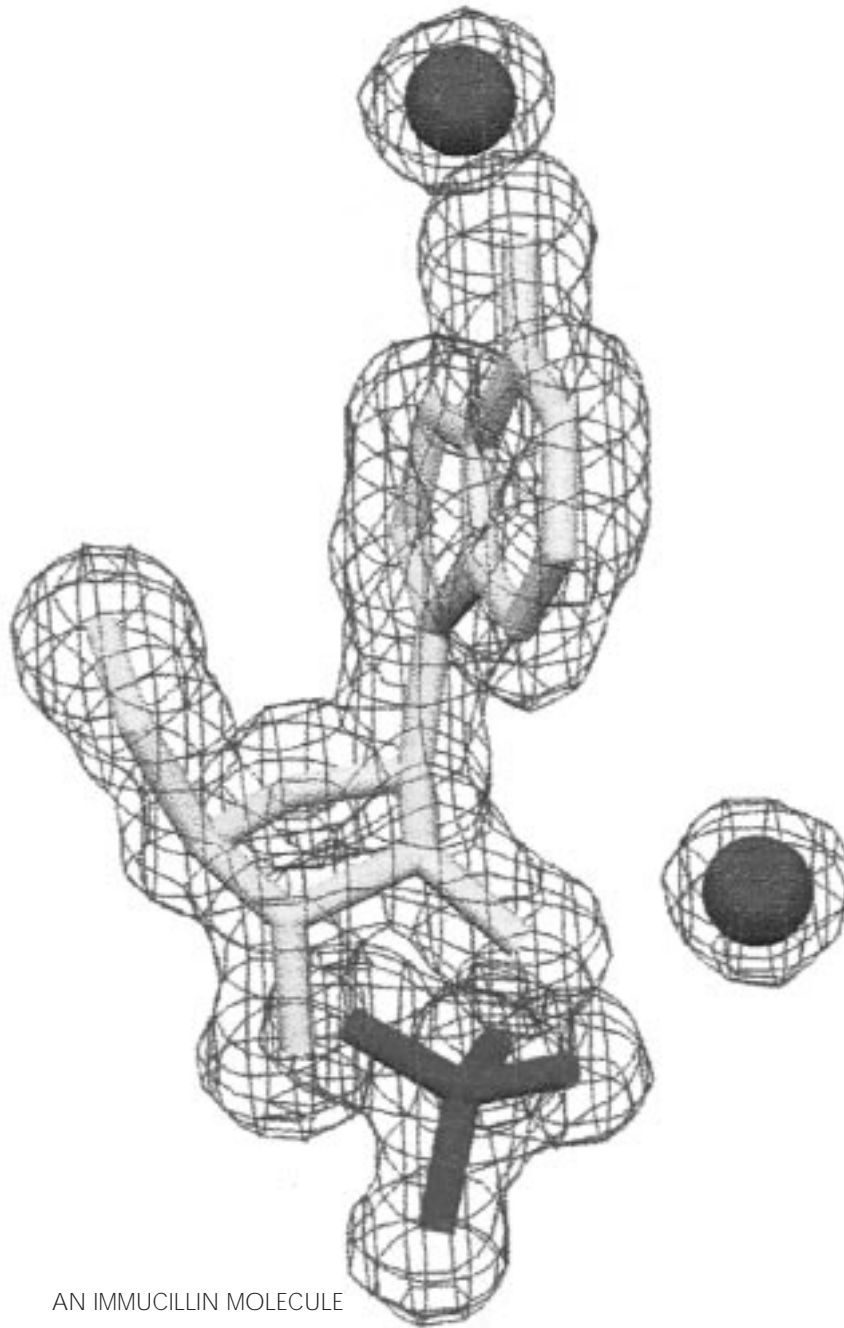
*continued on page 14*

# Put a Lock on It

Designer molecules that take advantage of the lock-and-key paradigm of enzymes and their substrates are poised to fight disease.

**M**ost things in life could benefit from some extra engineering, from the cupholders in your car to the latest mission to Mars. Dr. Vern Schramm, chair and Ruth Merns professor of biochemistry, brings that notion of precision engineering to biochemistry. Schramm's targets are the enzymes that catalyze the cellular biochemical reactions that influence how cells grow, function and, in some cases, become cancerous or subject to other diseases. His approach is to develop drugs to strategically lock up key enzymes. The goal is to build a better monkey wrench—to throw into the machinery.

Take the enzyme purine nucleoside phosphorylase, or PNP. This enzyme is crucial for the survival of the immune system's T cells, usually front line soldiers in the battle to keep us healthy. Unfortunately, sometimes things go wrong—errors involving T cells are behind a variety of serious conditions. In many autoimmune diseases, such as psoriasis, inflammatory bowel disease, multiple sclerosis and rheumatoid arthritis, T cells turn treasonous and misdirect their attacks. "T cells recognize foreign invaders and kill them," says Schramm. "So if they start to react against your own tissues, whether it's in your joints or skin or your gut, you get a variety of these inflammatory symptoms." Then there are the cancers known as T-cell leukemia and T-cell lymphoma. "The T cells just keep dividing without control," he explains. Patients may exhibit enlarged lymph



AN IMMUCILLIN MOLECULE

nodes, livers or spleens, or skin abnormalities, as their bodies literally fill with T cells.

Meanwhile, an exceptionally rare disease that is the polar opposite of these cancers may, paradoxically, point to an answer. Worldwide, about 50 babies have been born with what is known as a PNP deficiency. They lose their T cells at an early age, with devastating effect. "They're born perfectly normal," explains Schramm. "But at about one or two years old, their T cells disappear, which is a very bad thing. Most of these babies used to die from secondary infec-

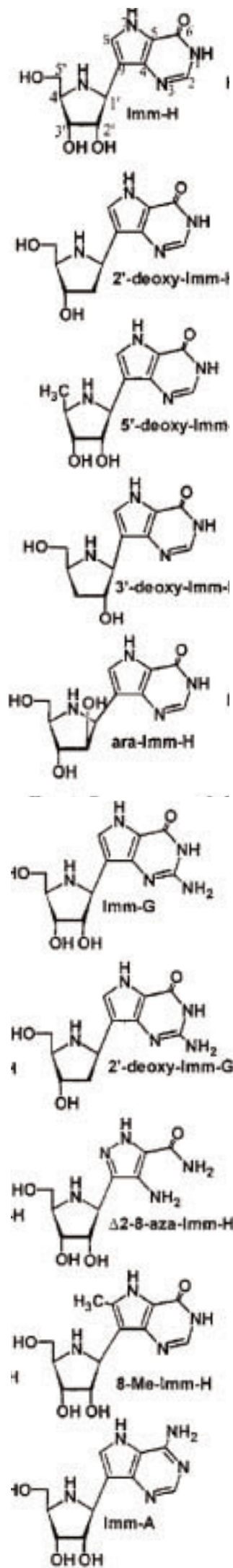
tions, primarily viral infections."

Luckily, however, there now exists an effective treatment in which doctors replace the missing protein. But the babies' predicament got researchers to thinking: perhaps the disease, with its paucity of T cells, could somehow serve as a model for the treatment of the cancers and other conditions in which T cells run amok. In other words, deliberately inhibiting PNP, the enzyme that keeps T cells going, might be a therapy for diseases of T-cell proliferation.

PNP, however, is a difficult enzyme to inhibit chemically, because of its

abundance and ubiquity in the body. "If you look in the patent literature, there are 33 patents by seven drug companies that have tried to do the same thing and weren't able to," says Schramm. That difficulty was an opportunity for him and his colleagues to employ their "precision engineering." They have now designed a related family of molecules, dubbed Immucillins, that inhibit PNP about a thousand times better than any of the previously patented compounds. The College of Medicine has licensed the inhibitor to a biotechnology company, which completed laboratory trials in the past year. And combined Phase I and II human clinical trials have begun on Immucillin H against T-cell leukemia. "This compound," Schramm says, "looks as though it really might work."

PNP also has a critical role in the survival of the bacterium *Plasmodium falciparum*, which is responsible for the majority of life-threatening malaria cases. The bacterium cannot synthesize its own necessary purine molecules, but instead relies on PNP to produce purine. Dr. Kami Kim, associate professor of medicine (division of infectious diseases) and associate professor of microbiology and immunology, has therefore tested the PNP-inhibiting Immucillin H molecule against *P. falciparum*. Working with Schramm and Einstein student Gregory Kicska, along with colleagues from New Zealand, Kim found that Immucillin H does indeed show activity against the malaria bacterium in culture. They have also cloned *P. falciparum* PNP,



with which they will try to design an Immucillin analog that might be an even more effective inhibitor of that species-specific molecule.

Schramm and his colleagues can engineer such powerful inhibitors because they are able to observe the fleeting structure known as the transition state of the enzyme. To explain the concept, Schramm sounds like a verbally coherent Yogi Berra. “You can think of the enzyme as a catcher’s mitt,” Schramm says, “and the molecule it works on, the substrate, as the baseball. In the first step, the ball goes into the mitt, and you know that if you don’t clutch your fingers around it, the ball will pop right out again. It’s the same way in an enzyme. Many times the substrate hits the pocket and flies right out again. Usually, though, the enzyme will close around the substrate in the same way as a catcher’s fingers will close over a baseball. The transition state is analogous to when that ball is being held tightly.”

The technology at Schramm’s disposal allows him to determine what the substrate-enzyme system looks like during the one-tenth of one-trillionth of a second when the substrate is bound tightly by the enzyme in the transition state. He then designs a chemical inhibitor that is structurally similar to the bound substrate. A well-designed inhibitor will cause the enzyme to close tightly around it. And an enzyme closed tightly around an inhibitor molecule is an enzyme that cannot accept an actual substrate molecule: the enzyme is effectively blocked from acting. “The practical effect of such molecular design is to make inhibitors that are extremely powerful,” Schramm notes.

He and his colleagues are now applying this design principle to other inhibitors that could be important for disease treatment. “Our general program,” he explains, “is to pick an interesting enzyme target, solve the transition state of the enzyme, use that as a blueprint to make powerful inhibitors, and test those inhibitors in biological systems.”

One such interesting enzyme target is 5’-deoxy-5’-methylthioladenosine phosphorylase, or MTAP. The molecule plays a role in the production of polyamines, chemicals that

coat and protect DNA. Rapidly multiplying cancer cells require large amounts of polyamines to coat their ever-replicating DNA. Therefore, stemming the production of polyamines is known to prevent the progression of, for example, prostate cancer. But the existing inhibitors of polyamine production have nasty side effects. The trick then is to target an enzyme that is part of the polyamine production line and that has absolutely no other function. MTAP is such an enzyme, and Schramm and his colleagues are developing an inhibitor for it.

Another project involves harnessing the lethal power of a toxin called ricin, extracted from castor beans, and a potential “magic bullet” against cancer. Historically, ricin has grabbed the attention of KGB assassins in addition to scientific researchers, as a milligram of it is enough to kill a horse. “You may remember the story of Georgie Markoff, a Bulgarian defector who was a radio broadcast announcer for radio free Europe,” Schramm says. “He left Bulgaria because he had denounced the Communist leadership of the country during the Cold War. He moved to England and continued his broadcasts, which upset the Communists. So the Bulgarians enlisted the aid of the KGB, who made a little umbrella gun that shot Markoff in 1978 with a tiny iridium pellet that was filled with ricin.” Markoff’s death was initially unexplained. But the death of another Bulgarian, in Paris, raised eyebrows. Forensic researchers found a small welt on each man’s leg. Further examination revealed that the welt contained a tiny sphere with pores on its surface. Within the sphere were traces of ricin, which had exited through the pores, attacking both victims.

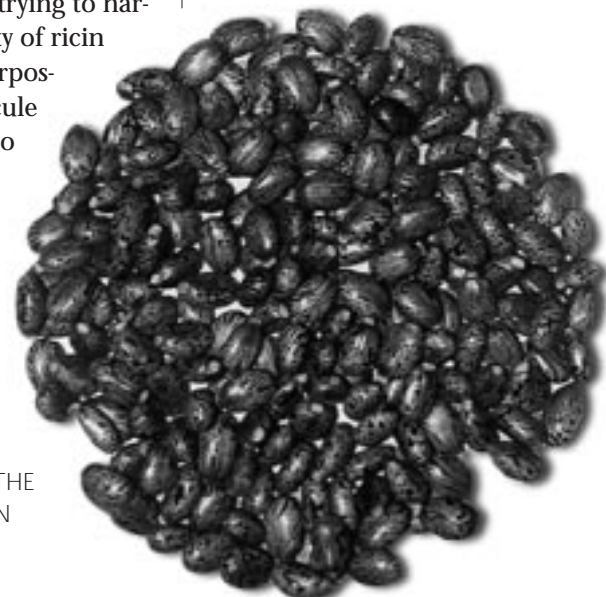
Researchers are now trying to harness the extreme toxicity of ricin for more beneficent purposes—a single ricin molecule can kill a cancer cell. “So the idea,” Schramm explains, “is to take that toxin, attach a monoclonal antibody that will recognize cancer cells and inject

it in a patient. It should bind to a cancer cell, be taken up and kill the cancer cell specifically.”

Such guided-missile ricin-based medications exist, and patients have been treated with them on an experimental basis. “There have been some remarkable remissions with this therapy,” says Schramm. “However, the side effects are very bad.” In fact, there have been more deaths caused by the treatment than there have been remissions brought about by the treatment. The problem, of course, is that not every ricin molecule is absorbed by cancer cells, which leaves some ricin free to wreak havoc on healthy cells.

Schramm is therefore working on a “rescue therapy” to be administered shortly after the ricin-based drug. The idea is to design a transition-state inhibitor of ricin to use as an antidote, in the hope that it would prove specific enough and strong enough to shut down the deadly toxin before it harms more than cancer cells. In this proposed protocol, a patient would receive a dose of ricin-modified antibodies that find and bind rapidly to cancer cells, which absorb the toxin. Then, before ricin has a chance to damage healthy cells, the remaining lethal molecules circulating in the body would be neutralized by the rescue therapy. The first generation of these inhibitors has already been made in the laboratory.

The utility of the molecular design approach is endless. Schramm foresees a future where researchers will know all human enzymes intimately, from their function and role in disease to the structure of their transition states, allowing scientists to engineer inhibitors for any of them. “The evolution of genomics into protein structure and into mechanism,” Schramm says, “gives us tremendous power.” ■



CASTOR BEANS, THE SOURCE OF RICIN



A SECTION OF THE EINSTEIN CENTER FOR SYNCHROTRON BIOSCIENCES AT BROOKHAVEN NATIONAL LABORATORY

# Crystal Clarity

From years to hours in the brave new world of x-ray crystallography

**W**ith the Human Genome Project a resounding success, scientists now have at their disposal the entire genetic blueprint of *Homo sapiens*—a sort of how-to guide for the construction of the species. (See “Frank Talk From Francis,” page 13.) But the completion of the sequencing and mapping of most of the human genome’s three billion letters, representing the four basic building blocks of DNA—a run-on sentence to put Faulkner to shame—really only sets the stage for the truly difficult and profound work to come. Deep in the alphabet soup are approximately 30,000 genes, which are the blueprints for the proteins that do the chores within the trillions of cells in a typical human body. With the genes in hand, researchers now need to figure out what the proteins coded for by these genes look like (the three-dimensional structure), what their jobs are, how they do them, and what role those proteins might play in disease.

At the forefront of the College’s effort in this area is the Albert Einstein Center for Synchrotron Biosciences. Key Center personnel are director, Dr. Mark Chance, pro-

fessor of physiology and biophysics and of biochemistry; Drs. Steve Almo and Anne Bresnick, professors of biochemistry; and Dr. Mark Girvin, associate professor of biochemistry and scientific director of Einstein’s structural NMR facility.

The most versatile technique for determining protein structure is x-ray crystallography, which played such a fundamental role 50 years ago in the elucidation of DNA structure that first set us on the path that led to the unraveling of the entire human genome. In the simplest terms, researchers shine x-rays on a crystal of protein, which diffracts the light. To the untrained eye, what you get in return looks like nothing more than a bunch of spots. The trained eye, however, also sees a bunch of spots, but knows what to do with them. Powerful computers translate the unique patterns of spots into a picture, in three-dimensions, of the protein that must have created that particular spot pattern—the protein’s overall shape, its internal geometry, the juxtaposition of its parts. And all of this sheds light on how the protein works.

The protein crystallographer has chosen a hard lot in life. Proteins

can be fiendishly tough to obtain in large quantities, to purify and to get into crystal form. The data is hard to gather—the more detail you want, the longer that process takes, and over time the crystal loses its structural integrity. Also, the calculations are numbingly complex. The months or years it can take to nail down the structure of a single refractory protein has led many a crystallographer to the brink of despair.

**G**ood news for crystallographers, and bad news for their therapists, is the revolution going on in crystallography that is being led by scientists such as Chance and his colleagues. The instrument of their salvation is a behemoth called a synchrotron light source. Chance uses Einstein-owned parts of the synchrotron at the Brookhaven National Laboratory on Long Island. There, electrons race near the speed of light in a doughnut-shaped tunnel ringed by powerful magnets. As the magnets guide them in their circular path, the electrons emit intense light, a nuisance to particle physicists but a bonanza for crystallographers. The light is sent down tracks called beamlines, to



A BULLETIN BOARD AT THE SYNCHROTRON FACILITY, WITH EINSTEIN RESEARCH ON THE COVER OF NATURE STRUCTURAL BIOLOGY.

be focused on dozens of simultaneous experiments in a room that literally hums and throbs with electronic equipment. “Steve Almo is our crystallographic expert,” Chance says. “I supply the photons and he figures out what to shoot them at.” Einstein owns four beam lines, and shares synchrotron data and research projects with the National Cancer Institute, Rockefeller University and Memorial Sloan-Kettering.

In June, Dr. Wladek Minor of the University of Virginia analyzed the Protein Data Bank, which has records of the methods and raw data of every published protein structure worldwide. Minor found that one of the Einstein beamlines, the X9B, produced 20 structures in 2001, more than any other beamline in the world, with the exception of one operated by a much larger institution—the United States Department of Energy, which obtained 25 structures from a beamline at Argonne National Labs. The X9B’s 20 structures put it ahead of beamlines operated by the Stanford Synchrotron Radiation Laboratory and the European Synchrotron Radiation Facility (which tied for third place), and the Lawrence Berkeley National Laboratory (in fifth place). And in sixth place worldwide was a second Einstein beamline, the X-9A, with 15 more structures. The 35 structures produced overall by Einstein far outpace anyone else.

“The productivity of the X9B beamline is all the more remarkable given that about 30 percent of the beamline’s time is not being used for crystallography,” Chance notes, “but is devoted to an x-ray absorption spectroscopy program.” In 2004, another Einstein beamline goes on line at Brookhaven, “which will keep us in front for many years to come.”

*One Einstein beamline, the X9B, produced 20 structures in 2001, more than any other beamline in the world, except for one operated by the U.S. Department of Energy.*

The appeal of the synchrotron to the protein crystallographer has three major elements. First, it’s fast. “The speed at which we can collect the data is up by a factor of at least 100 to 1000, because of the brightness of the synchrotron beam,” explains Chance. “The analogy is that of a light bulb to a laser. While a light bulb radiates light in all directions, with the laser beam you can get all of its radiation focused onto a small spot. So we can get data in hours as opposed to days.”

Moreover, the fact that the synchrotron beam can be tuned to different wavelengths of light—colors, as it were—lets crystallographers play some mathematical tricks that remove the old necessity of making multiple types of crystals for each protein, thus saving headache, heartache and time. Though the technique is called MAD (for multi-wavelength anomalous dispersion), it makes crystallographers smile. Finally, the pictures the synchrotron gives are high-resolution, often revealing details down to near a ten-millionth of a millimeter.

Chance and his colleagues have had some spectacular successes with the synchrotron, and numerous members of the Einstein community benefit. Almo’s group pushed one protein structure from data collection to the cover of *Nature Structural Biology* (July 1999, vol. 6, no. 7) in a mere six weeks. (The protein was EVH1, “a novel proline-rich ligand-binding module involved in cytoskeletal dynamics and neural function,” according to the journal.) Only a few years ago, such work literally took years. “Now,” Chance points out, “they finished the structure before they left the beamline that day. Another group was working on it and we beat them because of the technology available here at Einstein.” The synchrotron’s resolution also is critical, for example, for the immuno-oncology research of Dr. Stanley Nathenson, professor of microbiology and immunology, of cell biology and the Samuel H. Golding professor of microbiology, and for the cancer drug-design work of Dr. Vern Schramm, chair and Merns professor of biochemistry (see page 3).

So far there is no Rosetta stone of protein structure—researchers cannot simply look at the DNA sequence in the gene and know the structure

of the protein encoded for by that gene. They still have to tackle each new gene and its protein the hard way. But as more and more structures are solved, and computers recognize patterns, the job is likely to get easier (see page 7). Genes from other organisms will be helpful as well. Sometimes structure determination goes easier with a non-human protein, letting researchers make inferences about the human version.

A case in point is *Xeroderma pigmentosum* group C protein, found in radiation-sensitive cells at levels 13 times as high as in radiation-resistant cells. When Chance and colleagues tried to produce the protein in bacteria to obtain large quantities for crystals, the bacteria all died. But the analogous protein in the flatworm *C. elegans*, is easy to work with. “Do we have any idea why?” Chance asks. “No. Do we care? No. All we care about is that we have a protein that’s very close to the human protein, so we’re going to push ahead with that.” Other Einstein researchers are using a similar approach to study DNA repair genes that are defective in colon cancer.

To speed the conversion of genome information to protein structure, Einstein has teamed up with the Brookhaven National Laboratory, Rockefeller University, Mt. Sinai Medical School and Cornell University to form the New York Structural Genomics Research Consortium, which the National Institutes of Health is funding to the tune of \$25 to \$30 million over the next five years. (Eight other such multicenter teams exist across the nation.) Chance compares the endeavor to efforts like the Manhattan Project and the space program: “We don’t think it’s possible that one investigator, one cancer center, one institution can solve the complex problems that we’re talking about alone.” He also thinks competition among such partnerships will drive innovation and speed. “It’s a big project,” he says. “You need to pool the resources of many institutions, but at the same time the competition is good too, because there’s rarely one correct answer.” The Albert Einstein Center for Synchrotron Biosciences itself can be considered an answer. ■

# Structural Biology in the 3rd Millennium

by Steven C. Almo, Ph.D.

In 1948, Max Perutz, the father of modern protein crystallography, summed up his progress on the structural analysis of hemoglobin: “Due largely to the absence of any direct method for obtaining the atomic positions from the observed intensities of the diffracted rays, a detailed analysis of an organic compound of comparatively moderate size such as sucrose or cholesterol, takes two or more man-years to complete. On the face of it, therefore, an attempt to analyze the crystal structure of hemoglobin, or of any crystalline protein for that matter, looks about as promising as a journey to the moon.” Perutz thus demonstrated almost clairvoyant abilities. He finally published the full atomic structure of hemoglobin in 1968; Americans orbited the moon later that year and walked on it the next.

Fortunately, the situation has changed dramatically. The emergence, and convergence, of numerous technological advances, starting in the mid-1980s, now provides the unique opportunity to systematically approach protein structure solution. The advent of modern molecular biology now allows for the production of virtually any protein, and new detector and synchrotron technologies make possible the collection of protein-crystal X-ray diffraction data in hours instead of weeks and months. These remarkable advances have resulted in an exponential increase in the rate of structure solution: the protein database (PDB) currently contains more than 15,000 individual entries.

These advances also have resulted in the establishment of the NIH-sponsored Protein Structure Initiative (PSI), which currently supports nine National Structural

Genomics Centers. The stated mission of these Centers is the development of an efficient pipeline for high-throughput structure discovery, including cloning, expression, purification, crystallization, data collection, structure solution and homology modelling. The PSI envisions the solution of 10,000 new structures over the next decade with the long-term goal being nothing less than the production of “useful” structural models for all individual globular protein domains in nature.

Albert Einstein College of Medicine is a founding member of the New York Structural Genomics Research Consortium (NYSGRC—see page 5 and [www.nysgrc.org](http://www.nysgrc.org)), one of the National Centers, which

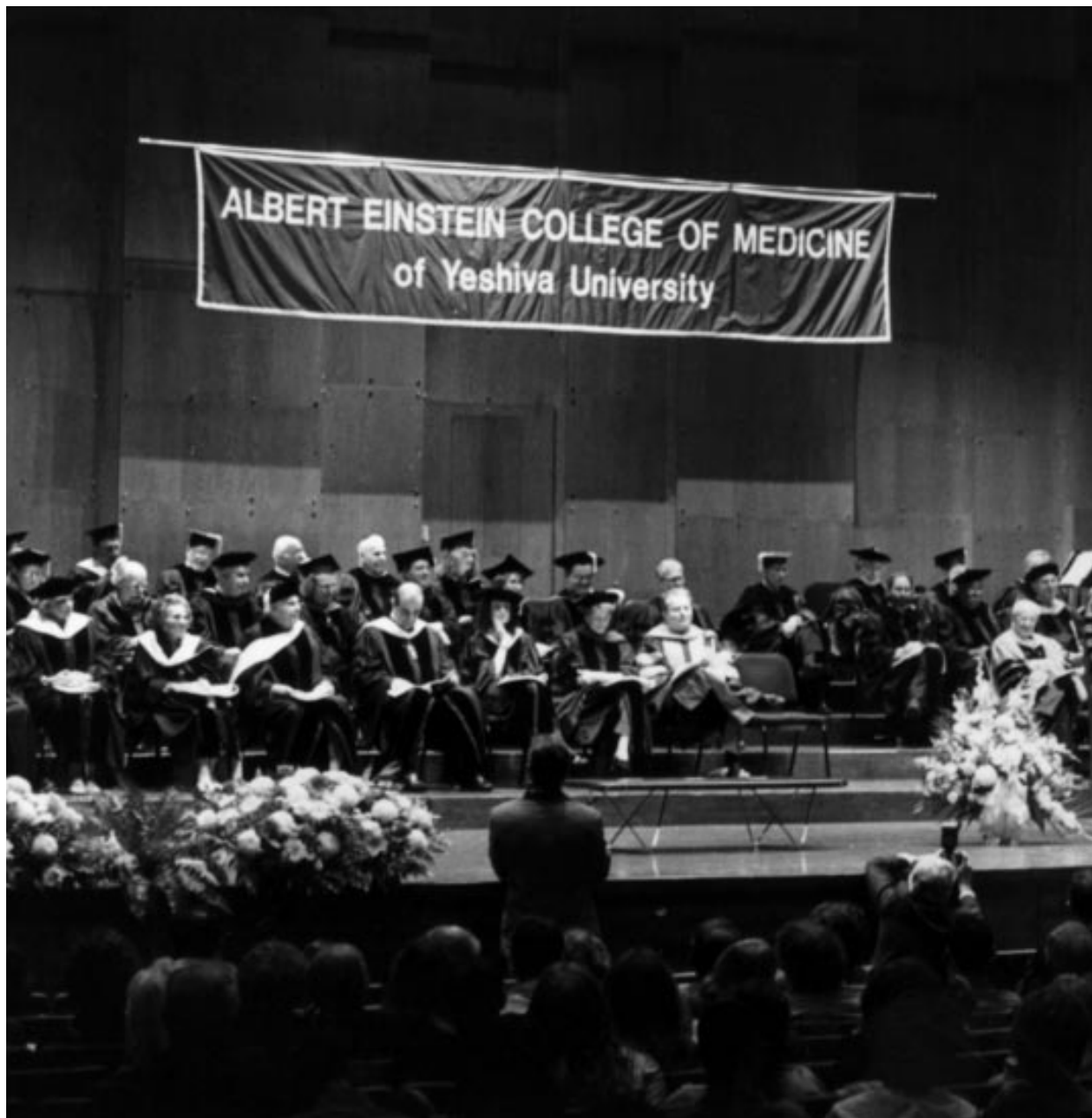
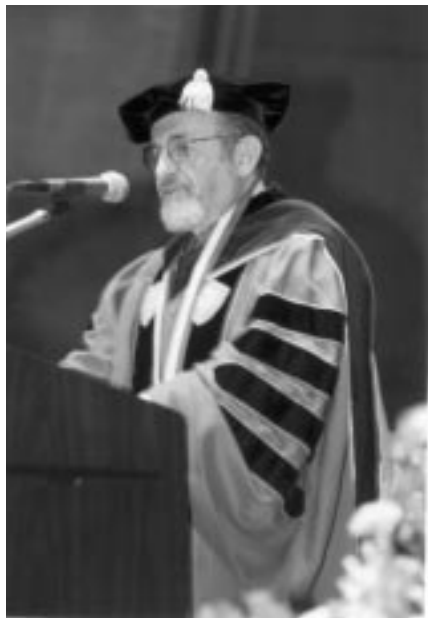
includes teams at Brookhaven National Laboratory, Cornell Medical School, Rockefeller University, Columbia University and the commercial partner Structural Genomix, based in La Jolla, CA. Four years ago, the NYSGRC established a pilot program by targeting for structural analysis 120 open reading frames from the budding yeast *Saccharomyces cerevisiae*, which had no significant sequence homology to any existing entry in the PDB. From that humble beginning, the NYSGRC has gone on to solve some 50 full structures. The first five years, the major aim of which is identifying and overcoming bottlenecks in the pipeline, could end with 300 structures in hand. The next half of the

*continued on page 10*



YEAST PNP OXIDASE, FOR WHICH NO STRUCTURAL INFORMATION PREVIOUSLY EXISTED. ALSO SHOWN ARE COFACTORS (STICK REPRESENTATIONS) THAT ARE REQUIRED FOR CATALYSIS. JOHN BLANCHARD, PROFESSOR OF BIOCHEMISTRY, WUXIAN SHI, INSTRUCTOR OF BIOCHEMISTRY, AND DAVID OSTROW WERE INSTRUMENTAL IN SOLVING THE STRUCTURE AND CONFIRMING ITS FUNCTION.

# Commencement



## CONFERRED

177 M.D. degrees; 39 Ph.D. degrees, including 11 combined M.D./Ph.D. degrees; 47 Belfer Institute for Advanced Biomedical Sciences diplomas.

## PRESIDING

Dr. Norman Lamm, President, Yeshiva University; Dr. Dominick P. Purpura, The Marilyn and Stanley M. Katz Dean; Dr. Stephen H. Lazar, Grand Marshal.

Keynote Speaker: Dr. Norman Lamm.

## AWARDED

**Samuel R. Rosen Outstanding Teacher Award for Preclinical Teaching:** Todd R. Evans, Ph.D., professor of developmental and molecular biology; Laurie J. Ozelius, Ph.D., assistant professor of molecular genetics.

**Samuel R. Rosen Outstanding Teacher Award for Clinical Teaching:** Serban Fotino, M.D., professor of medicine.

**Harry Eagle Award for Outstanding Basic Science Teaching:** Joan G. Jones, M.D., professor of pathology (clinical), and professor of clinical obstetrics & gynecology and women's health.

**Harry Gordon Award for Outstanding Clinical Teaching:** Susan M. Coupey, M.D., professor of pediatrics.

**Lifetime Achievement Award for Outstanding Teaching:** Michael I. Cohen, professor and chair of pediatrics; Matthew D. Scharff, professor of cell biology and of medicine, Harry Eagle Professor of Cancer Research/National Women's Division.

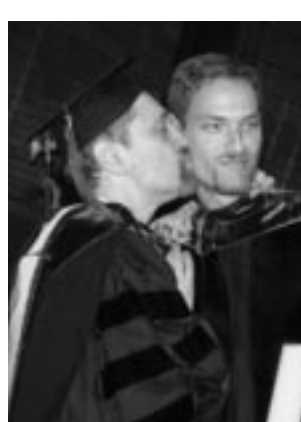
## ALUMNI HONORS

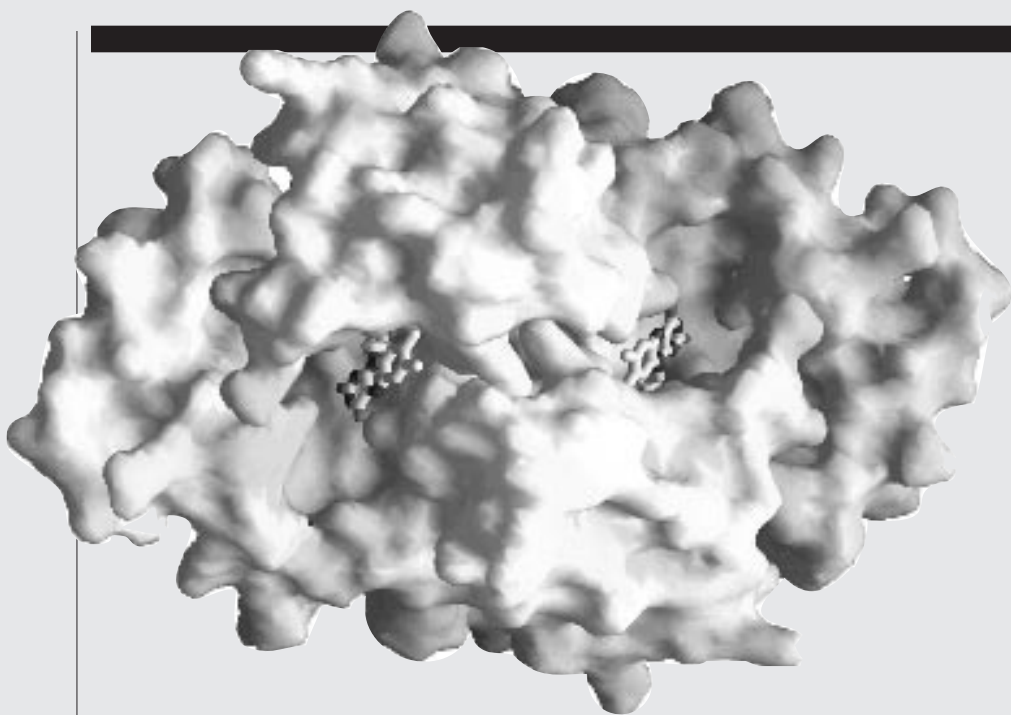
**40th Anniversary Alumni Class:** Class of '62; **25th Anniversary Alumni Class:** Class of '77.

**Distinguished Alumnus Award:** Dr. Robert Sherwin, Class of '67, C.N.H. Long Professor of Medicine, Yale University.

**Honorary Alumnus Award:** Dr. Matthew D. Scharff.







A SURFACE REPRESENTATION OF THE SAME YEAST PNP OXIDASE SHOWN ON PAGE 7. THIS VIEW HIGHLIGHTS A CLEFT OF HIGHLY CONSERVED RESIDUES LIKELY REPRESENTING THE ACTIVE SITE.

decade will be devoted to the high throughput production phase: cranking out structures for the 3,500 additional genetic sequences on our wish-list.

A major issue associated with structural genomics is whether functional information can be derived solely from the high resolution structure of a protein. We believe that this question can be answered with a resounding yes. For example, consider a protein for which there is either no functional or mechanistic information. A simple linear sequence alignment of other, homologous proteins identifies conserved amino acids. And the remarkably simple exercise of “mapping” these conserved residues onto the surface of the three-dimensional structure will immediately identify conserved surfaces that represent active sites, ligand binding sites and regulatory sites for further biochemical characterization.

An important aspect of structural genomics is the fact that the purified proteins represent an enormous resource, as they provide material for direct biochemical and biophysical characterization. Though it is common to ascribe similar function and mechanism to proteins that share even modest sequence similarity, that is 30 percent identity or less, recent studies have highlighted that this practice is highly suspect. Even relatively few amino acid differences can result in novel mechanisms and ligand/substrate binding specificities. Thus in addition to the primary purpose of structural studies, the

availability of these materials allows for the direct challenge, or validation, of widely accepted functional annotations, and will thus play a significant role in directing the design and interpretation of a wide range of biological studies.

Based on the accumulated experiences of the NYSGRC and the other Structural Genomics Centers, every likelihood exists that the ambitious goals of the PSI will be achieved. And as a consequence of this remarkable promise, structural biologists are now faced with both the luxury and the requirement of reassessing the future of structural biology, in terms of direction and scope. For example, the infrastructure is now emerging for the targeted and systematic structural analysis of specific areas of biological interest. Mechanistically inclined biologists could target the entire ensemble of kinases in a given organism (for example, the 122 kinases in *S. cerevisiae*) to gain a global understanding of mechanistic diversity and the evolution of specificity and function. The same concept is true of any collection of functionally related proteins, such as those involved in cell motility, neural development or RNA splicing.

Furthermore, the infrastructure within the Structural Genomics Centers is allowing for large-scale projects to be tackled that are beyond the scope and capabilities of individual laboratories. As a particular example, the NYSGRC is now focusing on the structural analysis of the approximately 260 open reading

frames of unknown function that are essential for the viability of *Haemophilus influenzae*. This work will provide a wealth of functional information on a set of previously uncharacterized genes and may provide novel drug targets.

The success of structural genomics is reshaping structural biology in another important respect. In particular, as the PSI continues to describe the structures of unique folds and individual domains, there must be a deliberate and concerted shift towards the examination of multi-component assemblies. This shift in focus is essential, as individual gene products rarely function independently. Rather, it is these “consortiums” of different proteins, working together, that are the true operational units of biological function. Indeed, large multi-component protein complexes are typically the ultimate effectors of complex cellular functions.

Accordingly, one of the outstanding challenges in the post-genomics era is the quantitative description of the regulatory circuits that control the spatial and temporal assembly, organization and function of these complex biological machines. (The effort has been dubbed “systems biology.”) And the infrastructure of the structural genomics movement is already providing the basis for a concerted national effort to examine the multi-component biological machines responsible for complex biological processes. In June, I and my collaborator Ron Milligan, of the Scripps Research Institute, hosted the first organizing meeting to establish the team and the goals for the assault on protein complexes. Here at Einstein, I am establishing two pilot projects, one with Charles Query, assistant professor of cell biology, on complexes in *Schizosaccharomyces pombe*, and another with William Jacobs, professor of microbiology & immunology and of molecular genetics, on complexes in both *Mycobacterium tuberculosis* and *Mycobacterium smegmatis*. The goal is to begin isolating sufficient quantities of complexes for systematic, high-throughput structural analysis, by both x-ray diffraction and cryo-electron microscopy. The resulting structural database promises unprecedented mechanistic infor-

mation describing the function of the complex biological machinery involved in normal physiology and human pathology, and will form the foundation for experimental design and interpretation by the next generation of biologists.

As with the PSI, this Complex Structure Initiative (CSI) has a number of enormously beneficial subsidiary aspects associated with it. The strains and the purified complexes, which are the natural products of the production pipeline, represent an enormous resource. Having these complexes in hand will provide numerous unique opportunities. We could develop a novel paradigm for drug target selection that focuses on the disruption of assemblies. We may also be able to attain high-throughput quantitative analysis of all gene products as a function of cell cycle and growth conditions. Ultimately, we envision the technologies and reagents arising from the CSI as serving as the impetus to generate reporter cell lines and whole animal models. These resources will in turn make it possible for researchers to examine complex organization, composition and post-translational modification status as a function of cell or tissue type, cell cycle, nutritional status and responsiveness to therapeutic regimens. The CSI thus represents the next logical step in the evolution of structural biology and promises to have a significant impact throughout the life sciences.

The exciting recent developments in structural biology clearly are already changing the course of biological research. These advances promise new opportunities for the entire life sciences community. And I invite everyone at the College of Medicine to take advantage of the structural genomics pipeline that exists here at Einstein. The Nobel Laureate Perutz said, “A discovery is like falling in love and reaching the top of a mountain after a hard climb all in one, an ecstasy induced not by drugs but by the revelation of a face of nature that no one has seen before.” The structural genomics pipeline is now at work unveiling nature’s faces. ■

*This article is based on a lecture by Dr. Almo, professor of biochemistry, at the College of Medicine in April.*

# AlumNews

1959

Since retiring in 1997, Dr. Leon Chameides enjoys traveling, genealogy, music, his five grandchildren, reconnecting with former classmates and continuing to do some medical writing for the American Heart Association.

1960

Dr. Robert G. Bernstein has retired as chief of radiology at Weiler Hospital, a post he has held since 1969, and has been named professor emeritus of radiology at Einstein, where he continues to teach ... Dr. Evan Charney recently retired as chair of pediatrics at the University of Massachusetts Medical Center and as chair of the Board on Children, Youth & Families, of the Institute of Medicine ... Dr. Gerald Galst is an associate clinical professor of medicine at Einstein, as well as a member of the Cardiology Private Practice Group at Weiler ... Dr. Jack L. Katz chairs the department of psychiatry at North Shore University Hospital in Manhasset ... Dr. Sidney Levitsky is still doing cardiac surgery and recently completed 35 years of ROI/NIH grant funding... Dr. Irwin E. Librot, a neurologist, maintains a full-time private practice in West Nyack, NY... Dr. Arthur Mostel has retired from practicing obstetrics and gynecology, although he continues his sexual therapy practice.

1961

Dr. Chester Pearlman has retired from practicing psychiatry, which leaves him lots of time to enjoy his hobby, music... Dr. Albert Taub has a private practice in psychiatry and also serves as faculty for the resident training program at St. Elizabeth's Hospital in Washington, D.C... IN MEMORIAM Dr. Daniel Goldberg, on January 7, 2002. His colleagues and patients remembered him as a gentle, dignified member of the medical community. Deepest condolences to his wife of 40 years, Audrey; son, Dr. Howard S. Goldberg (Class of '88); daughter, Dr. Beverly Goldberg; and the entire Goldberg family.

1964

Dr. Joel Feiner was recently named medical director for Telecare Mental Health Services of Texas. He also is professor of psychiatry at the University of Texas Southwestern Medical Center and president of the American Orthopsychiatric

PROFILE: KAREN HOPKIN, PH.D., SUE GOLDING CLASS OF '92

## The Write Stuff

The cool thing for me has always been telling stories about science," says Dr. Karen Hopkin. "I always enjoyed giving journal clubs, piecing together the logic behind a certain area of research. Science journalism was a logical destination." Hopkin took her first steps down the science writing road even before completing her doctorate in 1992 on superoxide dismutase in the laboratory of Dr. Howard Steinman, professor of biochemistry. A 1991 "mass media fellowship" from the American Association for the Advancement of Science (AAAS) placed her at WOSU, the radio station of Ohio State University, writing and reporting. And while still at Einstein, Hopkin also interned for National Public Radio's "Science Friday," a program covering current science, broadcast from New York City.

After finishing her Ph.D., Hopkin went to work for the AAAS communications office in Washington, DC. "There were no men in the office," she notes, "so I thought maybe I'd get a calendar with guys in it. But Chippendale dancers

don't do it for me. I realized I needed a calendar of male scientists." Hopkin thus came up with the idea for the infamous "Studmuffins of Science" calendar, which she went on to produce in 1997 and 1998, selling about 7,000 copies each year. The swimsuit calendar parody featured actual male scientists—including Nobel Laureate Richard Roberts.

When a producer's job opened up at "Science Friday" in 1993, Hopkin returned to New York. For three years she prepared each show, and occasionally wound up hosting it. "That was frightening," she remembers. "If [host] Ira Flatow called in sick, suddenly I'd be on live national radio for two hours." A yearning to write more brought Hopkin back to DC with the *Journal of NIH Research*. That publication, unfortunately, folded in 1997, but today Hopkin successfully freelances, contributing regularly to *Scientific American*, *New Scientist*, *The Scientist* and *Science*. Now living in Boston following a 1999-2000 Knight Science Journalism Fellowship at M.I.T., Hopkin has been on a major assignment: helping to revise "The Molecular Biology of the Cell," co-authored by National Academy of Sciences president Dr. Bruce

Association... Dr. Stuart Wollman is chair of anesthesiology at St. Vincent's Catholic Medical Center, Brooklyn and Queens Division.

1965

Dr. Bernard Zazula recently became the proud grandfather of twins.

1966

Dr. David Schick is president of the Montefiore Staff and Alumni Association.

1967

Dr. Stephen Levis maintains his gynecologic practice but has given up practicing

obstetrics ... Dr. Henry Rosenberg is very busy as residency director at Thomas Jefferson University's department of anesthesiology, president of a patient advocacy group and editor in chief of the *American Journal of Anesthesiology*.

1968

Last winter Dr. Peter Heiman performed the role of Scalza in the Bronx Opera Company's production of Franz von Suppe's operetta, "Boccaccio."

1970

Dr. Douglas Drossman is a co-director of the University of North Carolina Center for Functional Gastro-Intestinal and Motility Disorders, associate editor of the Gastro-Intestinal section of the *Merck Manual* and of *The Journal of*



Alberts. She's also updating a companion book designed for undergraduates, "Essential Cell Biology." Her work on the latter volume so impressed Alberts that Hopkin was made a co-author. "Actually, I was thinking it would be fun to have the credit be something like, "Essential Cell Biology—As Told To Karen Hopkin," she smirks.

Currently guest editing an issue of *Muse*, a science magazine for children published by the Smithsonian, Hopkin still gets a rise from telling the story of science. "If you make this transition from science to writing, many scientists will ask if you don't miss the process of discovery, the moment that you're the first person to know something," she says. "But it doesn't bother me. I'm perfectly happy being the second person to know something. When you find it out, give me a call." ■

*Gastroenterology*, and chair of the multinational working teams for diagnosis of functional gastro-intestinal disorders.

1971

Dr. Gary D. Rifkin is an associate professor of medicine at the University of Illinois College of Medicine at Rockford. He was recently appointed acting chair of medicine.

1973

Dr. Jay A. Berzofsky is chief of the molecular immunogenetics and vaccine research section of the metabolism branch of the National Cancer Institute where his research focuses on vaccines for HIV, cancer, and viruses that cause

cancer. He chairs the NCI Vaccine Working Group, and was elected a fellow of the American Association for the Advancement of Science... Dr. Richard S. Frankenstein, a specialist in chest diseases, was elected Speaker of the California Medical Association. A solo practitioner in Garden Grove, CA, he also chairs the Governing Body of Garden Grove Hospital and Medical Center... Dr. Joel Gernsheimer is working in the ER at Lincoln Hospital... Dr. Joe Okon's twin sons, Benjamin and Ezra, recently celebrated their bar mitzvah... Dr. David Siegel was recently elected to the Association of Professors of Medicine from the University of California, Davis, where he is vice chair of internal medicine and chief of medicine for the affiliated Veterans Administration program.

## 1974

Dr. Susan Chernow Gilman is medical director of the Elder Center at Roxborough Memorial Hospital and assistant clinical professor of psychiatry at Thomas Jefferson University... Beth Kaplan, daughter of Drs. Mitchel and Ronnie (Resnik) Kaplan (Class of '75), is a third-year medical student at Einstein... Dr. Murray M. Pollack recently received the 2002 Distinguished Investigator Award from the American College of Critical Care Medicine. Last year he received a Distinguished Career Award from the American Academy of Pediatrics.

## 1975

Dr. Laura Fox has an ophthalmology practice with her husband in Beverly Hills, CA ... Dr. Sidney Goldfarb has a urology practice in Princeton, NJ ... Dr. Eugene Peters has a busy pediatric practice and recently celebrated the birth of his third grandchild... Dr. Adam Rowen, a pulmonary disease specialist in New Jersey is involved in anti-bioterrorism planning and lectures about the subject.

## 1976

Dr. Relly Chern has a private ophthalmology practice in Manhattan and teaches at Einstein. She and her husband celebrate their 40th wedding anniversary this year... Dr. David A. Gorelick has worked in the Intramural Research Program of the National Institute on Drug Abuse for the past 12 years ... Dr. Harvey Karp received the Socially Responsible Physician of the Year Award

from the Physicians for Social Responsibility, in recognition of his work on children's environmental health. This spring, Random House published his book, "The Happiest Baby on the Block," which explains what colic is and how to help calm colicky babies... Dr. Ross S. Levy is part of the Mt. Kisco Medical Group, a multi-specialty group for which he offers dermatology services... Dr. Stanley Scott has had his private practice in internal medicine in the same location in Queens, NY, for 22 years. His wife Joan is his office manager... Dr. Matthew J. Soff has moved to Plantation, FL, where he is part of a gastro-intestinal/internal medicine group practice.

## 1977

Drs. Mitch Fishbach and Val Overton (Class of '82) practice cardiology and ophthalmology, respectively, in Scarsdale, NY. Mitch also teaches at Montefiore and Columbia ... Dr. Marcia Naveh is chief medical officer for a medical start-up company dedicated to providing services to the elderly in long-term care settings.

## 1978

Dr. Michel I. Bergman is associate chief of pulmonary medicine and director of ICU at Long Island College Hospital in Brooklyn, NY. For the past four years he has been listed among the "Best Doctors in NY" in *New York Magazine*... Drs. Shoshana Englard-Falconer and David Falconer live in St. Paul, MN, with their two sons, Ben and Noah... Dr. Robert L. Perkel teaches clinical medicine and medical ethics at Thomas Jefferson University Medical College, where he is a professor of family medicine.

## 1979

Dr. Robert Marion continues as professor of pediatrics and of obstetrics & gynecology and women's health at Einstein. He also is director of pediatric genetics at Montefiore. His daughters, Dori and Davida, are a junior at Cornell and a freshman at Vassar, respectively, while his son Jonah recently celebrated his bar mitzvah... Dr. David Wiener is the director of clinical operations for the Jefferson Heart Institute at Thomas Jefferson University in Philadelphia.

## 1980

Dr. Kenneth J. Davis recently became senior partner of his pediatric group in Elizabeth, NJ... Dr. George Fulop is senior director of Medical Policy and Programs at Merck-Medco.

## 1981

Dr. Ronald A. DePinho received the 2002 ASCI Award from the American Society for Clinical Investigation, recognizing his fundamental discoveries spanning the fields of cancer research, aging and chronic degenerative disease. He is professor of medicine and of genetics at Harvard Medical School, as well as a member of the department of adult oncology at the Dana Farber Cancer Institute and an American Cancer Society Research Professor.

## 1982

Dr. Francis Farraye recently relocated to Boston Medical Center, where he is the clinical director of gastroenterology... Dr. John Fazio practices pathology in Syracuse, NY, where he lives with his wife and two daughters... Dr. Jeff Lefkowitz's son, Matthew recently celebrated his bar mitzvah... Dr. Kurt Nolte is an associate professor of pathology at the University of New Mexico School of Medicine in Albuquerque... Drs. Ann Silverman and Robert Spitzer (Class of '80) have four children and live in Michigan. Dr. Silverman is the director of Gastro-intestinal/Hepatology Research at William Beaumont Hospital and is on the voluntary faculty at Wayne State University.

## 1983

Dr. Susan Soeiro has relocated her internal medicine practice to White Plains, as part of Primary Care/Cardiology Associates. Her husband, Dr. Ruy Soeiro, continues as a professor of infectious diseases at Einstein. Their son, Dr. Damon Soeiro (Class of '00) is completing his residency in radiology in Boston at Beth Israel/Deaconess. This year, he will marry Dr. Rebecca Tenny (Class of '01), who is a pediatrics resident at Boston Children's Hospital.

## 1985

Dr. Marcia W. Suval is working in a community mental health center in New Bedford, MA, and lives in RI... Drs. Susan Zimmerman and William Tham are in private practice with the Maryland Neurological Institute in Annapolis,

which is a group of psychiatrists, neurosurgeons and neurologists practicing together to coordinate care of spine, pain and neurology patients.

## 1986

Dr. Maryirene Ilchert Flynn practices orthopedic surgery and sports medicine in Staten Island... Dr. Ileana Vargas is working at the Naomi Berrie Diabetes Center, researching the prevention of obesity and type 2 diabetes in children and adolescents.

## 1988

Dr. Michael J. Clements has opened a solo practice in family medicine near his home in South Windsor, CT... Dr. Howard Goldberg is director of research and development at CST Corporation in Framingham, MA. The company specializes in informatics related to health care. He also practices, part-time, at Jordan Hospital, in Plymouth... Dr. Margaret Levitt is the medical student and resident coordinator at Sound Shore Medical Center in New Rochelle, NY... Dr. Rachel Seidel recently celebrated the marriage of her daughter, Zoe Gilman, to Daniel Feldman.

## 1991

Dr. Camille Nelson is practicing nuclear cardiology in Atlanta.

## 1993

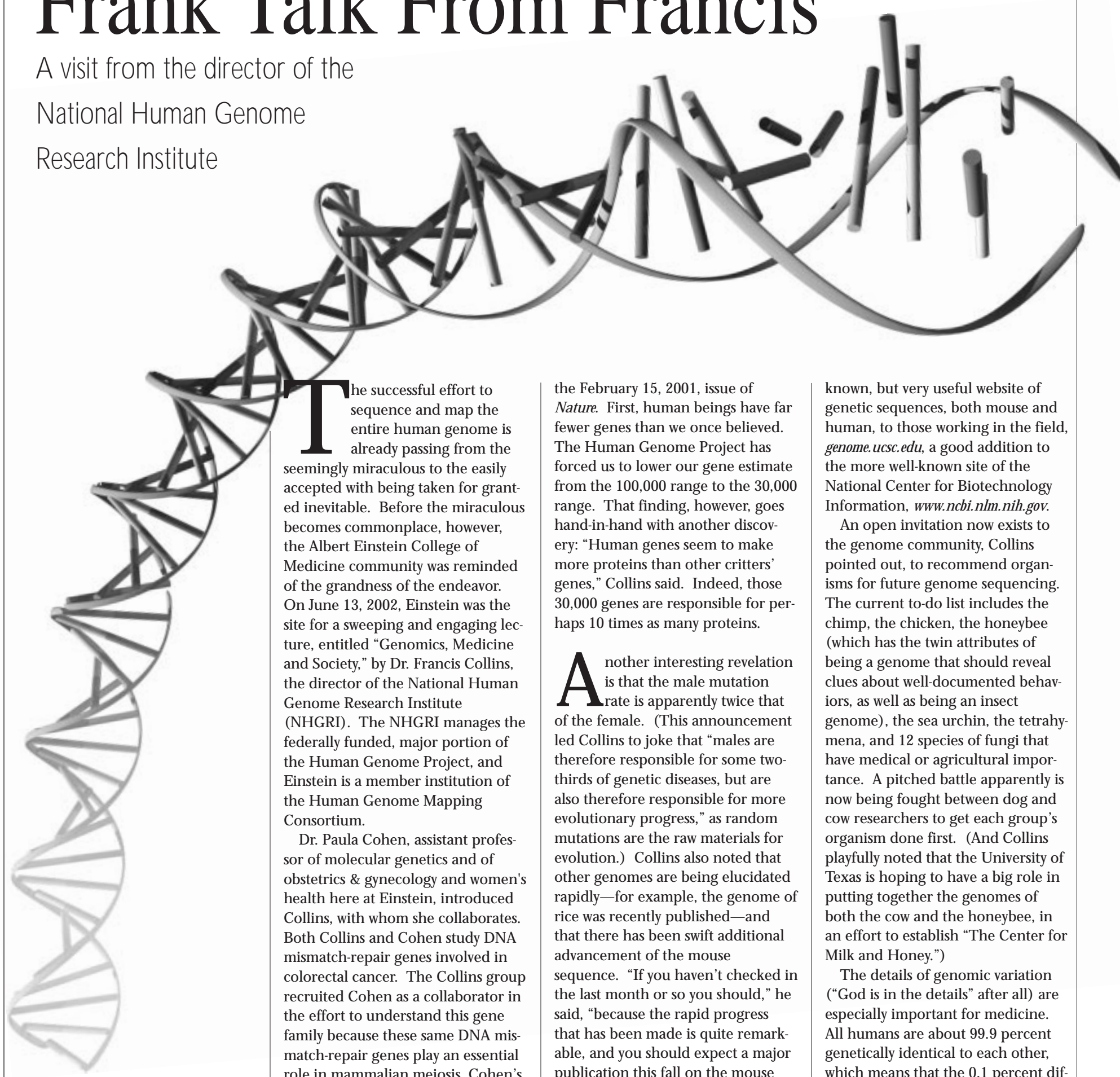
Dr. Ghary Gappelberg's son, Eli, recently celebrated his first birthday... Dr. Marc Levitt is a pediatric surgeon at the Children's Hospital of Buffalo, and assistant professor of surgery at the State University of New York at Buffalo.

## 1995

Drs. Kim Starer Landzberg and Brian Richard Landzberg recently expanded their family with the birth of their third child. Kim is an ophthalmologist with Riverdale Eye Associates and serves on the voluntary faculty at Montefiore. Brian is in a private gastro-intestinal practice in Manhattan that is affiliated with Cornell/NY Presbyterian Hospital... Dr. Cassandra Milling was presented the 2002 American Academy of Neurology Education & Research Foundation Clinical Research Training Fellowship Award for her research in epilepsy and sleep medicine. She is a lecturer at the University of Michigan. ■

# Frank Talk From Francis

A visit from the director of the  
National Human Genome  
Research Institute



**T**he successful effort to sequence and map the entire human genome is already passing from the seemingly miraculous to the easily accepted with being taken for granted inevitable. Before the miraculous becomes commonplace, however, the Albert Einstein College of Medicine community was reminded of the grandness of the endeavor. On June 13, 2002, Einstein was the site for a sweeping and engaging lecture, entitled “Genomics, Medicine and Society,” by Dr. Francis Collins, the director of the National Human Genome Research Institute (NHGRI). The NHGRI manages the federally funded, major portion of the Human Genome Project, and Einstein is a member institution of the Human Genome Mapping Consortium.

Dr. Paula Cohen, assistant professor of molecular genetics and of obstetrics & gynecology and women's health here at Einstein, introduced Collins, with whom she collaborates. Both Collins and Cohen study DNA mismatch-repair genes involved in colorectal cancer. The Collins group recruited Cohen as a collaborator in the effort to understand this gene family because these same DNA mismatch-repair genes play an essential role in mammalian meiosis, Cohen's area of expertise. She noted that since 1996, there have been 251 references to Collins in *The New York Times*. (Professor Albert Einstein is still ahead with 1,142.)

Collins reviewed some of the surprising findings of the first draft of the genome, which was published in

the February 15, 2001, issue of *Nature*. First, human beings have far fewer genes than we once believed. The Human Genome Project has forced us to lower our gene estimate from the 100,000 range to the 30,000 range. That finding, however, goes hand-in-hand with another discovery: “Human genes seem to make more proteins than other critters' genes,” Collins said. Indeed, those 30,000 genes are responsible for perhaps 10 times as many proteins.

**A**nother interesting revelation is that the male mutation rate is apparently twice that of the female. (This announcement led Collins to joke that “males are therefore responsible for some two-thirds of genetic diseases, but are also therefore responsible for more evolutionary progress,” as random mutations are the raw materials for evolution.) Collins also noted that other genomes are being elucidated rapidly—for example, the genome of rice was recently published—and that there has been swift additional advancement of the mouse sequence. “If you haven't checked in the last month or so you should,” he said, “because the rapid progress that has been made is quite remarkable, and you should expect a major publication this fall on the mouse sequence, and its comparison to the human sequence.” He then mentioned one important aspect of having numerous organisms' genomes available: “Multiple species comparisons will help show how the genome works—it's like looking at evolution's lab notebook.” He also cited a lesser

known, but very useful website of genetic sequences, both mouse and human, to those working in the field, [genome.ucsc.edu](http://genome.ucsc.edu), a good addition to the more well-known site of the National Center for Biotechnology Information, [www.ncbi.nlm.nih.gov](http://www.ncbi.nlm.nih.gov).

An open invitation now exists to the genome community, Collins pointed out, to recommend organisms for future genome sequencing. The current to-do list includes the chimp, the chicken, the honeybee (which has the twin attributes of being a genome that should reveal clues about well-documented behaviors, as well as being an insect genome), the sea urchin, the tetrahymena, and 12 species of fungi that have medical or agricultural importance. A pitched battle apparently is now being fought between dog and cow researchers to get each group's organism done first. (And Collins playfully noted that the University of Texas is hoping to have a big role in putting together the genomes of both the cow and the honeybee, in an effort to establish “The Center for Milk and Honey.”)

The details of genomic variation (“God is in the details” after all) are especially important for medicine. All humans are about 99.9 percent genetically identical to each other, which means that the 0.1 percent differences in the genomic makeup of individuals is the place to look for the propensities of contracting specific diseases. The development of haplotype maps that catalog the genetic variations of most importance for health and disease should transform medicine. Moving past

*continued on page 16*

continued from page 2

Symposium guest speakers included: Dr. Frank Wood, professor of neurology, Wake Forest University School of Medicine, who spoke on "The Genetics of Dyslexia: Current Status of the Art and the Science"; Drs. Sally E. Shaywitz, Class of '66, and Bennett Shaywitz, professors of pediatrics at Yale University and co-directors of the NICHD-Yale Center for the Study of Learning and Attention, who jointly delivered a lecture on "Science and Reading"; and Dr. Mary Kelly, director of CERC's Adult Literacy Program and acting director of the Fisher Landau Center, who spoke on "Progress in Defining the Clinical Characteristics and Effectiveness of Treatment in Adults with Literacy Problems."

Gottesman, began her career at Einstein 33 years ago, after graduating from Barnard College and earn-



DR. GOTTESMAN

ing her M.A. and Ed.D. degrees from Teachers College, Columbia University. She has trained thousands of physicians, nurse practitioners, psychologists, teachers, school volunteers and parents on how to identify and help children and adults with learning problems. The creator of a widely used screening test to identify children at risk for learning disabilities, she has published numerous articles in professional journals about the developmental course of reading disabilities and the nature of reading disabilities in adults. For her significant contributions to the field, she has been honored by, among others, the LD Access Foundation and the International Dyslexia Association. ■

## Laurels

Dr. Valiere Alcena, Class of '73, clinical professor of medicine, received the Jerome H. Holland Sciences and Technology Award from the American Red Cross of Westchester, and a Distinguished Public Health Service Award from the Westchester County Board of Health.

Dr. M. Donald Blaufox, chair and professor of nuclear medicine, has authored "An Ear to the Chest: An Illustrated History of the Evolution of the Stethoscope" (Parthenon Publishing/CRC Company), which offers an informative and entertaining look at the development of the stethoscope. Recently, Dr Blaufox also received a special Lifetime Achievement Award presented by the International Society of Radionuclides in Nephrology, recognizing his pioneering work in the application of radioactive materials to the study and treatment of kidney diseases and hypertension.

Dr. Susan M. Coupey, professor of pediatrics, and Mimi McEvoy, principal associate in pediatrics, received a John Templeton Foundation Spirituality & Medicine Curricular Award from the George Washington Institute for Spirituality and Health.

Dr. Darwin Deen, Class of '81, associate professor of clinical family medicine and community health and of clinical epidemiology & social medicine, has received the Dale Rasmann Nutrition Education Award from the American Dietetic Association and the Society of Teachers of Family Medicine.

Dr. Betty Diamond, the Murray and Evelyne Weinstock Professor of Microbiology and Immunology, and professor of medicine, recently received the American College of Rheumatology's Distinguished Investigator Award, presented annually to a senior scientist making significant contributions to the field of rheumatology.

Dr. Madhur Garg, a 4th-year resident in radiation oncology, has been selected to receive the American Society of Clinical Oncology's prestigious young Investigator Award. The award recognizes Dr. Garg's innovative research into a novel anti-angiogenic approach to radiation sensitization. His research mentor was Dr. Chandan Guha, assistant professor of radiation oncology.

Dr. Ivan Hand, Class of '82, associate professor of pediatrics, has been elected to the Society for Pediatric Research. He is director of neonatology at Jacobi Medical Center/North Central Bronx Hospital.

Dr. Susan Horwitz, co-chair of molecular pharmacology and the Rose C. Falkenstein professor of

cancer research, is president of the American Association of Cancer Researchers.

Dr. Nadine Katz, assistant professor of obstetrics & gynecology and women's health and director of undergraduate medical education, received an award for "best oral abstract presentation" at the annual meeting of the Council of Residents Education in Obstetrics and Gynecology and the Association of Professors in Gynecology and Obstetrics.

Dr. Harold Klinger, professor of molecular genetics, is co-founder of a new international society, the International Cytogenetics and Genome Society (ICGS). The society's mission is to provide a forum for better communication between plant, invertebrate, and vertebrate cytogeneticists worldwide. Dr. Klinger, who also is chief editor and founder of the journal *Cytogenetic and Genome Research*, established the ICGS in collaboration with journal co-editor Dr. Michael Schmid, professor of human genetics at the University of Wurzburg in Germany.

Einstein student Jean Lee was selected an NIH-Oxford University Scholar in Biomedical Research, through which she will pursue a Ph.D. in the biomedical sciences at the Oxford University School of Medicine.

Dr. Sridhar Mani, assistant professor of medicine, is the recipient of a 2002 Damon Runyon-Lilly Clinical Investigator Award. The award is granted to outstanding young physicians and their research mentors to address the national shortage of clinical investigators. His mentors are Drs. Susan Horwitz and Roman Perez-Soler, professor of medicine, chief of the division of medical oncology and chair of oncology at Montefiore.

Dr. Thomas Rohan, chair and professor of epidemiology and social medicine, has accepted an invitation to serve on the Epidemiology and Disease Control Study Section of the National Institutes of Health's Center for Scientific Review. His term runs through June 2005.

Dr. Zachary Rosen, Class of '87, assistant professor of family medicine and community health and of epidemiology & social medicine, received the Montefiore Medical Group Director's Award for Clinical Excellence for his roles as physician and medical director of the Montefiore Family Health Center.

Dr. Peter Satir, professor of anatomy and structural biology, is the 2002 recipient of the Henry Gray Laureate, the highest honor accorded by the American Association of Anatomists.

Nilda I. Soto, assistant dean for Minority Student Affairs, has been selected to serve on the Association of American Medical College's 2002 Award for Outstanding Community Service Selection Committee.

Dr. E. Richard Stanley, Renée and Robert A. Belfer Professor of Developmental Biology, and professor and chair of developmental and molecular biology, received a MERIT Award from the National Cancer Institute. The award acknowledges Dr. Stanley's major contributions to the understanding of CSF-1 and its receptors.

Sandie Torres, Class of 2004, received a NYC Community Service Scholarship Award from the NY Community Trust. Ms. Torres has chosen to complete two clerkships in emergency medicine. Her sponsor/mentor is Dr. Steven Nazario, assistant professor of emergency medicine.

Dr. Mark Winiarski, assistant professor of psychiatry and behavioral sciences, of epidemiology and social medicine, and of family medicine and community health, has been selected a Fulbright Scholar. He will study indigenous understandings and mental health care interventions related to HIV/AIDS in Namibia.

## IN MEMORIAM

Charlotte K. Lindner, who served as director of the D. Samuel Gottesman Library from 1978 until her retirement in 1989. ■

# Sam He Is

by Karen Hopkin, Ph.D.

**A** visit with Sam Seifter, original Einstein faculty member and distinguished university professor emeritus of biochemistry, is a singular treat. First, he usually has fruit. Even better, he always has a story: Sam searching for a snack cake he first encountered while sleeping on a beach in Fiji; wrestling proteins from a bucket of cell soup in the days when chromatography tanks were the size of the Ullmann building; or simply observing science through the decades. And peppered throughout the mix are puns of all shapes and sizes, delicious as the piece of fruit almost invariably offered.

Now Sam has collected some of his reflections, in verse, in book form. "To Every Truth Its Season" (Fithian Press, Santa Barbara, 2002) offers a small sampling of vintage Seifter. His thoughtful yet playful approach to literature and life shines through in this



compilation. We have Sam's family to thank for embarrassing him into pulling together these pieces, penned periodically over the past 40 years.

Nothing can substitute for spending time with Sam Seifter. But if you're looking for Sam and he's off at a seminar or pressing some flowers, pick up the book. Then pull up a chair and a pear and enjoy your visit. Here is a sample...

*Karen Hopkin, Ph.D., (see page 11) is a 1992 graduate of the Sue Golding Graduate Division.*

## A PRINCIPAL UNCERTAINTY

One fine day,  
in the late defining years of my life,  
I allowed my mind  
the irresponsible pleasure  
of unabridged playfulness,  
and leafed through my dictionary  
in unaccounted search  
for funny-looking words:  
words, which when met head-on,  
free of guardian qualifiers,  
seem quaint and even hilarious.  
Towards the end of my quest,  
having reached the nether region of  
words,  
I found  
yes.

I have not  
consulted my psyche sufficiently  
to know the funny that is yes,  
but I know the finality  
that it holds.  
Three laughing letters:  
first, an hermaphroditic vowel,  
then a most certain vowel,  
that knows its self,  
and finally, a sibilant consonant  
that could go on hissing forever,  
as though it had begun in Eden  
and is working its way through eternity.

This accordion word,  
so compressed and enfolded,  
holds the affirmation of all the truths  
that have arrived, and those that are yet  
to come.

It is the principal certainty of all we are  
and will ever be  
and the verdict that speaks the truth.  
It is anagrammatic  
in every Odyssey,  
and in Ulysses himself,  
and is even misanagrammed in Joyce.  
Shouted in one sharp Archimedean cry,  
or whispered in a Galileian sotto voce,  
it can also be a prolonged exhalation  
of some exploding truth;  
or alternatively  
it can sound like Nora-Molly Bloom's  
permissible breathless yess,  
so full of promise.

In my dictionary,  
yes,  
so vast in consequence,  
needs only four lines  
for definition and usage; while  
a,  
so indefinite an article,  
and the first word in my catalog of  
words,  
needs more than half a column.

So there, I thought,  
so ends my search for funny words,  
ending with the bang of certainty.

And then my eyes  
(also brimming with a yes)  
advanced three words  
in the alphabetic march from  
yes.

And there was  
yet,  
a transformation not to be devoutly  
wished;  
a mutation, a shift in the generic code,  
from s to t  
(as in the word shift itself).

Gone was the funny,  
gone was the certainty;  
enter the serious,  
enter uncertainty.

And then I knew:  
to every truth its season,  
to every yes its yet.

## HAIKU—EVOLUTION

*Written in Dr. Noda's Tokyo house, dining  
room overlooking a garden full of shrubs,  
flowers and toads*

Inside the warm house  
we talk of evolution.  
Outside, toads evolve.

## THE CHILDREN OF MA'ALOT

Children of Ma'alot,  
battered children of our hope,  
your ordeal is over  
and in the hill beds of Safaad  
you rest in gentler cover  
than any we could give in life.

Children of Ma'alot,  
guide us clearly,  
for our grief is too confused;  
and there is peril  
that our only legacy to you  
could be the vengeance we will do.

Children of Ma'a lot,  
you are also the children of  
Theresienstadt,  
of Maidanek-Lublin, Mi Lai, Belfast,  
Mozambique, and a crowded  
geography  
of death in dust-dry villages,  
quick-dug ditches, huddled school-  
houses,  
gas and napalm chambers,  
rifled huts and cobbled streets;  
and, lest we forget,  
soul-consuming refuge camps.

Children of Ma'alot,  
and all the others,  
there was no escape in your time,  
although for each many thousand  
years  
of generations of children  
had grown and multiplied  
to bring you to this point and then to  
death.

Each child returned  
to the stones of Safaad  
or the sands of the Sahara  
or the smog over the Ganges  
is the cruel cut-off  
of so many centuries of hope.

And now begins again  
the endless wait  
for the generation  
that can kill the hate.

*continued from page 13*

the simpler cases of single genes responsible for illness, such as sickle cell disease, Collins predicts that within a decade medical science will identify the constellation of genes that heavily contribute to chronic conditions such as diabetes, heart disease, cancer, mental illness, Alzheimer's, Parkinson's and asthma. "Once you've identified the genes, then you have opportunity for diagnostics, prevention, pharmacogenomics, gene therapy and an understanding of biological defects and drug interventions," he notes.

Collins also recognized the potential for misuse of genetic information. Such concerns led to the inclusion within the NHGRI of the Ethical, Legal and Social Implications (ELSI) Research Program. "You need effective federal legislation to protect against discrimination in light of what you're

going to learn from the genome," Collins says. "And you need to prepare health care providers and the public to deal with statistical risk analysis," as genomic information will point to predispositions rather than definitive outcomes. "You have to make sure that the advantages that the understanding of the genome will confer are accessible to everyone," Collins stresses. (Such advantages may be incalculable. Collins recalled that Bill Clinton would admonish all sides in the Balkan conflict that "you guys shouldn't fight, you're 99.9 percent genetically the same." The response was confused silence.)

After quoting the famous warning that "prediction is very difficult, especially about the future," Collins nevertheless made some prognostications. He believes that by 2020, there will be accessible individualized medicine, because cheap sequencing technology will allow us

to have our personal genomes sequenced for less than \$1000, or about the price of a full-body CT scan today. And gene-based designer drugs may be available to treat your unique condition, which would masquerade as a standard illness with the diagnostic and interventional techniques currently available. Collins implored current Einstein students and researchers to become involved with research aimed at employing genomics in the service of medicine, noting that "we need the best and brightest minds of the next generation to engage in this effort." He concluded by emphasizing that point with a quote not from a great scientist or physician, but from a great hockey player, Wayne Gretzky. "Skate," said Gretzky, "where the puck is *going* to be." ■

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