

Still The Second Best Thing About Payday

The Disease of Obesity

Fat Is a Stubborn Foe, Columbia's Leibel Reports

By Rich McManus

Nothing seems to love the human body like fat, arriving oftentimes unbidden, and remaining snuggled up close until substantial means—including regular exercise, diet, drugs, or even surgery—are employed to thwart its lusty embrace.

Something about the human body just wants to be fat, gravitates toward lushness of flesh, and it is investigators such as Columbia University's Dr. Rudolph Leibel—who spoke at the Clinical Center's Contemporary Clinical Medicine: Great Teachers segment of Grand Rounds on Jan. 14—who are discovering the genetic and hormonal elements that feed the body's hunger for adiposity.

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Verfaillie To Deliver NIH Director's Lecture, Feb. 11 in Masur

Dr. Catherine Verfaillie will deliver the NIH Director's Lecture on "Greater Potency of Adult Stem Cells," at 3 p.m. on Wednesday, Feb. 11, in Masur Auditorium, Bldg. 10. Verfaillie is director of the Stem Cell Institute and professor of medicine, division of hematology, oncology, and transplantation in the department of medicine at the University of Minnesota. The lecture will focus on her discovery of multipotent adult progenitor cells (MAPCs) and her laboratory's ongoing research on their properties and potential therapeutic uses.

Verfaillie and her colleagues identified MAPCs and were the first to show that these cells, derived from adult bone marrow, can differentiate *in vitro* and *in vivo* into almost all cell types of the body.

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'Tangible Benefits Not Created in a Vacuum'

Zerhouni Discusses Principles of Collaboration at 87th ACD Meeting

By Carla Garnett

When the advisory committee to the director (ACD) last met in June 2003, NIH director Dr. Elias Zerhouni described for them his ambitious Roadmap for Medical Research initiative, which embodies the concept of team science. At the most recent ACD meeting on Jan. 12, he expressed great satisfaction that the fall 2003 public rollout of his three-pronged research strategy had been widely reported and enthusiastically received.

In reassuring ACD members that despite recent criticism of some grants and some consultancy arrangements, NIH must not shrink from its duty to provide health research for the benefit of all, Zerhouni also reemphasized a large part of the Roadmap strategy—NIH's need to

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NIH director Zerhouni (r) and deputy director Kington meet with the ACD.

Admission to 'A Circle of Trust'

King Program Features Stimulating Conversation

By Rich McManus

Masur Auditorium was transformed into a family living room Jan. 15 as NIH observed the 75th birthday of Martin Luther King, Jr., with an intimate conversation between civil rights movement legends Dr. Dorothy Height and Rep. John Lewis (D-GA), both of whom knew and worked with Dr. King. Moderating the discussion—in the manner of Brian Lamb conducting *Booknotes* interviews on C-SPAN—was NICHD deputy director Dr. Yvonne Maddox, who elicited moving testimony from the special guests, both of whom have published memoirs.



Dr. Dorothy Height gives perspective on civil rights movement.

"I grew up on a farm 50 miles from Montgomery,

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"Finding MAPCs opens the possibility that 'adult' stem cells from easily accessible sources like marrow could be used to treat degenerative and inherited disorders," Verfaillie said. "But a lot of questions remain. Is their plasticity due to co-existence of multiple tissue-specific stem cells in marrow or can a single cell turn into most types? What is the mechanism underlying differentiation of MAPCs? These are the types of questions that still need to be answered."

Her research has shown that MAPCs can be cultured from human, mouse and rat marrow. Ongoing work in her laboratory is aimed at further characterizing these cells and developing approaches for using them in the treatment of mucopolysaccharidosis, hemophilia, muscular dystrophy, sickle cell anemia and other diseases.

A hematologist known for her work on leukemia, Verfaillie's research career has focused on the microenvironment of bone marrow, specifically hematopoietic stem cell regulation and proliferation, stem cell therapy for leukemia, and most recently, the potential therapeutic value of MAPCs. She has a long

association with NIH, having received grants from various institutes since 1994 and currently holds grants from NHLBI, NIDDK and NCRR.

She earned her M.D. *summa cum laude* from the Catholic University of Leuven in Belgium, her native country. After a residency in internal medicine and a fellowship in hematology at the University of Leuven, she moved to the University of Minnesota in 1987 to do a postdoctoral fellowship in hematology. In 1991, she was appointed assistant professor in the department of medicine and then in 1998 was named professor of medicine.

Verfaillie has published extensively in the scientific literature and has received numerous honors and awards for her work. She holds the Anderson chair in stem cell biology; the Tulloch chair in stem cell biology, genetics and genomics; and the McKnight's presidential chair in stem cell biology. Among her other honors are the Young Investigator Award from the International Society of Experimental Hematology, membership in the Royal Belgian Academy of Medicine, and the 2003 Jose Carreras Award from the European Society of Hematology. The Leukemia Society of America has also honored her with the designations of special fellow and scholar. In 2000, *U.S. News and World Report* named her "one of the ten leading innovators for 2001."

The lecture is part of the NIH Director's Wednesday Afternoon Lecture Series. For information and reasonable accommodation, contact Hilda Madine at (301) 594-5595 or hmadine@nih.gov. ■

Duke, Pitt Training in Clinical Research

The Clinical Center's Office of Clinical Research Training and Medical Education offers two opportunities for training in collaboration with Duke University and the University of Pittsburgh.

The NIH-Duke Training Program in Clinical Research, implemented in 1998, is designed primarily for physicians and dentists who desire formal training in the quantitative and methodological principles of clinical research. The program, offered via videoconference at the CC, offers formal courses in research design, research management and statistical analysis.

Academic credit earned by participating in this program may be applied toward satisfying the degree requirement for a master of health sciences in clinical research from Duke School of Medicine. For more information, visit <http://tocr.mc.duke.edu/> or email tocr@mc.duke.edu. The deadline for applying is Mar. 1, 2004.

The University of Pittsburgh Training in Clinical Research Program is designed for Ph.D.'s and allied health professionals and consists of a curriculum taught over three semesters starting with an intensive 8-week summer session. NIH trainees are only required to spend the first 5 days of the summer session in residence at the University of Pittsburgh. Physicians and dentists are also eligible to matriculate in this program.

For more information, including tuition costs, visit http://www.cc.nih.gov/cc/cc_pitt/index.html or email tcrp@pitt.edu. The deadline for applying is Mar. 1, 2004. Prospective participants should consult with their NIH institute or center regarding the official training nomination procedure. ■



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The American Federation of Government Employees (AFGE) Local 2419 raised \$1,500 for the R&W Foundation's patient care fund during its annual holiday raffle. This donation, which tripled last year's gift, will be used to support monthly events and activities for the Clinical Center's pediatric patients. The union recently presented a check to R&W officials at the Clinical Center. Shown are (from l) George D. Peters Jr., AFGE; Randy Schools, R&W president; Charles Butler, CC rehabilitation medicine department; Richard A. Laubach, Local 2419 president; Todd Loveless, AFGE treasurer. "We support all of the efforts of NIH," said Laubach. "The holiday raffle allows us to participate, give something back to NIH and the patients, and hopefully provide a little more joy and comfort for the kids." In addition, the union collected and donated more than 200 toys to pediatric patients for the holidays.

Minority Students Learn About NIAID

NIAID's Office of Training and Special Emphasis Programs is hosting the second annual Intramural NIAID Research Opportunities (INRO) program Feb. 1-5 on campus. INRO 2004 brings together 21 students from underrepresented minority groups across the country interested in exploring career opportunities in allergy, immunology and infectious diseases.

The program introduces students to research and training opportunities in the Division of Intramural Research and the Vaccine Research Center. The 5-day INRO program includes scientific lectures by NIAID researchers, discussions with scientists, tours of the laboratories in the Research Technology Branch and the VRC. Current NIAID postbaccalaureate and postdoctoral minority trainees are participating in the program, giving the visiting students an opportunity to learn more about laboratory projects and training experiences.

For more information, contact Dr. Wendy Fibison, wfibison@niaid.nih.gov or (301) 496-6400. ■

Have Kidney Disease?

Call NIH at 1-800-411-1222 for new kidney studies, including lupus nephritis, membranous nephropathy and focal segmental glomerulosclerosis. Treatment provided at no cost. Transportation may be provided. Email prpl@cc.nih.gov (TTY: 1-866-411-1010). ■

Intern Program Seeks New Recruits

Entering its 47th year, the NIH Management Intern Program—a competitive 2-year training opportunity—is seeking outstanding men and women interested in a career in public service to apply for the 2004 MI Program. The program offers an opportunity to explore different administrative career fields, gain invaluable insight into NIH and train for future administrative leadership positions.

The program will be open for applications through Tuesday, Mar. 2. NIH will select up to three participants for the 2004 program. Positions are offered at the GS-5/9 levels; the program has a career ladder with potential to the GS-12 level, depending on the candidate's grade at time of selection.

The program uses rotational assignments to introduce interns to potential career tracks. Participants accept management trainee positions and receive training in a variety of administrative fields including budget and finance, public information and education, program planning and evaluation, grants and contracts, public liaison and legislative analysis, program administration, information technology, human resources management and human capital management, central service management, science policy, program and management analysis, general administration, and public affairs and communications.

To be eligible to apply, candidates must be U.S. citizens, willing to work full-time and currently employed at NIH at GS-5 or above or wage-grade equivalent on a career or career-conditional appointment, or on any type of appointment that offers noncompetitive conversion during the application period.

Potential applicants should view the web sites at <http://internships.info.nih.gov>, <http://www.hhs.gov/careers/quickhirefaq.html> and <https://jobs.quickhire.com/scripts/hhs.exe> (click on New Users). For more information call (301) 402-3383. ■

Depression Study Needs Volunteers

If you currently experience symptoms of depression, you may be eligible to participate in a research study. Symptoms include sadness, losing interest in your activities and changes in eating and sleeping patterns. Interested volunteers, 18 years or older, may be eligible to participate. If you qualify, participation involves a 3-4-hour visit, including questionnaires. The study does not include treatment, but we provide referrals. You will be compensated for your time. For more information, call the Mood Laboratory at the Uniformed Services University, (301) 295-3241. ■

FEW Hosts NIH Ombudsman

Federally Employed Women, Bethesda chapter, will host Dr. Howard Gadlin, NIH ombudsman and director of the Center for Cooperative Resolution, at a brown bag chapter meeting on Tuesday, Feb. 10 from noon to 1 p.m., in Bldg. 31, Rm. 6C6. Gadlin will present "Cross Cultural Conflict Resolution: Mediating Disputes in the National Institutes of Health." Sign language interpreters will be provided. Individuals with disabilities who need reasonable accommodation to participate should contact Allyson Browne, (301) 451-0002 or the Federal Relay (1-800-877-8339).

Healthy Volunteers Needed

If depression has never been a problem for you and the fall and winter seasons do not affect how you feel very much, you may be eligible to participate in a research study. We are looking for volunteers with good mental health, 18 years or older. If you qualify, participation involves a 3-4-hour visit including questionnaires. Participants will be compensated for their time. For more information, call the Mood Laboratory at the Uniformed Services University, (301) 295-3241.

OBESITY, CONTINUED FROM PAGE 1

Lipsett Amphitheater swelled to standing-room-only proportion for Leibel's presentation, "Obesity: A Disease, Not a Character Flaw," reflecting medical interest in the booming rates of booming belllines in the United States.

"There has been an enormous increase in the prevalence of obesity in the U.S.," said Leibel, showing epidemiologic maps indicating steady weight gain in the past dozen or so years; Alabama appears to be the heaviest state at the moment. The rise in American obesity is paralleled by rising diagnoses of diabetes, not to mention a host of other illnesses, including hypertension. "Obesity results in lots of suffering, and lots of cost," Leibel noted. "About 5 to 7 percent of the total U.S. health budget is accounted for by obesity-related ailments."

Speaking from an evolutionary perspective about environmental, and by selection, genetic tendencies for holding weight up or down, Leibel noted two up-regulating factors for fat mass: reproductive requirements, and protection against environmental vicissitudes, such as famine. Opposing fat acquisition (in addition to glancing in the mirror) is at least one major factor—predator evasion. Or as Leibel explained, "You can't run away from your enemy if you're excessively overweight."

Fat mass is regulated chiefly by signals mediated through the hypothalamus (a pea-sized structure above the pituitary gland), Leibel said. In the short term, incoming signals are mainly metabolites; in the intermediate term, gut hormones such as ghrelin released from the stomach exert their effect; and in the long-term, adipocytes, or fat cells, send signals such as leptin, a substance that, when available in adequate supply, pushes you away from the table and, when in short supply, draws you back to the buffet. The net evolutionary sense of these systems appears to be this: defense against the *loss* of fat is much greater than defense against *gain* of fat.

"Obesity is a game of inches, like baseball," Leibel said. "Small differences add up, particularly over a long period." For example, a mere 3.6 percent excess in intake of calories versus output can account for the 30-35-pound weight gain most adults experience between ages 25 and 55 years.

Ranging away from the belly to the brain, Leibel stated, without irony, that "the guts of the (fat-determining) system is in the hypothalamus." The arcuate nucleus, or "nose" of the hypothalamus, is the seat of first- and second-messenger molecular action determining fat intake. Evidence in animal studies shows that when specific neurons in specific regions of the hypothalamus are either ablated or preserved, researchers can "adjust" for fat or thin rodents. Leibel described a sort of biological tango wherein orexigenic factors battle anorexigenic factors to maintain homeostatic balance in the body.

Partners in the dance include leptin and its receptors, neuropeptides Y, POMC (proopiomelanocortin) genes and a host of neuropeptides. It is likely that all of the molecular players have not been discovered. Causes of human obesity range from monogenic—as in mutations in the MC4R gene, which represents the most common form of human obesity syndrome (accounting for some 3-5 percent of severe obesity in children)—to polygenic. The genetic basis for most human obesity has not yet been identified. It is likely that the interaction of several genes, each with modest effects, determines one's predisposition to obesity, Leibel said.

He reported that the heritability of obesity, which is in the range of 65-70 percent, is much higher than in many other diseases. He guessed that some 30-40 genes play a role in the control of energy homeostasis. "The trick is, how do they play with one another, and with the environment, to produce the phenotype (obesity)?"

Pausing for some anthropological observations, Leibel noted that the modern environment—studded with cell phones and dotted with restaurants that provide take-out—is not well tuned to man's genetic makeup, forged as it was in hunter/gatherer days. "An organism designed in one environment (prehistory) now finds itself in the modern world...This helps explain why obesity is so hard to treat: We're just not designed to be skinny organisms in this environment."

Most current treatments for obesity don't work, Leibel said, because they are bucking such powerful biological defense systems. But that's no reason to toss out the Adidas, for "even a little bit of weight loss can do a lot of good—modest weight loss improves health." He urged, "Use whatever works, but is healthy. Try different approaches." He cautioned that diet composition is "not a major player" in weight control because "a calorie is a calorie, no matter where it comes from."

He mentioned two drugs licensed for weight loss, sibutramine and orlistat; the latter blocks absorption of fat, but can have unpleasant "social consequences" as users may have to take frequent bathroom trips. He called bariatric surgery a "draconian" approach, but allowed that it is the most effective intervention, especially the procedure known as gastric bypass roux-en-y.

Peering into the future of body mass reduction, Leibel said there is a great need for new molecular targets, especially gut-related signals, and called for reduced consumption of calorie-dense foods. He also repeated the prescription that nobody wants to hear, especially when it's 15 degrees outside—a need for increased exercise.

To view Leibel's talk in its entirety, visit <http://videocast.nih.gov>. ■

Storm Water Management Project Generates 'Field of Streams'

Occupants of Bldg. 31's B and C wings inadvertently find themselves overseeing a curious project under way outside their windows on the campus's northeast corner: creation of a network of large underground pipes that will serve to retain storm water runoff from the new Clinical Research Center, the new Bldg. 33 and garage complex, and essentially "the entire north half of campus," said Yong-Duk Chyun, CRC project director.

The project—wherein massive pipes are laid side by side in a pit the size of several football fields then covered with gravel, tarps and fill dirt—is designed "to manage the quantity of storm water flowing into the stream" feeding Rock Creek, said Chyun.

"They are basically water retention pipes—they will hold the water temporarily as it is discharged into the stream at a slow rate."

The 60-inch corrugated pipes are made of polyethylene, but their installation is engineered to support a large dirt berm atop them in order to provide



The black polyethylene pipes, each 5-feet across, stacked at left are to be buried beneath dirt and gravel, and form an underground network that retains storm water runoff from the north half of campus, including the construction sites for the Clinical Research Center and the new Bldg. 33 biodefense facility. A dirt berm will be built atop the network, to shield the garage (r) from view.

landscaping that will help shield the new 1,200-car parking garage from the sight of neighbors across Cedar Ln.

Chyun reported that CRC construction will be complete in August. The CRC occupancy plan calls for lab space to be populated first, beginning in September, followed by the various hospital departments, and finally the patients themselves, who will be transferred from the old Clinical Center over the course of a weekend. "The patients will move last," said Chyun, "when the facility is fully operational and ready for them."—Rich McManus ■

Career Center Web Site Launched

Contemplating a career in health sciences or looking for more opportunities for funding and training? NIH recently launched a new Virtual Career Center developed by the intramural Office of Education and designed to meet the needs of the NIH community as well as students and professionals in science and medicine, from the college level to postdoctoral and beyond.

The center, <http://www.training.nih.gov/careers/careercenter/index.html>, has four major areas of interest: exploring career options, continuing education, employment options and opportunities, and the job search process. Containing 55 pages and more than a thousand links, the site also allows for a quick focus on areas that meet a user's particular needs.

"The range of career options open to young scientists is broad and continually evolving," says Brenda R. Hanning, acting OE director. "Many of the jobs students will have in the future may not have been invented yet. Our site will work to keep pace with new avenues of opportunity."

The "Exploring Career Options" section enables users to explore their interests through self-assessment mechanisms, discover careers and pathways, and learn important career skills such as writing grants and publishing articles.

The section titled "Continuing Your Education" provides information on admissions, application services, financial aid, loan repayment, grants, fellowships, education survival skills, and medical schools and other professional programs.

Information on conducting employment searches and learning about opportunities available in industry, academia and government are found in the "Employment Options and Opportunities" section.

Last, important skills to be used for applying, interviewing and negotiating for a position are found in the "Job Search Process" section. Because users will have specific needs and come from different backgrounds, each section can be searched independently and includes related links that will provide additional information on particular areas of interest. ■

Are You a Woman Who Has Been Depressed?

NIMH is looking for female volunteers to participate in a study that examines the role of hormones in depression. Participants should not be currently depressed, be between ages 18-45, be medically healthy and not be taking any medications, including birth control pills. Study includes medical and psychiatric evaluations. Financial compensation and transportation reimbursement provided. For more information call Linda Simpson-St. Clair, (301) 496-9576 (TTY 1-866-411-1010). ■

Malaria Vaccine Study Needs Volunteers

Healthy men and women ages 18-45, without previous history of malaria or receipt of a malaria vaccine, are needed to participate in a study on the safety and effectiveness of a new investigational malaria vaccine at Walter Reed Army Institute of Research in Silver Spring. Health screening and financial compensation provided. Call 1-866-856-3259 toll free or (301) 319-9335/9320, or visit www.wrairclinicaltrials.com.

KING PROGRAM, CONTINUED FROM PAGE 1

Alabama," Lewis recalled, "so I had a taste of segregation and discrimination. I didn't like it. I didn't like what I tasted. I asked my parents, 'Why?' and they told me, 'That's the way it is—don't get in trouble.'

"I hated racial segregation and discrimination," he continued, noting that when he first applied for a library card in 1956, at age 16, he was denied. But when he went back to that same library in 1998 to sign copies of his newly published book, he was welcomed.

Lewis, who marched from Selma to Montgomery with King in his role as chairman of the Student Nonviolent Coordinating Committee, said, "I would still be on the farm raising chickens if it weren't for Dr. King. He freed me. He liberated me. He taught me how to stand up to segregation."

Height, now 91, who was president of the National Council of Negro Women for 41 years and still serves as president emerita, recounted an upbringing in a relatively tolerant Pennsylvania steel

mill town. It was there that she learned, through events such as an Elks Club-sponsored debate on the U.S. Constitution, what America promised its citizens and what it could be, ideally.

"I think my life and that of blacks in America has been characterized by rising expectations, and rising frustra-

tions," she said. Commemorations such as this, she noted, only slowly erode a sense of indignation at how long it is taking for justice to arrive for all people in America.

She offered a fascinating footnote to the story of King's famous March on Washington, culminating in the "I Have a Dream" speech on the steps of the Lincoln Memorial on Aug. 28, 1963: "One thing that we were never able to do that day was convince the leadership that there should have been a woman speaker on the platform."

Quipped Lewis, "We were male chauvinists," to which Height replied without missing a beat, "Now I feel better."

Height said she had wanted a woman on the dais to speak for women, not for any particular organization. "Mahalia Jackson was the only female voice you heard that day, when she sang the National Anthem." The following day, at a post-march meeting, organizers resolved "never again to lack a woman's voice," Height said.

Lewis was only 23 on that hot summer day, he recalled. "I had heard Martin Luther King speak many times. We had been in meetings on [Capitol] Hill earlier in the day, and we didn't expect such a huge crowd when we came out. We had to walk—you

couldn't drive. A sea of humanity just pushed us toward the Lincoln Memorial. Martin Luther King was so moved. He just went into his heart and soul and said 'This is it.' He had an executive session with himself, and decided to let himself be used by God Almighty. He transformed those marble steps into a pulpit."

Lewis returned to the site of the famous speech on the 40th anniversary of its delivery last August. "It was too much—I was overcome by it," he said. A plaque on the site reading, "I have a dream..." will be there as a memorial "for generations yet unborn," Lewis predicted.

Maddox asked the two heroes of the civil rights movement to share their dreams for America. "Let America be America," said Height, quoting a famous Langston Hughes poem.

"We have all these things that we stand for—why not start living up to them?...If we go on with this 'eye for an eye' business, everyone will be blind." She remembered the initial exhilaration of the



Clinical Center employees Thao Mai (l) and Kathleen Spaid were among those who recited the King Litany.

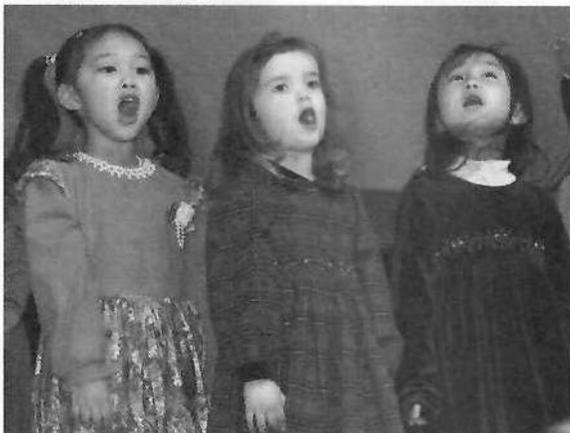
Brown v. Board of Education decision that abolished the doctrine of separate but equal, but laments continued efforts to circumvent its intent. "I don't want to see just law and order," she said, "but also equality and justice."

Said Lewis, "I want to see an America that lays down its tools and instruments of violence here and around the world," and the audience erupted in applause. "I want an America where we all live like



Rep. John Lewis (D-GA, l) is greeted by NCMHD director Dr. John Ruffin.

PHOTOS: ERNIE BRANSON



The NIH Pre-school Singers, which included these three youngsters, sang two songs and wished MLK a happy birthday.

a family. We're all one family, and we live in the world house, not just the American house." Quoting King, he added, "We must all learn to live together, or we'll perish separately."

Maddox got each of them to address the roots of their own activism.

"It's what I was doing at 19 that made a difference in my life," said Height. She had protested injustice even earlier than that, at age 12 outside a YMCA pool. "Being active in committees and having faith in my purpose in life got me involved in the civil rights movement," she added. "When you see something that is not right, does your blood boil or do you look the other way? You have to learn how to use yourself in ways that can be positive." A combination of caring about what was happening and seeing what she could do for others motivated Height. She also said that inspiring adults served as role models. "I met Eleanor Roosevelt and Mary

NIH director Dr. Elias Zerhouni greets Height before the King program began in Masur.



McLeod Bethune on the same day," she remembered. "I will never forget the benefits of dealing with caring adults—we need much more of this approach today."

Lewis recalled that he was heavily influenced by both philosophy and King in the late fifties and early sixties. "I didn't see myself so much as a leader... We used to call ourselves a circle of trust, a band of brothers and sisters, a big family... We had to learn to lay our differences aside sometimes. It was more important that we spoke with one great, mighty voice. In those days, we didn't have any web site. We had no email. We had no fax. But we had ideas, we believed in something, and we laid our bodies on the line." The audience clapped in assent.

Earlier in their remarks, both guests recounted the importance of friends in high places. Height said she often thinks "it was the hand of God" that enabled civil rights activists to remain nonviolent after the assassination of Medgar Evers in 1963; that event actually led to unanticipated unity among all ages in the movement, she related. She remembered the words of a 72-year-old marcher, who when offered the mercy of a car ride replied, "My feet

may be tired, but my soul is rested."

Lewis recounted the importance of civil rights leaders' friendship with both President John F.

Kennedy and his brother Robert, who was then attorney general:

"Without them, we wouldn't have survived." He remembered a 1961 Freedom Ride that turned ugly when a mob surrounded the marchers in the Montgomery church led by the Rev. Ralph Abernathy. "We all went down to the basement, and Dr. King called the Kennedy brothers, who got the National Guard to come out and protect us. If it hadn't been for that act, I might not be here today."

Testifying to King's international influence, NIH director Dr. Elias Zerhouni told the crowd that his father had always hailed King, JFK and Gandhi as heroic role models. "In no small measure, my position [as NIH director] is due to [King]," said Zerhouni in an emotional recollection. "I want to formally commit us to Dr. King's vision of the world... The diversity of those who serve must parallel the diversity of those who are served. My father always told me that you are not defined by what you receive from others, but by what you give to others. That was Dr. King's challenge, too: 'What are you doing for others?'"



NINDS retiree Levon Parker presents award to Dr. Ruth Kirschstein at ceremony.

to bestow upon Dr. Ruth Kirschstein, senior advisor to the NIH director, a crystal obelisk "in appreciation for your courageous leadership in promoting true equal opportunity at NIH."

In closing remarks, NIAMS director Dr. Stephen Katz observed that the audience "was truly mesmerized" by the conversation between Maddox, Height and Lewis. "I think we should have part two next year."

The complete event may be viewed at <http://videocast.nih.gov>. ■



NICHD deputy director Dr. Yvonne Maddox served as moderator of the conversation at the Jan. 15 observance.

The ceremony also included musical selections from the NIH Preschool children and from guest musicians Wydell Croom (piano) and Bryan Mills (saxophone), who performed a medley of "Precious Lord" and "Amazing Grace." Also, recent retiree Levon Parker of NINDS returned

ACD MEETING, CONTINUED FROM PAGE 1

establish and maintain strong collaborations with both public and private sector scientists.

"The public will not be served," he remarked in his state-of-the-NIH report to the ACD, "if we completely eliminate the ability of government scientists to interact with the private sector—either non-profit or for-profit—in appropriate ways."

Roadmap Hits the Road Running

Describing the media response to the Roadmap public unveiling, Zerhouni said, "I'm told that this was one of the largest press conferences at NIH. Most important, though, was that the stories were accurate and well-reported. In that sense we have done what we needed to do, what you asked us to do in June, which was communicate extensively with multiple constituencies."

There are 28 initiatives in the Roadmap; several have been launched already and all will be launched in the coming months, with the help and guidance of NIDCR deputy director Dr. Dushanka Kleinman, who was introduced as assistant director for Roadmap coordination, a post she assumed on a temporary detail to the Office of the Director.

New ACD member Dr. R. Sanders Williams, a cardiologist and dean of Duke University's medical school, applauded the Roadmap for "making room

for mavericks, but providing a structure" for trends in biology.

In a discussion launched by ACD member and former U.S. Sen. Connie Mack on balancing investigator-initiated research and targeted research, Zerhouni explained that 57 percent of NIH-supported research can be classified as so-called investigator-initiated or basic science, 33 percent is research targeted toward a specific disorder, and 10 percent represents research training.

"You can't dictate what will be done and how," stressed Zerhouni. "[However] we can identify grand challenges and let scientists self-assemble research teams."

ACD member Phillip Williams, retired vice chair of the Times Mirror Co., said that communicating to non-scientists about the benefits of basic research versus targeted research will be essential in garnering public support of the NIH research agenda.

People will want to know why you seem to be studying something without a purpose, he commented. "You must communicate the tension [between the two] as you have here."

Issues in the News

In his fourth ACD session as director, Zerhouni took the opportunity to discuss two issues that have

PHOTOS: ERNIE BRANSON



Zerhouni welcomes advice of a blue-ribbon panel he appointed to consider intramural clinical research.

'Landscape Is Completely Different'

ACD Contemplates Future of Intramural Clinical Research

A lot can change in half a century, and in a thoughtful discussion about the revitalization of NIH's intramural clinical research program, advisory committee to the director (ACD) members and guests at their Jan. 12 meeting heard innovative suggestions for returning the program to its past glory. Looking forward to the opening later this year of the Clinical Research Center, NIH director Dr. Elias Zerhouni had enlisted a blue-ribbon panel to study the status quo and seek ways to meet the demands of a 21st century clinical environment that has changed dramatically since the Clinical Center first opened in 1953.

"What can and should NIH do in the realm of clinical research?" he asked. "If you compare clinical research in 2003 with 1953, you will see that the landscape is completely different in our country."

Noting that in the early fifties, "there were very few, if any, centers that could conduct interventional clinical trials, or train a large cadre of talented physician-scientists," Zerhouni said there were not many alternatives to the NIH Clinical Center back then. "Today, you have dozens of outstanding programs in academic health centers, and the specific role of a national center such as the Clinical Center became not only an issue of managing the

program internally, but also an issue of strategy and priority. We believe that in the next few years, the role of the Clinical Center may actually increase in importance compared to 5 to 10 years or so ago. Academic health centers are facing very difficult fiscal times. Margins of clinical activity have pretty much collapsed; the margins have come down from 5 or 6 percent to 1 or 2 percent. It's very hard to invest boldly as a trustee or chancellor or dean of an academic health center into high-risk clinical research that requires any kind of margin of excellence. So perhaps there is a role for the Clinical Center in that context."

Chaired by Dr. Edward Benz, president of Dana-Farber Cancer Institute, and cochaired by Nobel laureate Dr. Joseph Goldstein, professor and chair of the department of molecular genetics at the University of Texas Southwestern Medical Center, the 15-member blue-ribbon panel brought together top-notch investigators from a range of specialties and research disciplines both within and outside NIH. On a fast-tracked assignment, they met three times in 2003 and were briefed extensively by a number of intramural NIH'ers and outside experts.

"The charge to the panel was to give some thought and recommendations to how the NIH intramural clinical research program (ICRP) could revitalize the

gained a lot of attention in the past 6 months, both inside and outside NIH.

In no uncertain terms, Zerhouni said, NIH stands behind its peer-review system, which determines which research grants the agency funds. A model for others in the international research community, NIH's system of evaluating which research proposals are worthy of funding is sufficiently rigorous—second to none—he pointed out, and its decisions should not be second-guessed. Justification for several NIH-funded grants on such topics as sexual behavior was questioned by some members of Congress, who requested that NIH look into the specific grants and report back.

“We have reviewed this field,” said Zerhouni, who explained that each grant cited was examined for public health relevance and each was determined to be quality research whose results would benefit the public. “There is absolutely no evidence whatsoever that these grants are not in the interest of the public. Our peer review system is working. It is actually one of the most comprehensive processes that can assure one that we are performing and funding good science... We found that in every case, when you looked at the details and when you looked at the public health relevance, that there was no question that these grants should have been funded, and should continue to be funded.”

national mission in clinical research, take advantage of the unique resources and deal with the unique disadvantages that come from an intramural program on this campus,” said Benz, presenting the panel's final report. Specifically, he said, Zerhouni asked the group to consider where the ICRP can produce paradigm-shifting research, whether its current portfolio is appropriate, how accomplishments can be made by reassigning existing resources and how success can be evaluated.

First among six recommendations is that a “single high-level oversight committee” be created to handle all responsibilities related to NIH's ICRP. The committee replaces all current oversight boards and would report to the NIH director. It would govern, plan strategy, set priorities and develop budget, in addition to making recommendations about transdisciplinary clinical initiatives and resource allocation. A new external advisory committee to the NIH director would monitor the overall quality and vitality of the ICRP. The panel also recommended that a new deputy director for clinical research position be created on par with the deputy director for intramural research post.

“While no one would claim that the entire [nation's clinical research] enterprise is where it should be,” Benz said, “the idea that the Bethesda campus is a unique place or the only place that the very most talented people are going to pass through in the

Zerhouni also provided details about his response to Congress regarding possible conflicts of interest that were suggested by a December series of *Los Angeles Times* articles.

The stories raised questions about several NIH intramural scientists who receive compensation from outside organizations for consulting on research, and the propriety and public disclosure of such agreements. A thorough review of all outside consulting arrangements by NIH scientists was ordered by the director and is under way. Zerhouni also pointed out that—contrary to suggestions by the media reports—all of the arrangements had been disclosed, reviewed and approved under existing ethics rules.

Open Doors, Disclose Facts

“The philosophy we used [to answer the allegations] fairly immediately was to be completely transparent and completely proactive,” Zerhouni said, noting that his first concern was to refute implications by the articles that patient safety may



Dr. Michael Gottesman (l), NIH deputy director for intramural research, and ACD member Dr. Cecil Pickett, president of Schering-Plough Research Institute, listen to reports at the recent ACD session.

CONTINUED ON PAGE 10

course of their training and career development is not true anymore. The NIH intramural program needs to develop a unique position in what is now a very fertile field for clinical research.”

In finding a “niche that is distinct and complements what goes on in the extramural community,” the ICRP should emphasize study of rare diseases, stressing pathophysiology and novel therapeutics, he said.

Other recommendations by the panel require the ICRP to develop new training and career pathways in patient-oriented research, and reduce regulatory barriers to clinical research. Benz said clinical research should be as respected and valued as laboratory research.

Currently 17 institutes use the Clinical Center for some part of their intramural clinical research portfolio, according to CC director Dr. John Gallin, who briefed the panel and who served—along with Dr. Michael Gottesman, NIH deputy director for intramural research, and NIDDK director Dr. Allen Spiegel—as an *ex-officio* participant.

Zerhouni thanked Benz and the panel for their recommendations, noting the challenge presented in reconciling this group's ideas with those offered last year in an Institute of Medicine report. He indicated that the intramural clinical research issues would be further deliberated at an upcoming Office of the Director staff retreat.

have been compromised by the relationships. "I'm pleased to tell you," he stressed, "that we have gone through the reviews—all the reviews for NIH aren't completely done at this point—but for the cases that were mentioned, there is absolutely no indication whatsoever that a patient was harmed because of this relationship. I want the committee to understand that our actions were to, as completely as possible, shed light on the facts alleged, so that we can at least be sure that the reality of conflict was not there."

Beyond patient safety, Zerhouni said his next major concern was the research itself, to determine that no "tainting of the decision-making process" occurred during the consultancies. "In each case we found the appropriate recusals," he explained. "We found no evidence that what was alleged in the [original] article relates to reality."

Still, the director acknowledged the public perception left by such media reports cannot be allowed to impugn NIH's reputation, or impede its mission.

"When you look at the reality, we find very little," Zerhouni said. "However, the fact that the article triggered such a reaction tells you that we have an appearance problem, and not only an appearance problem, but we have a limit problem. Do we have the ability to have our scientists consult without limits—limits on time, on dollars, on kinds of relationships? I think that's a valid question."

To address such questions and others involving conflict of interest and human subject research, he has called for an independent committee to look at NIH policies.

"Our mission is too important to have it undermined by the sense that there was no independent review of the process," Zerhouni said. "The situation is not as bad as it was portrayed, but [it] could be improved so that the appearance of conflict is eliminated. We all feel very strongly that collaborations between public and private scientists are important and essential to translating basic science into tangible products, methods and...that there is a way to assure the public of the lack of conflict."

"We are subject to conflicting tensions," he continued. "On the one hand the public expects us to create tangible benefits. Those tangible benefits cannot be created in a vacuum. They have to be created in connection and in conjunction with the non-governmental sector, because of the high level of complexity related to research. That connection needs to be reinforced and appropriately managed. The principles in my mind are full transparency—there's nothing in a relationship that should not be done in full light of day, full disclosure, appropriate review and proactive monitoring."

On the Administrative Front

In addition to Williams, another new ACD member

attending his first meeting of the group was Dr. Raghavendra Vijayanagar, a cardiovascular surgeon from Florida.

Two newly appointed institute directors were introduced—Dr. Story Landis, who took the reins of NINDS last August, and Dr. Jeremy Berg, who claimed NIGMS's top job in November.

Further lauding the agency's "continued success in recruiting outstanding individuals," Zerhouni also announced recent appointees Dr. Norika Ruiz Bravo, NIH deputy director for extramural research, and Richard Turman, NIH associate director for budget. Zerhouni mentioned that NHGRI director Dr. Francis Collins is leading the search committee to replace Dr. Claude Lenfant, who retired as NHLBI director last summer.

Reiterating his commitment to pursue diversity in all aspects of NIH operations—not only in research and research training, but also in the workforce—Zerhouni also acknowledged a rare honor for a federal agency, an award for best diversity practices that he accepted on behalf of NIH a few months ago. NIH was the only government organization among 2003's 10 recipients, and is only the second federal group so honored.

"I think it is important to continue to pay attention to the need for diversity," Zerhouni said. "There is no greater need for diversity than in health and health research. We are providing research to a diverse population and we need a workforce that reflects that diversity. We are not there yet. There is a lot more to do, but I think the intent and the momentum are there."

Other issues addressed at the meeting include the NIH budget: Zerhouni reported that at the time, NIH continued to operate under a fourth Continuing Resolution, using fiscal year 2003 funding levels. Congress was expected to complete the 2004 budget process before the end of January, he said.

In NIH deputy director Dr. Raynard Kington's report, he gave updates on several administrative fronts, including the NIH steering committee, which employs a 9-member panel of institute and center directors to streamline agency decisionmaking; the administrative reorganization advisory committee (ARAC), whose summer 2003 report was accepted by HHS Secretary Thompson as a blueprint for NIH; and the reactivation of 5-year reviews for IC directors. The review process has been expanded to include Office of the Director components such as the Office of AIDS Research and the Office of Disease Prevention.

Commenting on the strong potential for flat NIH budgets over the next few years, Zerhouni concluded that "scientific opportunity has never been better" and that NIH will be looking to capitalize on "synergy, efficiency and prioritization." ■

Stopping Your HRT? Worried About Mood?

The Behavioral Endocrinology Branch, NIMH, is investigating whether mood, anxiety and irritability accompany hormone replacement therapy (HRT) withdrawal. Participants should be ages 45-60, with a past history of perimenopausal mood symptoms responsive to estrogen therapy (ET) or HRT, who are currently on ET or HRT and in good physical health. For information call Linda Simpson-St. Clair, (301) 496-9576.

Former NINDS Director Masland Dies

By Shannon E. Garnett

Dr. Richard L. Masland, 93, former NINDS director, died Dec. 19 of pneumonia.

Widely recognized as an expert on mental retardation, Masland served as the second director of the institute (then named the National Institute of Neurological Diseases and Blindness—NINDB) from 1959 to 1968. Among outstanding contributions during his administration was the development of the National Collaborative Perinatal Project—a very large prospective study that followed more than 50,000 women from their pregnancies until the children reached 8 years old. The study was designed to find and clarify the causes of cerebral palsy, mental retardation and other neurological disorders.



Dr. Richard L. Masland

Masland's interest in this subject began before coming to NIH and included a nationwide survey he conducted from 1955 to 1957 of research facilities and potential in the field of mental retardation. The results of the study were published in 1958 in the book *Mental Subnormality*.

As NINDB director, Masland recruited many noted researchers to develop and expand the institute's research programs, including Dr. Carleton Gajdusek and Dr. Clarence Gibbs—who together created a research program on human prion disease. Their work later led to Gajdusek's winning a Nobel prize for research on kuru (a rare, devastating neurological disorder). Masland also started an epidemiological division, headed by Dr. Leonard Kurland. In 1961, Masland established a series of clinical research centers—bringing together teams of investigators working on related research—as well as important programs in head injury led by Dr. William F. Caveness, and in epilepsy led by Dr. J. Kiffin Penry.

Under Masland's directorship, neurological and sensory research and training programs expanded rapidly, and the institute's budget grew from \$40 million in 1959 to \$129 million in 1967.

"During his tenure, Dr. Masland developed and strengthened NINDS's programs in clinical research, epidemiology, infectious diseases and perinatal research—establishing himself as a legendary scientist and visionary, and positioning the institute as the nation's cornerstone for brain research," said NINDS director Dr. Story Landis. "Many of the programs he started are still critical to our mission today."

Born in Philadelphia, Masland earned his under-

graduate degree from Haverford College in 1931, and his medical degree from the University of Pennsylvania School of Medicine in 1935.

After a 2-year internship at the Pennsylvania Hospital, his neurological career began and continued a steady climb to distinction as a clinician, teacher, author and researcher in neurology and clinical neurophysiology. At the University of Pennsylvania, he was appointed fellow in neurology in 1938, and associate in neurology in 1940. While at the Pennsylvania Hospital, he was assistant neurologist from 1939 to 1946. In addition, Masland was a veteran of the U.S. Army—serving from 1942 to 1945, including 2 years as director of the department of physiology at the School of Aviation Medicine. In 1946, he was appointed fellow in psychiatry at the Pennsylvania Institute for Mental Hygiene.

Before coming to NINDB, Masland was professor of neurology and psychiatry at Bowman Gray School of Medicine at Wake Forest College in Winston-Salem, N.C. He took a leave of absence from Bowman Gray in 1955 to become research director of the National Association for Retarded Children. In 1957, he was named assistant director of NINDS. He became director in 1959.

Masland left NINDS in 1968 to join the staff of Columbia University as professor of neurology and chairman of the department of neurology at the University's College of Physicians and Surgeons. He also served as director of the Neurological Service at Presbyterian Hospital's Neurological Institute in New York City. He later became president of the World Federation of Neurology—serving from 1981 to 1989.

During his career, Masland held offices in numerous professional organizations and served on many committees and advisory groups. He was widely published in such research areas as convulsive disorders, the effect of anoxia on the central nervous system, voluntary muscle disorders and drug therapy for neuromuscular disease.

Throughout his lifetime, Masland received countless awards and accolades including the 1963 Award of Merit from the National Association for Retarded Children for his research on the causes of mental retardation. The award—which cited Masland as a "scientist, humanitarian and pioneer for his achievements in alleviating mental retardation"—was presented by President John F. Kennedy.

Masland is survived by his wife, Mary Wootton Masland of Englewood, N.J., a speech and language pathologist; two sons, Prof. Richard Masland of Weston, Mass., and Tom Masland of Cape Town, South Africa; two daughters, Frances Masland, of Newton, Mass., and Sarah Bender of Colorado Springs; and seven grandchildren. ■

NIH Chamber Singers Auditions

The NIH Chamber Singers welcome men and women in all voice ranges to round out its merry band of troubadours. In February, the group will begin rehearsing for its Spring concert. If you are interested in joining the Singers, contact Susan Hauser at hauser@nlm.nih.gov for details.

New Ways To Enter the Campus Debut

The fence surrounding the NIH campus is nearing completion. Once finished, it will include eight vehicle/pedestrian access gates and nine stand-alone pedestrian access gates.

All of the vehicle access gates will have a security guard presence, and pedestrian access will be available during business hours. The other nine pedestrian access gates stand alone, that is, they do not require a security guard. "Once the fence is completed and the gates are in operation, we can rely more on electronic access security systems rather than having a guard present at each post," said Arturo Giron, associate director, security and emergency response.



This pedestrian portal near the Children's Inn shows the double-gating that will require two waves of an employee's ID card.

"The pedestrian access gates, or portals, will be equipped with an electronic security system allowing all NIH employees entry just by waving their NIH ID badge in front of a card reader," Giron said.

For added security, the pedestrian-only portals were designed such that once employees wave their ID in front of the reader, they open the gate to an entryway where they wave their ID card in front of another reader and then enter campus. "This additional security measure will prevent any 'piggy-backing' and help ensure only those who are authorized gain entry," said David Chung of the Division of Physical Security Management.

The electronic systems for the pedestrian entrances will be fully operational by March 2004. Until then, employees will be able to open the gate manually to enter and exit the campus.

For more information on the perimeter fence and its access gates, contact Chung at (301) 496-6893.

Wednesday Afternoon Lectures

The Wednesday Afternoon Lecture series—held on its namesake day at 3 p.m. in Masur Auditorium, Bldg. 10—features the NIH Director's Lecture given by Dr. Catherine M. Verfaillie on Feb. 11; her topic is "Greater Potency of Adult Stem Cells." See story on p. 1.

On Feb. 18, Dr. Barry J. Everitt will lecture on "Neural and Psychological Basis of Compulsive Drug Seeking: Implications for Treatment." He is professor, department of experimental psychology and MRC Center for Behavioral and Clinical Neuroscience, University of Cambridge, UK.

For more information or for reasonable accommodation, call Hilda Madine, (301) 594-5595. ■

Pedestrian-Only Entrances

On Cedar Lane:
West Drive
Garden Drive

On Old Georgetown Road:
South Drive
Northeast corner between Center Drive and Cedar Lane
Lincoln Drive (Just south of)

South End of Campus:
Near Bldg. 14 Trailers
Between 41 lots and MLP-7

Rockville Pike:
Two entrances, one on each side of the planned Visitor's Center near the South Drive entrance (Metro)

Vehicle and Pedestrian Entrances

On Old Georgetown Road:
South Drive
Lincoln Drive (vehicle exit only)
Center Drive

On Cedar Lane:
West Drive
(Patient/Patient Visitor vehicles only.
Open to employees for pedestrian access.)

On Rockville Pike:
North Drive
Wilson Drive
South Drive
Center Drive

NIH Sailing Association Open House

The NIH Sailing Association invites everyone to its open house on Thursday, Mar. 4 from 5 to 8 p.m. at the FAES House on the corner of Old Georgetown Road and Cedar Lane. Would you like to learn to sail? Does the idea of racing sailboats appeal to you? Can you imagine being part of a group filled with skilled sailing instructors, enthusiasts and boat owners? Membership includes instruction, sailboats for charter, racing, cruises, parties and fun. Admission is \$5 at the door and includes pizza and sodas; \$2 for beer or wine. For more information, visit www.recgov.org/sail. ■