

THE NIH RECORD

Still The Second Best Thing About Payday

Genes, Mother Nature and Youth

Kenyon To Give Mahoney Lecture On Aging, Sept. 25 in Masur

By Doug Dollemore

Mother Nature is smarter than some scientists suspect. Take aging, for instance. It doesn't "just happen," says Cynthia Kenyon, a professor of biochemistry and biophysics at the University of California, San Francisco.

"Biologists often underestimate nature. They are always surprised by the order and logic of cells," Kenyon says. "For example,



Dr. Cynthia Kenyon

everyone was surprised by the 'intelligent' way that information is encoded in DNA. Aging was the same way. Many people considered aging to be an inevitable, passive process caused by the gradual corrosion of cellular components over time. The

hourglass runs, and then it stops. For some years, I have felt that this view might be

SEE MAHONEY LECTURE, PAGE 2

CFC Kickoff Set, Oct. 3

NIH Combined Federal Campaign deputy coordinators and keyworkers are invited to attend the annual CFC kickoff at 11:45 a.m. on Tuesday, Oct. 3, on the patio behind Bldg. 31A. A highlight of the event will be "Tree House," a puppet show (for adults) about goal-setting by the Blue Sky Puppet Theater. NIAMS will host this year's CFC campaign. For more information about how you can contribute to the NIH CFC, contact your area keyworker.

HIGHLIGHTS

- 1** New Look for www.nih.gov
- 2** Patient Works Magic at CC
- 3** Chemist Improves Drug Synthesis
- 4** Film Festival Draws Some 25,000
- 5** Glimcher To Give Kinyoun Lecture
- 8** CIT Announces Fall Computer Classes
- 12** Youngsters Enjoy Redskins Park



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3-Year-Old Site Refreshed

NIH Home Page Updates Its Look

By Carla Garnett

Most people see 3-year-olds and think, "Cute toddler, just barely starting life." That is, unless the 3-year-old "toddler" is a web page. Then, most people might consider it a relic. Time moves a lot faster on the World Wide Web. That's one reason NIH recently revamped the look and organization of its home page.

"With the web, things tend to change rapidly," says Dennis Rodrigues of the NIH Office of Communications and Public Liaison, which manages the NIH web site. "By refreshing the look, you're letting people know that your site is evolving and healthy. You're encouraging users to explore. You want to avoid the impression that the site is old and stale."

Altered States

Last year, a team that included Richard Barnes, CIT web graphics designer, and Ginny Vinton, CIT home page server administrator; the NIH web coordinating committee, a group of IC and OD representatives that acts as an executive board for the

SEE HOME PAGE, PAGE 6

Cancer Survivor Makes Magic with Patients

By Jemarion Jones

If laughter is the best medicine, Jeff Desind is doing his part to make sure children in the pediatric ward of the Clinical Center get their proper dose.

Card tricks, disappearing sponge balls and mysterious length-changing rope have enabled the charismatic 54-year-old to bring smiles to the faces of children undergoing treatment for cancer and other conditions.



Jeffrey Desind (c) works his magic on Clinical Center patients Andrew Scott (r), 18, and Walter Winston, 16, during the pediatric ward's recent crab feast.

Desind knows first-hand the importance of smiling and keeping a

SEE MAGICIAN, PAGE 4



Dr. Angela Ng recently joined the Center for Scientific Review as scientific review administrator of the metabolic pathology study section in the oncological sciences integrated review group. This section is responsible for reviewing applications concerning effects of nutritional deficiencies/excesses on cellular pathology, immunological and molecular aspects of carcinogenesis, and chemoprevention. Ng received her Ph.D. in pathology from Northwestern University in 1990, then spent 4 more years there as a research associate conducting studies in molecular developmental biology and endocrinology. In 1994, she joined UroCor, Inc. in Oklahoma City, where she conducted basic and applied research on urological diseases and the development of diagnostic products for urological cancer.

MAHONEY LECTURE, CONTINUED FROM PAGE 1

too simplistic, and that the aging process might be subject to regulation.”

To prove it, she has generated a slew of fundamental research that, in the next few decades, may help scientists determine if human aging can be slowed down through genetic alteration. Kenyon will discuss this once-unimaginable possibility when she delivers the Florence Mahoney Lecture on Aging, “Genes From the Fountain of Youth,” at 3 p.m., Monday, Sept. 25, in Masur Auditorium, Bldg. 10. A reception will follow the lecture.

“Her studies have played a key role in initiating the modern molecular analysis of aging in model organisms,” said Dr. Richard Hodes, director of the National Institute on Aging. “She is clearly a pioneer in a rapidly growing, exciting and productive research field.”

Kenyon, who earned her Ph.D. at the Massachusetts Institute of Technology in 1981, began her research with a simple query: Why does a mouse live about 2 years and a bat about 50 years? Since these animals likely evolved from a common mammalian ancestor, she theorized that diversity in the lifespan of these and other animals arose from changes in genes that influence aging.

To test her hypothesis, she chose to study *Caenorhabditis elegans*, a tiny, self-replicating nematode or roundworm. *C. elegans* is useful for aging studies for several reasons: its genome has been deciphered; 70 percent of our genes have worm counterparts; and the worm has a relatively short lifespan (it achieves sexual maturity, produces about 300 progeny, ages and dies—all in less than 3 weeks). These factors allow Kenyon to alter a single gene and, in just a few months, observe its impact through several generations of the worm. What she has found is *C. elegans* are “little gold mines of gene discovery.

“By changing certain genes, we can keep our animals young much longer than normal,” Kenyon reported. “It’s as if they have discovered the fountain of youth.”

At least two genes, *daf-2* and *daf-16*, appear to regulate aging in *C. elegans*. *Daf-2* controls a special stage in the worm’s development called dauer formation. A dauer forms if, in the first few hours of its brief life, a prepubescent worm finds food scarce. In this state, *C. elegans* grows a cuticle for protection and can go into hibernation for several months. When the food supply is ample again, the worm emerges from its dauer state and continues its normal lifecycle. *Daf-2* is a gene that essentially drives the worm’s development past or out of the dauer state. But Kenyon and her colleagues have found that *daf-2* does much more. It also can regulate the lifespan of normal, fertile adults. By altering this gene so that its activity is reduced, Kenyon’s team found lifespan of well-fed worms,

who did not enter a dauer state, could be doubled.

“So we now know the worm has its own kind of death gene,” Kenyon says. “In *C. elegans*, this gene, *daf-2*, speeds up the aging process. When its activity is inhibited, the worms live much longer and remain active and youthful for much longer than normal.”

The *daf-2* gene is similar to a gene in humans that functions in hormone control, she adds. In the worm, this gene makes a protein that looks much like the receptors for hormones such as insulin and IGF-1. In humans, these hormones control food utilization pathways, metabolism and cell growth.

Kenyon has recently found evidence that aging in the worms also may be regulated by hormonal changes in the reproductive and sensory organs. These discoveries may place aging in a similar category as hormonally triggered events such as puberty and menopause.

“This raises the question of whether there might be a simple hormonal treatment to retard aging in humans substantially,” Kenyon said. “It is difficult for me to imagine that such an elaborate system evolved for nematodes alone. To me, it seems likely that a similar system regulates the life spans of higher organisms, possibly including humans. If so, someday we may be able to use this information to improve the quality of life of old age in humans. This would be a wonderful accomplishment. It is my goal.”

Earlier this year, Kenyon was a recipient of the King Faisal International Prize for her studies of the aging process. She is a member of the American Academy of Arts and Sciences, and is an Ellison Foundation scholar. ■

N I H R E C O R D

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Chemist Improves Synthesis of Scarce Drugs

By Michael Vatalaro

A Nobel Prize-winning chemist has devised a simpler and more effective method of synthesis for two experimental anticancer drugs, each 100 times more powerful than Taxol. The new process could allow the previously scarce compounds to become widely available treatment options if they are proven effective in clinical trials and approved by the Food and Drug Administration.

Dr. Elias J. Corey, a professor of chemistry at Harvard University and winner of the 1990 Nobel Prize in chemistry, and Eduardo J. Martinez, a predoctoral student in Corey's lab, improved the original synthesis of ecteinascidin, a potent antitumor agent discovered in 1988. Until recently, the compound was not widely available; it had to be purified from its natural source, where it exists in tiny quantities.

Now, with the new, highly efficient method of synthesis, it is possible to produce ecteinascidin and a related drug, phthalascidin, commercially. "The number of lives [the drugs] will save will not be limited by supply," said Corey. The new method was reported in the April issue of *Organic Letters*, a publication of the American Chemical Society.

Ecteinascidin has shown the ability to shrink drug-resistant soft tissue sarcomas—tumors of the muscles, tendons and supportive tissues. Approximately 10,000 Americans each year develop soft tissue sarcomas, which typically are treated with surgery and radiation. Chemotherapy is not a first-line treatment in many forms of the cancer. As many as 40 percent of sarcoma patients who do receive chemotherapy experience a short remission followed by the return of the tumor—now impervious to chemotherapy. Clinicians are concentrating their testing of ecteinascidin on these drug-resistant tumors.

Preliminary results from phase 2 clinical trials indicated that tumors stopped growing or shrank in 47 percent of patients (14 of 30) given ecteinascidin. The results were announced in May at the American Society of Clinical Oncology meeting in New Orleans.

Both ecteinascidin and phthalascidin show remarkable antitumor activities, killing living tumor cell lines in the lab with an efficiency roughly two orders of magnitude greater than that of Taxol, a leading anticancer drug. Isolated from a marine organism collected in the Caribbean by Dr. Ken Rinehart, a professor of chemistry at the University of Illinois, Urbana-Champaign, ecteinascidin soon was found to show dramatic levels of anticancer activity, even at minuscule doses. Until 1996, the only source of the drug was a small reef-dwelling tunicate called *Ecteinascidia turbinata* found in the West Indies (see photo). Researchers had to harvest over 1 ton of these sea squirts to produce 1 gram of ecteinascidin.

In 1996, Corey and his collaborator Dr. David Gin, now at the University of Illinois, published the first successful chemical synthesis of the molecule. This synthesis offered hope that the production of ecteinascidin could be done independent of the natural source. Both Corey and Rinehart are long-time grantees of NIGMS, having received a combined 63 years of support.

PharmaMar, a Spanish pharmaceutical company, bought the rights to the compound and began harvesting the tunicate to produce it. Currently, PharmaMar grows *Ecteinascidia* in an aquaculture facility in Spain, a more practical and environmentally sound practice than harvesting the creature from the wild. The new synthesis, which has fewer steps and is more efficient overall, may make raising *Ecteinascidia* in tanks unnecessary, as it potentially enables the production of the drug in lots measured in kilograms instead of grams. Since each patient treated receives just 4.5 milligrams of ecteinascidin over a 3-week period, Corey estimates that 5 kilograms of the drug could supply the world's research and clinical needs for the next few years.

Recent research indicates that ecteinascidin may even be able to prevent tumors from becoming drug-resistant in the first place. According to a study conducted by Dr. Kathleen Scotto at Memorial Sloan-Kettering Cancer Center in New York City, ecteinascidin prevents the formation of P-glycoprotein, a protein associated with multidrug-resistant tumors. P-glycoprotein is a membrane protein that transports toxins such as chemotherapy agents out of cancer cells, preventing the chemotherapy drugs from destroying the tumor. Previous studies by Scotto's lab have indicated that when some tumors are exposed to chemotherapy agents, they quickly boost the activity of the MDR1 gene, which is responsible for the formation of P-glycoprotein. By interfering with that process, ecteinascidin may keep the tumor cells vulnerable to chemotherapy. Even if ecteinascidin is not proven effective on its own, it may become a key ingredient in chemotherapy "cocktails" to prevent tumors from developing resistance to drugs currently in use. The work was published in the *Proceedings of the National Academy of Sciences* in June and supported in part by the National Cancer Institute.

Phthalascidin, which is a derivative of the natural compound, was developed in Corey's lab. It is not being tested in humans at this time although its simpler structure and synthesis give it even greater potential as a drug. "This type of research is driven by the great power of modern chemistry. I hope that ecteinascidin and phthalascidin will be useful as life-saving drugs, but it will be another 5 years before we know for certain," said Corey. ■



A cluster of *Ecteinascidia turbinata*, the tunicate from which the drug ecteinascidin is purified. Photo courtesy of PharmaMar.

Stress Hormones, Depression Studies

The Clinical Neuroendocrinology Branch, NIMH, is seeking people with current or past depression to participate in an evaluation study at the Clinical Center. Participants should be 18 to 65 years old; medically healthy; nonsmokers within the past year; and able to participate in studies involving at least one night's stay at the Clinical Center. Eligible volunteers will receive a physical evaluation, metabolic studies and participate in studies for possible heart disease and osteoporosis in depression. They will also be paid. For more information, call 496-5831 or 496-1892 voice mail #1 for Dr. June Cai.

MAGICIAN, CONTINUED FROM PAGE 1

positive attitude during treatment. In 1994, he was diagnosed with hairy cell leukemia, an uncommon cancer of B lymphocytes in which the cancer cells appear to have hairlike projections when examined under a microscope.

Hairy cell leukemia makes up 2 percent of all leukemias. Although for most patients the disease is controlled with standard chemotherapy, up to 25 percent of patients with the disease become resistant to traditional treatment.

After chemotherapy and other traditional treatments failed, Desind was unsure of his next step. "When other treatments don't work, you ask, 'What do I do next?'" he said.

The next step turned out to be enrolling in an immunotoxin protocol at NIH. In June, Desind began taking an experimental immunotoxin called BL22. After three rounds of treatment, the leukemia now appears to be in remission.

"I don't want to jinx it, but my white blood cell and platelet counts are up," he said.

The use of immunotoxins, small antibodies linked to a toxin, is part of a promising experimental strategy to treat cancer by directly targeting and delivering deadly poisons to tumor cells. Because the antibody specifically binds to the cancer cells, normal cells are spared and there are fewer side effects such as bone marrow damage.

"The remarkable response of Jeffrey and several others like him proves that immunotoxin therapy can benefit some cancer patients for which there is no other type of treatment," said Dr. Robert J. Kreitman, chief of the clinical immunotherapy section and principal investigator for the BL22 protocol. "The next step is to make and test immunotoxins targeting other types of cancer."

Even though Desind is grateful that the immunotoxin therapy has so far succeeded where other treatments have failed, he does not give all the credit to modern medicine.

"The key is attitude," he said. "I was never worried... I'd rather be positive than negative. I wasn't going to let [leukemia] affect the way I lived my life."

For now, living his life involves making children smile as much as possible. When he is not working at a New York City investment firm, Desind, the amateur magician, takes his act to various pediatric patient events in the Clinical Center.

"He just brings instant smiles to the kids' faces," said Kristin Johnson, a recreational therapist in the Clinical Center's rehabilitation medicine group. "Magic can bring amazement and smiles when kids have had a hard day or they're not feeling well."

"Magic spans all ages," said Karen Bergeron, a research nurse who assists Kreitman and works with Desind. "His enthusiasm is passed on to the audience and it gets recycled back to him. He gets

energized working with the kids."

At times, Desind's dedication to entertaining children has taken precedence over his own health. During a bout with pneumonia and tuberculosis, he still managed to perform for some of the pediatric ward patients.

"I like bringing a smile to a kid's face," he said. "I enjoy making people happy. There's nothing better."

He has become so popular that he's now getting magic show requests from individual patients. For now, Desind will take those requests and continue to make magic wherever he is needed. ■



More than 25,000 people attended the fourth NIH Outdoor Film Festival, held Aug. 18-27, according to R&W, which sponsored the event. R&W thanks all who helped make the festival a success. In the photo above, hundreds gather before dusk to get good seats in front of the large screen erected near the Medical Center Metro station. Below, a family celebrates a birthday on the lawn before the movie starts.



Renewal of Carpool Permits

NIH carpool parking permits expire on the last day of October 2000. To get a new one, each member of the pool must appear together at the NIH Parking Office in Bldg. 31, Rm. B3B04. Hours are 7:30 a.m. to 4 p.m., Monday through Friday. Carpool permits can also be obtained Oct. 11 at EPN, Conf. Rm. C, from 1 to 2:30 p.m., and Oct. 18 at Rockledge II, Conf. Rm. 9104, from 1 to 2:30 p.m. ■

Glimcher To Give Kinyoun Lecture, Oct. 6

On Friday, Oct. 6, Dr. Laurie H. Glimcher will speak on the topic "T Helper Cells: Genes and Development." She is the Irene Heinz Given professor of immunology, Harvard School of Public Health, and professor of medicine at Harvard Medical School. Her presentation, part of NIAID's Kinyoun Lecture series, will be at 3:30 p.m. in Lipsett Amphitheater, Bldg. 10.



Dr. Laurie Glimcher

The major focus of Glimcher's laboratory is the study of T-helper-cell differentiation. There is now abundant evidence to show

that the ratio of Th1 to Th2 cells is highly relevant to clinical diseases, including autoimmune, infectious and allergic diseases. Therefore, the ability to alter the ratios of Th1 and Th2 subsets provides exciting therapeutic possibilities.

Her laboratory has concentrated its efforts on ways in which this manipulation can be achieved. The researchers demonstrated that co-stimulatory molecules can differentially drive T-helper-cell development. Another approach to altering Th subset ratios, they found, is to increase or block the synthesis of or effects of selected cytokines.

Glimcher's laboratory studies both the function of *'Ability You Can Count On'*

October Is Disability Employment Awareness Month

The theme for this year's National Disability Employment Awareness Month (October) is "Ability You Can Count On." The skills and talents of 7.8 million working-age people with disabilities are ready to be tapped by NIH employers. Persons with disabilities can get jobs done in a cost-effective, high-quality manner. They represent ability you can count on.

Listed below are two activities planned for this October. These events highlight the abilities and skills of Americans with disabilities.

The kickoff will start Wednesday, Oct. 4. There will be a fast and furious game of basketball played by 10 persons in wheelchairs. The NIH Police are challenging the Baltimore Ravens Wheelchair Basketball Team. Tip-off time is high noon on the Bldg. 1 parking lot. Dr. Ruth Kirschstein, acting NIH director, will throw the first jump ball. For those who can't make the noon game, another match is scheduled for later that evening in the Bldg. 10 gymnasium, on the 14th floor. It promises to be a fun day for all.

interleukin-4 (IL-4) and the mechanisms that underlie tissue-specific cytokine gene transcription. Her laboratory has recently defined the genetic basis of IL-4 expression in T cells. Her group identified the proto-oncogene *c-maf* as the transcription factor responsible for Th2-specific IL-4 expression and subsequently isolated a second novel nuclear protein, NIP45, which together with *c-maf* and NF-AT allows reconstitution of IL-4 transcription in non-T cells.

Her laboratory has also produced and characterized mice deficient in cytokine-specific transcription factors. Such mice have provided insight into the differential control of cytokine gene expression and have provided powerful models of allergic and autoimmune disease. Her laboratory has isolated a novel transcription factor, T-bet, that singlehandedly controls the transcription of the interferon-g gene. Even more significant, T-bet appears to be the master switch for Th1 lineage commitment.

Glimcher earned her B.A. degree from Radcliffe College in 1972 and her M.D. from Harvard Medical School in 1976. Among the numerous honors and awards she has received are the Distinguished Young Investigator Award from the American College of Rheumatology, the Arthritis Foundation's Lee S. Howley Award and the FASEB Excellence in Science Award.

All attendees are invited to join Glimcher at a reception to be held in the Lipsett lobby after her talk.—Karen Leighty ■

On Tuesday Oct. 24 in the Visitor Information Center, Bldg. 10, a variety of national and local vendors will display disability-related resources and services from 11 a.m. to 2:30 p.m. The Disability Awareness Fair's objective is to highlight the benefits of tapping into the labor pool of persons with disabilities and provide practical information and resources about assistive technologies to the NIH community.

If you are an individual with a disability who needs any assistance or special accommodation, call Carlton Coleman, 496-2906. ■

Postmenopausal Women Sought

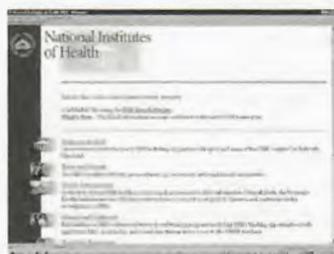
Postmenopausal women not currently taking hormone replacement therapy are needed to participate in a study. Participants will be required to give a small blood sample (about 2 tablespoons) in an initial screening. Total visit time required is about 30-45 minutes. The study, which takes place at the Clinical Center, does not require you to take any new medications or stop any current ones—it involves only a blood sample and there is no age cut-off. Compensation (\$50) is provided for each blood draw. For more information, call 496-5150. ■

HOME PAGE, CONTINUED FROM PAGE 1

home page; as well as staff at Rodrigues' branch, began considering ideas to renovate the site.

As with any redecorating project, everything from color choices to photos and other artwork were picked at and analyzed. But, Rodrigues admits, a lot more went into the update than simply rearranging words and pictures on a page. A pilot project to evaluate the site's effectiveness was also undertaken. That project produced about a dozen videotapes of people actually accessing NIH's home page, navigating the site and searching for information they wanted. Using the results of the pilot, the redesign team considered a number of changes—both cosmetic and substantive.

Take white space, for example, says Rodrigues. The team found that, unlike a paper product, web pages can get away with filling in a lot more space.



The August 1997 version

“Over the last several years, we've learned a lot about effective design techniques for the web,” he points out. “There's a difference between how much white space is appropriate in hard copy and how much is appropriate on screen. Studies suggest people don't need as much empty space on screen. They tend to like a lot more choices on web pages.”

Barnes came up with several drafts, which were pored over and tweaked. The final pick went through several rounds of revision before it was adopted.

“After we chose the design,” Rodrigues recalls, “we went about reorganizing the content. Our existing information didn't always fit easily into the new design templates; the team had to do quite a bit of creative restructuring so that everything made sense.”

The new NIH page features a white background with main headings in blue type and borrows a few elements from its predecessor, including some of the graphics and accent colors. It also features several ways the user can access the major sections of the site: simple file folder-like tabs along the top, a list

with brief details about each section down the left center of the screen, and bracketed links along the bottom. Several frequently requested items—Q&As, employment information and visitor information—are set off in a different color and different typeface, and are now easier to find, grouped along the right side of the page.

Other navigation tools added to the site can be found on secondary pages, which prominently feature “On this page” or “Quick links” (short contents lists) along the left side. Users no longer have to scan the entire page for its highlights.

More Than a Pretty Face

Many of the site's pages were re-examined for accessibility issues as well, Rodrigues continues. A lot of work was done to make the site accessible to users with disabilities.

Overall, the text on the new site is presented in clean and easier-to-read type. Use of photos has been minimized, and all graphics have what are called “alt tags,” which appear as the user's cursor passes over the pictures and contain short explanations of the graphics for people who cannot see.

Accounting for the wide variety of computers and software available in the online community, the new design was tested on different size monitors, using several different web browsers.

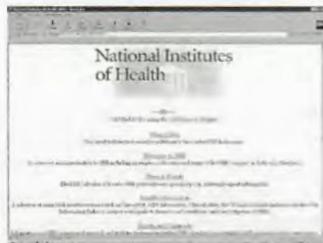
Next Update Not Far Away

Because the web site could not be closed while renovations were made, the technical team built the new site as a mirror image on a test machine; the new page would have to replace the old in mere moments to minimize downtime. On a low-usage Sunday afternoon, Aug. 20, the moment of truth arrived. The switch was made—not without a few technical snafus that kept the team working deep into the 9 p.m. hour.

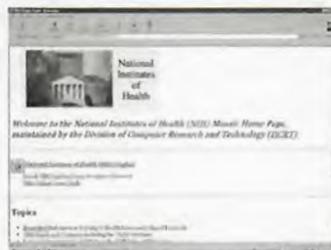
“You have this maze of interconnected elements,” Rodrigues explains, “and you're moving the elements around. The potential for things to become disconnected is very high. We had a few problems with some of the links, but given the amount of material we were moving, the swap went fairly smoothly.”

So far, most of the feedback on the new site has been positive, he reports.

“It was a great example of teamwork—Richard created an elegant design, we reorganized and transferred the content, and Ginny's group handled switching the files to the production server.” The team that worked on the redesign is not done yet, though.



The December 1996 version



The December 1993 version



Above is the latest iteration of the NIH home page on the World Wide Web. The address is a simple www.nih.gov. Several independent auditors have found recently that the NIH home page is popular with the public. According to PC Data Online's Top 10 Hit List, the NIH site ranks ninth (as of Aug. 26) in hits in the category of Health and Family; NIH was also the only federal site ranked in any category.

Rodrigues acknowledges that the web is constantly introducing new concepts and new elements to consider. For example, technology for palm pilots—handheld computers and electronic organizers—seems to be gaining momentum, he says. Will the NIH site work well with that technology, or might there be a better way to design for this much smaller format?

“You have to keep up with new trends and design techniques,” concludes Rodrigues. “The evaluation data we used was by no means exhaustive. The plan now is to conduct studies on the revised site, identify any problems and find ways to adjust the site to solve them. These new studies will provide us with even better data for the next update. With the web, you really can’t ever rest on your laurels.” ■

Hispanic Heritage Month Observance

NIH’s observance of Hispanic Heritage Month continues in October with a morning symposium titled, “¡Salud! To Your Health—Bridging the Gap in Health Disparities,” on Wednesday, Oct. 4 in Bldg. 10’s Lipsett Amphitheater and Visitor Information Center.

The talks begin at 9 a.m., with welcoming remarks. At 9:20, Dr. Carlos Camargo, assistant professor of medicine, Harvard Medical School, will discuss “Body Mass Index and Risk of Developing Asthma.” He will be followed at 10:30 by Dr. Amelie G. Ramirez, deputy director, Chronic Disease Prevention & Control Research Center, Baylor College of Medicine, whose topic is “Hispanics and Cancer: Charting a Course for the Future.” A reception follows the talks at 11:30 a.m. in the VIC. For more information contact Raymond Mejia, 496-9972. ■

Hrynkow Named FIC Deputy Director

Dr. Sharon Hemond Hrynkow has been named deputy director of the Fogarty International Center. She will take a leadership role in guiding FIC’s



Dr. Sharon Hrynkow

efforts to reduce the global burden of disease through research and research training.

Dr. Gerald T. Keusch, FIC director, said, “Dr. Hrynkow’s strong scientific and diplomatic expertise, coupled with her experience as a scientist working abroad, will be invaluable to the center as we work to address global health issues in partnership with a range of international colleagues.”

Hrynkow joined FIC in 1995. Most recently, as

acting associate director for program coordination, she helped implement new FIC programs and initiatives on topics such as bioethics, ecology and infectious diseases, and health and economics. Previously, as FIC’s assistant director for international relations and director of the Division of International Relations, Hrynkow advanced regional initiatives on behalf of FIC and NIH and served as FIC’s chief advisor on foreign policy matters.

As a science policy analyst, she was one of the lead organizers of an international conference on malaria in Dakar, Senegal, in 1997. This conference launched the Multilateral Initiative on Malaria (MIM), a collaboration of NIH partners, African and European scientists and the World Health Organization to support malaria research while building research capacity in malaria-endemic countries. FIC assumed the rotating role of MIM secretariat from the Wellcome Trust in May 1999. Prior to joining FIC, Hrynkow served as a science officer at the State Department, where she played a key role in mobilizing foreign policy efforts to address the HIV/AIDS pandemic.

She graduated from Rhode Island College and earned her doctoral degree in developmental neurobiology at the University of Connecticut. She received a Letten Saugstad fellowship to conduct postdoctoral studies at the University of Oslo and was named a science, engineering and diplomacy fellow of the American Association for the Advancement of Science. Hrynkow was elected to the Council on Foreign Relations in 1996. Her interests include the advancement of science education for women in developing countries and the prevention of congenital brain deformities worldwide. ■

Female Paid Volunteers Needed

Are you female, 18 to 35 years old, in good health and not on birth control pills? You may be eligible to participate in a study of commonly prescribed medications. The study involves multiple visits to the Uniformed Services University (next to the Naval Medical Center, across the pike from NIH) over a 3-month period. Earn up to \$880 and get a free medical exam. Call (301) 319-8204 for more information and a preliminary telephone screening.



The NIH Police’s recent observance of “Police Week” included a fundraising barbecue to benefit the Friends of the Clinical Center. More than 1,500 people attended the gathering, which was held in front of Bldg. 1. On hand for the presentation of the donation were (from l) Kip Fenton, FOCC administrative assistant; O.W. “Jim” Sweat, director of the Division of Public Safety; NIH Police Capt. Lawrence Brown, Deputy Chief Robert Fuller, and Police Chief Alvin Hinton; and Maria Stagnitto, FOCC president.

CIT Computer Training Classes for Fall 2000

Registration is now open for the fall term of computer classes, which will begin at the end of September.

With 16 different statistical offerings, this term presents a record-breaking set of options for everyone who uses statistics at NIH. Those just getting started or who need a refresher can take *Introduction to Statistics*, a 2-day class that offers an overview of the topic. For instruction in popular statistical software, the *SAS Programming Fundamentals I and II* series or the *Introduction to S-PLUS* and *Programming in S-PLUS* sequence offer an in-depth introduction to each type of software. Those who are further along in their use of SAS have many options with advanced classes taught by CIT staff and by the SAS Institute. As a new offering, SAS Institute will teach a number of classes including *Using SAS/STAT Procedures to Perform ANOVA and Regression*, *Categorical Data Analysis Using Logistic Regression in SAS Software*, and *Introduction to Statistics Using SAS/INSIGHT Software*. Finally, in addition to his popular course, *Avoiding Pitfalls in Statistical Analysis*, Dr. James Malley will be offering a second course. The new course will deal with advanced statistical questions and is intended for anyone who took the first course and wishes to pursue further topics.

Another highlight of the fall program is Helix and Unix training. You can begin with *Introduction to the Helix Systems*, which gives an overview of CIT's offerings in that system, and then continue to more general Unix courses. The *Fundamentals of Unix* course acts as a platform-free introduction to Unix for those without previous experience, and then *Basic Security for Unix Workstations* offers information about keeping the workstation secure. For beginning Unix administrators, *Unix Systems Administration Concepts* offers an introduction. Dr. Lewis Lipkin will teach a new four-session hands-on class, *Using Linux*. Finally, those with programming experience in other languages who would like to program in C can begin with Dr. Richard Troxel's newly expanded C language course.

These are just a few of the many classes planned for this fall, so check the web site <http://training.cit.nih.gov> to get complete information on the fall offerings, and to fill out an application (the paper catalog is no longer produced). As always, there is no tuition for attending CIT courses and seminars. Courses are open to NIH employees and to other users of CIT computing facilities where the coursework pertains to use of the facilities. Students should obtain their supervisor's approval before submitting applications. You may also register by calling 594-6248. ■



Michael Beauchamp (l) of NIMH's Laboratory of Brain and Cognition pitches a frisbee into a goal on a field near parking lot 41B. Games of Ultimate Frisbee are played on

this field Tuesday and Thursday evenings, from about 5:30 to 7. Anyone who shows up is welcome to play.

Below, Beauchamp (r) contests Pierre Ledoux of NLM's National Center for Biotechnology Information for possession of a tossed frisbee.



PHOTOS: DAMON TIGHE

Chamber Music Concert, Oct. 1

On Sunday, Oct. 1, the Rock Creek Chamber Players will begin their eighth consecutive season of monthly concerts in the Clinical Center's 14th floor assembly hall. The free public concert, sponsored by the recreation therapy section, will begin at 3 p.m. It will include Devienne's Quartet, Op. 73 No. 1, for bassoon and strings; solo piano works by Rachmaninoff and Prokofieff; and Schumann's Piano Trio No. 1 in D minor. For reservations and information call (202) 337-8710. ■

Wednesday Afternoon Lectures

The Wednesday Afternoon Lecture series—held on its namesake day at 3 p.m. in Masur Auditorium, Bldg. 10—features Dr. John Carlson on Sept. 27, discussing, "Olfaction in *Drosophila*: Genetics and eGenetics." He is professor of molecular, cellular and developmental biology, Yale University. For more information or for reasonable accommodation, call Hilda Madine, 594-5595.

'Medicine for the Public' Lecture Schedule

The Medicine for the Public lecture series, sponsored by the Clinical Center, is now in its 24th year. The talks, which are free and open to the public, are held at 7 p.m. on Tuesdays, Sept. 19 through Oct. 24 in the Clinical Center's Masur Auditorium.

Sept. 19—New Directions for Organ and Tissue Transplantation. Dr. Allan D. Kirk, chief of the transplantation section, NIDDK, will explain how diabetes, renal failure and other end-stage organ diseases can be treated more successfully by immunologic strategies that make the body believe that the transplanted tissues are its own.

Sept. 26—Adolescents and AIDS: Millennium Milestones. Great progress has been made in the last two decades in the fight against HIV/AIDS, yet there's still far to go. Dr. Lauren Wood, senior clinical investigator in the HIV& AIDS Malignancy Branch, NCI, will discuss some of the positive and negative milestones reached to date, including advances in care and research, as well as the changing epidemiology of the HIV epidemic.

Oct. 3—Dangerous Liaisons: Drugs and Herbal Products. Every day, as more Americans begin using herbal products, how many actually consider the risks? Drs. Stephen Piscitelli and Aaron Burstein of the Clinical Center's pharmacy department will describe the widespread use of complementary medicines in the United States, focusing on the benefits and dangers of herbal products.

Oct. 10—Stroke: Rapid Diagnosis, New Treatments. Stroke happens every 43 seconds, and is the third leading cause of death. Dr. Alison Baird, visiting scientist at the Stroke Branch, NINDS, will discuss advances in how physicians use new imaging technology to confirm strokes, and review new options to treat them.

Oct. 17—Women's Health Research for the 21st Century. The NIH Office of Research on Women's Health was established 10 years ago. Dr. Vivian Pinn, NIH associate director for research on women's health and director of ORWH, will discuss current status and future direction in this field.

Oct. 24—Prostate Cancer. Dr. Marston Linehan, chief of the Urologic Oncology Branch, NCI, and Dr. William Dahut, who heads the prostate cancer clinic in NCI's Medicine Branch, will outline risk factors for prostate cancer and how the disease develops.

For more information, call 496-2563 or visit <http://www.cc.nih.gov/ccc/mfp/series.html>. ■

Fair Addresses Quality of Work Life

What makes your life complicated? What would make it easier for you to balance the demands of work, home and your personal needs? On Thursday, Oct. 5, the NIH quality of work life committee is sponsoring a resource fair, "Real People, Real Choices: Quality of Work Life at NIH." The fair, held in Bldg. 10's Visitor Information Center (lower level exhibit area) from 10 a.m. to 3 p.m., will provide an opportunity to learn more about employee services. Twenty-six offices and organizations will be on hand showcasing programs that help enhance quality of life. At the fair, you will be able to find out more about NIH's family-friendly workplace policies; talk to on-campus child care centers about programs and availability; find out about programs that make the campus safe; get information about R&W's new concierge service; and more.

The fair's keynote speaker is Linda Breen Pierce, author of *Choosing Simplicity: Real People Finding Peace & Fulfillment in a Complex World*. Her talk is at noon in Lipsett Amphitheater, Bldg. 10.

For more information about the fair, call the Work and Family Life Center at 435-1619, or visit its web site at <http://wflc.od.nih.gov>. ■



There is a small afterthought of a courtyard near Lipsett Amphitheater in Bldg. 10 where only light and shadow are welcome; no doors offer passage. Inside are pyramids of mirrored glass, breaking images into shards as they trade reflections. It seems a good place from which to be barred.



Those bright red numbers on the sides of NIH buildings are good for more than simple identification. This numeral is also home to a bird's nest, although it was unattended at the time this photo was taken.



A squadron of motorcycles is parked under a shed behind Bldg. 13. Come winter, the same crowd probably won't be on hand.

PHOTOS: DAMON TIGHE

Help Plan Asian/Pacific Heritage Program

The first planning meeting for NIH's 29th annual Asian/Pacific Islander American Heritage Program is scheduled at 2:30 p.m on Tuesday, Sept. 26 in the Natcher Conference Center, Rm. D. All are welcome to this meeting and to participate in the planning of the program, which will take place in May 2001. For more information, contact Victor Fung by email vf6n@nih.gov or call Joanne Wong at 496-9147. ■

NIDDK's Taylor Offers Parting Comments on Diabetes

By Anna Maria Gillis

"Diabetes is much more complicated than I ever dreamt," reflects Dr. Simeon Taylor, as he leaves his post as chief of the Diabetes Branch at NIDDK to become Lilly research fellow at Lilly Research Laboratories in Indianapolis. Still, he believes the scientific advances of the past 30 years and current research directions provide hope.

"Undoubtedly, the most striking progress has been in understanding how insulin works," said Taylor. In 1979, when he began at NIH as a research associate, scientists knew that insulin bound to receptors on the outside surfaces of cells and helped glucose into cells, but they were "clueless," he says, about how it happened. They had a general model for how hormones functioned: straightforward pathways with few steps. The pathway for insulin action, however, has proved to be nonlinear and multi-stepped.

Over the years, Taylor and his colleagues have made major contributions to understanding the insulin action pathway and insulin resistance. The inability to use the hormone effectively is characteristic of type 2 diabetes. In particular, Taylor's group has determined how and why insulin fails to act

in patients with leprechaunism, Type A insulin resistance and other genetic forms of insulin resistance. They also have developed a mouse model for a form of insulin-resistant diabetes.

"Simeon was the lead person in the world studying genetic defects in the insulin receptor," said Dr. Phillip Gorden, director emeritus of NIDDK. "He attracted collaborators from all over the world, and they were able to relate specific receptor mutations to particular kinds of insulin resistance and to individual patients." These mutations reduced the number of receptors or inhibited the receptors' ability to mediate the effects of insulin on cells.

In 1992, Taylor received the American Diabetes Association's Outstanding Scientific Achievement Award for his discoveries. "He has done classic work," said Dr. Jesse Roth, professor of medicine at Johns Hopkins and former NIDDK scientific director. "Simeon's work has permanence. It will be work people look back on in 30 years."

"When I started in research, there was one camp that thought the whole problem in (type 2) diabetes was with insulin secretion and another that thought it was with insulin resistance," says Taylor. "Increasingly, the consensus is that the two are both important, and possibly not entirely independent of each other. In a given person, there may be one problem with the pancreatic beta cells that produce

insulin, and a second defect in the insulin action pathway causing insulin resistance."

Seeing the relationship between obesity and insulin resistance is another advance, said Taylor, adding that progress has been rapid since the 1995 discovery of leptin, a protein secreted by fat cells. Leptin will soon be given to NIH study volunteers with lipoatrophic diabetes. They have lost a significant portion of their fat cells and are extremely insulin resistant. Published studies of lipoatrophic mice have encouraged the hope that leptin will lead to improvements in the metabolic abnormalities in the lipoatrophic patients, noted Taylor.

Taylor believes significant study is critical in two areas. First, people with type 2 diabetes need more effective behavioral and pharmacological therapies to help them lose weight and, especially, maintain it. The second great challenge is to understand diabetes complications such as blindness, kidney failure and cardiovascular disease.

"There is so much more that is unknown than known," he said, about how high blood sugar causes the development of problems. When scientists get a better understanding of these pathways, it may be possible to develop drugs to prevent or postpone chronic complications, he observed. "Maybe we can someday save people from going blind or having amputations.

"My patients have taught me just how hard it is to have diabetes and how much suffering it causes," he added. "It's one of the reasons I'm interested in drug development."

Increasingly, pharmaceuticals are being developed that target specific proteins on disease pathways. Yet, "it's humbling that none of the oral diabetes drugs presently on the market have grown out of a prior understanding of mechanisms," says Taylor. "They grew out of discoveries that a compound was lowering blood sugars, and only later was it determined how the drugs worked. In the case of metformin, we still don't know how it works."

With his many scientific accomplishments, Taylor is still most proud of having trained researchers at NIH who have gone on to start their own labs. He encourages those he mentors to be persistent and to take a long-range view. "When you do things that no one else has ever done, most of the time they're bound not to work," he cautioned. In science, as in baseball, "if you're hitting 30 percent of the time, you're doing well."

Still, he maintains, "We're in a golden age of biomedical science. With the genome available—with its amazing amount of relevant information—our challenge is to understand it to help people." ■



NIDDK's Dr. Simeon Taylor has taken his expertise in diabetes research to a drug company.



HRDD Training Tips

The Human Resource Development Division, OHRM, offers the following courses. For more information about these and other HRDD offerings, visit the web site at <http://trainingcenter.od.nih.gov/> or call 496-6211.

Administrative Systems

Fellowship Payment System 9/21, 22

If you don't see your class: some HRDD classes are already full through September. The new FY classes will be available starting Oct. 1. Check out the web site in October to see the new catalog. For hard-to-get classes, apply early to ensure yourself a seat. ■

CIT Computer Classes

All courses are on the NIH campus and are given without charge. For more information call 594-6248 or consult the training program's home page at <http://training.cit.nih.gov>.

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|---|---------|
| Creating Presentations with PowerPoint 2000 | 9/21 |
| BRMUG - Macintosh Users Group | 9/26 |
| An Introduction to S-PLUS 2000 | 9/26-27 |
| Bitplane User Training | 10/2-3 |
| Data Warehouse <i>Query</i> : Human Resources | 10/3 |
| MATLAB 5 - Matrix Laboratory | 10/3-5 |
| Meet Your PC - What's Inside the Box | 10/4 |
| The NIH Contractor Performance System for New Users | 10/4 |
| Creating Presentations with PowerPoint 2000 | 10/4 |
| Data Warehouse <i>Query</i> : Travel | 10/5 |
| Introduction to JavaScript Programming | 10/6 |

Conference on Sjögren's Syndrome

NIDCR and the Sjögren's Syndrome Foundation will host a clinical conference titled, "Sjögren's Syndrome: Treating the Whole Patient," on Saturday, Sept. 23 from 8 a.m. to 5 p.m. in the Natcher Bldg.'s conference room E. This continuing education conference, which includes continental breakfast and box lunch, is designed to promote better understanding, evaluation and treatment of this systemic autoimmune disorder.

Sjögren's syndrome is one of the most prevalent autoimmune disorders, affecting mostly women and between 1 million and 4 million Americans. Patients are often underrecognized and misdiagnosed. The conference will address new therapies on the horizon for Sjögren's, and include talks by several authors on self-management of chronic illness. ■

'Come Back to Bethesda' on Oct. 7

The tenth annual Come Back to Bethesda Benefit Car Show will be held Saturday, Oct. 7 at Chevy Chase Cars in Bethesda from 11 a.m. to 4 p.m. Proceeds benefit the Children's Inn at NIH. Also that day are the Taste of Bethesda and the American Heart Walk. Spend the day and do all three! ■

Former CC Radiology Chief Doppman Mourned

Dr. John Leo Doppman, 72, chief of the Clinical Center diagnostic radiology department for 26 years, died of cancer on Aug. 21 at the Clinical Center. A diagnostic and interventional radiologist at the CC for 36 years, he retired in April.

Doppman developed, refined and performed numerous semi-surgical radiologic procedures. He was a pioneer in angiography, a technique that uses injections of radio-opaque dye to visualize blood vessels and tumors. He researched vascular malformations of the spinal cord and developed ways to visualize and treat them. His research culminated in the publication of the first text on this subject in 1969. Later, he concentrated on endocrinology research and developed techniques for locating ectopic or elusive glandular tumors. Many of these techniques are now standard practice in medical centers worldwide.



Dr. John Doppman

"John was a pillar of the NIH clinical research community," said Dr. John Gallin, Clinical Center director. "He was a respected clinician, prolific writer, dedicated teacher and generous friend. He will be missed."

Doppman received an M.D. from Yale and interned at Mercy Hospital, Springfield, Mass., served in the Navy from 1954 to 1957 and completed a residency in radiology at the Hospital of St. Raphael, New Haven, Conn. He was a Fulbright fellow in radiology research at the Postgraduate Medical School at Hammersmith Hospital, London, and the Karolinska Institute, Stockholm.

He joined the Clinical Center in 1964 as deputy chief of the diagnostic radiology department. From 1970 to 1972, he was a radiology professor at the University of California, San Diego. He returned to NIH, where he was chief of the CC diagnostic radiology department from 1972 to 1996. Under his direction, the department acquired among the first CT and MRI scanners in the country.

"He was a keen, compassionate clinician, an enthusiastic teacher and an innovative thinker," said Dr. Andrew Dwyer, CC radiologist. "He was a strong, positive influence on the clinical, educational and research environment of the Clinical Center."

On Aug. 2, Doppman was awarded scientist emeritus status. Among his many honors were the Gold Medal from the Society of Cardiovascular and Interventional Radiology (1997); Gold Medal from the American Roentgen Ray Society (1998); the Copeland Award from M.D. Anderson Cancer Center (1992); and the Public Health Service Distinguished Service Medal (1982), the highest award granted by PHS.

He also received several NIH awards including the Distinguished Clinical Teacher Award (1997); the Clinical Center Director's Award (1997); and the NIH Director's Award (1999). He was an honorary member of the radiological societies of England, Ireland, Germany and Hungary, as well as of the American Society of Endocrine Surgeons. He authored 38 textbook chapters and 516 articles in scientific journals.

Survivors include his wife, Anne-Marie; a daughter, Corinna, a son, Christopher; and a granddaughter, Nicole.

Free Wisdom Teeth Removal

NIDCR seeks volunteers in need of wisdom teeth removal to participate in clinical studies evaluating new pain medicines. Patients will have their wisdom teeth removed at no cost by a board-certified oral surgeon using local anesthesia and intravenous sedation. Patients will be evaluated for participation in ongoing research studies. For more information contact Michael Burke, 496-6242.

Community Health Forum Set, Oct. 21

The NIH Office of Community Liaison will hold its third annual community health forum, Share the Health: An Exposition of Health Resources from NIH to Its Neighbors. The event, which features free health-related information, lectures and screenings, will be held on Saturday, Oct. 21 from 8:30 a.m. to 3 p.m. at the Natcher Conference Center.

Community members will have an opportunity to participate in free health screenings, collect health information, visit exhibits by NIH institutes, visit NIH's web site and its links to health information sources, attend free health seminars, see computer demonstrations on how to access health information on the Internet, tour the National Library of Medicine and Children's Inn, participate in dance workshops, learn about volunteer opportunities and hear about efforts to promote health within the community. Children's health activities will also be featured.

Confirmed seminar topics include Alcohol and the Brain; Dry Mouth and Dry Eyes: Could It Be Sjögren's Syndrome?; and the Mission and Focus of the National Center for Complementary and Alternative Medicine. Additional lecture topics may include child and adolescent depression, an assessment of tools enabling children to read, and a look at advances in cardiovascular disease research. Dr. Francis Collins, director of the National Human Genome Research Institute, will give the keynote lunch presentation on "Medical and Societal Consequences of the Human Genome Project."

Save the date and plan to bring the entire family. For more information, call Terry LaMotte or Monique Simpson of Palladian Partners at (301) 650-8660 or visit <http://health.info.nih.gov/forum2000>. ■



The annual R&W bullpen party at Oriole Park was a big success in July, when the O's faced interleague rivals from the Atlanta Braves. Relief pitcher Mike Timlin (above) signed autographs for the children. Shortly after this event, Timlin was traded to the St. Louis Cardinals.



R&W and NBC Channel 4 recently hosted a day at Redskins Park for children of NIH and Special Love/Camp Fantastic, along with kids from Metropolitan Police Boys and Girls Clubs.



Sports anchor George Michael (above, c) clowns with patient John Steres (r) and a youngster from the Boys Club. At left,

the family of Jason Nwachukwu (l) gets into the spirit of the new season. Massive Redskin rookie tackle Chris Samuels (r) looms over patient Justin Horner. Several youngsters were allowed a no-holds-barred shopping spree at the Redskin store, courtesy of Michael, reports R&W President Randy Schools.



Eckelman Elected Society President

Dr. William C. Eckelman, chief of the positron emission tomography department in the Clinical Center, has been elected by the board of directors of the Society of Nuclear Imaging in Drug Development to serve as president for a 2-year term. SNIDD is an all volunteer, educational organization whose goal is increasing the appropriate use of noninvasive, nuclear imaging technology as tools in drug research and development. The society is holding a conference Oct. 23-25 in the Natcher Bldg. titled "Nuclear Imaging and Biomarkers in Drug Development Using Established Radiopharmaceuticals." ■