

nih record

Studies of Consciousness Reawakening, Panel Reports

By Rich McManus

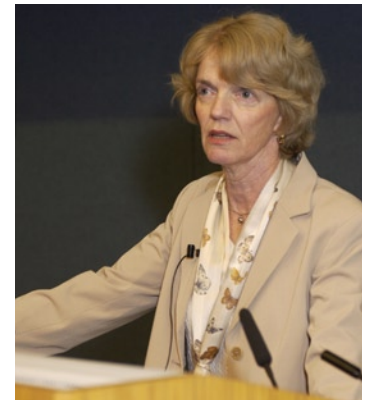
For many decades considered too obvious, or mysterious, to be studied scientifically, the notion of human consciousness and how it is generated is once again under the microscope, reported a panel of experts convened for a Mar. 22 STEP Science for All session on “Consciousness: How Does the Brain Create Mind?”

The scientists were not all of one mind (heck, the mind itself might not be all of one mind), but a consensus emerged that, in the words of philosopher Dr. Patricia Churchland, “It looks very likely that what we consider mental phenomena is actually brain phenomena... There is no mind-independent substance, just the physical brain” that is responsible for consciousness. “It’s not 100 percent certain, but highly probable.”

That probability is the fruit of broad surveys of neuroscientific study, narrowly focused investigations of an emotion as simple as fear, and on fascinating glimpses into minds damaged by stroke or other brain injury.

Churchland, professor of philosophy at the University

SEE CONSCIOUSNESS, PAGE 4



Dr. Patricia Churchland suggested that we are as naïve today about the true nature of consciousness as the ancients—who thought that the same “element” that consumed firewood also illuminated stars, comets and the northern lights—were about fire.



ABOVE • R&W treated thousands of area kids to a night at the circus. See coverage, p. 12.

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During move-in day Apr. 2, Erias Hyman cuts the ribbon on a newly occupied patient care unit of the CRC.

Patients, Staff Celebrate CRC Move-In

By Kathryn Boswell

The lobby of the Mark O. Hatfield Clinical Research Center was relatively still on Saturday morning, Apr. 2. A few people lingered at the café tables by the fountain, while others quietly prepared for the day ahead—wiping countertops, sweeping hallways and turning on computers. The calm was soon broken by the sound of wheels rolling across tile floors somewhere in the south end of the first floor.

SEE CRC MOVE-IN, PAGE 6

Hopeful Strategy vs. Protean Foe NIAID Tackles Malaria in Vaccine Lab

By Anne Oplinger

Across great stretches of the globe, malaria is an inescapable fact of life. In some places, everyone is infected by this energy-sapping malady. Every 30 seconds, someone—usually an African child under 5—dies of malaria.

Unlike diseases such as measles, in which a single encounter confers life-long immunity, malaria can strike again and again, bringing its victims recurring bouts of racking chills, high fevers, sweating and extreme fatigue. Along with AIDS and tuberculosis, malaria forms a deadly troika that not only takes millions of lives every year, but also casts a deep shadow on the world’s poorest countries. According to some estimates, malaria costs the continent of Africa \$2 billion in lost gross domestic product annually.

There is no vaccine to prevent malaria, a parasitic disease spread by *Anopheles* mosquitoes. Indeed, no vaccine exists against any human

SEE TACKLING MALARIA, PAGE 8



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briefs

Event Honors Julius Axelrod, May 23

“Celebrating Julie,” an event to honor the life and achievements of NIH scientist and Nobel laureate Dr. Julius Axelrod (1912-2004), will take place on Monday, May 23 in Masur Auditorium, Bldg. 10. NIH director Dr. Elias Zerhouni and NIMH director Dr. Thomas Insel will host protégés, colleagues and friends for a day of scientific reflection on Axelrod’s discoveries in his long and successful career. Axelrod spent most of his 50 years as a researcher at NIMH. Overflow rooms for NIH staff will be available in Natcher auditorium. The symposium will also be videocast at <http://videocast.nih.gov>. For more information, or reasonable accommodation, contact Jennifer Loukissas at (301) 443-4536 or loukissj@mail.nih.gov.

Bike To Work Day, May 20

Celebrate National Bike to Work Day with the NIH Bicycle Commuter Club, Friday, May 20, 7:30-9:30 a.m. in front of Bldg. 1. Those arriving by bike qualify for gifts from local Bike to Work Day sponsors. If you have never tried bike commuting, group rides along common routes, led by veteran bike commuters, have been organized.

Planned group rides depart from Lake Needwood (North Rock Creek route), Georgetown (Capital Crescent route), Columbia Heights (South Beach Drive route), North Arlington (Virginia route), Seven Locks Rd. (Gaithersburg route) and Silver Spring Metro (Jones Bridge route).

Thanks to the NIH Fitness Center, all NIH cyclists have free access to Fitness Center shower facilities on Bike to Work Day 2005. You can get detailed information about routes and planned drop-in points or sign up for a group ride or find a one-on-one bike commuting mentor by contacting the bike club’s ride mentor administrator Samantha Smith (samantha.smith@mail.nih.gov).

Even if you don’t plan to commute by bike, stop by on May 20 and meet fellow NIH’ers who have chosen to drive one less car, use one less parking space, maintain local paths for your enjoyment and advocate for improved roadway safety on and around the NIH campus. The NIHBCCG goal is to make commuting to and from NIH safer and saner for all. Visit the club’s web site at <http://www.recgov.org/r&w/nihbike/bike.html> for more Bike to Work Day and bike commuting information.

STEP Forum on Food, Population

The staff training in extramural programs (STEP) committee will present a Science in the Public Health forum on the topic, “Food for Thought: Sustaining the Global Population,” on Tuesday, May 10 from 8:30 a.m. to 12:30 p.m. in Lister Hill Auditorium, Bldg. 38A.

Proper food and nutrition have long been recognized as key to achieving and maintaining good health. However, human population continues to grow while food production may shortly encounter natural limits. We should not take food security for granted. Our actions today may make a world of difference for future generations.

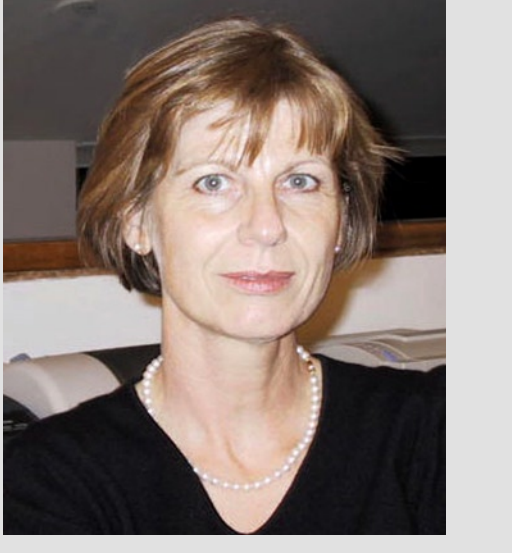
This forum will examine the factors behind the agricultural “green revolution,” threats to and solutions for future food production, population and fertility trends and possibilities for the future. NIH supports a broad portfolio of related research including human population dynamics, nutrition and basic biology relevant to agriculture.

Wednesday Afternoon Lectures

The Wednesday Afternoon Lecture series—held on its namesake day at 3 p.m. in Masur Auditorium, Bldg. 10—takes the day off on May 11, but returns May 18 with a presentation by Dr. Stephen C. West. He will address, “Making Ends Meet: Double-Strand Break Repair in Human Cells.” He is principal scientist, Cancer Research UK, London Research Institute, Clare Hall Laboratories, South Mimms, UK.

On May 25, Dr. JoAnn E. Manson will give the Robert S. Gordon, Jr., Lecture on “Postmenopausal Hormone Therapy: Can the Divergent Findings from Clinical Trials and Observational Studies Be Reconciled?” Manson is Brigham professor of women’s health, Harvard Medical School.

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



Solowey Awardee Heberlein To Lecture, May 12

You know the advice—don't drink on an empty stomach. Now Dr. Ulrike Heberlein and her group at the University of California, San Francisco, think they have the basis for this slogan. On Thursday, May 12, at noon in Lipsett Amphitheater, Bldg. 10, Heberlein will be honored for her work by receiving the 2005 Mathilde Solowey Lecture Award in the Neurosciences and delivering a lecture entitled, "Drugs, Flies and Videotape: Can Fruit Flies Teach Us About Drug Addiction?"

By studying drunken fruit flies, Heberlein and colleagues discovered that the hormone insulin, which surges after we eat, may make the brain less sensitive to alcohol intoxication. If confirmed in humans, the finding also suggests a promising way to treat alcoholism using drugs that control insulin activity. The UCSF group showed that when the normal function of insulin-like molecules in the brain of fruit flies is reduced, the intoxicating effect of alcohol increases.

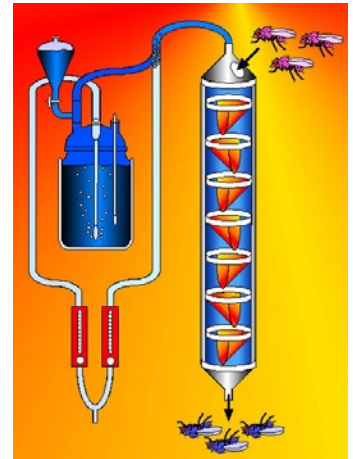
In her pioneering 10-year research effort to determine the genetic basis of alcohol-induced behavior, Heberlein has employed an apparatus she calls the inebriometer, in which normal fruit flies and those with genetic mutations are placed at the top of a cylinder and exposed to ethanol. The genetic contribution to alcohol sensitivity is measured by how quickly the fruit flies lose their grip and fall to the bottom of the device. Earlier research demonstrated that fruit flies and humans display many of the same vulnerabilities and behavioral responses to alcohol.

Heberlein and her colleagues showed that the molecule protein kinase A modulates sensitivity to alcohol. When its activity is inhibited, the amount of alcohol needed to cause inebriation decreases. Her group had also examined different regions of the fruit fly brain to determine where protein kinase A had its effect. In the new research, they zeroed in on a small group of neurons in the brain that produce so-called insulin-like peptides, or DILPs.

In 1999, President Clinton named Heberlein as one of 60 young researchers receiving Presidential Early Career Awards for Scientists and Engineers, the highest honor bestowed by the United States government on young professionals at the outset of their independent research careers.

Heberlein received her Ph.D. in biochemistry in 1987 from the University of California at Berkeley. In addition to the PECASE award, she has received a McKnight Investigator Award. She has published papers in *Cell*, *Nature* and *Nature Neuroscience*. She is currently a professor in the department of anatomy, UCSF.

For more information call the Foundation for Advanced Education in the Sciences, Inc. at (301) 496-7975 or Dr. Miles Herkenham at (301) 496-8287. 📞



The inebriometer intoxicates hapless flies.

Mental Health Month Observed in May

During May, which is Mental Health Month, the Work/Life Center and NIMH, with support from the Employee Assistance Program, are sponsoring two events for NIH staff interested in learning more about anxiety and its disorders.

The first event, to be held Thursday, May 19, from 2 to 3:30 p.m., is a research-based lecture by NIMH's Dr. Daniel Pine, chief of the section on development and affective neuroscience, Mood & Anxiety Disorders Program. He will discuss what is known about anxiety disorders. The lecture, which will be in Bldg. 10's Lipsett Amphitheater, will also be broadcast at <http://videocast.nih.gov>.

On Tuesday, May 24, employees are invited to attend a walk-in, anonymous and confidential anxiety-disorders screening from 10 a.m. to 3 p.m. at three NIH sites:

Bldg. 10, Rm. 6C401 (OMS)

Bldg. 31, B2-B57 (EAP)

Neuroscience Center, Rm. B (6001 Executive Blvd.)

Participants will be able to view a brief video about anxiety disorders, complete a questionnaire about symptoms, meet privately with a mental health professional and/or pick up information—all of which generally takes less than an hour.

Employees whose native language is not English and who will attend the Bldg. 10 or 31 sites may request an interpreter for the screening by contacting Andrea Rander (301-496-1807) by May 17.

Sign language interpretation will be provided at the lecture. For other reasonable accommodation for either event, contact the NIH Work/Life Center at (301) 435-1619 (TTY 301-480-0690), or send an email to wlc@od.nih.gov.

For more information about either event, contact Sophia Glezos Voit, NIMH (301-443-4533, sglezos@mail.nih.gov).

Family members who would like to be screened may call (888) 442-2022 to find out about privately sponsored sites. This referral line is coordinated by Freedom From Fear, the mental health organization that sponsors National Anxiety Disorders Screening Day each year. However, NIH does not necessarily endorse this organization or any referrals they may provide. 📞



CONSCIOUSNESS

CONTINUED FROM PAGE 1

*Above:
Speakers at the STEP
forum on human con-
sciousness included (from
l) Dr. Todd Feinberg, Dr.
Joe LeDoux, Churchland
and Dr. Bernard Baars.*

PHOTOS: ERNIE BRANSON

of California, San Diego, proceeded on the assumption that “mind is what the brain does,” but cautioned that we are far from being able to assign any particular conscious state to the firing of specific neurons. Even so, she argued, “We won’t have defined consciousness if all we find are the cortical correlates of it.”

Just as fundamental concepts such as temperature, proteins and genes were only understood after years of theoretical fine-tuning—what she called “the profile of discovery”—consciousness itself might one day yield to scientific analysis.

She used the metaphor of fire, which in ancient times was thought to be the root of such disparate phenomena as stars, comets, the northern lights, as well as forest fires, to explain how a definition of consciousness might mature.

We now know that fire is rapid oxidation, she observed, but it has taken millennia to realize that only terrestrial fires depend on oxidation, and that stars are fueled by fusion, comets are cold iceballs lit by starlight, and that no flame ignites the northern lights.

“I suspect that consciousness will go the way of fire,” she said. “Neuroscience is still very much in its nascent stages,” and cannot yet approach the major puzzles of consciousness, including information storage, modularity, computation, integration, functional organization and time management, she said.

Science’s ability to ask good questions about the nature of consciousness has itself been hampered in the past 40 years by a fashionable arm of inquiry known as behaviorism, said Dr. Bernard Baars, a research fellow at the Neurosci-

ences Institute in San Diego. “Consciousness has only been spoken of in euphemisms, as in the way Victorians used to speak of sex.” His approach, now more than 2 decades in the making, has been to study consciousness as a variable—states characterized, like gravity, by more and less of it. He has pioneered the concept of “global workspace theory.” It posits that the brain—with its 20 billion neurons each firing 10 times per second—is like a “massive society of information processors.” Consciousness, in Baars’ view, involves brainwide distribution of information; unconscious input stays, by contrast, quite limited in distribution.

Like Churchland, he agrees that it is “too early in the field’s history” to arrive at a conceptual definition of consciousness. But just as with fire, and temperature and genes, some fairly smart operational definitions are maturing toward actual concepts.

Interestingly, Baars argued that dreaming is actually a conscious state—studies have shown it (and common sense suggests that humans would have no record of having dreamed if not for this quality).

Lest the discussion become too abstract, Dr. Joe LeDoux of the Center for Neural Science at New York University illuminated the basic neural pathways underlying consciousness of a very raw kind—the sense of fear. Examining the nature of feelings and how the brain makes them, he showed that our emotional responses aren’t necessarily dependent on feelings. There are unconscious pre-processes that generate conscious feelings.

If you see a snake, for example, you unconsciously recoil, and only later form an emotion.

LeDoux advanced a “reconsolidation” theory of memory in which our recollections are only as good as the last time they were retrieved; we have no access to the virgin events that originally created them. Perhaps that explains why people habitually revisit bad memories; repeated rinsing might dilute their unpleasantness.


Commenting on the role of the unconscious, LeDoux noted, “There’s more to the self than meets the mind’s eye.”

If consciousness can be defined as self-awareness, what better way to study it than to look at how it changes when damaged by head injury, or stroke or aneurysm? Dr. Todd Feinberg of Albert Einstein College of Medicine offered a clinician’s view of the impact of neurological disorders on sense of self.

He focused on delusional mental syndromes in

which victims don't recognize their own body parts as belonging to them. In one, married women who are afflicted commonly misidentify the limb as belonging to their husband; men affected by it are likely to attribute ownership to the mother-in-law, he insisted with a straight face.

These conditions, including Capgras syndrome, asomatognosia and alien hand syndrome (in which, in its classical form, a person's hand systematically tries to undo the actions of the other) yield evidence for Feinberg of a "neural hierarchy theory" making consciousness not the king atop a mountain of subservient neurological input, but rather a democracy moved by forces erupting within it.

The four guest speakers might not fully have answered the question, "What is the real nature of conscious awareness?" posed by the meeting's lead organizer, NCI's Dr. Grace Ault, but they certainly reached the borderlands. To see the whole program, visit www.videocast.nih.gov. 



NHLBI director Dr. Elizabeth G. Nabel (l) welcomes council members (from l) Dr. Charles T. Esmon, Dr. Patricia Wahl, Dr. Jeffrey McCullough and Dr. Katherine High. (Not shown is J. Hoxi Jones.)

NHLBI Appoints New Council Members


Five new members were recently appointed to the National Heart, Lung, and Blood Advisory Council. They are:

Dr. Katherine High, professor of pediatrics and professor of medicine and pathology at the University of Pennsylvania School of Medicine, and an investigator with the Howard Hughes Medical Institute.

Dr. Charles T. Esmon, chair in cardiovascular research and head of the cardiovascular biology research program at the Oklahoma Medical Research Foundation, as well as an investigator with the Howard Hughes Medical Institute and a member of the National Academy of Sciences.

J. Hoxi Jones, director of public information and volunteer services at the Texas Department of Human Services, and an experienced administrator in health training programs.

Dr. Jeffrey McCullough, professor of laboratory medicine and pathology at the University of Minnesota, as well as the director of the Biomedical Engineering Institute at the University of Minnesota.

Dr. Patricia Wahl, professor of biostatistics and dean of the School of Public Health and Community Medicine at the University of Washington. 

NIH Home Page Staff Captures Honors

Staff members from the Office of Communications and Public Liaison, OD, recently earned seven outside awards in connection with their contributions to facilitating health communications via the web at health.nih.gov.

OCPL's Online Information Branch (OLIB), headed by NIH home page manager Dennis Rodrigues, received three awards in the category of Consumer Portal

from CorHealth, a California-based organization that analyzes critical health care trends and issues for businesses. OLIB received awards for best design and best user interface, as well as an honorable mention for outstanding content. The National Cancer Institute and the National Institute on Aging also captured awards from CorHealth for their web site contributions.

Meanwhile, OLIB also picked up four bronze awards in the Fall/Winter 2004 Web Health Awards Program from WWW. Evaluated by a distinguished group of judges, the office was noted for providing exemplary online health information in the category of "Health Promotion/Disease and Injury Prevention Information." The National Center for Complementary and Alternative Medicine and NIH's stem cell unit, managed by the National Institute on Deafness and Other Communication Disorders, also took home awards from the same organization.

The new health information web site debuted in May 2004 with a specific purpose: "Our primary focus was to create a resource that accurately and intuitively guides users to the full range of NIH health information on any given topic," said Rodrigues. "We recognized that users want answers to their specific health concerns and, after doing considerable research, we found a way to bring online information together to meet those needs."

The web site features many opportunities for health consumers. A "one-stop online shopping" vehicle, the page is laden with links to vital research, medical findings and information. The site also helps users appreciate the role of research in furthering NIH's mission. The health information page received more than 400,000 visits in February 2005; the most heavily requested topics were depression, endometriosis, diabetes, nutrition and heart disease.

It is estimated that the NIH web site, as a whole, receives several million visits in an average month.—

Jan Ehrman 



Right:
Clinical Center director Dr. John Gallin (r) greets Marcos Arrieta of El Paso, Tex., the first pediatric patient to move into the Hatfield Center.

Middle:
Jim Wilson (l), Frank Kelly (c) and Gallin discuss last-minute logistics on move day.

Bottom:
Nurse Siu-Ping Ng helps Nicole Hofhine get settled in new digs.

PHOTOS: BILL AND ERNIE BRANSON



CRC MOVE-IN

CONTINUED FROM PAGE 1



It echoed through the CC lobby. “The patient is on his way,” someone hollered over a radio.

Every person who had been answering phones, mopping floors, scrubbing desks or checking files, stopped what they were doing, walked into the lobby and turned to look in the direction of the growing clamor. Doctors, nurses, hospitality staff, housekeepers, construction workers and visitors all strained to get a glimpse of the convoy heading toward the pediatrics unit. As the sound grew louder, people’s faces changed from looks of expectation to welcoming smiles. The CRC’s first pediatric patient had arrived. Marcos Arrieta, reclining in his bed, was escorted by a crew of nurses, volunteers, other staff, and his mother, Maria, as he made his way from the old hospital to the bright, new rooms of the CRC, where he was formally welcomed by CC director Dr. John Gallin as the new pediatrics unit’s first patient.

Arrieta shyly smiled as Gallin shook his hand and began pointing out some of the new features in the boy’s room, including the flat-

screen television set that also serves as a computer monitor, the keyboard and mouse, and the glow-in-the-dark animal footprints on the ceiling.

Following Arrieta’s arrival, the new pediatrics unit and Gallin welcomed four more patients and their family members: Derek Aldona Reyes, Valeria Rivero, Kathryn Yokoyama and Nicole Hofhine.

They were excited about the move. A couple of them kept asking, “Can we go? Can we go now?” all through the night,” said nurse Siu-Ping Ng, watching the beds wheel in.

Hofhine’s mother, Michelle, walked into the room and exclaimed, “Look at this view! You can see the Children’s Inn right across the street.” Nicole and her mother have been coming to the Clinical Center for almost 10 years and had been anxious to see the new building. “We were here when they broke ground for this building,” Michelle says. “It’s great to finally see the inside.” Nicole seemed pleased with her room



At left, the medical board room serves as move headquarters for the day. At right, cleaning crew members (from l) Aida Atistibha, Woine Hagos, Zerfe Argaw and Precious Moko put on the final touches just before patients arrive.



too as she arranged her two stuffed dogs beside her in bed and smiled at the sight of her very own computer keyboard.

The pediatrics unit was not the only area of the hospital alive with movement and transition. Hundreds of staff, movers and volunteers were on hand to coordinate the moving of 89 patients from the old building to the new. Proudly wearing their bright blue T-shirts with the, "Follow Me to the CRC" logo designed especially for the Clinical Center move, volunteers and staff tended to every need—whether it was moving furniture, cleaning new work stations, stocking pharmacy shelves, preparing patients' meals for the day, translating for non-English-speaking patients and their families, reassuring patients or communicating updates from the move headquarters in the medical board room.

The most challenging part of the move was that it had to be completed in one day, but it was the only realistic option. Senior Nurse Executive Laura Chisholm, who served as co-chair of the relocation task force, explains, "Logistically, we could not split our patient services between two locations. We had to move all of our equipment and patients at the same time, which made it all the more challenging. Thankfully, we had a great team working together, so it made the whole move go exceptionally well."

For months leading up to the move, employees participated in a multitude of simulated tests, drills and exercises to prepare them for any situation that might arise on the move date and the days following. The relocation task force led practice walks through various routes from the Magnuson to Hatfield building many times, looking for anything that might interfere with the movement of patient beds and determining the best path to take. "We have been through every scenario, prepared for every possible thing that could happen," said one volunteer. "We're ready. No one is nervous; we're just excited."

The move finished ahead of schedule at 3:38 p.m., but not without a few obstacles. "The



facilities staff did an amazing job," Chisholm says. "Throughout the day, they fixed a broken elevator, tended to two small floods, built a ramp to allow beds to travel over a path that had a bump in it, took care of door access issues and finished last-minute housekeeping needs."

In spite of the day's challenges, the consensus among staff, patients and their families was one of excitement. Family members joined doctors and nurses as they all snapped photos of loved ones moving into the sparkling new facilities. Patients shook hands with the movers who had pushed their beds, and smiled and waved to staff as their beds progressed down hallways.

The move was one of great historical significance for NIH, but it was also a memorable day for those present.

Said Gallin, "Getting to this point has been an adventure—like climbing Mt. Everest. It's been a 12-year hike, and this last thrust may be short, but we'll reach an awesome goal."

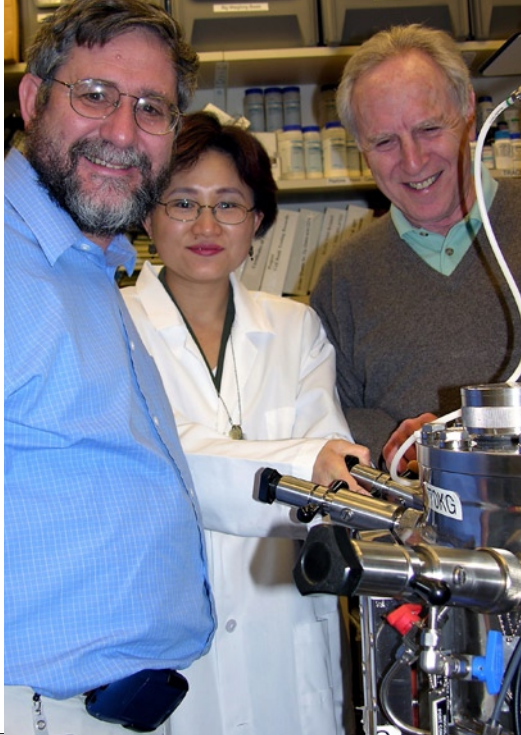
Reflecting on the journey to completion, he added, "Watching this enterprise move forward, watching what you do so well—we have made history in this house of hope." ①



Top left:
Pediatrics patient Dereck Aldona Reyes gets situated in sparkling accommodations.

Top right:
Patients are transported through the CRC's signature open atrium.

Bottom:
Excited hospital staff line the hallways as Gary Bowman is escorted to his new room.



TACKLING MALARIA

CONTINUED FROM PAGE 1

didate is guided by a “task force” of researchers through the vertical threads of vaccine development, which begin with molecular analysis; journey through scale-up, purification and quality control; continue through immunological studies in cells and animals; and end in clinical trials.

The unusual approach is a response to the difficulties of designing a vaccine against *Plasmodium falciparum*, the parasite that causes the most lethal kind of malaria. As it passes back and forth between its human and mosquito hosts, the parasite shifts between sexual and asexual forms. This shape-shifting hinders the ability of the hosts’ immune systems to pin down and eliminate the invader. The parasite’s many forms also present a daunting challenge to vaccine designers. Vaccines work by giving the immune system a “preview” of a disease organism. So the more complex and changeable the microbe is, the harder it is for scientists to identify what kind of preview will best stimulate the protective might of the immune system.

An optimist could view the complexity of the malaria parasite’s lifecycle as a boon to vaccine designers. Theoretically, vaccines could be aimed at any point in the cycle. At the MVDB, several candidate vaccines target malaria parasites during their sexual stage within mosquitoes, while others are aimed at the blood stages in humans that cause disease. The violent chills, high fever and drenching sweats of malaria come when large numbers of parasite-laden red blood cells burst at once, releasing tens of thousands of *Plasmodium* in a form called merozoites. Many of the released merozoites go on to infect additional blood cells, thus prolonging the infection. A vaccine that halts or inhibits the parasites at this stage would also eliminate or reduce malarial disease and deaths.

But to craft such a vaccine, the researchers must first identify which of the parasite’s 5,300 antigens provoke a strong immune response. At each stage of its lifecycle, the parasite has a different set of antigens, further complicating vaccine design. Finding, purifying and making the appropriate antigens in sufficiently large quantities are among the tasks awaiting the vaccine developers.

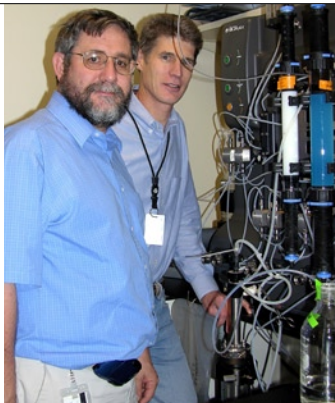
Dr. Carole A. Long, who heads the lab’s immunology team, says the MVDB offers “soup to nuts” in the vaccine process. The first course is made inside a gleaming chrome fermenter where a soup of bacteria containing parasite DNA churns out quantities of parasite antigens that the scientists believe may have what it takes to become a vaccine. The mailbox-sized

parasite. But in a state-of-the-art laboratory in Rockville, a team of NIAID scientists is at work to change that. Dr. Louis Miller and Dr. Allan Saul, co-chiefs of the Malaria Vaccine Development Branch (MVDB), believe the lab’s holistic approach to vaccine development makes the idea of a malaria vaccine feasible.

Several dozen scientists with a wide range of expertise moved into the 7,000 square-foot MVDB lab in early 2001. Their mission: bridge the gap between basic research and commercial vaccine production. The MVDB, explains Miller, focuses on product development—taking a promising vaccine candidate from concept through scale-up and the early phases of clinical testing—a bottleneck in malaria vaccine research and development.

In its organization, the lab departs from tradition, where each researcher or small group works more or less in isolation. Instead, every aspect of the facility, from the physical layout to the range of expertise of the workers, is designed on an industrial model, enabling a smooth transition from one phase of vaccine research to the next. Essentially, says Saul, the MVDB is a small biotech company. Beyond the scientific challenges inherent in creating any new vaccine, the researchers also have had the challenge of adopting a more business-oriented mindset, he adds. This means that the team objectively assesses various vaccine candidates, abandoning those that are weak while pursuing more promising ones.

Miller’s sketch of the lab’s many projects looks like a woven textile. Each horizontal thread represents a different vaccine candidate. Every can-



Top: Malaria researchers (from l) Co-chief Allan Saul, Jin Wang and Co-chief Louis Miller at the MVDB’s fermenter.

Bottom: Following fermentation, recombinant proteins are highly purified using this device. Saul and David Narum, who heads process development, stand by the machine.

fixture cost \$100,000 and is built to good manufacturing practice standards, which means candidate vaccines are prepared to sufficient standards of purity to meet Food and Drug Administration requirements for eventual human use.

Once produced in quantity, the antigens must be tested for their ability to arouse the desired immune responses. The tests, or assays, are indirect indicators of the candidate's protective value. Lab measurements—the amount of antibody produced in an animal following inoculation with a test vaccine, for example—may or may not correlate to protection from infection or disease in humans. Devising assays to detect meaningful correlates of protection is one of the hardest tasks for immunologists, notes Long.

Still another hurdle for the MVDB researchers is the quest for a suitable adjuvant to include in the vaccine's formulation; an adjuvant is a substance that improves the immune system's response to an antigen. Currently, only one kind of adjuvant—made from aluminum salts—is widely used in human vaccines. The pharmaceutical industry does not have much incentive to pursue new adjuvants, says Saul, because the existing one is satisfactory. Exotic adjuvants are essentially a niche business, pursued by smaller biotech companies. The MVDB is partnering with these smaller companies to devise adjuvants specifically designed to work well in malaria vaccine formulations, Saul adds.

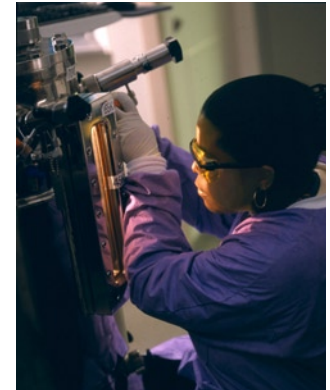
Miller emphasizes the important collaborations between MVDB researchers and scientists both inside and beyond NIH. Lab personnel work closely with scientists in NIAID's Division of Intramural Research and the extramural Division of Microbiology and Infectious Diseases, for example. Partnerships also exist with other U.S. agencies, nonprofit organizations and biotech companies, all of which bolster efficient production of viable vaccine candidates.

Of course, all the technical success in the world means nothing unless the vaccines can be tested and shown to work in malaria-endemic settings. Ensuring that African scientists and clinicians have the training and infrastructure support to conduct successful vaccine trials in their own countries is a critical piece of the malaria puzzle, says Miller. NIAID has a decade-old relationship with the National School of Medicine of Mali and has worked with scientists there to create the Malaria Research and Training Center in Bamako. The MRTC addresses all aspects of the malaria problem, ranging from strategies for distributing insecticide-impregnated bed nets to formulating a national malaria drug use policy.

One of the MRTC's most important tasks in the future will be testing and evaluating vaccine candidates as they emerge from the MVDB and elsewhere. The MVDB has had substantial success in making clinical-grade antigens, says Miller, which makes increasing the capacity for phase I and II trials a top priority. The necessary technology and trained personnel are being put in place in Mali to make clinical trials there safe and scientifically productive. The first trials of malaria vaccines were conducted by the MRTC last year. One vaccine, called FMP-1, was developed by the Walter Reed Army Institute for Research and GlaxoSmithKline Biologicals and the second was produced at the MVDB called AMA1.

Ironically, notes Saul, malaria's ubiquity works to the advantage of vaccine researchers when candidates move from the lab into clinical testing. Because infection rates are so high—in some places reaching 100 percent—any reduction in parasite burden shows up readily in the vaccinated person's blood, and researchers can rapidly learn whether a particular vaccine approach is working, he explains.

Considering the mountain of difficulties to be overcome on the way to a successful malaria vaccine, victory might seem elusive. Saul, though, is cautiously optimistic. A quarter-century ago, when he first entered the field, Saul admits to being a bit starry-eyed about vanquishing malaria. Now his optimism is tempered by what he calls healthy skepticism. Nevertheless, he says the last 5 years have been ones of steady progress. Both he and Miller emphasize that the road to an even partially successful malaria vaccine will be long, but they are both equally convinced that preventing malaria through vaccination is not a vain hope. The MVDB has already played an important role in advancing malaria vaccine science, they say. With the commitment and expertise of its personnel clearly evident, there's every reason to believe the branch will be instrumental in lifting the burden of malaria from countless millions. ●



A technician operates a gleaming chrome fermenter where a soup of bacteria containing parasite DNA churns out quantities of parasite antigens.

CIT Computer Classes

All courses are given without charge. For more information call (301) 594-6248 or consult the training program's home page at <http://training.cit.nih.gov>.

Web Sponsor	5/10
SAS Programming I	5/10
Statistical Analysis of Microarray Data	5/11
nVision Travel	5/11
Seeking Information on the Web	5/11
Reference Manager 11 (PC) Basics	5/12
Complementary & Alternative Medicine: Databases, E-Journals and Other Sources	5/12
PubMed	5/12
Statistical Graphics in R	5/12
Introduction to Flash Application Development	5/13
Getting Started with Medical Image Processing Analysis and Visualization (MIPAV)	5/16
Beginning Perl	5/16
Writing Scripts for MIPAV	5/17
Wireless LAN & VPN Client Training	5/17
NIH Data Warehouse Query: Advanced Query & Reporting Workshop	5/18
Visualization in MIPAV	5/18
Introduction to Novell SUSE Linux Enterprise Server	5/18
Writing MIPAV Plugins	5/19
Building a Home Network	5/20
Mapping to the Talairach Coordinate System using MIPAV	5/20

NIH Training Center Classes

The Training Center supports the development of NIH human resources through consultation and provides training, career development programs and other services designed to enhance organizational performance. For more information call (301) 496-6211 or visit <http://learningsource.od.nih.gov>.

NIH Foreign Travel (NBS Travel System)	5/16-17, 6/6-7
NIH Domestic Travel (NBS Travel System)	5/23-25, 5/31-6/2, 6/1-3
Introduction to NIH Property Management	6/2-3
Consolidated Purchasing Through Contracts	6/6
Federal Supply Schedules	6/6
Professional Service Orders	6/6
Buying from Businesses in the Open Market	6/7
Purchase Card Training	6/7

NIH Shares Health at Local Event

NIH is sponsoring a day of free health-centered fun for the entire family on Sunday, May 15 at the newly renovated Westfield Shoppingtown (Wheaton Plaza). "Share the Health: NIH's Premier Health and Fitness Expo" offers interactive health exhibits, health screenings, hands-on lab experiments, lab-art workshops, fitness activities and more. Held from 11 a.m. to 3 p.m., the event provides health information and activities for children, teens, adults and seniors.

Sponsored by the Office of Community Liaison and the R&W, the newly redesigned event promotes community health through the prevention of disease. Scientists at NIH will share easy and fun ways to improve fitness and maintain good health.

Attendees can discuss their health concerns with NIH physicians and scientists while visiting interactive exhibits from nearly all 27 institutes and centers. Visitors can learn about the effects of drugs and alcohol on the brain, dental hygiene, diabetes, bone health, alternative medicine and infectious disease prevention.

Local area hospital staff and members of the Commissioned Corps will offer free health screenings to help community members discover if they are at risk for stroke, high blood pressure, skin problems, head and neck cancer or obesity. NIH health educators will also sponsor a variety of fun, interactive exhibits.

Children can don lab coats and goggles to experience what it is like to be an NIH scientist for the day, performing hands-on lab experiments. They can also jump on a Moon Bounce, play games and win prizes.

Other activities include scaling a rock-climbing wall, exploring the "Drunken Brain," and navigating an obstacle course with Fatal Vision Goggles. For more information, call the Office of Community Liaison, (301) 496-3931 or visit <http://sharethehealth.od.nih.gov>.

Career Fair for Foreign Fellows

Visiting fellows are invited to participate in NIH's second annual Career Fair for Foreign Fellows on Tuesday, May 17, from 1 to 4 p.m. in the CRC atrium on levels B1 and 1. The program will include information about enhancing career skills, funding research in various nations, supporting career development in home countries, and facilitating post-NIH career progression with the assistance of selected international organizations.

Welcoming remarks, scheduled for 12:45 p.m., will be given by Dr. Sharon Hrynkow, FIC acting director, and by Dr. Joan Schwartz, acting deputy director of the Office of Intramural Training and Education.

For more details, contact Dr. Kamala Tirumalai at tk8oi@nih.gov or visit <http://felcom.nih.gov/NIHVFC/>.



Healthy Volunteers Sought

Doctors at NIH are seeking healthy volunteers to take part in a study. Participants will be required to give a small sample of blood (about 2 tablespoons). Total visit time required is about 30-45 minutes. The study involves only a blood sample and there is no age cut-off. Compensation is provided. For more information, call (301) 496-5150.

Can Chocolate Help Your Health?

The National Center for Complementary and Alternative Medicine seeks volunteers to participate in a 6-week study evaluating the effect of dark chocolate on blood pressure and the blood's glucose and insulin levels. Participants will help researchers learn more about chocolate's impact on hypertension and diabetes. Participants will be asked to take dark chocolate and a placebo (inactive treatment). To participate, you must be: persons with hypertension (high blood pressure) who can be safely taken off anti-hypertensive medications; age 21 to 60; not taking other medications or nutritional supplements for any illnesses besides hypertension. Compensation and dark chocolate will be provided. For more information, call (301) 496-3244.

Female Volunteers Needed

The Behavioral Endocrinology Branch, NIMH, is seeking female volunteers ages 18-55 to participate in studies of the effects of menstrual cycle hormones on brain and behavior. Volunteers must have regular menstrual cycles with no changes in mood in relationship to menses, be free of medical illnesses and not taking any hormones or medication on a regular basis. Payment will be in accordance with the duration of each visit and the type of protocol. For more information, call Linda Simpson-St. Clair, (301) 496-9576 (TTY 1-866-411-1010).

Ever Have Postpartum Depression?

If you have a history of postpartum depression (PPD) following the birth of any of your children, consider participating in a PPD study with NIMH. The study seeks to examine if your PPD was caused by hormonal changes during or after pregnancy. The study is recruiting female participants between the ages of 20-45. Call Linda Simpson-St. Clair, (301) 496-9576 (TTY 1-866-411-1010).

Stopping Your Estrogen Therapy?

NIMH is investigating whether mood, anxiety and irritability occur when you stop taking your estrogen or estrogen/progesterone combination therapy. Participants should be ages 45-60, have a past history of perimenopausal mood symptoms responsive to estrogen therapy (ET) or combination therapy, be currently taking ET or combination therapy and be in good physical health. For information call Linda Simpson-St. Clair, (301) 496-9576 (TTY 1-866-411-1010).

NIDA Welcomes New Councillors

The National Institute on Drug Abuse has announced the appointment of three new members to its advisory council: Dr. John Rice, Dr. Barry Lester and Dr. Mark Greenberg.

Rice is a professor of mathematics in psychiatry at the division of biostatistics at Washington University Medical School in St. Louis. He has received a number of NIH awards and has extensive experience with multi-site collaborative studies.

Lester is a professor of psychiatry and human behavior, and pediatrics at Brown Medical School. He has received many NIH grants to study high-risk infants including research on prenatal cocaine exposure and child outcome.

Greenberg is Bennett chair of prevention research and director of the Prevention Research Center at Pennsylvania State University. Much of his work has been devoted to understanding ways to promote healthy social and emotional development and better school-based prevention programs.



Dr. Timothy Condon (l), NIDA deputy director, and Dr. Nora Volkow, NIDA director, welcome new council members Dr. Barry Lester (second from l) and Dr. John Rice (r).

Asian and Pacific Islander American Heritage Month Observance

Everyone is invited to the 2005 NIH Asian/Pacific Islander American Heritage Month Program. The theme for the 33rd anniversary observance is "Progress with Diversity." The program consists of two parts—a scientific lecture and a cultural dance festival.

On Thursday, May 26 from 11 a.m. to noon, Dr. Morgan Sheng of the Massachusetts Institute of Technology will present recent developments in the field of synaptic plasticity. This event will be held in Lipsett Amphitheater, Bldg. 10.

On Friday, May 27 from 11:30 a.m. to 1 p.m. in Masur Auditorium, Bldg. 10, the cultural program will feature Chinese, Indian, Korean and Indonesian dances and music performances by the Washington Jin Ling Chinese Dance Academy, Pushpanjali School of Dance, Washington Korean Dance Company and the Seni Budaya Theater Dance Association. Dr. Richard Nakamura, NIMH deputy director, will present the keynote address. Immediately following the program, a reception will be held in the old Visitor Information Center exhibit gallery; guests can meet the performers and sample Asian pastries.



R&W Hosts Circus Night at MCI Center

PHOTOS: ERNIE BRANSON

More than 10,000 people attended Premier Evening of the Ringling Bros. & Barnum and Bailey Circus at the MCI Center recently as guests of the R&W. Since it started producing the children's charity event 8 years ago, R&W has hosted more than 50,000 children and their families at the circus's first night in town, said Randy Schools, president. "The R&W has given out over \$500,000 worth of free tickets to children in local hospitals, such as NIH, Children's Hospital, Fairfax, Walter Reed and Georgetown," he said. R&W also works with local social service agencies to treat at-risk youth and those in need of partnership with Easter Seals, he added. "The joy of the event is seeing all of the children with their smiles and eagerness to have a good time," Schools said. The event began with a pizza dinner, at which circus clowns mingled with guests, then everyone entered the arena to see the Three-Ring Adventure.

