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September◆1997

Gene Therapy In Mice Delays Onset Of Lou Gehrig's Disease (ALS)

Researchers Fighting Programmed Cell Death

by Jeremy Kay, *ASN&R* Staff Writer

Amyotrophic lateral sclerosis (ALS), better known as Lou Gehrig's disease, is not only among the more prevalent of neurological disorders, affecting approximately 8 people out of every 100,000 — it is also among the most cruel. Its victims, who are usually young adults in the prime of life, quickly lose strength and physical coordination as their motor neurons — the cells of the brain and spinal cord that operate muscles throughout the body — mysteriously begin to die.

The patient becomes increasingly debilitated, eventually suffering near total paralysis. Within five years of diagnosis, most patients are dead. Now, however, a study conducted by researchers at Columbia University provides hope for a new type of treatment that could delay the onset of the disease's debilitating symptoms.

The Columbia team, working with a mouse model of ALS, showed that expression of extra copies of a gene called Bcl-2 allows mice to live symptom-free for an average of 19% longer than afflicted mice without Bcl-2. The Bcl-2 protein is known to regulate the life and death of cells through a process called programmed cell death. These results, which were obtained in collaboration with a group at the University Hospital in Geneva, Switzerland, are published in the July 25 issue of the journal *Science.*

According to Dr. Serge Przedborski, Assistant Professor of Neurology at Columbia and principal investigator on this project, these findings are exciting not because they directly suggest a way to treat ALS patients, but because they shed light on the cellular process by which motor neurons die in this disease. "Bcl-2 itself might not necessarily be the answer" for treatment, he said in an interview, "but it suggests a mechanism . . . and if we know the mechanism we can figure out ways to interfere" and delay or prevent cell death. Moreover, he said, the mechanism responsible for cell death in ALS might also be relevant to other neurodegenerative diseases, such as Parkinson's and Alzheimer's diseases.

The death-causing mechanism Dr. Przedborski and his colleagues have targeted with this experiment is known as programmed cell death (PCD), or, alternatively, as apoptosis. The process of PCD has received a lot of experimental attention recently as researchers have come to the somewhat coun-

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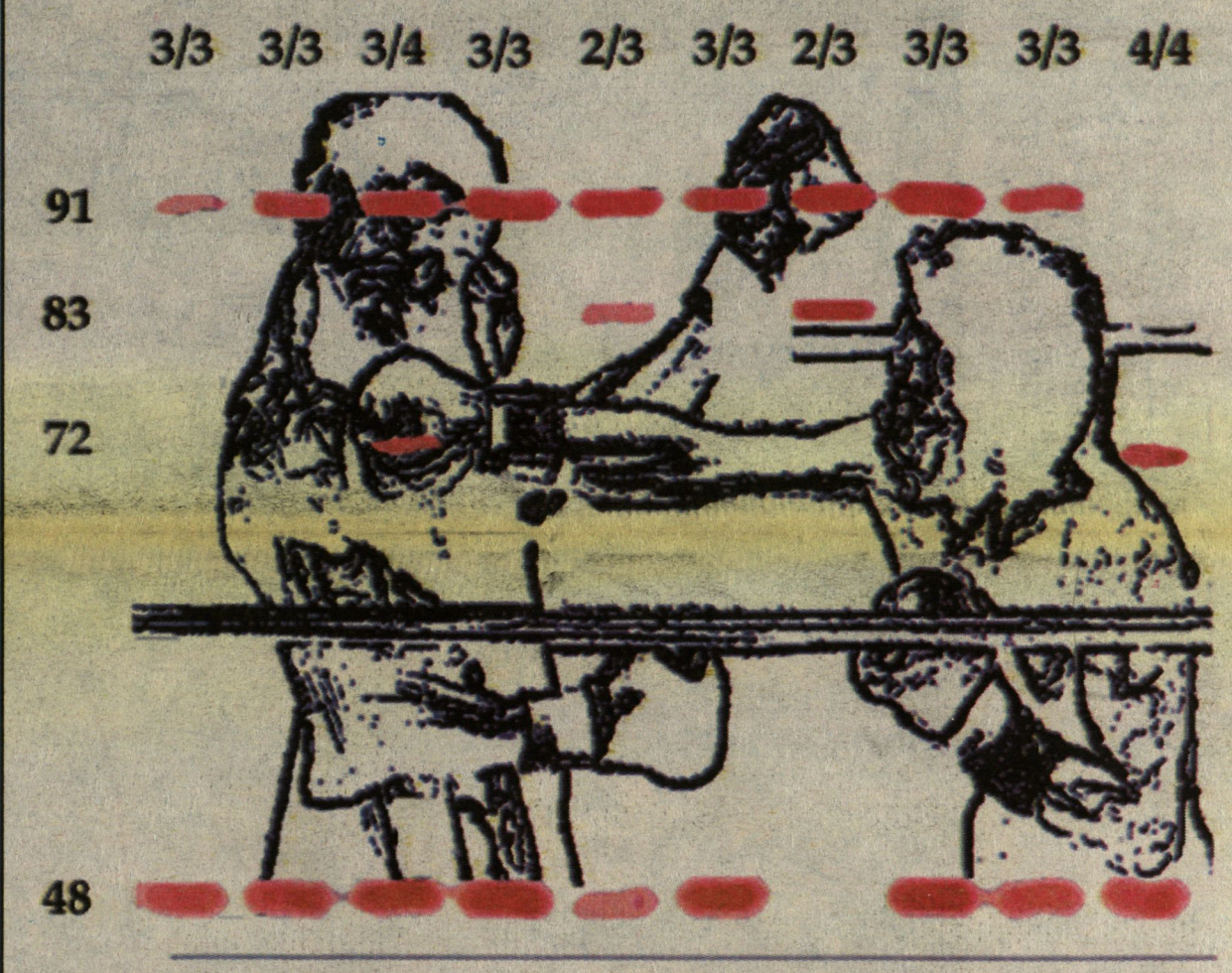
Boxers At Risk

Study Finds Genetic Factors May Increase Likelihood of Permanent Neurological Injuries

by Elizabeth Belton, *ASN&R* Staff Writer

If Rocky Balboa was predisposed to Alzheimer's, chances are that after a twenty year professional boxing career he should be experiencing severe motor and cognitive impairment even at a relatively young age. A new study indicates that some boxers may be predisposed to dementia following excessive head trauma. The study suggests a relationship between a gene and the predisposition, and points out that the gene in question is also possessed by Alzheimer's victims.



A boxer in the act of inflicting head trauma on his opponent, superimposed upon an electrophoretic gel used in apolipoprotein E (APOE) genotyping. Possession of the e4 allele of APOE was found to correlate with more severe long-term neurologic impairment in professional boxers, suggesting that genetic factors play a role in the development of the punch drunk syndrome *(dementia pugilistica).* (Graphic courtesy Dr. Norman Relkin, Cornell University Medical College)

The study, "Apoliprotein E e4 Associated with Chronic Traumatic Brain Injury in Boxing," authored by doctors and scientists at Cornell University Medical Center was published in the July issue of the *Journal of the American Medical Association.* It presents the results of a two-year study of thirty amateur and professional boxers.

The study attempted to establish a relationship between chronic traumatic brain injury (CTBI) which many boxers experience, and the apoliprotein E APOE4 genotype to see if the gene predisposes the boxers to "punch-drunk" syndrome, or dementia.

The boxers were assembled from a variety of sources, ranging in ages from early twenties to early seventies.The average age was 49, and boxers were either black, White or Hispanic. Those running the study, which ranged over two years, established that, based on a previous study, boxers who had a high exposure to head trauma were those who had participated in 12 or more professional fights.

They were ranked for boxing exposure, amateur and professional bouts. The boxers were also subjected to a neurological evaluation, to determine if they had any evidence of sensory/motor impairment. Boxers classified as "probable" candidates for CTBI

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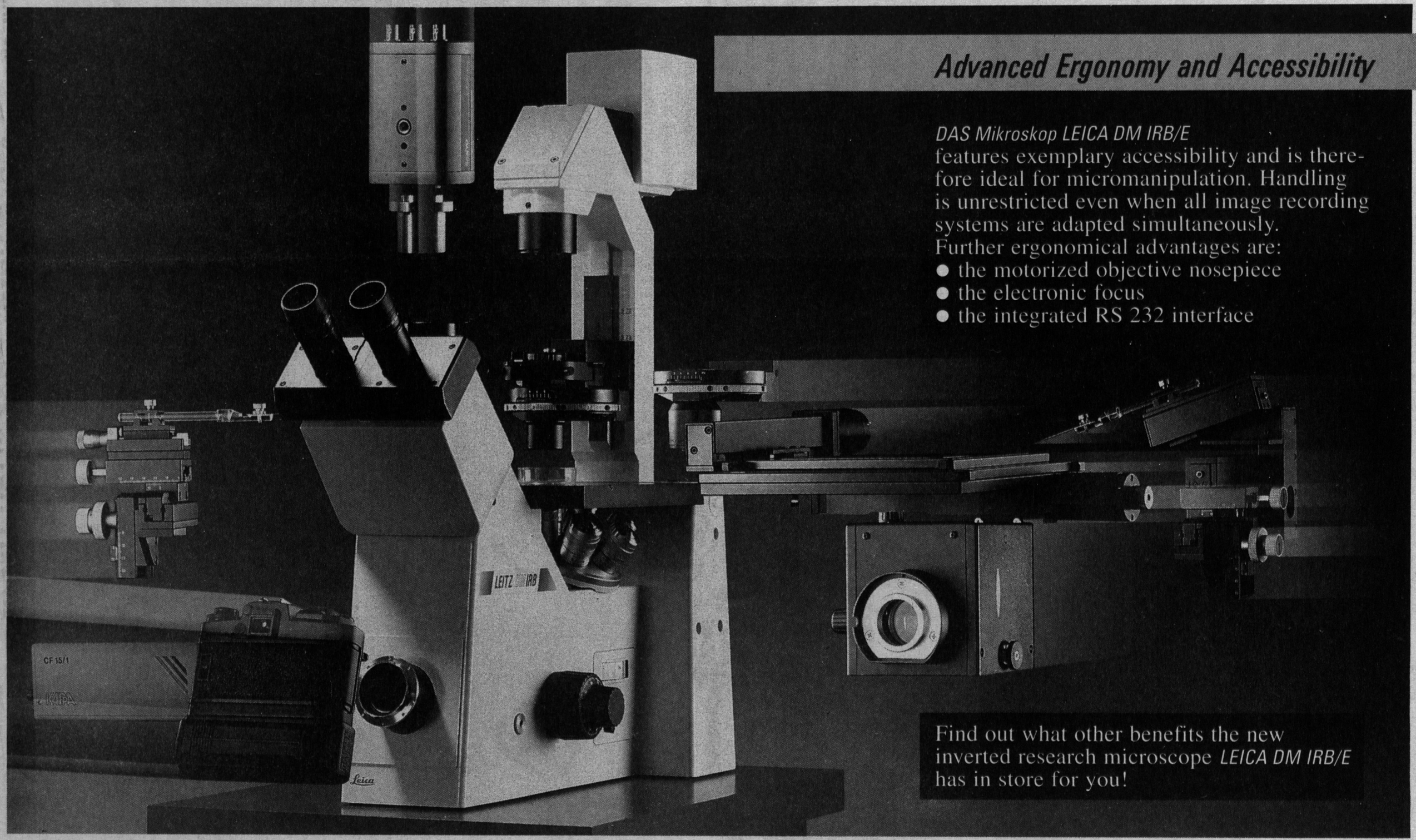

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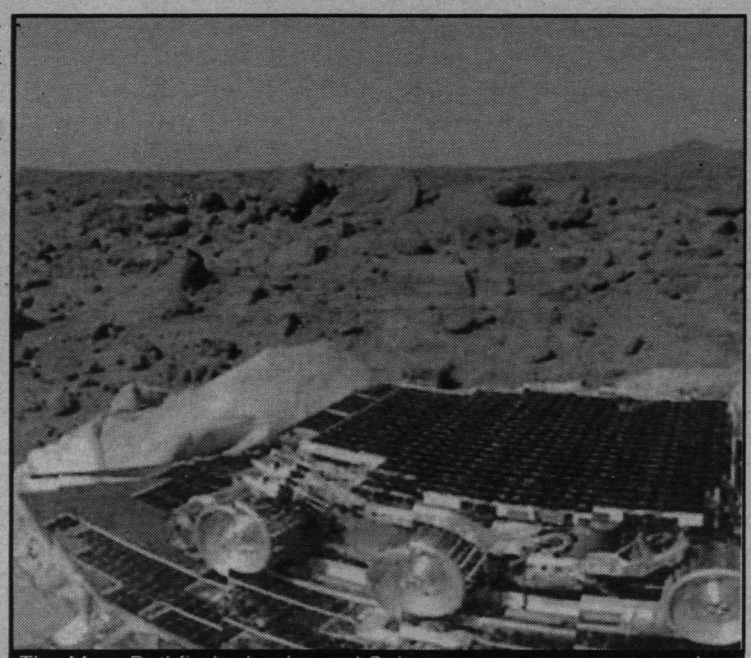
Making Mars Pathfinder "Ray-Proof"

BNL Accelerator Aids in Mission's Preparation

by Kathryn Gavin

The summer's biggest science story, NASA's mission to Mars, had a suspenseful moment early on, when the Pathfinder lander and Sojourner rover couldn't communicate due to a modem error.

But the worldwide TV audience breathed a sigh of relief when engineers at the Jet Propulsion Laboratory fixed the problem in a matter of hours, using a trick that their colleagues in the Pathfinder construction team had learned two years earlier at Brookhaven National Laboratory.



The Mars Pathfinder lander and Sojourner rover prepare to explore the surface of Mars. photo: NASA/JPL

While building the Mars-bound machines out of commercially available parts, JPL engineers came to BNL to test their Motorola modem and other components for resistance to damage from cosmic rays. The rays — speeding atomic nuclei, or ions, of unknown origin and high velocity — can do significant and sometimes permanent damage to computer chips and other parts, whether they're on board a space vehicle or sitting on the surface of a planet whose atmosphere is as thin as Mars'. The impact of a single cosmic ray can turn a chip's digital "1" signal into a "0", or vice versa, causing an glitch called a single-event upset.

The tests took place at Brookhaven's Tandem Van de Graaff accelerator, which can produce and accelerate beams of high-energy ions — from hydrogen up to lead and gold — to simulate cosmic rays and aim them at components mounted in the beam's path. After a few days of work, the JPL team found that while their modem was in fact upset by impacts from heavier ions, it could shake off the problem if they turned it on and off a couple times. So, when the Pathfinder's modem malfunctioned on Mars, a few commands from Mission Control were all it took.

The Mars vehicles are only the most highly publicized of the Tandem's cosmic-ray customers — everyone from satellite companies to NASA's other teams have paid several hundred dollars an hour for a chance to stick their components in front of its beam and chart the damage it causes. Even while the Mars mission was captivating audiences, a team from Lockheed Martin was using the Tandem to evaluate the space-worthiness of chips for a future satellite.

Simulating cosmic rays is but one of the Tandem's jobs — its other mission is to provide the same kind of ions for use in BNL's Alternating Gradient Synchrotron, an accelerator used by both high-energy and nuclear physicists, and radiation biologists. The Tandem's straight-line accelerator path links into a transfer line that links with the AGS's circular tunnel.

BNL's Vladimir Zajic mounts a circuit board onto the target area for the Tandem Van de Graaff's cosmic ray simulation facility. The target is then placed in the cylinder in the background and bombarded by speeding heavy ions. Photo: Brookhaven National Laboratory

Beginning in 1999, the Tandem's ions will feed from the AGS to the Lab's new Relativistic Heavy Ion Collider, which will create head-on collisions between clouds of ions traveling nearly the speed of light, in an attempt to re-create a phase of matter known as the quark-gluon plasma. Last seen a few moments after the Big Bang, quark-gluon plasma requires the constituent particles of nuclear particles such as protons and neutrons to break free of their bonds, if only for 10^{23} seconds.■

FEATURES

September 1997

- A new study has found that possession of an Alzheimer's succeptability gene correlates with more severe long-term neurological impairment in professional boxers, suggesting that genetic factors play a role in the development of "punch drunk" syndrome. p 1.
- Research into blocking programmed cell death leads to progress in ALS treatment in a mouse model of the disease. Gene therapy allows treated mice to live symptom-free for longer. p 1.
- Brookhaven's Tandem Van de Graaff accelerator was used to test Mars Pathfinder's resistance to cosmic rays before its mission. The testing can uncover problems and their solutions before distant missions probe the solar system. p 3.
- Should NASA be focussed on sending humans into space? In light of the Cold War's end and recent unmanned successes, one earth scientist thinks not. p 4.
- Experimental balloons launched high into the stratosphere let astronomers peer into the mysterious gamma ray part of the spectrum, which hardly penetrates the atmosphere. p 6.
- Two scientists at Cold Spring Harbor, who discovered a family of genes controlling the formation of long-term memory, have formed a company which will seek drugs to treat neurodegenerative diseases such as Alzheimer's. p 8.
- Stanley Schachter, a Columbia Psychologist noted for his research into the social determinants of emotion and behavior, has died at the age of 75. p 15.
- The fate of the High Flux Beam Reactor, Brookhaven's main research reactor which has been at the center of environmental controversy lately, is to be decided in the coming months. p 17.

– O P I N I O N –

NASA Should Focus on Unmanned Missions

By Frank A. von Hippel, Ph.D.

The International Space Station currently being built by the U.S., Russia, and other participants of the Cold War will serve as a conspicuous symbol of the end of the Cold War and as a stepping stone to manned missions to the moon, Mars, and other celestial bodies. Neither of these reasons are sufficiently compelling to spend over 100 billion dollars. We all know the Cold War is over. Additionally, a stepping stone to further manned missions is unnecessary because humans are rarely needed on board to guide spacecraft (with the exception of missions to repair or upgrade satellites, such as the Hubble Space Telescope, few missions require humans on board).

Furthermore, the space station, as a stepping stone to further manned missions, should not be used to justify the existence of a manned space program to begin with. NASA needs the support of the American people, but that support should target unmanned missions that are designed to monitor the environmental health of our planet and to engage in scientific exploration of our solar system, including the search for life outside Earth.

Biosphere 2 provides a good metaphor for the direction that NASA should take in an atmosphere of increasing demands and decreasing funds. Biosphere 2 is a 3.15 acre greenhouse in Arizona that was built by private investors at a cost of about $200 million as a prototype for the technology needed for a planetary base on Mars or other bodies in the solar system and as a laboratory for the study of the environment. The original corporate objective was "to design, build, and operate closed ecological systems for biospheric research and education towards better management on Earth, for applications in the exploration and settlement of the solar system — and perhaps beyond" (John Allen in his 1991 book *Biosphere 2: The Human Experiment*). Two teams lived sealed in Biosphere 2, the first team of eight people (along with 3,800 other species of animals and plants) for two years from 1991-1993, and the second team of seven people for six months in 1994. Management of Biosphere 2 was transferred to Columbia University on January 1, 1996; it is now run as a Western campus of Columbia for research and education (K-12, undergraduate, and for the public) in the environmental sciences. Humans no longer live inside Biosphere 2. The structure operates as an unmanned mission to study the Earth.

The engineer said that NASA astronauts would not tolerate a diet of algae, to which Tony Burgess replied that it would be less expensive to recruit astronauts who would eat such a diet than it would be to grow an inefficient food supply and supplement it with beef launched from Cape Canaveral

NASA is planning a space station that, as Biosphere 2 once did, would use plants both to supply food and to generate a hospitable atmosphere for its crew (instead of using oxygen tanks). Perhaps NASA learned from experiences at Biosphere 2: unlike Biosphere 2, NASA has envisioned a much simpler system of growing only a few species of plants hydroponically (without soil, the roots are bathed in a liquid nutrient solution) and densely on a series of shelves arranged in a special plant mod-

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ALS...Continued from Page 1

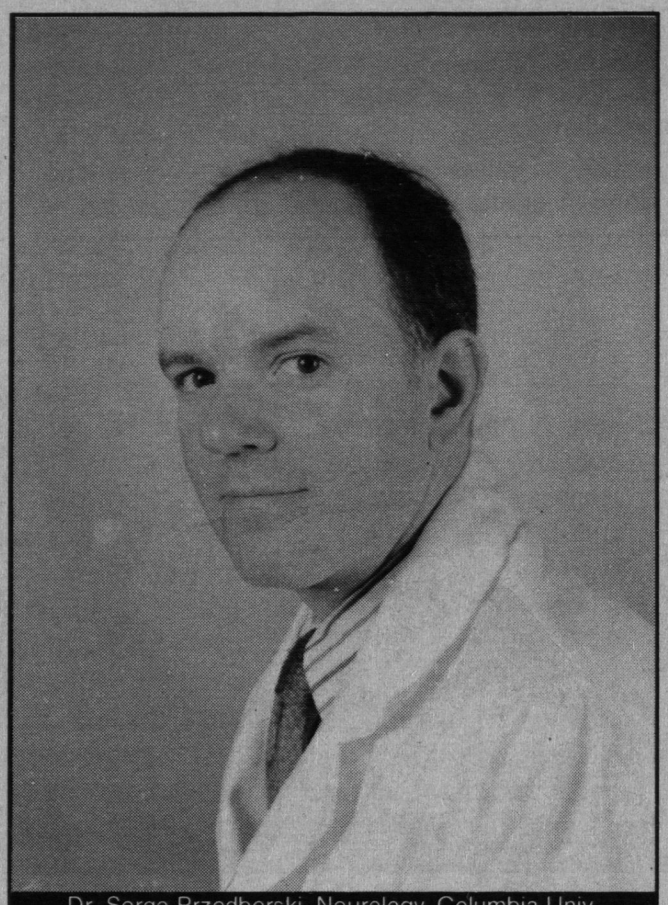
terintuitive realization that, in a healthy organism, cells are dying all the time.

Apparently, cells are capable of killing themselves for the good of the organism as a whole — they can activate a sort of intracellular "self-destruct mechanism" if they realize they have become extraneous or potentially harmful. For example, during development of the embryo, the fast pace of cell division produces unneeded cells; these are eliminated by PCD. The self-destruct program can also be triggered, through the well-publicized tumor suppressor protein p53, in a cell that has become a potential cancer threat as a result of DNA damage. In the immune system, cells that have begun producing antibodies that attack the body's own proteins sacrifice themselves by PCD, and in the nervous system, neurons that have made connections to inappropriate targets can also eliminate themselves in this way. (Normal, mature neurons, however, ordinarily would not do so.)

When a cell activates this "self-destruct" pathway, it shrivels up into a little package that can be conveniently swept away by the immune system with minimal disruption to surrounding tissues. This process is called PCD to emphasize that death is the result of an internal cellular program rather than external insult or injury.

The death program is thought to exist in nearly all animal cell types, and it is thought to be regulated and carried out by more or less the same set of proteins no matter where in the body or along the evolutionary ladder you look. Bcl-2 and a family of related proteins, for example, have been shown to constitute a key checkpoint in cellular life-or-death decisions in organisms ranging from nematodes to humans and in tissues ranging from the brain to the intestine.

Although the Bcl-2 family's checkpoint is only one part of a very complicated cascade of signals that eventually leads to cell death, it is one of the best understood parts of the pathway because Bcl-2 was the first cell death regulatory gene to be discovered. Bcl-2 acts as a late brake on the self-destruct mechanism, encouraging cells that have started down the road towards death to go on living.



Dr. Serge Przedborski, Neurology, Columbia Univ.

Other members of the family, meanwhile, are known to promote PCD by countering Bcl-2's effects.

Dr. Przedborski and his colleagues suspected that at least some of the motor neurons that die in ALS do so through a mechanism of apoptosis — that, somehow, the disease is forcing cells to trigger their own self-destruct mechanism, so that, although the disease initiates the chain of events that leads to death, the cell itself acts as its own executioner. If this were true, it would mean that interfering with PCD might improve the condition of ALS patients.

It was this suspicion that lead to the experiments reported recently in *Science.* There were several good reasons for forming this hypothesis — first, post-mortem examinations of ALS patients had indicated that some dying cells show the morphology characteristic of apoptosis. Second, an inherited version of ALS, familial ALS (FALS), had recently been linked in some families to a mutation in an enzyme known as copper/zinc superoxide dismutase (SOD). This enzyme has the important protective task of breaking down free-radical compounds such as hydrogen peroxide, which, if left unmolested inside a cell, can wreak havoc by oxidizing — and thereby destroying — DNA or vital proteins. The discovery that this SOD mutation causes familial ALS seemed to indicate that a lack of sufficient protection from free radicals might be an important cause of motor neuron death in all cases of ALS. Although FALS accounts for only 10% of ALS cases, and only a quarter of FALS cases are caused by the SOD mutation, researchers felt comfortable extrapolating from FALS to all

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Balloons to the Stratosphere: The Long Road Ahead in the Study of High-Energy Gamma Rays

by Ilana Harrus, Ph.D., *ASN&R* Staff Writer

These days, Professor Elena Aprile has been thinking about plastic balloons. No, she is not preparing a birthday party for one of her two daughters; the balloons that have occupied her thoughts are worth up to $100,000 each, require on average 40 million cubic feet of helium to fly, and are used to carry scientific payloads high into the atmosphere.

Prof. Aprile is a physicist at the head of a NASA-funded research project between the Columbia University Astrophysics Laboratory, the University of New Hampshire Marshall Space Flight Center, and Waseda University in Japan. On July 25, her team successfully completed the first test of a new kind of gamma-ray detector to be used in the next generation of space-based gamma-ray observations. This instrument operates in a range of energy that is still little explored, and has greater sensitivity and greater resolution than existing detectors.

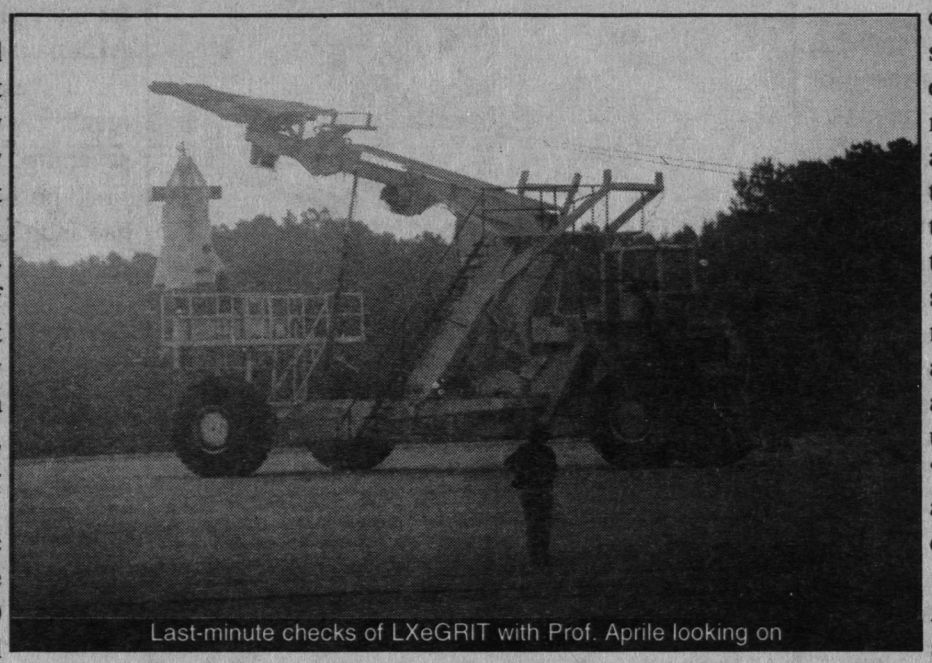
Gamma rays are the most energetic packets of light, also called photons, in the universe. They carry more than 20,000 times the energy transported by optical photons. Most are absorbed by the atmosphere and never reach the ground. Instead, gamma-ray astronomers have had to turn to satellite- or balloon-based detectors, studying the sky to explore this energy. The launch of the Compton-Gamma Ray Observatory (CGRO) has already proven the quality of space-based observations, and plans are being made to prepare the next generation of gamma-ray observatories.

With this objective in mind, a group at Columbia University started to develop a liquid xenon detector, giving birth to the Liquid Xenon Gamma-Ray Imaging Telescope (LXeGRIT) collaboration. Highly purified liquid xenon is among the most efficient elements in the detection of gamma rays, but because it is difficult, (though not dangerous) to handle, few had tried to use it for air-borne detectors. The interaction between an incoming gamma-ray photon and an atom of xenon produces a large number of electrons and scintillation photons which can be used to reconstruct the energy and position of the initial photon.

Imaging techniques in the gamma-ray energy range are still in their infancy: the anticipated precision, between 1 and 3 degrees, although better than that of current gamma-ray detectors in this energy range, is still significantly worse than what can be obtained with optical telescopes.

After 4 years developing the detector and checking its performance in the controlled environment of a laboratory, the LXeGRIT collaboration first tested the detector in a balloon flight in late July.

The launch was supervised by the National Scientific Balloon Facility (NSBF), a NASA sponsored institution based in Palestine, Texas. Every year during the May to October launch season, this small town becomes the world center of scientific ballooning. Launches vary according to scientific requirements: payloads for infrared observations can be operated at lower altitudes than a typical gamma-ray payload — the weight requirements are different and the balloons used are generally different as well. For the non-experts,however, it all looks pretty much the same. When all meteorological conditions have been cleared, a truck picks up the payload and brings it to the launch pad. The balloon is unfolded and brought to the launch pad as well. It is securely attached and filled with helium. When filled, the balloon is released in a two-step process. First, it is allowed to stabilize 100 feet above the ground. Then it is released completely. At that moment the payload is still tied on the back of the truck. During the short time the balloon rises, the truck driver maneuvers quickly to bring it directly below the balloon, Only then is the payload released. "It's like watching a ballet", said Prof. Aprile. After an hour and a half the payload reaches 130,000 feet. At that altitude, it is above more than 99.5% of the atmosphere and data collection begins.



Last-minute checks of LXeGRIT with Prof. Aprile looking on

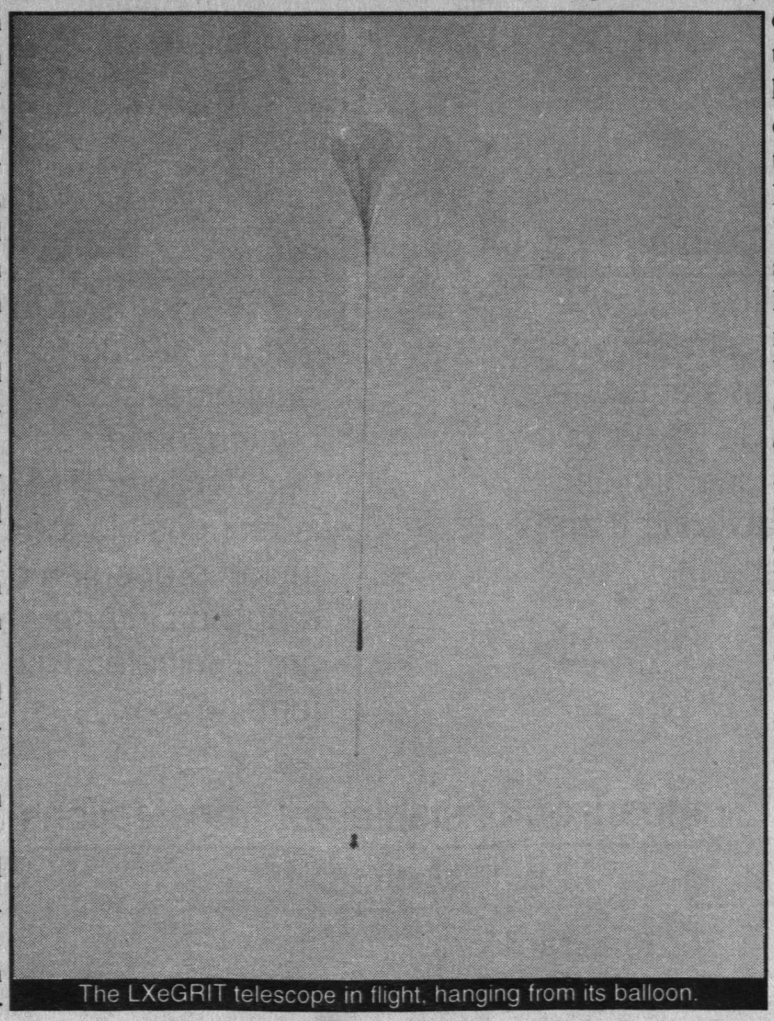
In the case of the first LXeGRIT flight, data were not recorded onboard but were transmitted directly to the control room. This need for direct telemetry coverage limits the distance the payload can fly to less than 300 miles, and was one of the limiting factors in the duration of the flight. In theory, as NSBF site-manager Dwight Bawcom said, "The end of flight is planned according to scientist requirements". In practice, many factors can affect the decision to terminate a flight. At all times, the trajectory of the system is monitored from the ground and from a plane which keeps constant visual contact with the balloon. Once the decision to end a flight is made, the NSBF team analyzes where the payload and its parachute and balloon will land, and makes sure that these landing sites are in deserted areas where any damage caused will be minimal. The payload and its parachute are released from the balloon which is then destroyed. For planned short flights the recovery team leaves the base at the time of the launch and is updated on possible landing sites. Usually, it will be no more than 350 miles from the launch site and at least ten miles from any inhabited area. There is no shortage of stories about unusual landings. According to Bawcom, "payloads typically land on private lands and we compensate landowners for any damage due to payload impacting".

Damage was what worried Prof. Aprile. On impact, even protected by a specially crash-padded gondola, the detector may suffer irreparable damage. To minimize the risk of damage when the payload is dragged on the ground by the parachute, the two are separated at the moment of impact. This requires excellent timing and is done manually by one of those onboard the plane keeping track of the payload. On the initial July 25th flight, the LXeGRIT payload was retrieved in an oil field with little damage to the detector.

A major objective of this first balloon test was to demonstrate that the team could overcome the difficulties in handling the detector in a flight. From this perspective the flight was a success. It is however too soon to be sure of the quality of the data collected. A longer flight is scheduled for this purpose early in September from a base in New Mexico.

There are many interesting phenomena to be studied in the energy range covered by LXeGRIT. One in particular is the evidence for matter-antimatter annihilation in our galaxy. When an electron and its anti-matter companion (called a positron) annihilate, two photons are created. The energy of these photons can provide a distinct signature of that process. It is this signature, a line of emission at the rest energy of an electron, that the LXeGRIT could detect. Electron annihilation is not the only process in astrophysics to give rise to line emission. Atomic elements do this as well, and a few (e.g., aluminum, titanium, iron) do so at energies accessible to LXeGRIT. In addition to the study of specific energy lines, scientists from the LXeGRIT group are planning to study the continuum emission- that is to say, the emission not concentrated in a narrow band of energy, but covering the complete range of their detector. Their "to-do" list includes the study of the contribution of Active Galactic Nuclei (AGN) at those energies, the measure of gamma-ray energy of isolated pulsars, the mapping of the diffuse gamma-ray background, and placing constraints on emission from black holes.

For the moment however, the group is still testing the instrument, preparing for the next balloon flights, when it's time to fly it higher in the sky.■



The LXeGRIT telescope in flight, hanging from its balloon.

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Discovery of a Genetic Switch in Brain Spawns Hope for Novel Memory Drugs

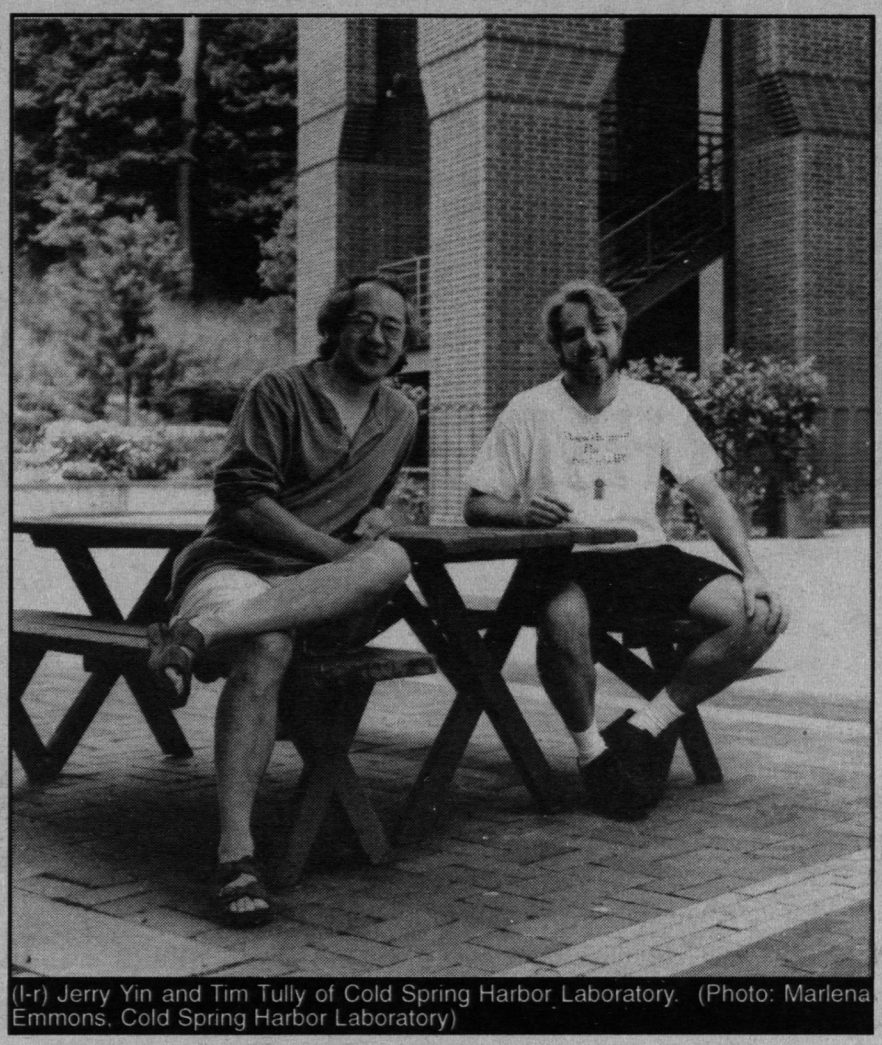
Helicon, "The Memory Company," Seeks Drugs to Treat Neurodegenerative Diseases

by Dan Coulter, ASN&R Staff Writer

On July 31, 1997, Cold Spring Harbor Laboratory announced its collaboration with Oncogene Science and Roche Holding Ltd. to form a corporation called Helicon Therapeutics. The company is to discover, develop, and commercialize novel drugs for the treatment of long-term memory disorders such as Alzheimer's and other central nervous system dysfunctions.

The company is based on the fundamental discovery by Drs. Tim Tully and Jerry Yin at Cold Spring Harbor of a genetic "memory switch" in the brain that controls the formation of long-term memory. Under terms of the agreements, Oncogene Science will contribute its proprietary, high-speed robotic screening technology to identify drug leads and Roche will provide research funding, a capital contribution, their "CNS-enriched" drug library, and expertise in CNS research, molecular biology, advanced chemistry and product development.

Helicon is presently headquartered at Cold Spring Harbor Laboratory and at Oncogene Science in Uniondale. Should a viable drug candidate be found, the company intends to move into a biotechnology incubator on Long Island.



(l-r) Jerry Yin and Tim Tully of Cold Spring Harbor Laboratory. (Photo: Marlena Emmons, Cold Spring Harbor Laboratory)

THE CREB GENE FAMILY — THE MEMORY SWITCH"

A few years ago, Tully and Yin collaborated to determine how long-term memory is formed within the brain. Prior to the team's collaboration, Dr. Tully had been studying the mechanisms of learning and memory in *Drosophila,* the common fruitfly. Using a self-designed fly training apparatus, Tully was able to show that the fruitflies did, in fact, develop long-term memory by subjecting them to a shock-odor standardized test. Just how this was accomplished on a molecular level however, remained elusive. Enter Jerry Yin. Dr. Yin specializes in the study of the molecular biology of learning and memory. With Yin's expertise, the team hoped to go one step further, showing how long- term memory is dependent upon protein synthesis and gene regulation.

Scientists have known for several years that long-term memory could be blocked by drugs that prevent the synthesis of new proteins in nerve cells. This implied that long-term memory was dependent on structural changes that strengthen connections between nerve cells. In order for these structural changes to occur, new proteins have to be made, which means that genes have to be turned on.

The team identified a key molecule known to function centrally in long-term memory formation. In a paper published in the journal *Cell* in 1995, Tully and Yin reported their findings involving transgenic flies, genetically engineered to produce copious amounts of a protein called CREB. Essentially, these flies formed photographic memory after a single trial of Tully's standardized shock-odor learning experiments.

The CREB gene can produce two forms of a protein. In the brain, both can affect long-term memory, but in opposing ways, as activators or repressors. The CREB proteins are transcription factors or proteins that act on DNA to turn on other genes. The CREB activator acts as an "on-switch", and the CREB repressor as an "off-switch", of the downstream gene expression. When copious amounts of the repressor are produced, long term memory formation is blocked. In contrast, large amounts of the activator enhance long-term memory formation.

In a recent interview, Dr. Tully pointed out that the enhancement of memory occurring from hyper-activation of the CREB activator is to be regarded as the creation of a photographic memory. The team was able to show that fruitflies can form this protein-synthesis-dependent long-term memory after only one standardized training session, instead of the ten sessions usually required for fruitflies.

This phenomenon has also been demonstrated in mouse studies conducted by Alcino Silva, also at the Cold Spring Harbor Laboratory. Originally, Silva showed that a partial knockout of the CREB gene in mice suppressed the formation of long-term memory. More recently, Silva and co-workers published a paper suggesting that the whole CREB switch mechanism controlling the formation of long- term memory in flies can be applied to their mouse studies as well.

"The point is that we think that this is a very hopeful sign — that things are working in the same way for both the fly and mouse studies," said Tully. "This is an important step because a mouse is a mammal and the CREB gene found in mice is identical to the CREB gene in humans. Our observation that it is sufficient to simply increase activator or repressor levels to affect memory formation is the premise for forming Helicon. Our notion is that if we can find drugs that simply increase the relative concentration of activator vs. repressor, it should have the same effect as in our genetic experiments. We will however, try to pinpoint the mechanism behind memory formation," said Tully.

Yin's lab is largely involved now in trying to understand the mechanism by which CREB normally functions. Tully's lab is involved primarily in trying to find the downstream genes that are regulated by CREB during memory formation. Dr. Yin suggested that the fly CREB gene is a predecessor of the mammalian genes, and that there are two or three genes that have diverged from the fly gene. "This fly CREB gene looks as if it were an ancestor gene before it was duplicated and more specialized in function. In mammals, it's a little more complicated to understand the CREB mechanism," commented Yin, "especially with two to three genes involved and all the protein products from them in the mix."

CREB AND HUMAN NEURODEGENERATIVE DISEASES

Current evidence suggests, then, that CREB functions as a long-term memory switch for all types of memory. With respect to vertebrates, there are two distinct types of learning; declarative and non-declarative. Declarative learning is based upon factual knowledge, such as remembering events or places. Non-declarative learning involves things like motor skills that are learned by repeated training. CREB appears to be involved in long-term memory for both. It is also believed that different anatomical regions of the brain are involved in declarative vs. non-declarative types of learning.

"The hippocampus is the part of the brain that everybody is excited about these days because it appears to be centrally involved in the formation of declarative memories," said Dr. Tully. In Alzheimer's disease for example, neurodegeneration occurs more rapidly in the hippocampus than it does in the rest of the brain. Once a nerve is gone, it can no longer participate in memory formation. There is also some neurodegeneration in the rest of the brain where non-declarative things are learned, and Alzheimer's disease eventually affects these areas as well.

"The evidence so far is that neurodegeneration appears to occur preferentially in the hippocampus," notes Tully. "Alzheimer's patients tend to

Continued on Page 18

Continued from Page 4

ule attached to the station. An engineer consulting for NASA presented the plan to our scientific staff at Biosphere 2 last summer. The simpler and more intensive approach envisioned by NASA is a sensible way to grow food while maintaining a viable atmosphere by having food plants convert the crew's exhaled carbon-dioxide to oxygen.

The engineer also explained that meat would be added to the astronauts' diet via shuttle flights that would dock with the space station. Noting that shuttle payload is at a premium (a side of beef delivered to the astronauts means one less satellite deployed or one less experiment run), Tony Burgess, Biosphere 2's site ecologist, pointed out that it would be cheaper and more food and oxygen would be generated if NASA grew algae that would meet the crew's nutritional needs instead of flying in meat and growing potatoes and other common food plants. The engineer replied that NASA astronauts would not tolerate a diet of algae, to which Tony Burgess replied that it would be less expensive to recruit astronauts who would eat such a diet than it would be to grow an inefficient food supply and supplement it with beef launched from Cape Canaveral.

At that point I questioned the logic of manned space flight at all. Space exploration and space science are cheaper and obviously safer if no astronauts are involved. But as the engineer correctly pointed out, manned exploration of our solar system has been NASA's mandate since its inception.

Shortly after the NASA presentation, NASA's David McKay and his colleagues published their paper in the August 16, 1996 issue of the journal *Science* suggesting that life may have existed on Mars several billion years ago. My brother and I discussed some of the implications of these findings in a letter to *Science* (September 20, 1996 issue); in response, I received a letter with the criticism that "a tiny nothing comes to justify a hugely expensive space mission."

The possibility of life on Mars has improved the prospects for manned missions to Mars. One of Biosphere 2's original objectives was to serve as a prototype for the technology needed for a planetary base on Mars. Several other locations in our solar system could also harbor bases or space stations, including the moon, some of the moons of Jupiter, and in orbit around Earth where the Russians already have a beleaguered space station. But what is the value of such planetary bases and space stations? Certainly as much science can be gleaned from unmanned probes, which are also more robust than man in the harsh environment of space. The cost of ejecting humans into space and maintaining them there is exorbitant (e.g., costs of training astronauts, engineering space vehicles and space stations for human habitation, maintaining conditions in space suitable for human life, etc.; together these costs amount to billions of dollars a year in NASA's budget).

What about space stations and planetary bases as alternative human habitats to an increasingly polluted and environmentally disrupted Earth? Here some back-of-the-envelope accounting allows one to reach the simple conclusion that only a handful of people could ever be carried to and installed in a space station or base (and only the extremely wealthy or those supported by the richest governments), while the costs of putting those people in space would easily support an improved environment here on Earth for a large number of inhabitants of all walks of life, including nonhuman. Furthermore, the fuel consumed and pollution produced delivering people to a space station or base would further degrade the environment for the rest of us left behind.

Biosphere 2 has redirected its focus to improving the quality of the environment here on Earth, a move that NASA should consider as well. This is not an argument for a reduction in NASA's budget; rather, it is an argument for a redirection in its expenditures. Unmanned space missions such as the Mars Pathfinder should continue; the potential gains in basic science, technology, and environmental monitoring of Earth are enormous. But in most cases, sending people into space can only be justified with decision based on romance, not logic. We can no longer afford to send humans into space just to captivate Americans into support for NASA. Rather, we should recognize the important scientific gains that unmanned space flight can bring us, particularly with regard to monitoring climate change, tropical deforestation, other land-use changes, and stratospheric ozone depletion here on Earth. As John Allen, one of the founders of Biosphere 2, wrote in his 1991 book *Biosphere 2: The Human Experiment,* "It looked like there might be only a fairly narrow 'window of opportunity' before urgent terrestrial demands completely swamped any prospect of funds being allocated to travel to other worlds." Those urgent terrestrial demands have long ago swamped us, making manned space stations and bases an unnecessary expense. The money could be better spent by NASA improving the quality of the environment on our own space station Earth.■

The author is Assistant Professor in the Department of Earth & Environmental Sciences at Columbia University and is based at the Biosphere 2 Center in Oracle, AZ.

THE U(1) PROBLEM IN CHIRAL RANDOM MATRIX MODELS

Janik RA. Nowak MA. Papp G. Zahed I.
Nuclear Physics B. 498(1-2):313-330, 1997 Aug 4.

We show that conventional asymmetric chiral random matrix models (ChRMM), with a gaussian distribution in the asymmetry, provide for a screening of the topological charge and a resolution of the U(1) problem in the unquenched approximation. Our exact results to order 1/N are in agreement with numerical estimates using large ensembles of asymmetric ChRMM with gaussian distributions.

BCL-2 - PROLONGING LIFE IN A TRANSGENIC MOUSE MODEL OF FAMILIAL AMYOTROPHIC LATERAL SCLEROSIS

Kostic V. Jacksonlewis V. Debilbao F. Duboisdauphin M. Przedborski S.
Science. 277(5325):559-562, 1997 Jul 25.

Mutations in the gene encoding copper/zinc superoxide dismutase enzyme produce an animal model of familial amyotrophic lateral sclerosis (FALS), a fatal disorder characterized by paralysis. Overexpression of the proto-oncogene bcl-2 delayed onset of motor neuron disease and prolonged survival in transgenic mice expressing the FALS-linked mutation in which glycine is substituted by alanine at position 93. it did not, however, alter the duration of the disease. Overexpression of bcl-2 also attenuated the magnitude of spinal cord motor neuron degeneration in the FALS-transgenic mice.

SIMPLIFICATION OF DNA TOPOLOGY BELOW EQUILIBRIUM VALUES BY TYPE II TOPOISOMERASES

Rybenkov VV. Ullsperger C. Vologodskii AV. Cozzarelli NR.
Science. 277(5326):690-693, 1997 Aug 1.

Type II DNA topoisomerases catalyze the interconversion of DNA topoisomers by transporting one DNA segment through another. The steady-state fraction of knotted or catenated DNA molecules produced by prokaryotic and eukaryotic type II topoisomerases was found to be as much as 80 times lower than at thermodynamic equilibrium. These enzymes also yielded a tighter distribution of linking number topoisomers than at equilibrium. Thus, topoisomerases do not merely catalyze passage of randomly juxtaposed DNA segments but control a global property of DNA, its topology. The results imply that type II topoisomerases use the energy of adenosine triphosphate hydrolysis to preferentially remove the topological links that provide barriers to DNA segregation.

A FLUCTUATING CHARGE DENSITY FORMULATION OF THE DIELECTRIC BEHAVIOR OF LIQUIDS - WITH APPLICATIONS TO EQUILIBRIUM AND NONEQUILIBRIUM SOLVATION

Raineri FO. Perng BC. Friedman HL.
Electrochimica Acta. 42(18):2749-2761, 1997.

The usual molecular formulation of the dielectric properties of fluids is based on the equilibrium spatial and temporal fluctuations of the local density of vector dipole moments. In this work we discuss an alternative statistical mechanical theory of the longitudinal dielectric response of liquids comprising molecules with arbitrary shape and charge distribution. The molecules are represented by models comprising interaction sites carrying fluctuating partial charges; in this way the role of the electronic polarizability of the solvent molecules is taken into account. The emphasis of the theory is on the fluctuations of the microscopic charge density at equilibrium. It leads to a compact molecular formulation of the frequency- and wavevector-dependent longitudinal dielectric function of the solvent. It also leads to charge susceptibilities required for the description of the solvent response to a time-varying external charge distribution. The theory provides a simple unified description of the dielectric properties of dipolar as well as "non-dipolar" solvents. In the latter case the solvent molecules lack a permanent dipole moment; the solvent "polarity" originates from the molecular electrical multipoles of higher order that are a consequence of the finite size of the molecular charge distribution. We show that the molecular formulation of the dielectric response is especially useful for the discussion of the energetics and dynamics of the solvation process relevant to electron transfer reactions in solution. Thus we examine the dependence of the solvent reorganization energy on the distance between the donor and acceptor groups in an intramolecular charge transfer reaction in acetonitrile and in benzene. The dynamical theory is illustrated by calculating the solvation time correlation function for Coumarin-153 in acetonitrile.

EXPERIMENTAL ANALYSIS OF FOOD DETECTION IN CAPUCHIN MONKEYS - EFFECTS OF DISTANCE, TRAVEL SPEED, AND RESOURCE SIZE

Janson CH. Dibitetti MS.
Behavioral Ecology & Sociobiology. 41(1):17-24, 1997 Jul.

Knowing how far away animals can detect food has important consequences for understanding their foraging and social behaviors. As part of a broader set of field experiments on primate foraging behavior, we set out artificial feeding platforms (90 x 90 cm or 50 x 50 cm) throughout the home range of one group of 22 brown capuchin monkeys, at sites where they had not seen such platforms previously. Whenever the group approached such a new platform to within 100 m, we recorded the group's direction and speed of approach, and the identity and distance from the platform of the group member that detected the platform or came closest to it without detecting it. We used logistic regression on these data to examine the effects of group movement speed, platform size and height, and focal individual age and sex on the probability of detecting the platform as a function of distance. Likelihood of detecting a platform decreased significantly at greater distances - the probability of detecting a platform reached 0.5 at 41 m from the group's center and 25.5 m from the nearest group member. These results show that detectability of platforms by the entire group (9 adults, 13 juveniles) was less than twice that for single group members. Detectability at a given distance decreased severely as the group moved faster, at their fastest speed, individuals had to approach a platform to within less than 10 m to find it. The large platforms were significantly more likely to be detected than the small ones, suggesting that increased use of larger food patches by wild primates may not necessarily reflect foraging preferences.

COMPUTER SIMULATION OF HYDRATED IONS NEAR A MERCURY ELECTRODE

Eck B. Spohr E.
Electrochimica Acta. 42(18):2779-2788, 1997.

We present previously unpublished results and summarize recent computer simulation studies of the interfaces between water or aqueous solutions and liquid or solid mercury which serve as realistic molecular-level models of the electrochemical interface. Most simulations were performed employing a simple rigid crystal model of mercury. It is first shown that the water structure is not strongly affected by using a more realistic liquid model, thus justifying the simpler approach. Structural, dynamic and thermodynamic properties near the rigid mercury crystal are calculated for Li+, F- and I- ions dissolved in water. The differences between the ions are rationalized on the basis of solvation and steric interactions.

SAPO-11, SAPO-31, AND SAPO-41 MOLECULAR SIEVES - SYNTHESIS, CHARACTERIZATION, AND CATALYTIC PROPERTIES IN N-OCTANE HYDROISOMERIZATION

Meriaudeau P. Tuan VA. Nghiem VT. Lai SY. Hung LN. Naccache C.
Journal of Catalysis. 169(1):55-66, 1997 Jul 1.

Large-pore SAPO-5 and medium-pore SAPO-11, SAPO-31, and SAPO-41 have been synthesized using a hydrothermal method. These catalysts were characterized by chemical analysis, XRD, SEM, IR, TPD of NH3, and MAS NMR; Pt dispersion was measured by Hz adsorption. n-Octane hydroconversion over the Pt-SAPO catalysts has been tested. High selectivity for n-octane isomerization has been observed on medium-pore PtSAPO-11, -31, and -41, while preferential hydrocracking has been found for large-pore Pt-SAPO-5. Isomerization products consisted of monobranched isomers with a negligible amount of dibranched isomers. Interestingly, among the medium-pore SAPOs, SAPO-41 exhibits the highest isomerization selectivity. The selectivity decreases in the order SAPO-41 > SAPO-31 > SAPO-11. The differences in isomerization selectivities of the SAPOs are explained by considering diffusional restriction and steric constraints, SAPO-41 channel dimensions adequately fitting the dimensions of the monobranched isomers.

ESTIMATING EXPOSURE TO METHYLMERCURY - EFFECTS OF UNCERTAINTIES

Lipfert FW.
Water, Air, & Soil Pollution. 97(1-2):119-145, 1997 Jun.

Uncertainties in exposures can lead to biased estimates of slopes and thresholds in the exposure-response relationships that are developed from regression analysis. This paper reviews published exposure and epidemiological studies of methylmercury (MeHg) from the perspective of the accuracy and precision of the estimates used to represent the actual doses received. Sources of such uncertainties, collectively referred to as "exposure errors", include instrumental and analytical errors, sampling and survey uncertainties, and individual variability in the

relationships between the exposure metrics and the actual doses to target organs. Because the relationship between maternal intake and the consequent dose to the fetal brain varies among individuals, epidemiological studies of the effects of prenatal exposure must necessarily be accompanied by larger exposure uncertainties than comparable studies of effects on the mothers. The increased exposure errors typically result in attenuated slopes of the dose-response functions and under-estimates of thresholds, so that part of the apparent increased sensitivity of the fetus that has been developed from epidemiological studies may in fact be due to their inherently less certain exposures. Sources and magnitudes of exposure error found in the literature are discussed and their statistical ramifications are explored with Monte Carlo simulations. The paper also finds that, after adjusting for exposure error, the relationship between dietary intake and blood concentration is consistent with an average half-life shorter than has typically been used and that using population averages yields a consistent but sub-linear relationship between dietary intake of Hg and hair concentration. Investigators are urged to obtain (and present) data on more than one exposure metric, so that their relative uncertainties may be assessed independently.

X-RAY AFTERGLOWS FROM GAMMA-RAY BURSTS

Tavani M.

Astrophysical Journal. 483(2 Part 2):L 87-L 90, 1997 Jul 10.

We consider possible interpretations of the recently detected X-ray afterglow from the gamma-ray burst source GRB 970228. Cosmological and Galactic models of gamma-ray bursts predict different flux and spectral evolution of X-ray afterglows. We show that models based on adiabatic expansion of relativistic forward shocks require very efficient particle energization or postburst reacceleration during the expansion. Cooling neutron star models predict a very distinctive spectral and Aux evolution that can be tested in current X-ray data.

HEMATOLYMPHOPOIETIC AND INFLAMMATORY CYTOKINES IN NEURAL DEVELOPMENT [Review]

Mehler MF. Kessler JA.

Trends in Neurosciences. 20(8):357-365, 1997 Aug.

It is now clear that cytokines traditionally viewed as immune modulators participate in inflammatory responses within the adult nervous system. However, in the developing nervous system hematolymphopoietic cytokines also play a role unrelated to neural-immune interactions. Instead, many of these factors subserve primary regulatory functions related both to the morphogenesis and to the cellular maturation of the central and peripheral nervous systems. This article focuses specifically on cytokine actions in neural development.

CRYSTAL CHEMISTRY OF LUPD2O4 AND OTHER SPINEL-RELATED NDCU2O4-LAPD2O4-TYPE COMPOUNDS

Chen BH. Walker D. Scott BA.

Chemistry of Materials. 9(7):1700-1703, 1997 Jul.

Lutetium palladium oxide (LuPd2O4) has been prepared in a multianvil apparatus at 60 kbar pressure and 1000 degrees C. It crystallizes in the tetragonal LaPd2O4-type structure with space group I4(1)/a, a = 5.681(1) Angstrom, c = 9.881(2) Angstrom, and Z = 4. The structure of this compound, like that of NdCu2O4 and other members of this new class, is closely related to that of spinel except for the difference in oxygen arrangements, leading to a difference in coordination of the A, B, and O ions. It can be derived from spinel by oxygen displacements. A new version of Kugimiya and Steinfink's AB(2)O(4) correlation map in the region 0.04 < K-ab < 0.18 and 0.8 < r(a)/r(b) < 1.7, has been generated. It shows that the new AB(2)O(4) class lies in the area between the spinel- and CaFe2O4-type regions.

PREFERENTIAL EXPRESSION OF KIN, A NUCLEAR PROTEIN BINDING TO CURVED DNA, IN THE NEURONS OF THE ADULT RAT

Araneda S. Angulo J. Touret M.
Sallanonmoulin M. Souchier C. Jouvet M.

Brain Research. 762(1-2):103-113, 1997 Jul 11.

The KIN17 gene product has been identified by cross immunoreactivity with anti-RecA antibodies and by DNA recombination techniques, and is probably part of the DNA recombination-repair machinery. Following Western blotting and immunocytochemistry using anti-RecA antibodies, and in situ hybridization with specific KIN17 cDNA probes, we here report the detection of high levels of KIN protein and KIN17 mRNA in the CNS of adult rats. The RecA cross-reacting protein has an apparent molecular weight of 41 kDa and is located in the nucleus of brain cells. Both the KIN17 transcript and the protein were found to be widespread, but they were present in different proportions, depending on the type of brain cells. High levels of KIN protein were seen in neurons of the motor nuclei of the brainstem, the locus coeruleus, hippocampal formation, entorhinal cortex, Purkinje cells, pyramidal cells of the cortex and mitral cells. In contrast, using a combination of KIN17 mRNA in situ hybridization and GFAP immunocytochemistry (a marker of glial cells) showed that the KIN17 messenger is preferentially transcribed in neurons, the post-mitotic and long lived brain cells. We postulate that KIN17 play a role in the illegitimate recombination of DNA sequences and/or the repair of alterations of the genome in neurons.

STRUCTURE OF NEUTRON-RICH NUCLEI AROUND SN-132

Andreozzi F. Coraggio L. Covello A.
Gargano A. Kuo TTS. Porrino A.

Physical Review C-Nuclear Physics. 56(1):R 16-R 19, 1997 Jul.

Recent studies have provided new experimental information on neutron-rich nuclei around doubly magic Sn-132. We have performed shell-model calculations for the two- and three-proton N=82 isotones Te-134 and I-135 using a realistic effective interaction derived from the Bonn A nucleon-nucleon potential. The results are in remarkably good agreement with the experimental data evidencing the reliability of our realistic effective interaction.

BOTH HIGH- AND LOW VOLTAGE-ACTIVATED CALCIUM CURRENTS CONTRIBUTE TO THE LIGHT-EVOKED RESPONSES OF LUMINOSITY HORIZONTAL CELLS IN THE XENOPUS RETINA

Akopian A. Krizaj D. Witkovsky P.

Brain Research. 762(1-2):121-130, 1997 Jul 11.

We examined the contribution of two intrinsic voltage-dependent calcium channels to the Light-evoked responses of a non-spiking retinal neuron, the horizontal cell (HC). HC's isolated from the Xenopus retina were studied by the whole cell version of the patch clamp. In a mixture of agents which suppressed Na- and K-dependent currents, we identified a transient, low voltage-activated Ca current suppressed by Ba2+ and blocked by Ni2+ (T-type) and a sustained, high voltage-activated, dihydropyridine-sensitive Ca current that was enhanced by Ba2+ (L-type). We made simultaneous intracellular recordings from rods and HC's in the intact, dark-adapted Xenopus retina. Under certain stimulus conditions, transient oscillations appeared in HC responses but were absent in rod light-evoked waveforms. One type of transient was seen at relatively hyperpolarized potentials (< -45 mV), was enhanced by Sr2+ and inhibited by Ni2+. It thus appears to depend on a T-type Ca-current. A second type of oscillation was seen to be superimposed on a prolonged depolarizing wave following light off in the HC and as spike-like depolarizations in rods. These oscillations were enhanced by Ba2+ and Sr2+, but blocked by the dihydropyridine, nifedipine, indicating their dependence on an L-type calcium conductance. All calcium-dependent oscillations were suppressed by 0.05-0.5 mM Co2+. Suppression of glutamate neurotransmission with CNQX or kynurenate, or glycine neurotransmission with strychnine, enhanced the HC oscillations.

DILEPTON AND/OR PHOTON PRODUCTION IN HEAVY ION COLLISIONS AND THE QCD PHASE TRANSITION

Hung CM. Shuryak EV.

Physical Review C-Nuclear Physics. 56(1):453-467, 1997 Jul.

We study the electromagnetic production from highly excited hadronic matter created in heavy ion collisions. The rates include the usual lowest order processes in quark-gluon plasma plus the usual reactions in the hadronic phase, related with rho,a(1) mesons. The space-time integration is done using a hydrodynamical model. Conventional (q) over bar q (pi(+)pi(-)) annihilation in quark-gluon plasma and hadronic phase cannot explain the observed dilepton spectrum, especially that by the CERES experiment at CERN. A decreased rho mass can account for the observed effect, provided it shifts into the region of 0.4-0.5 GeV near the phase transition. In order to test this hypothesis one should also look at the chiral partner of rho, the axial a(1) meson: its mass must then behave similarly. Its decay a(1) --> pi e(+)e(-) populates the low mass region seen in the same experiment. The results for direct photon production are below the current WA80 experimental bounds, for all variants considered.

HUMAN PARVOVIRUS B19 IN BONE MARROWS FROM ADULTS WITH ACQUIRED IMMUNODEFICIENCY SYNDROME - A COMPARATIVE STUDY USING IN SITU

NEW YORK REGIONAL CALENDAR OF SEMINARS

AUG 27-SEP 10

Aug. 27: "Gene Regulation in Immature Lymphocytes: Characterization of Ikaros Complexes and Initiator Elements," Dr. Steve Smale, Dept. of Microbiology and Immunology, Howard Hughes Medical Institute, UCLA School of Medicine, 12:00, Medical Science Building, Room 657, New York University Medical Center

Sep 3: Introductory Meeting, Dept. of Ecology and Evolution, 3:30, Life Sciences Bldg. Rm. 038, SUNY Stony Brook

4: "Structure and Mechanism of T7DNA Helicase," Dr. Smita S. Patel, Ohio State University, 4:00, Dept. of Biochemistry and Cell Biology, Room 038, Life Science Building, SUNY Stony Brook

5: "Atmospheric Wave Coupling in the Middle and Upper Atmosphere," Dr. Marvin Geller, Institute of Terretial and Plantery Atmospheres / Marine Sciences Research Center, SUNY Stony Brook, 12:30, Dept. of Marine Sciences Research Center, 120 Endeavour Hall - South Campus, SUNY Stony Brook

5: "TBA," Dr. Nahum Sonenberg, Dept. of Chemistry, McGill University, 12:00-1:00, Dept. of Molecular Genetics & Microbiology, Room 038, Life Science Building, SUNY Stony Brook

8: "Signaling by SH2-Containing tyrosine phospatases," Dr. Ben Neel, Beth Israel Hospital, 12:00-1:00, Dept. of Molecular Genetics & Microbiology, Room 038, Life Sciences Building, SUNY Stony Brook

8: "Information Representation, Action Potentials, and Neural Computation," John Hopfield, Dept. of Molecular Biology, Princeton University, 12:00, Center for Neural Science, Room 122, 4 Washington Place, New York University

9: "Water permeability of red blood cells in human subjects and in various animal species: studies by several techiques," Dr. Gheorghe Benga, Dept. of Cell and Molecular Biology, University of Cluj Napoca, Romania, 12:00, Rover Physiology Conference Room, P&S 11-505, Dept. of Physiology and Cellular Biophysics, Columbia University

10: "Conceptual and Empirical Approaches to Estimating Interaction Strength in Ecological Communities," Mark Laska, TAMS Consultants, NYC, 3:30, Room 038 Life Science Bldg., SUNY at Stony Brook

SEP 12-19

12: "Multiscale Variability of the Planktonic Fields of the Ocean," Dr. Sergey Piontkovski, Dept. of Marine Sciences Research Center, SUNY Stony Brook, 12:30, Dept. of Marine Sciences Research Center, 120 Endeavour Hall - South Campus, SUNY Stony Brook

15: "Oscar Klein and the Compton Effect," Oscar Klein, 2:10-3:10, Dept. of Theorical Physics, Room 831, Pupin Hall, Columbia University

15: "TBA," Dr. Vinayaka Prasad, Albert Einstein College of Medicine, Dept. of Microbiology & Immunology, 12:00-1:00, Dept. of Molecular Genetics & Microbiology, Room 038, Life Sciences Building, SUNY Stony Brook

16: "Genetic Analysis of Pattern Formation in the Zebrafish Embryo," Dr. William S. Talbot, Developmental Genetics Program, Skirball Institute, Department of Cell Biology, New York University, 12:00, Medical Science Building, Room 657, New York University Medical Center

17: "X Enantioselective Radical Reactions. Dream or Reality?," Prof. Mukund P. Sibi, Dept. of Chemistry, North Dakota State University, 4:00, Dept. of Chemistry, Room 412, Chemistry Building, SUNY Stony Brook

17: TBA, Charles Fox, Insect Evolution & Ecology, Fordham University, 3:30, Rm 038 Life Science Bldg., SUNY Stony Brook

17: "Molecular Mechanisms of Iron Transport," Dr. Marianne Wessling-Resnick, Dept. of Nutrition, Harvard School of Public Health, USB, 12:00-1:00, Dept. of Biochemistry and Cell Biology, Room 038, Life Sciences Building, SUNY Stony Brook

18: "Molecular Photonic Devices from Artifical Photosynthesis: Towards Molecular Internal Procession," Jon Lindsey, Dept. of Chemistry, Univesity of North Carolina, 3:00-5:00, Dept. of Chemistry, Room 1003, Main Building, 31 Washington Pl. 10th Floor, New York Univesity

19: "Pyrite and the Origins of LIfe," Dr. Martin Schoonen, Dept. of Earth and Space Sciences, SUNY Stony Brook, 12:30, Marine Science Research Center, 120 Endeavour Hall - South Campus, SUNY Stony Brook

19: "The World Wide Web and the Academic Medical Enterprise," Second Annual One Day Conference held at NYU Medical Center. For information: 212-263-5295 or http://rcr-www.med.nyu.edu/rcr/web_conf.html

SEP19-29

19: "Electro-Dissection of Neurotransmitter Transporters," Dr. Cela Mager, Dept. of Physiology, University of North Carolina - Chapel Hill, 12:00-1:15, Dept. of Physiology & Biophysics, Floor 21, Room 92, Annenberg Building, Mount Sinai School of Medicine

22: "Cellular Mechanisms of Network Functions in the Mammalian Visual System in Sleep and Waking," David McCormick, Section of Neurobiology, Yale University, 12:00, Room 122, 4 Washington Place, New York University

23: "Personality and Personality Disorders: Conceptualization, Classifications and Measurement," Drew Western, Harvard Medical School, 3:00-4:30, Room 101A, Main Building, 100 Washington Sq. East, New York University

24: "Predicting Long-Term Consequences of Trophic Manipulation in Seasonal Environments: Blending Empirical and Computational Ecology," Oswald Shmitz, Yale University, 3:30, Room 038 Life Sciences Bldg., SUNY Stony Brook

26: "TBA", Dr. Steven Eisenrich, Dept. of Environmental Sciences, Rutgers University, 12:30, Marine Science Research Center, 120 Endeavour Hall - South Campus, SUNY Stony Brook

26: "Functional Expression of Cloned Vertebrate Odor Receptors," Dr. Stuart Firestein, Dept. of Biological Sciences, Columbia University, 12:00-1:15, Dept. of Physiology & Biophysics, Floor 21, Room 92, Annenberg Building, Mount Sinai School of Medicine

26: "Metal Chalcogen Multiplebonds, The Phenonmen of Bond Stretch Isomerism and the Perils of a "Poplar Axis"," Jerald Parkin, Dept. of Chemistry, Columbia Univesity, 3:00-5:00, Dept. of Chemistry, Room 1003, 31 Washington Pl. 10th Floor, New York University

29: TBA (Plant Communities), Deborah Goldberg, University of Michigan, 3:30, Room 038 Life Science Bldg., SUNY Stony Brook

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Publicize your department's seminars & conferences. Send them via mail, fax, or email to the address or fax number on page 4.

HYBRIDIZATION AND IMMUNOHISTOCHEMISTRY

Liu W. Ittmann M. Liu J. Schoentag R. Tierno P. Greco MA. Sidhu G. Nierodzik M. Wieczorek R.

Human Pathology. 28(7):760-766, 1997 Jul.

Human parvovirus B19, which infects and lyses erythroid precursors, can cause severe anemia in patients with immunodeficiency. The incidence of parvovirus infection in adult acquired immunodeficiency syndrome (AIDS) patients is unknown. Eighty-one archival formalin-fixed, paraffin-embedded (FFPE) bone marrow biopsies from 73 AIDS adults were immunostained with monoclonal R92F6 against B19 VP1 and VP2 capsid proteins using streptavidin peroxidase and streptavidin alkaline phosphatase techniques. In addition, the same tissues were hybridized in situ with a digoxigenin-labeled parvovirus B19 DNA probe. Five FFPE bone marrows, from 3 HIV-negative patients with positive immunoglobulin M (IgM) serology for parvovirus B19, and 1 parvovirus B19-infected fetal liver were positive controls. By immunoperoxidase, all tissues were negative with R92F6 except the fetal liver, which exhibited strong positivity predominantly in viral inclusions. With immunoalkaline phosphatase, all positive controls were immunoreactive with R92F6; however, the AIDS marrows were negative. With in situ hybridization (ISH), all positive controls and 7 of 81 (8.6%) of AIDS marrows were positive for B19 parvovirus DNA. We conclude that ISH is more sensitive than R92F6 immunohistochemistry in parvovirus B19 detection. A small but significant number of bone marrows from AIDS adults shows evidence of human parvovirus B19 infection.

FLOW AT BROOKHAVEN AGS ENERGY (11.6 GEV/NUCLEON) - A BAROMETER FOR HIGH DENSITY EFFECTS

Kahana DE. Pang Y. Shuryak E.

Physical Review C-Nuclear Physics. 56(1):481-485, 1997 Jul.

Preliminary data on transverse energy "flow" and event asymmetries reported by the E877(814) Collaborations are compared to ARC (a relativistic cascade) model calculations for Au + Au at full AGS Brookhaven (Alternating Gradient Synchroton) beam energy. ARC triple differential cross sections for protons and pions are presented. Proton flow is produced in ARC, with the maximum (P-x)similar to 120 MeV/c. For central events [P-x] for the pions is near zero, consistent with experiment. The comparison with data provides a constraint on the size of flow at the highest energy available, to be put beside that at Bevalac energy. This sets the stage for examining flow at intermediate energies, now being measured by E895, for signs of baryon rich plasma.

ATHEROSCLEROSIS AND THE MOUSE - A DECADE OF EXPERIENCE [Review]

Plump A.

Annals of Medicine. 29(3):193-198, 1997 Jun.

Atherosclerotic disease is the leading killer in Western societies, accounting for close to 50% of deaths, Relatively little ill known about the genetics of this disease in the general population despite its high prevalence, Several experimental systems exist for studying the pathology of this disease, but these larger animal models fail to offer insights into the genetics. Over the past decade the mouse has supplanted larger animal models of atherosclerosis to become the primary organism for the study of atherosclerosis genetics and, to some extent, pathophysiology, Lipoprotein biologists in particular have benefited from the ability to modify the mouse genetically to study the relationship of lipoprotein abnormalities to atherosclerosis. Given the complexity of the disease an in vivo system is requisite and since the mid-1980s the mouse has served as that system. Initial studies using classical mouse genetics first defined differing susceptibilities to atherosclerosis among distinct strains of mice, These studies acted at least in part to shed preconceptions among lipoprotein and vascular biologists that the mouse could not serve as an atherosclerosis model, Subsequent studies taking advantage of the ability to overexpress and knock genes out have advanced understanding of the in vivo function of genes involved in lipoprotein transport and the relationship between these genes (and their attendant lipoprotein disorders) and atherosclerotic disease, This review chronicles the advances made over the past 10 years and reviews the contribution that the mouse has provided lipoprotein and atherosclerosis research.

EXACT FOUR-SPINON DYNAMICAL CORRELATION FUNCTION OF THE HEISENBERG MODEL

Abada A. Bougourzi AH. Silakhal B.

Nuclear Physics B. 497(3):733-753, 1997 Jul 28.

In this paper we derive the exact expression of the four-spinon contribution to the dynamical correlation function of the spin S = 1/2 anisotropic (XXZ) Heisenberg model in the antiferromagnetic regime. We extensively study its isotropic (XXX) limit and derive perturbatively the Ising one. Our method relies on the quantum affine symmetry of the model, which allows for a systematic diagonalization of the Hamiltonian in the thermodynamic limit and for an exact calculation of matrix elements of local spin operators. In fact, we argue that the familiar criticism of this method related to the complication of these matrix elements is not justified. First, we give, in the form of contour integrals, an exact expression for the n-spinon contribution. After we compile recently found results concerning the two-spinon contribution, we specialize the R-spinon formula to the new case n = 4. Then we give an explicit series representation of this contribution in the isotropic limit. Finally, after we show that this representation is free of divergences, we discuss the Ising limit in which a simple expression is found up to first order in the anisotropy parameter.

THE USE OF ELECTROPHYSIOLOGY FOR THE ASSESSMENT OF DIABETIC NEUROPATHY

Arezzo JC.

Neuroscience Research Communications. 21(1):13-23, 1997 Jul-Aug.

Whole nerve electrophysiology can provide a battery of objective, reliable and specific measures that are sensitive to the progression of diabetic symmetrical polyneuropathy (DSPN). However, under standard conditions, these measures index limited aspects of neural activity, and then only in large diameter, myelinated axons. Nerve conduction is not synonymous with "nerve function." Electrophysiologic measures can be influenced by a variety of factors

with different time courses of action and with different sensitivities to manipulation. The value of whole nerve electrophysiology must be based on a firm appreciation of the strengths and limitations of the procedure.

EVIDENCE FOR QUASI-BIENNIAL OSCILLATIONS IN ZOOPLANKTON BIOMASS IN THE SUBARCTIC PACIFIC

Conversi A. Hameed S.

Journal of Geophysical Research-Oceans. 102(C7):15659-15665, 1997 Jul 15.

To investigate the possibility of climatic influence on the marine biosphere, we analyzed the decadal time series of zooplankton biomass and sea surface temperature (SST) measured at station P, Gulf of Alaska, during the period 1957-1980. A relationship between the two series is not apparent in the raw data. However, Fourier analysis revealed peaks at 28.8 months in both zooplankton and SST spectra. This period belongs to the range of the quasi biennial oscillation (QBO). Such a signal has been found originally in atmospheric and later in physical oceanographic variables. However, it has not been reported previously in biological variables. Cross-spectral and band-pass filter analyses indicate that temperature and zooplankton variations at this frequency may be related. Possible mechanisms are discussed. These results are important because they indicate that a climatic signal, the QBO, is present in the oceanic biota.

ATMOSPHERIC MUON NEUTRINO FRACTION ABOVE 1 GEV

Clark R. Beckerszendy R. Bratton CB. Breault J. Casper D. Dye ST. Gajewski W. Goldhaber M. Haines TJ. Halverson PG. Kielczewska D. Kropp WR. Learned JG. Losecco J. Mcgrew C. Matsuno S. Miller RS. Price L. Reines F. Schultz J. Sobel HW. Stone J. Sulak LR. Svoboda R. Vagins M.

Physical Review Letters. 79(3):345-348, 1997 Jul 21.

A 2.1 ktonyr exposure of data from the Irvine-Michigan-Brookhaven detector has yielded 72 atmospheric neutrino events with a vertex contained inside the fiducial volume and at least 0.95 GeV of visible Cerenkov energy. The ratio of these two ratios (muonlike/total)(Data)/(muonlike/total)(MC) was found to be 1.1(-0.12)(+0.07)(stat) +/- 0.11(syst). The zenith angle dependence of this ratio of ratios is consistent with being flat. The region of sin(2)(2 theta) > 0.5 and delta m(2) > 9.8 x 10(-3) eV(2) has been excluded to the 90% confidence level for nu(mu) --> nu(e) oscillations while the region of sin(2)(2 theta) > 0.7 and delta m(2) > 1.5 X 10(-2) eV(2) has been excluded to the 90% confidence level for nu(mu) --> nu tau oscillations.

ON STRONGLY POLYNOMIAL DUAL SIMPLEX ALGORITHMS FOR THE MAXIMUM FLOW PROBLEM

Goldfarb D. Chen W.

Mathematical Programming. 78(2):159-168, 1997 Aug 1.

Several pivot rules for the dual network simplex algorithm that enable it to solve a maximum flow problem on an n-node, m-arc network in at most 2nm pivots and O(n(2)m) time are presented. These rules are based on the concept of a preflow and depend upon the use of node labels which are either the lengths of a shortest pseudoaugmenting path from those nodes to the sink node or valid underestimates of those lengths. Extended versions of our algorithms are shown to solve an important class of parametric maximum how problems with no increase in the worst-case pivot and time bounds of these algorithms.

MONSOON FLUCTUATIONS OVER THE PAST 350 KYR - HIGH-RESOLUTION EVIDENCE FROM NORTHEAST ASIA NORTHWEST PACIFIC CLIMATE PROXIES (MARINE POLLEN AND RADIOLARIANS)

Heusser L. Morley J.

Quaternary Science Reviews. 16(6):565-581, 1997.

High-resolution analyses of pollen and radiolarians from northwest Pacific cores V28-304 and RC14-99 provide continuous, directly-linked evidence of oceanic-atmospheric climate processes through the past three Pleistocene glacial-interglacial cycles. Systematic fluctuations in marine pollen assemblages, which reflect changes in the forest communities of Japan, are compatible with fluctuations in faunal assemblages and inferred oceanographic properties offshore. Each interglacial has distinguishable characteristics which imply that the sequence, timing and magnitude of climatic change were not identical during the three most recent interglacial intervals. Most interglacials contain at least one 10-15 kyr period of exceptionally high percentages (>20%) of Cryptomeria, which we interpret as reflecting increased levels of precipitation in response to intensification of the summer monsoon. With the exception of Oxygen Isotope Substage 5e in RC14-99. integlacial summer sea-surface temperatures were similar to or slightly warmer than today. Glacial environments in central Japan and in the northern subtropical gyre were similar to those which now support cold-temperate and boreal forests on northernmost Japan and a dominant subpolar fauna and associated low sea-surface temperatures offshore. Climatic change was apparently not as severe in southern Japan (where temperate vegetation largely replaced warm-temperate flora) or in the southern subtropical gyre (where only winter SSTs were cooler than present). We attribute these changes in vegetation and surface-water conditions to shifts in the atmospheric polar and oceanographic subarctic fronts in response to the seasonal variations in the Siberian High. Maxima in Cryptomeria systematically lag maxima in solar insolation at 30 degrees N. This correlation between our summer monsoon indicator and summer insolation substantiates the view that the strength of the Asian monsoon is linked to variations in northern hemisphere solar radiation.

ULTRASTRUCTURAL CHARACTERIZATION OF HUMAN HERPESVIRUS 8 (KAPOSIS-SARCOMA-ASSOCIATED HERPESVIRUS) IN KAPOSIS-SARCOMA LESIONS - ELECTRON MICROSCOPY PERMITS DISTINCTION FROM CYTOMEGALOVIRUS (CMV)

Said JW. Chien K. Tasaka T. Koeffler HP.

Journal of Pathology. 182(3):273-281, 1997 Jul.

Kaposi's sarcoma (KS) has been shown by molecular techniques to be associated with infection with human herpesvirus 8 (HHV8/KSHV), but specific ultrastructural characterization of the virus has been impaired by the frequent presence in these lesions of other herpesviruses, particularly cytomegalovirus (CMV). Since the ultrastructural appearance of HHV8/KSHV has been studied in the cell line KS-1 uninfected with other viruses including CMV, it was possible to undertake a comparative study of CMV and HHV8/KSHV in KS lesions. KHV8/KSHV was sparsely present and lytic infection was restricted to endothelial cells. The following specific ultrastructural features allowed distinction between HHV8/KSHV and CMV: the viral particles were more delicate and less numerous in cases of HHV8/KSHV infection; the viral tegument was more electron-dense in CMV than in KHV8/KSHV; dense bodies characteristic of CMV were absent in HHV/KSHV; complete CMV viral particles were more variable in size and generally larger (150-200 nm) than HHV8/KSHV (120-150 nm); and finally, the viral envelope was more pleomorphic in CMV than in KSHV/HHV8. Similarities between CMV and HHV8/KSHV included the basic structure of the nucleocapsids and the presence of capsids lacking central DNA cores (so-called non-infectious enveloped particles). These observations show that electron microscopy can be used to identify HHV8/KSHV and confirm the relationship between KHV8/KSHV and KS.

MITOCHONDRIAL DNA MUTATIONS AND PATHOGENESIS [Review]

Schon EA. Bonilla E. Dimauro S.

Journal of Bioenergetics & Biomembranes. 29(2):131-149, 1997 Apr.

Approximately three years ago, this journal published a review on the clinical and molecular analysis of mitochondrial encephalomyopathies, with emphasis on defects in mitochondrial DNA (mtDNA). At that time, approximately 30 point mutations associated with a variety of maternally-inherited (or rarely, sporadic) disorders had been described. Since that time, almost twenty new pathogenic mtDNA point mutations have been described, and the pace of discovery of such mutations shows no signs of abating. This accumulating body of data has begun to reveal some patterns that may be relevant to pathogenesis.

IOFFE CURRENT CONSTANT OF THE ROPER RESONANCE FROM A RELATIVISTIC THREE QUARK MODEL

Strobel GL. Shitikova KV.

Physical Review C-Nuclear Physics. 56(1):551-553, 1997 Jul.

The Ioffe current constants for the proton and Roper resonance are evaluated using a linear confining potential model parametrized to reproduce the proton magnetic moment, spin, and energy. The three-body Dirac equation, for the (1/2(+))(3) positive parity configuration, is solved in hypercentral approximation. Quark masses of the order of 9 MeV are needed to reproduce the proton magnetic moment. When the proton rms charge radius and magnetic moment are reproduced, the Roper has an Ioffe coupling constant about 25% larger than the proton.

Stanley Schachter, Social Psychologist at Columbia, 75

Known For Work in Social Determinants of Emotion and Behavior

by Dan Coulter, ASN&R Staff Writer

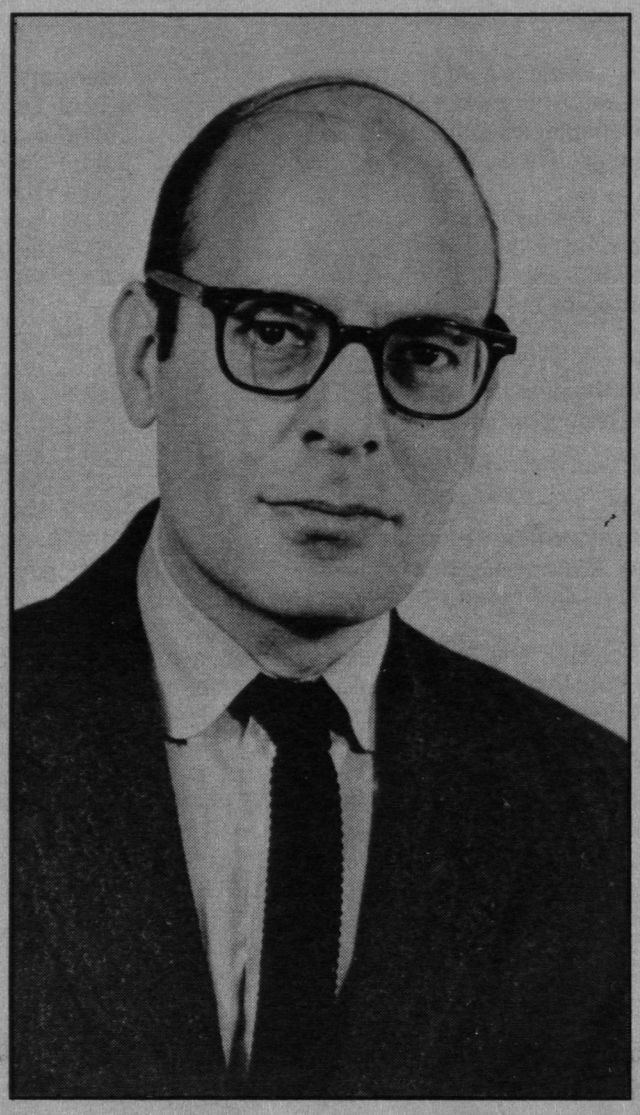
Stanley Schachter, the noted social psychologist at Columbia University whose wide-ranging curiosity brought him to studies of addiction and the emotions, among many other topics, died at home at The Springs, East Hampton, N.Y., on Saturday, June 7. He was 75.

He had suffered from cancer for more than six years, said his son, Elijah. Professor Schachter was internationally known for his work in social l determinants of behavior. His work has had a major impact on current views of emotion and of disorders such as obesity and nicotine addiction.

"One of the most remarkable things about Stanley was the variety of different areas in which he made contributions," said Robert Krauss, professor of psychology at Columbia. "His work ranged from the effects of deviating from a group consensus, to reasons people seek to affiliate with others, to the emotions, to the psychological factors underlying such appetitive behaviors as smoking and obesity, to decision making in the stock market, and most recently, to the sources of speech errors.

"I don't think there was anybody who had as broad a palette or who allowed his imagination to range as freely," Professor Krauss said.

Possibly his best known work was on the emotions. In the late 1950s, he proposed that our emotional experience is a function both of a physiological state and a cognitive interpretation of that state. That approach has had far-reaching impact not only in psychology but also the social sciences as well, Professor Krauss said.



He proposed the phenomenon of misattribution, in which people explain their own feelings and behaviors as the result of some source other than the real one. In one experiment, he gave participants a pill that stimulated them, but told them it would make them itch. When the participants were placed in an emotional situation, they responded with strong emotions because they believed the situation, not a drug, was the cause of the emotion.

He is also remembered for his studies of affiliation, in which he asked under what circumstances humans seek out one another. He was inspired by social comparison theory, proposed by Leon Festinger, his mentor at the University of Michigan, which holds that people understand their own beliefs, feelings and experiences by comparing them to those of others. He concluded that the need for social comparison is an important source of affiliation.

One consequence of the work on affiliation was a powerful set of findings on the effects of birth order, said Julian Hochberg, Centennial Professor Emeritus of Psychology at Columbia.

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Selected Funding Updates

Compiled by Peter M. Saal
Office of the Vice President for Research —SUNY Stony Brook

NSF: REVISED GRANT PROPOSAL GUIDE and PROPOSAL FORMS KIT

NSF has published an updated version of the NSF Grant Proposal Guide (GPG) (NSF 98-2) and Proposal Forms Kit (98-3). This document supersedes the prior version of the GPG (NSF 95-27) and the Proposal Forms Kit (95-28).

The principal purpose of this revision is to incorporate the revised NSF merit review criteria which were disseminated by NSF Important Notice No.121, New Criteria for NSF Proposals, dated July 10, 1997. (See GPG Chapter III.) Other sections have been revised, as appropriate, for clarity as well as to make the Guide consistent with current NSF policies, practices and procedures.

As stated in Important Notice 121, the new merit review criteria for reviewing proposals will be effective for proposals submitted on or after October 1, 1997. For consistency with this requirement, this version of the GPG also will be effective October 1, 1997. After October 1, 1997, the previous version of the GPG should be discarded.

The complete text of the GPG (as well as other NSF policy documents) is available electronically on NSF's home page at www.nsf.gov. In the near future, the GPG (including all forms) also will be available on the NSF home page in both Microsoft Word and HTML formats.

ACLS: Chinese Fellowships for Scholarly Development

CSCC Chinese Fellowships for Scholarly Development are non-degree visiting fellowships for Chinese scholars nominated by a U.S. host. Awards offer modest living allowance, health insurance, international airfare. Tenure: five months between August 1998 and December 1999.

The CSCC China Programs-Chinese Fellowships for Scholarly Development are to support Chinese scholars in the social sciences and humanities with the M.A., Ph.D. or equivalent, from a Chinese institution to carry out one semester of individual or collaborative research at the invitation of a U.S. host scholar. The program is directed in particular at younger scholars for whom a period of research in the U.S. at this time in their careers would enhance their scholarly potential after returning to China. Candidates must be nominated by the U.S. host; Chinese scholars cannot apply directly, and scholars enrolled in degree programs are not eligible. Support is provided for living and modest travel expenses for one semester. The deadline for posting completed applications: **October 31, 1997.** Decisions will be announced in late April, 1998. The U.S. host scholar may request nomination materials by Mail: Office of Fellowships and Grants, ACLS, 228 East 45th Street, New York, NY 10017-3398; Fax: 212-949-8058, or E-mail: grants@acls.org

EPA: Science to Achieve Results (STAR) Program

EPA's Office of Research and Development (ORD) is announcing the first phase of its 1998 Science to Achieve Results (STAR) Grants Program. ORD is requesting applications in three areas: exploratory environmental research; research into genetic and other influences on an individual's susceptibility to disease caused by pollution; and research that could be applied to provide indicators of global climate change. EPA expects that approximately $13 million will be available under this initial phase of the STAR program. Subsequent announcements requesting grant applications in other areas of research are scheduled for September and October. Specific details for the announcement can be found on the Internet at: **www.epa.gov/ncerqa**. The announcement also is available by contacting the National Center for Environmental Research and Quality Assurance at1-800-490-9194.

USDA: Fiscal Year 1998 National Research Initiative Competitive Grants Program

Applications are invited for competitive grant awards in agricultural, forest, and related environmental sciences under the National Research Initiative Competitive Grants Program (NRICGP) administered by the Competitive Research Grants and Awards Management Division, Cooperative State Research, Education, and Extension Service (CSREES), for fiscal year (FY) 1998. Topics and Deadline Dates are as follows:

November 15
22.1 Plant Responses to the Environment.
25.0 Soils and Soil Biology.
26.0 Water Resources Assessment and Protection.
31.0 Human Nutrition for Optimal Health.
51.4 Weed Biology and Management.

December 15
52.1 Plant Genome.
52.2 Plant Genetic Mechanisms.
53.0 Plant Growth and Development.
54.1 Photosynthesis and Respiration.
61.0 Markets and Trade.
62.0 Rural Development.
71.1 Food Characterization/Process/Product Research.
71.2 Non-Food Characterization/Process/Product Research.

January 15
32.0 Ensuring Food Safety.
41.0 Animal Reproductive Efficiency.
44.0 Animal Health and Well-Being.
51.1 Plant Pathology.
51.2 Entomology and Nematology.
51.7 Biologically Based Pest Management.
73.0 Improved Utilization of Wood and Wood Fiber.

February 15
42.0 Animal Growth, Development, and Nutrient Utilization.
43.0 Animal Genetic Mechanisms and Gene Mapping.
54.2 Nitrogen Fixation/Nitrogen Metabolism.
80.1 Research Career Enhancement Awards.
80.2 Equipment Grants.
80.3 Seed Grants.
100.0 Agricultural Systems.

The solicitation, which contains research topic descriptions, and the NRICGP Application Kit, which contains detailed instructions on how to apply and the requisite forms, may be obtained by writing or calling: Proposal Services Unit, Grants Management Branch, Office of Extramural Programs, Cooperative State Research, Education, and Extension Service, U.S. Department of Agriculture, STOP 2245, 1400 Independence Ave., SW., Washington, DC 20250-2245, Telephone: (202) 401-5048.

Requests for solicitations and application materials may also now be made via Internet by sending a message with your name, complete mailing address, (not e-mail), phone number, and materials that you are requesting to psb@reeusda.gov. Materials will be mailed to you (not e- mailed) as quickly as possible. The program description, application kit and abstracts of funded research are also available on the NRICGP Home Page on the Internet (www.reeusda.gov/nri).

Federal Highway Administration: Dwight D. Eisenhower Transportation Fellowship Program

Awards fellowships to undergraduate and graduate students, and faculty members in fields directly related to transportation. Durations range from three to twelve months and provide stipends which include tuition support during the fellowship. Contact: Dr. Ilene Payne, Director; 703-235-0538. Deadline: 10/15/1997

National Security Agency

Senior Investigators Grant for Research in Mathematics and Cryptology: support is provided to nonprofit institutions on behalf of senior mathematical scientists to conduct mathematics research in the areas of algebra, number theory, discrete mathematics, probability, statistics, and cryptology. Funds may be requested to support graduate students, and for travel, workshops, and equipment, for up to two months during the summer.

Standard Grants for Research in Mathematics and Cryptology: standard grants are provided to nonprofit institutions on behalf of principal investigators for no more than one month of summer salary each year for mathematics and cryptology research. Funds may be used for salary support, graduate students and postgraduate research assistants, workshops, and certain equipment purchases.

Young Investigators Grant for Research in Mathematics and Cryptology: support is provided to nonprofit institutions on behalf of young, promising investigators to conduct mathematics and cryptology research. Awards of $13,000 each provide two months summer salary each year for two years. In addition, proposals may also ask for graduate student support, not to exceed $5,000 per student per year, as well as limited funds for computer equipment.

Contact: Dr. Charles F. Osgood, Director; 301-688-0400. Deadline: 10/15/1997

Naval Surface Warfare Center: BAA 97-01

The Naval Surface Warfare Center, Dahlgren Division, Coastal Systems Station (COASTSYSTA) conducts research and development of techniques and technologies directed toward operations in a littoral environment. The COASTSYSTA is interested in receiving proposals for research and development in all of its mission areas. It is intended that this BAA be open for a period of two years from the date of publication.

Specific areas of interest include, but are not limited to: (1) environmental data collection, monitoring, analysis, or display; (2) multifunction underwater sensing designs and technology; (3) image and sensor data processing; (4) modeling and sim-

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What's Next For BNL's Main Research Reactor?

Two Sides Square Off; Decision Expected Early Next Year

by Kathryn Gavin

After a roller coaster ride of a year that has seen the High Flux Beam Reactor at Brookhaven National Laboratory go from world-class scientific facility to demonized symbol of the Lab's environmental woes, the ultimate fate of the 32-year-old research reactor will soon be decided.

Both scientists and Long Island residents are being given a chance to have their say about the future of the HFBR, which remains off-line following the January discovery of radioactive groundwater contamination near its dome-shaped building.

Their input, as well as cost considerations, will be delivered to U.S. Secretary of Energy Federico Peña before he decides in early 1998 if the facility will once again produce neutron beams for use by physicists, chemists, materials scientists and structural biologists, or if it will shut down for good. Over 250 scientists from 11 New York universities and labs, and 84 other institutions worldwide, used the HFBR in 1996.

Anti-nuclear activists have already made clear their desire to shutter the facility permanently, while some local elected officials, including Congressman Michael Forbes, have stated their conditional support for restarting it.

Meanwhile, a nationwide panel of scientists charged with assessing the HFBR's scientific worth, and the impact on the scientific community if it does not restart, met in Maryland in late July to begin formulating its official position.

And the public's first formal chance to learn about the HFBR and comment on its future, held on August 14 at a local library, drew media, Lab neighbors and a handful of scientists from BNL and SUNY Stony Brook. Several more such events have been planned, and the Lab is offering to send speakers to any local group or class that wants to hear more about the HFBR.

After hearing from all these voices, Peña has two choices: shut down the HFBR for good or work toward continuing its operation by conducting new environmental and safety studies and performing environmental upgrades, a process that could take up to two years. If the latter option is chosen, it could allow the HFBR to begin operating again with a boost in power level, resulting in 50 percent more neutrons for scientific users.

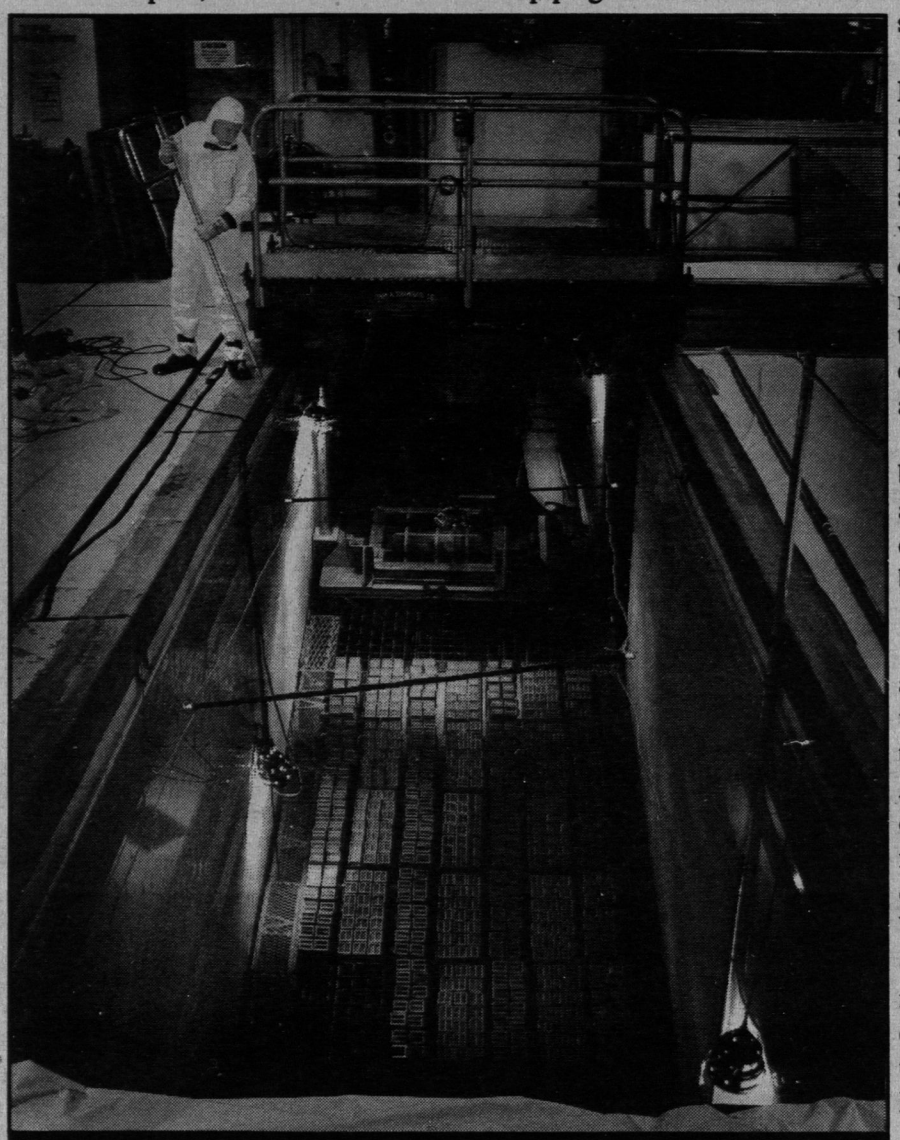
Trouble Beneath the Dome

Officials in the U.S. Department of Energy, which owns BNL and funds its assortment of large research facilities, have not allowed the HFBR to restart ever since the discovery in January of radioactive tritium in groundwater south of the reactor building.

Intense exploration of groundwater in the immediate vicinity revealed a contamination plume that extends a few thousand feet south of the HFBR under the Lab site and contains a total of about 5 curies of tritium — roughly equal to one-quarter the amout used in self-illuminating "exit" signs. No drinking water, either on or off the Lab campus, has been contaminated, and local health and environmental officials have had to reassure a concerned community that the leak does not pose a health threat.

Even as the HFBR's fate hangs in the balance, the contaminated groundwater is being pumped out of the ground at its southernmost point and recycled northward to a recharge basin to prevent it from leaving the Lab site.

Meanwhile, the contamination's source — a 68,000-gallon pool in the building's basement used to hold spent reactor fuel — is now being emptied of its contents so that a slow leak can be repaired and a leak-monitoring system installed. The upgrade to the pool, and similar renovations to piping and floors in the reactor building, are intended to bring the HFBR into compliance with Suffolk County's Article 12, one of the strictest groundwater-protection laws in the country.



The spent reactor fuel pool at the HFBR — source of recent controversy. (Photo: BNL)

Despite the rapid response, the damage to BNL's reputation, and the scientific community that had sprung up around the use of the HFBR, has been done. Many scientists who have used the reactor have been forced to seek beam time at the nation's only two other comparable research reactors, at Oak Ridge National Laboratory in Tennessee and the National Institute of Standards and Technology in Maryland.

DOE's Basic Energy Sciences Advisory Committee, or BESAC, is examining the potential effect on science if that kind of shuffling had to be done on a permanent basis. Their findings, and a recommendation on the HFBR's future, are due October 1.

BNL's other research reactor, the three-megawatt Brookhaven Medical Research Reactor, is much less powerful than the HFBR. It is largely used for clinical trials of an experimental brain tumor therapy in conjunction with the University Medical Center at Stony Brook and the Beth Israel Medical Center.

Science on Hold

Before the shutdown, the HFBR had a history of providing neutrons to scientists in many fields of study, from solid-state physics, materials science and surface chemistry to nuclear medicine, structural biology and even archaeology.

The subatomic particles produced in the reactor's uranium-235 core were used in both neutron-scattering experiments, which diffracted neutron beams off crystal samples to determine atomic-level characteristics of proteins, ceramics, polymers and other substances, and in irradiation experiments that lowered samples directly into the HFBR core and allowed radio-decay dating of archaeological artifacts and structural studies of materials.

The facility complements another of BNL's large research machines, the National Synchrotron Light Source, because neutrons from the HFBR can reveal the position of a sample's light atoms, such as hydrogen, which the NSLS's X-ray and UV light beams cannot. Studies of superconductivity and magnetism at the HFBR have also drawn on the unique properties of neutrons, which essentially act as tiny magnets while passing an atom's nucleus.

All that research is now on hold or being done elsewhere, from studies of an antigen found on the surface of the Lyme disease bacteria to analyses of polymers being developed to clean up oil spills.

The Sides Square Off

At the same time, anti-nuclear activists are gearing up for a fight the likes of which they have not seen since the demise of the Shoreham nuclear power plant. At the August 14 information session, they handed out flyers publicizing a Labor Day protest in front of the Lab's entrance, and a civil disobedience at DOE headquarters in Washington D.C. in late September.

Many of their claims against the reactor allege it gives off cancer-causing emissions, though BNL and DOE report that the HFBR emits far less than permitted by Environmental Protection Agency emissions standards for air and water. Other allegations describe horrific consequences in the case of an accident at the HFBR, despite conservatively calculated risk analyses that BNL and DOE believe show otherwise.

As the two sides square off, the battle for the HFBR's future will be fought in the middle ground, where both parties will be competing for the attention and sentiments of community members who may not know more about the HFBR than what they heard, saw and read during the months of the tritium saga.

Toward that end, BNL and DOE are offering to send speakers to any local group, class or organization that wants to hear about the HFBR, and will open the HFBR's doors on several occasions for tours. Independent groups, such as the Long Island Progressive Coalition, the Long Island Alliance for Peaceful Alternatives and Physicians for Social Responsibility, have hosted or are planning their own events to discuss the HFBR's pros and cons.

The next few months promise to be another roller coaster ride for the HFBR, the scientists who use it, the activists who oppose it and the community around it. None of them knows if it will be a smooth glide, a jarring derailment or another round of ups and downs for one of the nation's largest research facilities.■

To request a speaker for your organization or class, or to find out about upcoming events or tours related to the HFBR, call (516) 344-2345. To ask a question or give a comment, e-mail tellDOE@bnl.gov or write to Frank Crescenzo, DOE Brookhaven Group, Bldg. 464, PO Box 5000, Upton NY 11973.

Boxers.. Continued from Page 1

aggravated by the APOE gene were those who had the possibility of Parkinson's or actual Alzheimer's, or who had a history of alcohol abuse that might aggravate dementia.

The boxers, whose behavior and motor skills ranged from normal to severely impaired, were ranked from 0 (normal motor/sensory/behavioral characteristics) to 4 (severe impairment). The boxers' social and psychiatric history was also tabulated as a contributing factor — whether they used drugs and alcohol, how much, and if they had any history of psychiatric or medical problems.

One boxer, for example, had developed schizophrenia before becoming a boxer; another had suffered a concussion in a car accident.

The boxers' DNA was extracted and sent to a laboratory anonymously to isolate the APOE4 gene. These tests revealed that nineteen of the thirty boxers were homozygous for the APOE gene, and of the 12 boxers who were classified as "probably" suffering from CTBI, half had various types of APOE. The three boxers who exhibited very severe CTBI had at least one copy of the APOE gene.

"The results of this preliminary investigation," the report concludes, "suggest that the APOE e4 allele may predispose a boxer to developing CTBI, especially in those with high exposure to the sport." Race seemed to have little to do with the susceptibility to CTBI or to carrying the gene, although the report cautioned that the results may be somewhat biased because of the "self-selection" inevitable when people volunteer for a particular study.

"We don't know the mechanism that causes it [CTBI]," says Dr. Norman Relkin, who co-authored the study and who is an associate professor of Neurology and Neuroscience at New York Hospital at Cornell Medical Center. "There are two theories. One is the 'plasticity theory', where it's thought that APOE may influence the efficiency of CTBI after injury. The other is that APOE has a specific effect on the protein, beta-amyloid, which is also present in people with Alzheimer's, or on another element called the tangle."

In Alzheimer's patients, the beta amyloid protein is deposited in a neurofibrillary tangle, where the nerve cells have an irregular cytoskeleton, or supporting architecture.

Relkin commented that the dementia surfaced in boxers of all ages and, that unlike Alzheimer's, it doesn't necessarily manifest only in older people. "Astoundingly, some boxers were quite profoundly demented in their thirties. Our suspicion is that the possession of APOE will influence the age of the onset of the disease."

The other authors of the study include Barry Jordan, MD, MPH; Lisa D.Ravdin, PhD; Alan R. Jacobs, MD; Alexandre Bennett, PhD; and Sam Gandy, MD, PhD.■

Helicon... Continued from Page 8

show fairly intact non-declarative memory, even though their declarative memory goes more quickly. So for patients experiencing early stages of a neurodegenerative disease, the types of drugs that Helicon might find — based on using CREB as the initial target — will not be a cure for Alzheimer's but rather a therapy."

This therapeutic method will focus on increasing functionality of remaining neurons. "We hope to tweak the long term memory switch with a drug, and essentially turn up the gain of information converted to long term memory. If 20% of your neurons in the hippocampus are gone because of Alzheimer's disease, you can turn up the gain on the remaining 80% as a therapy for memory loss that is occurring during this neurodegenerative disease," said Tully.

Dr. Yin adds : "By targeting CREB, we're dealing with the bit components in neurons — the molecules that really underlie neuronal growth and structural change. And the feeling is that these CREB molecules affect growth and structural change in all neurons. This is how neurons work - its the building blocks. It looks like the CREB molecule participates in the very logic that all neurons use regardless of the anatomical location in the brain."

Another long-range goal for Helicon is to identify new classes of memory dysfunction where a CREB gene is mutated and inherited like the APP gene implicated in Alzheimer's. By focusing on CREB and its downstream genes as the central mechanism of the memory switch, the team feels it could begin to identify patient populations that suffer memory loss through such inherited mutated genes.

"Not only is there potentially a general therapy for neurodegenerative diseases, there's also the opportunity to identify new types of memory loss with a biological basis that comes from CREB and its downstream genes," said Dr. Tully. "And the economic impact is tremendous, the longer you can delay patients suffering neurodegenerative diseases from being admitted into nursing homes for supervised care. Society could save a lot of money even if admissions were delayed by two years. Helicon intends to develop therapeutic drugs that will do just that," concludes Tully.■

– Funding Updates –

Continued from Page 16

ulation; (5) innovative conventional and non-conventional MCM, amphibious warfare, naval mining, diving or special warfare techniques (and systems) for application in all phases of the battle timeline including surveillance, targeting, acquisition, and terminal phases; (6) shipboard MCM system modular integration concepts; (7) innovative and non conventional concepts for application of technology, engineering and systems to all phases of coastal operations and coastal warfare; (8) lasers, radar, millimeter wave, or other high energy sensor/weapon; (9)communications and data transmission of any type; (10) concepts and systems for remote control of sea mines; (11) remotely controlled vehicles: air, surface, sea surface, or undersea; (12) information processing, fusion, and display.

White papers should be no more than 5-7 pages in length. White papers (and any resulting proposals) will be evaluated using the following evaluation criteria: (1) Overall scientific, technical, and socio-economic merits of the proposed effort; (2) Potential naval relevance and contributions of the effort to the COASTSYSTSA's specific mission areas; (3) Degree to which new and creative solutions to technical issues important to COASTSYSTA programs are proposed as well as the degree to which technical data and/or computer software developed under the proposed effort are to be delivered to the COASTSYSTA with unrestricted rights; (4) The offeror's capabilities, related experience, facilities, techniques or unique combinations of these which are integral factors for achieving the proposal objectives; (5) The qualifications, capabilities and experience of the proposed Principal Investigator, team leader or key personnel who are critical in achieving the proposal objectives; (6) Realism of the proposed cost and the availability of funds. Based on evaluation of the White papers, participants may be selected and invited to submit full technical and cost proposals for evaluation by the COASTSYSTA using the above noted evaluation criteria. Point of Contact for White Papers and Proposals: John Miller, Contract Specialist, COASTSYSTA Dahlgren Division, NSWCDD, 6703 West Highway 98, Panama City, FL 32407-7001. Telephone: 850-235-5399. For details on white paper submission, contact Peter Saal at ext. 2-9033, or consult the 08/12/97 issue of Commerce Business Daily.

NSF/BIO: Doctoral Dissertation Improvement Grants

Doctoral Dissertation Improvement Grants support research in the biological sciences. Proposals whose focus is ecological, evolutionary, or behavioral and proposals to develop or exploit unique instrumental, informational or computational resources for biological research are eligible. Grants are typically awarded for 24 months and for amounts that range from $3,000 to $10,000. Contact telephone: 703-306-1400. Deadline:10/10/1997. (Ref: 96-132)

Am. Diabetes Association: Mentor-Based Postdoctoral Fellowship Program

Provides up to $30,000 per year for three years to support the training of scientists beginning a career in diabetes research. Awards are given to established investigators for the support of a postdoctoral fellow. Applicant investigators must hold appointments at U.S. university-affiliated institutions, and fellows must hold an M.D. or Ph.D. Contact telephone: 703-549-1500 x2376. Deadline: 10/01/1997

Leukemia Society of America, Inc.

Support for research toward a cure or control of leukemia, lymphomas, Hodgkin's disease, and multiple myeloma.

LSA Fellow Grants: grants of $30,250 per year for a three-year term Eligible applicants are promising investigators with less than two years of postdoctoral research training at the time of application. Application may be made for Special Fellow status in the third year of this award.

LSA Scholar Grants: grants of $54,000 per year for a five-year term. Awards are usually provided to independent faculty-level individuals in clinical/basic science departments of universities/associated research institutes who have competed successfully for research grants, and have completed at least five years of postdoctoral research.

LSA Special Fellow Grants: grants of $36,700 per year for a three-year term. Eligible applicants are scientists with at least two years of postdoctoral training at the time of application and are continuing their research training under the direction of a research sponsor.

Contact: Director of Research Administration; 212-450-8843. Deadlines: 10/01/1997

S.L.E. Foundation: Lupus Research

The S.L.E. Foundation, Inc., invites applications for financial support starting July 1998 for Research Projects relevant to Lupus Erythematosus, for Career Development Awards for young investigators interested in lupus research, and for Fellowship training in SLE and related disorders.

Research applications will be judged principally on the scientific quality, the qualifications of the investigators and the facilities available. Special attention will be paid to the proposal's relevance to lupus. Additional factors that will be considered are the institutional distribution of awards and appropriateness of the proposed budget. Career Development Awards will be evaluated primarily for the commitment of the individual to lupus research and his/her potential for an independent investigative career. Fellowship applications will be judged on similar grounds where relevant and, in addition, on the quality of the proposed training program.

Applicants should hold advanced degrees and be affiliated with institutions of higher learning. Annual funding of approved **Research Grant projects** will not exceed $50,000 per year; awarded for a term of up to three years. The **Career Development Award** is $50,000 annually for a term of up to three years. The annual **Fellowship** stipend is $20,000; fellowship grants are awarded for a term of one year.

Additional information and instructions for making application may be requested by sending a 9X12 manila envelope, stamped ($.78) and self-addressed to The S.L.E. Foundation, Inc., Grants Division, 149 Madison Avenue, New York, NY 10016. Telephone: 212-685-4118. Deadline for receipt of completed applications for Research Grants, Career Development Awards and Fellowships is **December 12,1997.**

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ALS... Continued from Page 5

ALS cases because the diseases are so clinically similar. Most ALS patients may not have faulty SOD protein, but they probably do suffer from excessive oxidative stress.

In other systems, free radical damage had been shown to induce cells to undergo PCD. Many in the ALS field, including Dr. Przedborski, began to investigate whether this might be true in ALS as well — whether the oxidative stress that now seemed to be at the heart of all ALS cases might kill cells by apoptosis.

Before long, experiments by Dr. Przedborski and others had shown that, in vitro, cells with the SOD mutation die by apoptosis more easily and at a higher rate than normal cells. These cell culture experiments showed that apoptosis was at least a possibility as a cause for neuronal death in ALS. To test whether it actually is a cause, Dr. Przedborski's group designed an experiment that asked if blockade of PCD was capable of affecting the course of disease or the survival of neurons in ALS-afflicted mice. As a blocker of PCD they chose Bcl-2, the prototypical anti-apoptotic protein. They obtained two transgenic mouse lines: One expressed several extra copies of Bcl-2 under the control of a neuron-specific gene promoter, while the other expressed several copies of the mutant SOD gene that causes FALS in humans. These SOD- mutant mice provide the best animal model of ALS yet produced, according to Dr. Przedborski — they develop an adult-onset neurodegenerative disease that resembles ALS very closely in its neuropathology and in its progression. By mating the two lines with each other, the researchers produced FALS-afflicted mice that overexpress Bcl-2 solely in the central nervous system. They then compared these FALS/Bcl-2 mice with FALS mice lacking the Bcl-2 transgene.

What they found was that these FALS/Bcl-2 mice were not spared from the disease — they still manifested all the clinical and pathological symptoms that afflict normal FALS mice. The duration of disease was not affected either — mice from both groups died about 70 days after first showing symptoms. However, the onset of symptoms was delayed significantly in comparison to FALS mice without the Bcl- 2 transgene. Mice possessing only the FALS gene first showed symptoms of the disease at about 6 months of age, on average; FALS/Bcl-2 mice, by contrast, came down with the disease an average of one month later. This amounts to a 19% increase in the time before disease sets in. The researchers also examined spinal tissue from the two strains of mice and found that the later onset of symptoms in FALS/Bcl-2 mice seemed to result from either a later onset or a slower rate of cell loss. Apparently, the FALS/Bcl-2 mice fared better because Bcl-2 was actually able to prevent cell death, at least for a while. Once degeneration began, however, Bcl-2 was powerless to stop it.

Although Bcl-2 did not turn out to be a magic bullet, Dr. Przedborski said, the results of this experiment are still important. The fact that Bcl-2 was able to interfere, if only temporarily, with the progression of the disease and the death of neurons provides strong evidence that apoptosis does play a role in ALS. "If apoptosis was not involved, we would not expect to see any effect" from an anti-apoptotic treatment like Bcl-2, Dr. Przedborski said. "But there was an effect, which means that, for the first time, we understand something about the mechanism of neuronal death in ALS and we have a potential way of interfering with it."

However, this experiment raises several nagging questions. Why, for example, does Bcl-2 eventually lose its battle to save the dying cells? If apoptosis is occurring, shouldn't the anti-apoptosis gene protect the cells indefinitely? One possible explanation for this result, Dr. Przedborski said, is that the transgenic Bcl-2 mouse simply does not express enough copies of the gene to protect cells sufficiently. People looking into how Bcl-2 works, Dr. Przedborski explained, have shown that, in general, "the more Bcl-2 you have, the more protection you have." Perhaps, then, a higher level of Bcl-2 expression would have succeeded in blocking death. "Another possibility," Dr. Przedborski said, "is that there's another form of cell death occurring that Bcl-2 can't prevent." In that case, anti- apoptosis therapy would be useful solely as a way of staving off ALS symptoms — it could never be a cure.

The experiment also leaves open the question of how and why the PCD pathway gets activated in ALS-afflicted neurons. Presumably a reduction in protection from free radicals is the initial cause, but, beyond this, little is known. According to Dr. Przedborski, there has been an aggressive search, ever since the FALS-causing SOD mutant was identified, for an explanation of exactly how this mutation causes cells to die.

Researchers have documented several abnormal intracellular pathways activated by the mutant protein, but no one has yet worked out how these pathways lead to death. There is clearly a lot of complicated cell biology between the starting point of ALS pathology and the final induction of neuronal death, and it may take years to work it all out. In this way, Dr. Przedborski said, ALS is similar to other neurodegenerative diseases like Parkinson's and Alzheimer's — in all these conditions, the initial source of pathology does not directly damage cells; rather, it sets up a complex network of intracellular interactions that somehow leads to death. Although researchers have discovered a variety of differences between diseased cells and normal ones, they have had great difficulty determining exactly how these differences cause cells to die.

The Columbia group's results are interesting because they in effect dodge the issue of how ALS kills cells, yet they still suggest a way to treat the disease. The experiment zeroes in on the ultimate mechanism of cell death, without worrying about the initial causes that are still so poorly understood. And when the aim is therapy, Dr. Przedborski emphasized, it is enough to understand only small parts of the disease process, as long as you can successfully interfere with them.

Several different ways of interfering with PCD are known. One possibility would be to treat ALS patients with Bcl-2 itself. That is unlikely to work, however, because Bcl-2 is such a big protein — "how do you get it across the blood-brain barrier?" Dr. Przedborski asked; "How do you get it into all the motor neurons?" — a task that would be next to impossible.

Another, more plausible treatment would target a class of proteins known as caspases, which are activated late in the signaling pathway that leads to PCD. Bcl-2 is known to inhibit cell death partly by inhibiting the activity of caspases. "There are small peptides that can inhibit caspases," Dr. Przedborski said; "they are only a few amino acids in length." These small molecules would be far more practical as drugs than Bcl-2. Already, a group at Harvard Medical School, headed by Dr. Robert Brown, Jr., has tested the efficacy of a small-peptide caspase inhibitor against the SOD-mutant mouse model of FALS. Their results, reported in preliminary form in the journal *Nature,* showed that the duration of disease, but not the time to onset, was extended by caspase inhibition. Of course, the actual development of human drugs based on this research is still years away. But the results of Dr. Przedborski's group, in conjunction with those of the Harvard group, make anti-apoptosis therapy look like a very promising potential treatment for ALS.

Dr. Przedborski also believes that his results might have implications not just for ALS patients, but for victims of neurodegenerative diseases in general. His lab has been working on both ALS and Parkinson's disease, testing the hypothesis that, although the clinical conditions are very different in these and other neurodegenerative diseases like Alzheimer's, the mechanisms of cell death might be shared.

"If you discover the mechanism that ultimately leads to death of neurons in one disease," he said, "it's tempting to believe these mechanisms will be involved in others." Why should such different diseases processes end with a common cell death mechanism? Dr. Przedborski and his colleagues reasoned that, since each of these diseases involves abnormal activation of a variety of cell biological processes, it is possible that the PCD pathway is among those processes that becomes accidentally triggered. If this turned out to be true, it would mean that all the diseases could be treated by attacking their common endpoint — there would be no need to laboriously unravel the knot of complex cell biology that leads to death in each different disease.

The finding that ALS seems to involve apoptotic cell death may well be a hint that PCD is an important part of these other diseases, but this is not necessarily so. The data implicating PCD in other diseases is still inconclusive, and, particularly in the Alzheimer's field, the potential role of apoptosis is the source of much controversy. More evidence about the role of apoptosis in Parkinson's and Alzheimer's will be necessary if Dr. Przedborski's notion is to be proven correct. Already, he and his lab are hard at work on the problem.

Even if PCD does not turn out to be the answer for other diseases, the recent report certainly is very important for the ALS field. Dr. Przedborski's results are only one part of what has been an explosion of hopeful news about ALS in recent years. The discovery of the SOD mutation and the development of a mouse model of ALS gives researchers, for the first time, a powerful tool to explore the causes of the disease. A detailed knowledge of what makes things go wrong inside these motor neurons might one day lead to a way to prevent ALS. On the therapy side, the FDA only last year approved the first drug designed to treat ALS, an inhibitor of glutamate-mediated cytotoxicity called rituzole, and it is currently considering several new treatments.

There is hope that neurotrophic factors, substances that encourage the growth and survival of neurons, might make an effective treatment, and the efficacy of antioxidant molecules such as vitamin E are being tested. In combination with these other therapeutic approaches, anti-apoptosis treatment might participate in a multi-faceted attack on ALS. Perhaps, some day soon, this approach will allow doctors to extend life, preserve quality of life, and possibly even provide a cure for ALS patients.■

Schachter... Continued from Page 15

The more anxious the subjects, the more they want to be with other people, a tendency particularly marked for first-born and only children, a finding that he applied to a great number of behaviors, such as fighter pilot effectiveness, alcoholism and receptiveness to psychotherapy.

"He was a brilliant experimentalist," Professor Krauss said. "In many ways, he was the virtuoso of the experiment. His experiments were simple, involving and incisive."

In a 1968 study of obesity, widely reported in the press, he found that obese people are prompted to eat by "external" cues unrelated to physical hunger, such as the immediate presence of food, surroundings, time of day and strong emotions, for example. And in a 1978 study, he showed that cigarette smokers are physiologically addicted to nicotine, and that when they switch to lower-nicotine brands, they smoke more to prevent symptoms of nicotine withdrawal.

He worked with Donald Hood, James F. Bender Professor of Psychology at Columbia, to "bring the individual back into the stock market," showing that market fluctuations could be traced to the psychology of individual participants. Greed and fear move the market, not efficiency, as many economists had proposed, Professors Hood and Schachter said. With tongue in cheek, Professor Schachter unveiled "bubbe psychology," after the Yiddish for "grandmother" at his 1981 University Lecture at Columbia. Any grandmother, he proposed, could outpredict an economist because she knows that people are not coldly rational about investing their money. "Bubbe psychology" was the topic of a front-page story in the Wall Street Journal.

His books were titled: "Social Pressures in Informal Groups" (1950) with Festinger and others; "Theory and Experiment in Social Communication" (1950) with Festinger and others; "When Prophecy Fails" (1956) with Festinger and Henry Riecken; "The Psychology of Affiliation" (1959), "Emotion, Obesity and Crime" (1971) and "Obese Humans and Rats" (1974), co-authored with a former student, Judith Rodin, now president of the University of Pennsylvania.

Professor Schachter was born in New York City in 1922 and received the B.S. and M.A. from Yale University in 1942 and 1944 respectively. From 1944 to 1946, he was a sergeant in the U.S. Air Force working on visual problems in the Biophysics Division of the Aero-Medical Laboratory at Wright Field. He returned to his graduate studies at MIT's Research Center for Group Dynamics, and, when that center moved to the University of Michigan, followed, receiving his Ph.D. in social psychology in 1949.

He was named assistant professor of psychology at the University of Minnesota in 1949 and taught there until 1952. After spending two years studying and conducting research in Amsterdam and Oslo, Professor Schachter returned to the University of Minnesota as associate professor in 1954. From 1954 to 1958, while research director of the Organization for Comparative Social Research at the University of Minnesota, he was also visiting professor at the University of Amsterdam and at Stanford. He was made full professor in 1959 and joined the Columbia faculty as professor of psychology in 1961.

Professor Schachter was elected to the American Academy of Arts and Sciences in 1976 and to the National Academy of Sciences in 1983, and was the recipient of Fulbright and Guggenheim fellowships. He was named Robert Johnston Niven Professor of Social Psychology in 1966 and retired in 1992 with an emeritus designation.

He was honored with numerous prizes and awards, including the James McKeen Cattell Award, the American Association for the Advancement of Science's Social-Psychological Prize, the General Electric Foundation Award (three times), the American Psychological Association Distinguished Scientific Contribution Award, and the Society for Experimental Social Psychology's Distinguished Scientist Award.

He was a significant teacher and mentor, and the generation of social psychologists who were his students are now the dominant figures in the field, Professor Krauss said.

He is survived by his wife, the former Sophia Duckworth, a consultant on historic preservation. They were married in 1967. Elijah, their only son, was born in 1969. Professor Schachter's wife and son reside in New York City. There are no other survivors.■

Continued from Page 19

Life Sciences Research Foundation: Postdoctoral Fellowships in the Life Sciences

Postdoctoral fellowships are offered to foreign scientists to study in the U.S, and to U.S. scientists to study at any nonprofit laboratory, in any field of the life sciences. Awards provide $35,000 per year for three years. Eligible applicants should hold M.D. or Ph.D. degrees. Contact: Susan DiRenzo, Assistant Director; 609-258-3551. Deadline: 10/01/1997

Skin Cancer Foundation: Research Grants Program

Grants of $10,000 each are provided for research projects relevant to skin cancer. Eligible applicants are researchers with a Ph.D. or M.D. Overhead or direct costs are not allowed. Contact telephone: 212-725-5176. Deadline: 10/10/1997

PA-97-086: Chemical Modifiers of Radiation Response of Tumors

The Division of Cancer Treatment, Diagnosis, and Centers of the National Cancer Institute (NCI) invites research grant applications for Program Projects (P01's) from interested investigators for preclinical exploration of the therapeutic potential of new and novel chemical modifiers of radiation response of tumors. Optimization of leads arising from the applicant's own work or from the published literature should include the design and synthesis of new compounds, using combinatorial chemistry, and preclinical evaluation in vitro and in vivo. The following classes of radiation modifiers are of particular interest:

- Small-molecule inhibitors that target genetic alterations associated with solid tumors
- Small-molecule modifiers of cell growth and regulation (modifiers of cell cycle checkpoints, cell signal transduction modifiers)
- Compounds that exploit or modulate tumor physiology (e.g., inhibitors of tumor cell respiration, modulators of the tumor micro environment, or inhibitors of tumor angiogenesis)
- Prodrugs activated by tumor physiology or by other innovative mechanisms

Support of the program will be through the program project (P01) award. The Principal Investigator of any new application requesting $500,000 or more in direct costs in any one year must notify the NCI Program Director and the NCI Referral Officer of intent to submit an application. Application Receipt Dates: October 1, February 1 and June 1.

PA-97-076: Immunological Aspects of Hematopoietic Stem Cells

NIH invites applications for studies of the early stages of lymphoid lineage commitment and development from hematopoietic stem cells. Although much has been learned in recent years to enhance understanding of the later stages of T, B and natural killer (NK) cell development, definition of the complex processes that regulate lymphoid lineage commitment and early lymphoid progenitor cell differentiation requires expanded research efforts. Work in this area is expected to provide basic information needed for future applications to human immunodeficiency diseases, autoimmune diseases, hematopoietic stem cell transplantation and gene transfer therapy. R01 and R29 grant applications will be accepted.

PA-97-081: Basic and Clinical Research on Immune Tolerance

The NIH invites applications that will elucidate basic mechanisms responsible for inducing and maintaining antigen-specific immune tolerance, that will facilitate translation of experimental knowledge on immune tolerance into clinical therapies for the treatment or prevention of immune-mediated disease, or that will promote more effective development of vaccines by preventing pathogen-induced immune tolerance. R01 and R29 grant applications will be accepted in response to this program announcement.

PA-97-075: Direct vs. Indirect Antigen Recognition in Allograft Survival

The National Institutes of Health invites applications for studies to further our understanding of the immune response to direct or indirect presentation of allogeneic major histocompatibility complex (MHC) antigens and to determine the contribution of each pathway to acute and chronic graft rejection. Research to date has focused on direct recognition of allogeneic MHC and therapies designed to block this pathway have been successful in reducing acute rejection of transplanted organs. However, chronic rejection is still an impediment to long-term survival. The indirect pathway of allorecognition has recently been implicated primarily in chronic graft rejection, however an additional role for this pathway in the enhancement of acute rejection has been suggested. Knowledge from basic, preclinical and clinical studies aimed at characterizing the relative role of the direct and the indirect allorecognition pathways in enhancing or preventing graft rejection could lead to the development of specific interventions to modulate immune recognition after transplantation and ultimately increase graft survival. The funding mechanisms to be used to support research under this PA are R01's and R29's.

PA-97-078: Inflamation in Asthma and Allergy

The purpose of this asthma and allergy research Program Announcement is to inform the scientific community of NIH interest in stimulating a wide range of basic and clinical studies to: characterize the role of tissue inflammation in the pathogenesis of asthma and allergic diseases; identify factors responsible for the initiation and maintenance of inflammation in asthma and allergic diseases; and, based on this knowledge, develop new and improved approaches to treat and prevent these disorders. The funding mechanisms to be used to support research under this PA are R01's and R29's.

PA-97-084: Innovative Approaches to Investigating Human Tuberculosis

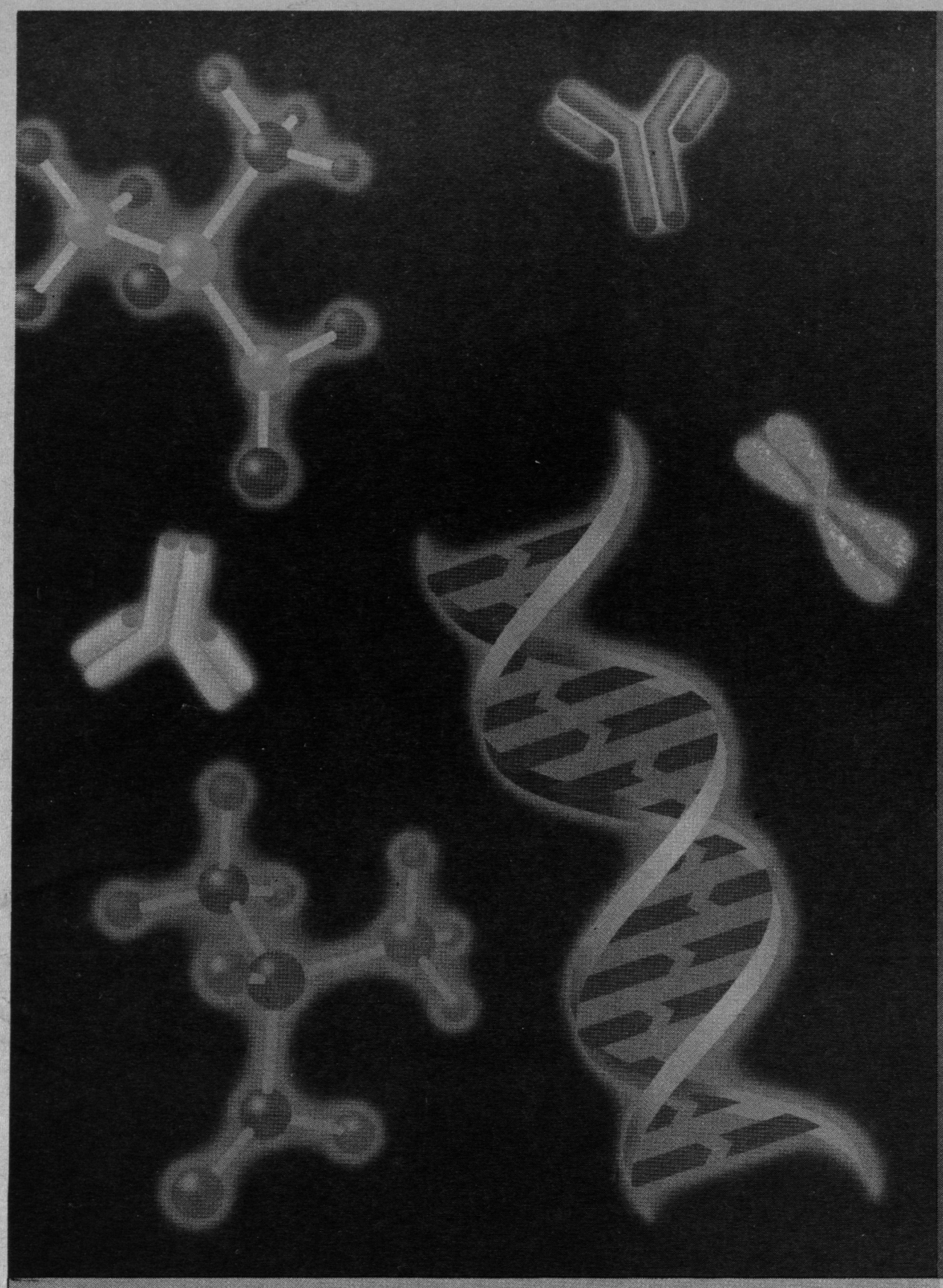
The National Institute of Allergy and Infectious Diseases and National Heart, Lung, and Blood Institute, National Institutes of Health (NIH), invite(s) applications that expand our knowledge and understanding of the organism Mycobacterium tuberculosis (M.tb) and its interaction with the human host. Applications for R01 and R29 grants will be accepted in response to this program announcement.

PAR-97-074: Innovative Approaches to Developing New Technologies

The purpose of this program announcement (PA) is to encourage submission of new Exploratory/Developmental Grant (R21) applications to explore new research paradigms in engineering, instrumentation, physical sciences, mathematics or computer science as applied to biomedical research. The projects should provide the opportunity to develop new technologies, methods, devices, and materials that provide greater understanding of fundamental elements of biological phenomena. These efforts should lead to new approaches to the solution of basic research questions in order to prevent, diagnose, and treat disease and disability and ultimately to improved human health. The technologies/instruments/ methodologies to be developed under this program must be applicable to a variety of NIH research areas. Applications to develop technologies that apply only to one categorical NIH institute or a specific disease, generally do not meet the guidelines for this program. Such applications will be considered only if the applicant clearly demonstrates the long-term potential of the technology for having a broad impact on biomedical research. Application Receipt Date: October 17, 1997.

PA-97-073: Mucosal Immunity in Pathogenesis/Prevention of Human Disease

The National Institutes of Health (NIH) invites applications for investigator-initiated basic and preclinical research into the human mucosal immune system and its regulation, including the gastrointestinal, oral, respiratory, reproductive, and urinary mucosa, with their specialized lymphoreticular structures and cells. The goal of this announcement is to increase high quality research on the mechanisms of response of the human mucosal immune system to disease specific antigens. Use of primate models may be appropriate. Increased understanding of the human mucosal immune system and its response in disease and to exogenous factors should allow the design of more rational immunotherapies and vaccines for the treatment or prevention of autoimmune and infectious diseases, including HIV infection and its complications. The funding mechanisms to be used to support research under this Program Announcement are research projects grants (R01) and First Independent Research Support and Transition awards (R29).■



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