"Uniting Academic Research"

# ACADEMIC SCIENCE NEWS&REVIEW™

New York Edition

Serving NYU, Columbia, SUNY Stony Brook & Brooklyn, Mt. Sinai, Cornell, Rockefeller, Einstein, North Shore, and Cold Spring Harbor & Brookhaven National Laboratories

October◆1997

## Researchers Find Gene for Crippling Neurological Disorder

### Dystonia, Often Misdiagnosed, is More Common Than MS, ALS, and Huntington's Disease

by Dan Coulter, *ASN&R* Staff Writer

A multi-institutional team of researchers from Mt.Sinai, Columbia, Massachusetts General Hospital, Stanford University and the Oregon Health Sciences University have discovered and cloned the gene responsible for early-onset childhood dystonia, a crippling, inherited neurological disorder.

The team's landmark discovery was announced in the September issue of *Nature Genetics* and is the culmination of more than 15 years of work. It contains clues that could lead to better understanding of the disease as well as to preventative procedures.

Although there are many forms of dystonia, the disease is generally marked by sustained, involuntary muscle contractions that can twist and contort parts of the body. Dystonia is six times more common than such well-known neuromuscular disorders as Muscular Dystrophy, Huntington's disease, and Amyotrophic Lateral Sclerosis (Lou Gehrig's disease), and affects over 300,000 people in North America.

According to Dr. Mitchell Brin of Mt. Sinai, one of the paper's co-authors, dystonia is often misdiagnosed or overlooked. This primarily is due to the lack of knowledge about the disease and its symptoms among medical and scientific professionals. "In addition to the 300,000 people estimated to have dystonia, there are still more that exhibit mild symptoms such as writer's cramp, frequent eye blinking or a misdiagnosed 'nervous tick'. "There are thousands of people out there with dystonia who don't even know it," observes Dr. Brin.

In general, dystonic patients may be categorized into two major groups. In the first are patients suffering from early-onset dystonia; In the second are those patients who have developed the disease during adulthood. The team distinguishes between these two groups because early-onset dystonia is most often the result of a specific genetic mutation on chromosome 9, whereas patients with adult-onset dystonia tend to carry different genetic mutations.

**EARLY-ONSET DYSTONIA**

Early-onset dystonia usually appears before the age of 11 and is the most severe hereditary form of the disorder, affecting up to 50,000 people in the United States. Symptoms usually begin in the legs and often spread to the rest of the body, causing it to twist into unnatural postures. Patients with

Continued on Page 4

## BNL Reactor Debate Heats Up

### Brookhaven Staff Rally Twice; Local Groups Join Opposition to Forbes, D'amato Over Reactor Closing

by Kathryn Gavin

After a strange twist of events that has led Brookhaven National Laboratory scientists and staff to take up picket signs, and local community and business groups to take up the Lab's cause, the future of BNL's High Flux Beam Reactor (HFBR) research facility is still unknown.

Several hundred Brookhaven National Laboratory Employees recently rallied in front of Rep. Michael Forbes' office to protest Forbes' (R-NY) and Sen. Alphonse D'Amato's (R-NY) call to close permanently Brookhaven's main research reactor.

In a surprise announcement on September 2, Representative Michael Forbes (R-NY 1st District) and Senator Alphonse D'Amato (R-NY) promised to introduce legislation to permanently close the HFBR immediately, rather than await the results of a thorough scientific, safety and environmental analysis planned by the U.S. Department of Energy.

The bills, which the congressional representatives said they crafted to protect the health of local residents, have been referred to the House's Science Committee, headed by James Sensenbrenner (R-WI) and the Senate's Energy and Natural Resources Committee, headed by Frank Murkowski (R-AK).

The announcement touched off an overwhelmingly negative response from BNL scientists, staff and HFBR users, and even local community and business groups.

Meanwhile, Secretary of Energy Federico Peña held firm to his commitment to DOE's thorough-going review process. A report on the HFBR's value to the nation's scientific community, including researchers in chemistry, solid state physics, structural biology, nuclear medicine, materials science and even art history and archaeology, is due shortly.

**Outrage from BNL Employees, HFBR Users**

Forbes and D'Amato got their first taste of the response to their announcement at their press conference itself, which was crammed with Lab employees despite being held with little advance notice and over 40 miles from the BNL site.

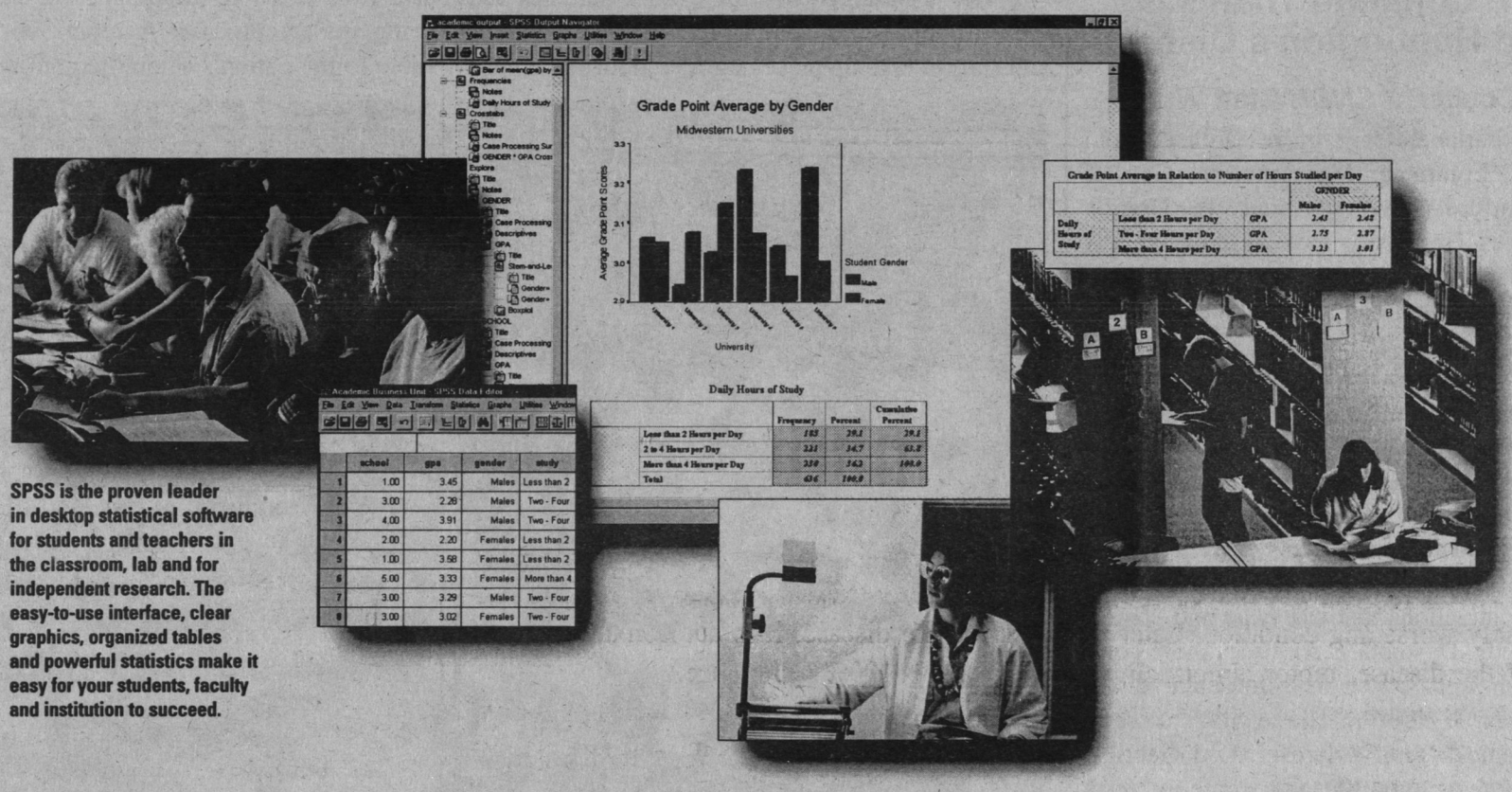
Continued on Page 5

## Inside...

Ask about the SPSS Graduate Pack for student home use

# What do the top 25 universities in the nation have in common?

# SPSS




**SPSS is the proven leader in desktop statistical software for students and teachers in the classroom, lab and for independent research. The easy-to-use interface, clear graphics, organized tables and powerful statistics make it easy for your students, faculty and institution to succeed.**

The top 25 of "America's Best Colleges"* all rely on powerful SPSS statistical software to enhance students' coursework in a broad range of disciplines. And, SPSS is perfect for *your* college or university, too.

SPSS is easy to teach and learn, freeing instructors and students to focus on course materials and research projects. For over 25 years, administrators, professors and researchers have incorporated SPSS in courses such as:

- **Statistics**
- **Research methods**
- **Social sciences**
- **Psychological/Behavioral sciences**
- **Political science**
- **Public policy**
- **Business, and more...**

In addition to teaching and research, SPSS has long been the choice for institutional research and resource management.

SPSS' flexible licensing programs make SPSS available on campus to students, faculty and staff. And, special student licenses make SPSS affordable for home use.

With SPSS, powerful add-on modules enable you to expand and customize your system. Plus, SPSS is available for a number of different platforms.

* Statistics provided by "America's Best Colleges" published by *US and News and World Report*. The 25 mentioned are listed on page 46 of the report as the top 25 national universities.

Find out how SPSS' broad range of products and pricing can enrich your college or university. Join the ranks of the best by improving your stats with powerful and flexible statistical tools from SPSS.

***For more information, call SPSS***

**1 (800) 543-5815**

Or, fax 1 (800) 841-0064
E-mail education@spss.com
World Wide Web http://www.spss.com

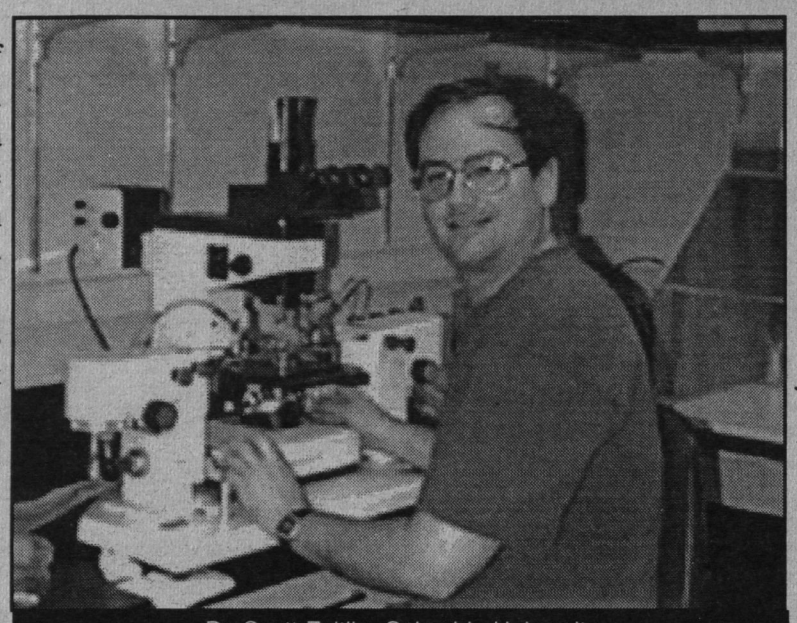
**SPSS**
***Real Stats. Real Easy.***℠

# New Studies Begin to Unravel the Enigma of Huntington's Disease

by Ian Hennessy

Perhaps the portentous repetition of four notes in the first movement of Beethoven's Fifth should have served as a harbinger, announcing the arrival of Fate at the door. For those poor souls that heard the fateful knock, death was assured.

In a twist of irony, a biological repeat also serves a death knell to those suffering from Huntington's disease.



Dr. Scott Zeitlin, Columbia University

Huntington's disease was first described by George Huntington in 1872, in his article "On chorea", and soon the disease became known as "Huntington's chorea". He called it chorea because the Greek derivation of the word 'chorea' means to dance. The term, still used in the medical literature, describes the involuntary and spasmodic movements of facial and limb muscles. The chorea is often the first symptom of an inexorably worsening condition. Later in the course of the disease, motor abnormalities become more pronounced, caloric intake increases, (yet patient's drop weight), cognitive function becomes impaired and seizures and rigidity become prominent. Patients who have suffered from the disease, which typically exhibits itself over a 15-20 year period, die from infections or suicide. Autopsy of the brains of these patients can sometimes reveal a staggering loss of up to 30% of brain mass. There is no effective treatment.

One of the features of the disease that had for years puzzled researchers was the age of onset. Usually the disease does not begin to manifest itself until the fourth or fifth decades of life, but about 10% of Huntington cases involve juvenile onset. It was also noted that when genealogies of affected families were examined, it was the offspring of affected males who seemed to develop the disease at a progressively younger age with successive generations.

In 1983 chromosome four was implicated as the area that contained the gene that caused Huntington's disease (HD). In 1986 it was localized to a region on the short arm of the chromosome, and in 1993, thanks to a large international effort, the gene was isolated. The gene now called the Huntingtin gene codes for a protein that weighed about 350 kDa (1 dalton is about the weight of 1 hydrogen).

Inspection of the gene quickly focused on the first exon (a region of the gene which codes for part of the protein). Researchers noticed that the exon contained many nucleotide repeats of sequence CAG. What they also found was that, when compared to normal individuals, the repeats in patients suffering from Huntington's were longer. In the normal person the repeated CAG sequence ranges from 6 to 39 repeats. In the later-onset Huntington patients, the range is from 40 to 55 repeats, while in the juvenile form these repeats can be between 70 and 100.

Investigators still do not know what causes the expansion of the CAG sequence. In addition, these trinucleotide repeats are not exclusive to Huntington's, but are implicated in other diseases as well. What is certain is that persons with 40 or more repeated sequences in one of their two chromosome 4 copies are fated to suffer from the disease. It is autosomal dominant and displays 100% penetrance.

DNA is a language whose letters (nucleotides) are A, T, C and G. The letters form words (amino acids) that are read by cellular machines (ribosomes) as combinations of three letters. For instance, GAA is read by the ribosomes as tyrosine. When the ribosome sees GAA it makes a tyrosine. When the ribosome sees GAC it makes the amino acid glutamine. When it sees a repeated CAG sequence it makes lots of glutamine, all lined up next to one another. This expansion of glutamines now serves as part of the huntingtin protein. These repeats seem to serve a function. The reason that scientists think so is because, when both copies of the gene are knocked out in mice, the animals die. Thus, the huntingtin protein is essential to life.

Up until last month, a provable biological model had not been shown for the poly-glutamine stretch. However, two papers in the August edition of the journal *Cell* have started to unravel this enigma. What is now believed to be the case is that the stretch of glutamines acts as a type of molecular Velcro to which other proteins, including other huntingtin copies, stick. When this happens, the proteins are prevented from doing their job and chaos begins to creep into cellular life. As the proteins continue to stick to the glutamine repeats, traffic in the nucleus, which is where the mutant protein ends up, starts to grind to a halt and cells begin to die.

One of these papers reported an *in vivo*

Continued on Page 21

# FEATURES

## October 1997

Continued from Page 1

advanced dystonia may be confined to a wheelchair or bedridden. This lifelong condition tends to have a higher frequency among Ashkenazi Jews — i.e., those of East European ancestry, although there are numerous non-Jewish individuals affected as well.

The team recently discovered the gene responsible for childhood onset dystonia, known as DYT1. They found that almost all cases of early-onset dystonia share a specific mutation on chromosome 9 called the "GAG" deletion, regardless of the patient's ethnic background. Dr. Brin explains, "The big breakthrough was finding out the identity of the gene. It turns out that whether you're Jewish or non-Jewish or African American, in this type of dystonia, the genetic mutation is often identical. Every single one of those individuals with early-onset dystonia has the same identical thing happen to chromosome 9 — it's called the GAG deletion — the deletion of the three base pairs guanine, adenine and guanine respectively. Statistically, since lots of deletions can happen by random chance, mutations on a Jewish person and an African American person should be a different — maybe an AGA deletion or a TAT deletion — yet it's always GAG. So there's something very special about this deletion. In early-onset dystonia, it is a very specific change and is independent of ethnic groups as far as we can tell."

One of the mysteries about dystonia is that not everyone who carries the gene shows signs of the disease. Those who carry the gene for dystonia have a 1 in 3 chance of showing signs and a 2 in 3 chance of passing on the gene with no evidence of symptoms. "Early-onset dystonia begins showing signs in the leg ... (while) in the beginning of adult-onset dystonia, signs start becoming evident in either the arm or the face. So the age of onset seems to determine where it is to begin in one's body," says Dr. Brin.

**ADULT-ONSET DYSTONIA**

As mentioned earlier, it is estimated that 50,000 people carry the mutated DYT1 gene. What then about the remaining 250,000 people with dystonia who do not develop the disease during childhood? What causes them to develop dystonia? "In adult-onset dystonia," comments Dr. Brin, "there are different mutations occurring on different genes. There's a mutation on chromosome 18, for instance, that the Germans announced, which predisposes people to getting torticollis — a form of dystonia where one's head pulls to the side or creates spasms of the vocal chords. The real challenge to us though, is to determine the function of the protein coded by the DYT1 gene on chromosome 9. Proteins are folded and can interact with other proteins to make molecules. "

Part of the team's studies involve a fifteen member family in upstate New York that is known to be predisposed to dystonia. Out of the fifteen members, eight developed dystonia within weeks after a physical injury to an arm or limb. "What we wish to determine then, is whether the body's response to that injury was compromised or modified in some way and triggered dystonia as a result. Our hypothesis is that the same areas of the brain are involved in both early-onset and adult-onset dystonia — you can get dystonia from many different routes" suggests Brin. "People with Cerebral Palsy, for example, who exhibit dystonic postures. are different than those with genetically based dystonia. Yet, the pathways that led to dystonia may be identical. Our hope is that if we can unlock the pure pathway associated with the DYT1 gene, then the spillover in terms of therapy and understanding for all these other forms of dystonias will be tremendous," says Dr. Brin.

**HEAT-SHOCK PROTEINS—A POTENTIAL LINK TO DISEASE**

"We look on dystonia as a stealth crippler," says Dr. Xandra Breakefield, of the Massachussetts General Hospital Molecular Neurogenetics Unit. "In contrast to other movement disorders, like Parkinson's disease, there is no visible evidence of damage to the brain and no truly effective drug treatment. Only after identifying the responsible gene and then determining the function of its protein can we understand exactly how this disease produces its symptoms." Dr. Brin speculates that the team might be able to uncover some answers by the

Continued on Page 18


# Academic Science News&Review–New York Edition

A Monthly Publication Dedicated to Academic Research in the Sciences.

Publishers
Peter S. Bernstein
Matthew S. Seidner

Editor-in-Chief
Peter S. Bernstein

Calendar Editor
Daniel Huber

Advertising Reps.
Cherylann Frank
Stephanie Rubino

Staff Writers
Elizabeth Belton
Dan Coulter
Ilana Harrus
Jeremy Kay

Contributors to this Issue
Kathryn Gavin
Sharon Cleary
James Polichak
Peter Saal
Ian Hennessy
Chris Verzulli

**Academic Science News&Review–New York Edition, 2780 Middle Country Road, Suite 213, Lake Grove, NY 11755**
**(516) 737-3415 editor@pdpub.com FAX (516) 737-3414**

Reactor...Continued from Page 1

Many voiced a sense of betrayal, recalling Forbes' earlier attitude toward the HFBR at his July 14 town meeting at the Lab. At that time, he had expressed support for restarting the HFBR after a safety review and the installation of a new, leak-proof liner for the spent fuel pool that has released low-level radioactive water into groundwater on the Lab site.

The HFBR has been kept off-line since the January discovery of the contamination; a remediation effort to prevent the contaminated groundwater from leaving the BNL site is now under way. Local, state and federal environmental and health agencies have all stated that there is no health threat from the contamination.

So strong was the reaction to Forbes' and D'Amato's Sept. 2 announcement that just two days later, over 500 BNL employees rallied outside Forbes' local office, located jut one mile south of the Lab. Carrying signs reading "Forbes and D'Amato: Over-reactors" and "Political Lies - BNL Dies," the protestors called for Forbes and D'Amato to "postpone introducing any legislation which short-circuits" the DOE process.

The rally attracted much attention but did not soften Forbes' or D'Amato's stance. Neither did the 1,600 signatures on a petition, nor a strong pro-BNL presence at all five of Forbes' town meetings throughout his district that weekend.

Soon, Lab employees unleashed a barrage of letters, phone calls and e-mails to their representatives, and enlisted their scientific professional societies, unions and users of all of Brookhaven's scientific research facilities to bring the issue to the attention of the House and Senate committees to which the bills have been referred.

In Question: the High Flux Beam Reactor, a 30-megawatt scientific research reactor at Brookhaven National Laboratory.

Just a week after his announcement with D'Amato, Forbes sent a letter to selected constituents - the vast majority of them female - to restate his position on what he called the "leaking HFBR" and take BNL to task for other environmental problems, nearly all unrelated to the research reactor.

"A re-started nuclear reactor that then encounters new and more troubling contamination leaks would mean a total loss of public confidence in the facility and, one fears, the larger question of whether BNL should be shut down entirely," he wrote. He also included a response card giving constituents the opportunity to laud his "tough decision," disapprove of his stance as "overblown" or provide additional comments.

The letter drew and even stronger response at BNL, leading to a second protest on Sept. 18 that drew over 1,000 employees, retirees, users and their families. Said co-organizer and scientist Ed Kaplan, "We've come together, exactly two weeks since we were here last, to impress upon all of our elected officials, in this case Congressman Forbes, that we in the Brookhaven National Laboratory community are outraged at how he and Sen. D'Amato continue to ignore facts, that he and D'Amato continue to disparage our laboratory, and that they continue to misinform their constituents about health and safety isuses."

The mood was only slightly marred by the recent arrest of the reactor workers' union leader for alleged aggravated harassment of Bill Smith, one of the most outspoken critics of the Lab and the HFBR.

**The Community Responds**

While Forbes and D'Amato gave their concern for the community as their main reason for taking their anti-HFBR stand, much of the community did

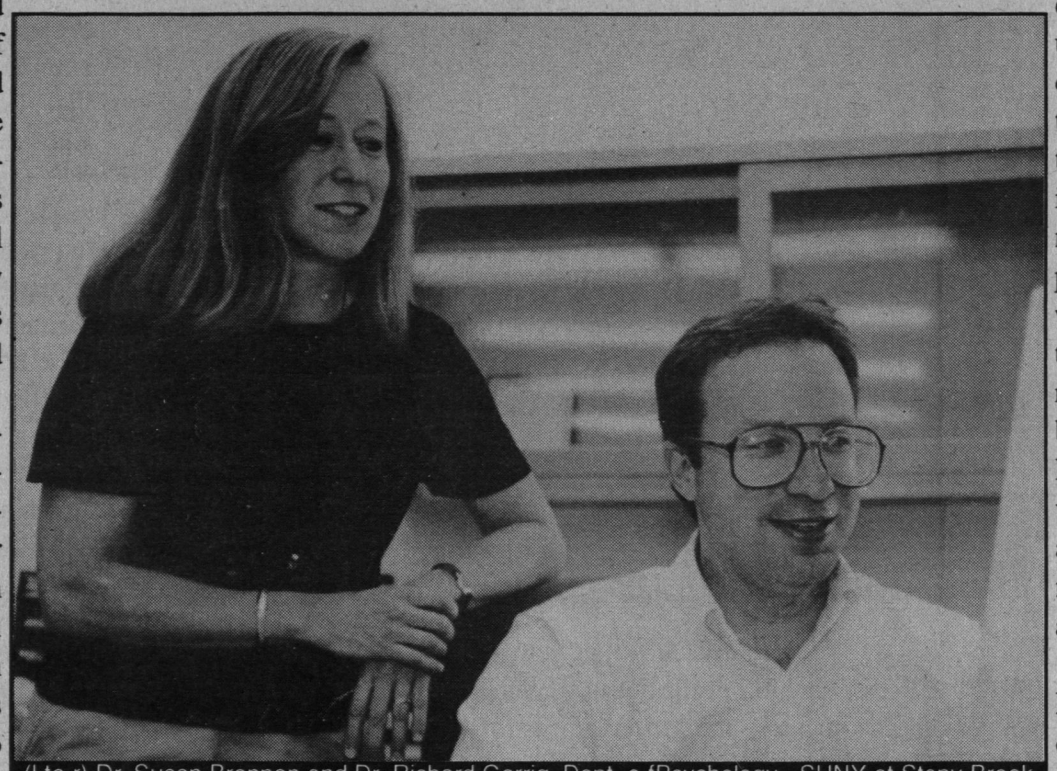
Continued on Page 18

# Do You Understand Me?

## Newly-Funded Research Will Study Discourse Comprehension, Develop Computer Model

by James Polichak

Drs. Richard Gerrig and Susan Brennan, of the Department of Psychology at SUNY Stony Brook, were recently awarded a grant of over half a million dollars from the Interactive Systems Program of the National Science Foundation (NSF) for research on discourse comprehension. The project, entitled "Psychological Representations of Multiple Agents in Text and Spoken Discourse", will examine the ways people extract and represent information from various sources in discourse, and will build upon previous work by Gerrig, Brennan, and others. It is intended to have both basic and applied scientific value.



(I to r) Dr. Susan Brennan and Dr. Richard Gerrig, Dept. o fPsychology , SUNY at Stony Brook

Researchers as well as government agencies have been interested in the factors that affect comprehension of discourse, whether spoken or written. Such research furthers basic knowledge of an important and complicated though commonplace activity. It also has applied value. It can be used to create computer models of the kinds of information people obtain from discourse. These models can then be used by computers to extract essential information automatically from large amounts of text.

Researchers have focussed on the basic cognitive processes that influence discourse comprehension, and on the long-term memory representations that people create from discourse comprehension. Government agencies and industrial concerns have been more interested in models that can process and summarize huge text databases.

The Interactive Systems Program of the NSF funds a number of research programs intended to develop understanding of the ways people process information and of how computers might do the same. Projects are funded for both computer scientists and cognitive scientists through this program. The funds that Gerrig and Brennan receive will be used to support their laboratories, a postdoctoral researcher, and graduate students as they develop materials, perform experiments, and develop their computational model.

Gerrig and Brennan, both cognitive psychologists, will perform their research in three stages. The first will examine how people process and represent in memory the differing information attributed to various characters in a text. The second will examine how the perspectives people hold, or are given while reading a text affect the memory representations they create. In the third stage, knowledge obtained from the earlier studies will be applied to the creation of a computational model of 'who knows what' in a text. This model will be used to create a partially automated system for extracting, representing, and coding information in a set of naturally-occurring texts, and for identifying the perspectives likely to affect this information.

The first stage of the research will examine the factors that affect representations of who knows what among agents in discourse. Much of our daily conversation is concerned with figuring out who among our friends or colleagues already has certain information and who does not. Our enjoyment of both high art and low entertainment can revolve around these issues—Claudius knows the wine is poisoned, but do Hamlet and Gertrude know as well? Janet and Chrissy know that Jack isn't really gay, but the Ropers do not, and therein lies much of the humor. A person's understanding of what a particular phrase might mean can depend upon what that person thinks the other person knows.

Psychologists have studied the ways that this mutual knowledge, or common ground, is built up and used in conversation. Participants in conversation use an assortment of cues to decide whether a piece of information is in common ground. The most obvious of these comes through asking questions, but more subtle cues are also used. For example, if something is salient in the immediate environment, like a siren, it is assumed to be in common ground through physical co-presence. If something has been mentioned in previous conversation, it is linguistically co-present. Information can also be assumed to be in common ground if the conversationalists believe they are members of a community. Community membership can range from a small circle of friends who use cute nicknames for each other to the community of all people who understand English.

The research by Gerrig and Brennan will specifically address how readers make decisions about common ground and co-presence among characters in given texts. Earlier research suggests that readers do not keep track of the differing knowledge that characters possess. This work seemed to show that readers believed that characters knew whatever the reader knew; an error called the "illusory transparency of intention" by Boaz Keysar of the University of Chicago.

Pilot work by Gerrig and Brennan, with Justina Ohaeri (Brennan's graduate student) argued otherwise. This work showed that the stories used in the earlier research did not contain the details of information that people use to establish the knowledge of characters— e.g. why one character might be concealing information from another. When such information was included, readers no longer made the "illusory transparency" error. It seemed that when information about the intentions of a character was missing, readers filled it in to maintain the belief that characters are rational. Readers, like participants in a conversation, attend to the social aspects of language used when making decisions about what characters know.

Further research by Gerrig and Brennan will focus on examining cues used by authors to indicate to readers whether a piece of information is known to a character. They will examine both features of narration and of utterances by characters that might indicate co-presence For example, a narrator might mention a dog barking in the distance. Unless the narrator specifically states that a character somehow did not hear the dog, readers should assume all characters heard it due to an implied physical co-presence. Alternatively, a character who had just seen a football game at home alone could say to another, "They lost." This would indicate to the reader that the character addressed can be assumed to know there was a football game and to know who the loser was.

The second stage of the research will examine the ways that the perspectives readers bring to texts affect the memory representations they form. It will also examine how these perspectives affect persuasion by a text. Readers can bring a variety of perspectives to any text. A powerful effect of personal relevance was found by Gerrig and collaborators Deborah Prentice and Daniel Bailis (both of Princeton). They presented students at Yale and Princeton with a long story containing a number of assertions that challenged common beliefs. For example, at one point in the story a character mentioned that mental disorders were contagious. They are not, and the readers knew it. Prentice, Gerrig, and Bailis manipulated one small element of the story for different readers. For some, the story was set at Princeton; for others at Yale. When people read the version set in the school they did not attend, their beliefs were changed more than for those who had read the version set at their own school. People scrutinized more carefully claims presented in a story

Continued on Page 9

PRINCIPLES *of* SOUND RETIREMENT INVESTING

# OVER ONE MILLION OF THE BEST MINDS IN AMERICA HAVE ALREADY CHOSEN THE BEST RETIREMENT SYSTEM.

# TIAA-CREF.

Nearly 160 Nobel Prize winners – and 1.8 million other forward thinkers – count on us to help them plan a comfortable future. With $170 billion in assets, we're the world's largest retirement company, the nation's leader in customer satisfaction, and the overwhelming choice of people in education, research and related fields.*

The reason? For more than 75 years, TIAA-CREF has introduced intelligent solutions to America's long-term planning needs. We pioneered portable benefits. We invented the variable annuity and helped popularize the very concept of stock investing for retirement planning.

Today, TIAA-CREF's expertise offers an impressive range of ways to help you create a comfortable and secure tomorrow. From the guarantees of TIAA's top-rated Traditional Annuity** to the additional growth opportunities of our nonguaranteed investment accounts, you'll find the flexibility and diversity you need to help you meet your long-term goals. And they're all backed by some of the most knowledgeable investment managers in the industry.

To learn more about the world's premier retirement organization, speak to one of our expert counselors at **1 800 842-2776** (8 a.m.-11 p.m. ET). Or better still, speak to one of your colleagues. Find out why, when it comes to planning for tomorrow, great minds think alike.

**Visit us on the Internet at www.tiaa-cref.org**

TIAA CREF

**Ensuring the future for those who shape it.**℠

*Source: DALBAR, Inc., *1995 Consumer Satisfaction Survey*, in which 96% of respondents expressed overall satisfaction with TIAA-CREF.

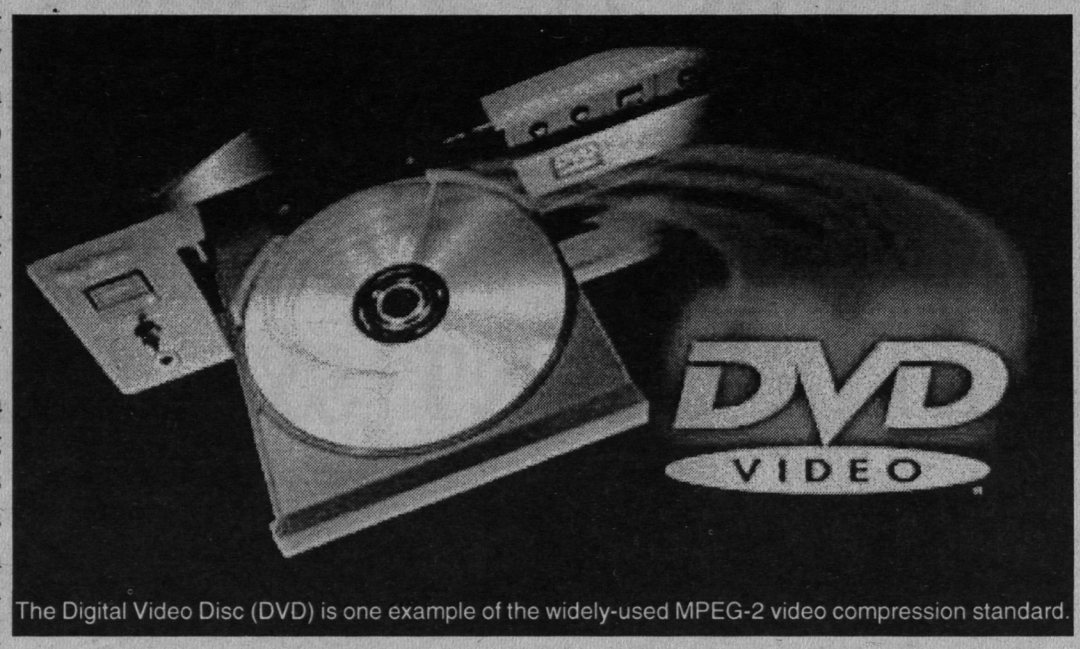
**TIAA is one of only a handful of companies that currently hold the highest marks from the nation's leading independent rating agencies for stability, sound investments, claims-paying ability, and overall financial strength: A++ (Superior), A.M. Best Co.; AAA, Duff & Phelps; Aaa, Moody's Investors Service; AAA, Standard and Poor's. TIAA's guarantees are backed by its claims-paying ability. These ratings of TIAA as an insurance company do not apply to CREF. CREF certificates are distributed by TIAA-CREF Individual and Institutional Services, Inc. For more complete information, including charges and expenses, call 1 800 842-2733, extension 5509, for a prospectus. Read the prospectus carefully before you invest or send money.

# MPEG Patent Group Created to License New Digital Technology

## Columbia to Receive Royalties

by Sharon Cleary

On June 26th, Columbia University together with eight electronics corporations received permission from the U.S. Department of Justice to create a patent pool, the MPEG Licensing Administrator, to license the video compression technology known as MPEG-2. The members of this patent pool, which includes corporate giants Sony, Mitsubishi, and Lucent Technologies, hold the 33 patents essential to develop products compatible with new video technologies such as high definition televisions (HDTV) and the next crop of camcorders and computers. Columbia University, the only academic institution in the licensing group, expects to begin receiving royalties as early as 1998.



The Digital Video Disc (DVD) is one example of the widely-used MPEG-2 video compression standard.

The MPEG technology is a means of compactly representing digital video and audio signals for consumer distribution. This technology transforms a stream of discrete samples into a bitstream of contiguous digital information, "tokens" in zeroes and ones, that takes less bandwidth space while still maintaining the quality of the image or sound.

MPEG, which stands for Motion Picture Experts Group, is an international organization first established in 1988 to develop standards for coded representation of moving pictures, audio transmission, and the combination of the two. The Group typically meets three times a year or more to discuss applications of this continually evolving technology.

MPEG-1, which made its debut in 1992, was the Group's first effort, developed to represent moving pictures digitally. Designed specifically for low definition television, it had the approximate resolution of a VHS tape. MPEG-2, a buffed-up version of MPEG-1 born in 1995, produces the broadcast quality image and sound used in high-definition television. The video capabilities of MPEG-2 technology eliminate redundant information such as images that are all the same color or figures that do not change from moment to moment, reducing the amount of data, storage, and transmission (bandwidth) required to reproduce video sequences. MPEG-3, the technology originally slated for use with HDTV, was incorporated into MPEG-2 once researchers realized they could produce broadcast quality with the existing technology.

Dimitris Anastassiou, Professor of Electrical Engineering at Columbia's School of Engineering and Applied Science and Dnowirector of the Columbia New Media Technology Center developed one of the MPEG-2 technologies with a graduate student. Prof. Anastassiou now looks forward to MPEG-4: "While the development of MPEG-1 and 2 dwelled upon decompression ratios, the key word for MPEG-4 is functionality. For example, say you have a video stream of a dozen joggers jogging. MPEG-4 will enable a user to extract a single person jogging in the background for interactive editing purposes. The MPEG technology will recognize the person you are highlighting as a specific stream of 0s and 1s within the digital signals." It will therefore be possible to cut and paste in a digital domain. MPEG-4, the fully developed version, is scheduled to receive full designation as an international standard in November 1999.

There will be no MPEG 5 or 6 however. Researchers have named the next standard MPEG-7. Why? "For fun; to be unpredictable!" says Prof. Anastassiou. Research here has not yet begun, but MPEG-7 is much talked about among researchers. While "functionality" is the key word for MPEG-4, "search" is the key word for MPEG-7 which will enable a user to search rapidly through an international multimedia library using key words.

MPEG-technology has broad applications for consumer products. The advent of the Digital Video Disc (DVD) will make it possible to play and view a computer game like "Myst" in broadcast quality images. DVD is also the enabling technology for high-definition televisions, camcorders and computers. A DVD looks much like a compact disc, but it stores roughly six times more information. They store the 0s and 1s that make up the digital audio and video bitstream while MPEG-2 is the syntax, which decodes the 0s and 1s. MPEG-2 technology also allows the Direct Broadcast Satellite to deliver digital information directly to satellites as well as to send the digitized programs directly to personal satellite dishes. The transmission is decoded by MPEG-2 technology. Finally, HDTV, which will soon be the only choice for television viewers, depends on digital video streams which obey the rules of MPEG-2. In a year, these products will be everywhere while MPEG research still continues at full steam ahead.

The formation of the patent group is well-timed, considering current advancements in consumer electronics. According to Robert Nelson, a spokesman for Columbia University, "Market analysts indicate that numerous consumer products, like high density televisions, computers and camcorders, will soon use digital technology for better quality audio and video. MPEG-2 is the international standard that decodes the sound and image and Columbia University is perfectly situated to reap the benefits of our research." The royalties generated from Columbia's MPEG-2 patents will be channeled into a Strategic Research Fund which will fund further research in engineering and life sciences.

The formation of a patent group like MPEG Licensing Agreement concerning a single new technology undergoes careful review by the Justice Department. When a new technology becomes the de facto standard, exclusive access to the technology is a primary concern. Imagine being unable to write a program for a PC without sending Bill Gates a check. But MPEG Licensing Agreement was formed as a non-exclusive patent group, allowing any company interested in utilizing the technology access to the patents.

Given the non-exclusive nature of the patent group, the U.S. Department of Justice expressed a favorable opinion of the group in a business review letter from Joel I. Klein, Acting Assistant Attorney General. Klein noted that it appeared the licensing program was well designed to capture all the efficiencies that come from joint licensing of complementary technologies, while incorporating many facets that should minimize the possibility of competitive harm. Particularly, MPEG Licensing Agreeement will employ an independent patent expert who will function as a mediator when the need arises. The mediator will decide whether an included patent remains essential to the licensing group, or whether an existing patent not already in the group should be included.

International technology standards are good for both consumers and producers. Consumers have greater choice when the technology in different products is interchangeable. Corporations no longer run the risk of pouring millions of dollars into researching a technology that could fail (e.g., consider betamax vs VHS systems). Further, a fax machine can communicate with another fax machine and accurately transmit messages anywhere in the world because the technology, which decodes the series of zeroes and ones that constitutes the fax is the same worldwide. An international standard allows digital video to be globally consistent as well.

The continuing development of international MPEG standards promises increasing rewards in the years ahead.■

Continued from Page 6

setting that was familiar and relevant, and were thus less persuaded by false claims.

The effects of a reader's perspective have usually been studied in terms of the reader's prior beliefs on the topic a text reports upon. The proposed research will use naturally-occurring texts from newspapers and other sources to extend these findings. Gerrig and Brennan hypothesize that different readers will have different reactions to texts that argue against something they believe. Some readers, they believe, will choose to ignore material inconsistent with their belief system, resulting in short reading times for that material. Others will try to combat material inconsistent with their beliefs by recalling other information that supports their belief systems. This will result in longer reading times and a different memory representation. The effects of these different reading strategies on persuasion and memory for the text will also be examined.

Gerrig and Brennan expect that a similar process may also occur when people read texts that present balanced statements. They believe that readers will focus more energy and time on reading the parts of the text that are consistent with their beliefs, and less time processing information that counters their beliefs. This should result in readers becoming more confident that their beliefs are true after reading a balanced text.

The proposed research will also examine these issues in terms of memory, when the information presented in a text can be represented in different forms. It may be integrated to varying extents into pre-existing memory structures, and thus be incorporated. Information not connected to other memory structures is said to be compartmentalized. For example, a person might read a story about a tenth planet in the solar system. This information could be incorporated into the reader's memory so that he now believes that there are ten planets in the solar system. Alternatively, this information could be represented in a form that labels it as part of a specific story that was read. A reader who does this will not believe there are ten planets, but if asked about the solar system in the context of the story will know that ten were mentioned there.

Factors like whether a story has a setting particularly relevant the reader thus affect the incorporation of information. Other factors that should affect such incorporation include whether the text is identified as fiction or non-fiction, what the specific source of the information is, and the kind of information included in the text. For example, reading a novel labeled "science-fiction" is unlikely to cause readers to believe that there are ten planets. However, identical information appearing in *Scientific American* or *the New York Times* should. Similarly, incorporation of political arguments should be affected by a reader's political beliefs, and by their beliefs about the political perspective of the source of the argument. Current models of text processing do not include the effects of perspective on the long-term memory representations readers create from a text, and thereby create problems. For example, according to Dr. Susan Brennan, current artificial intelligence approaches to automatically summarizing texts mistakenly assume that only one representation of a text is adequate. Gerrig and Brennan intend to examine systematically the effects of perspective, and to include them in their computational model.

Researchers developing standard models of text processing have assumed that all the information a text generates can be found in the text, independent of the reader. In other words, although some readers may comprehend a text better than others, they are all simply representing, to a greater or lesser degree, the information to be found in the text itself. Gerrig and Brennan believe this assumption is false. Different readers will comprehend a text in different ways, adding information to their representation or ignoring it, based on their own perspectives rather than on reading skill or intelligence.

Gerrig and Brennan will apply the basic findings on the way people represent the differing knowledge states of agents in a text, and on how perspectives affect memory representations in the third stage of their research. The intent here is to build a partly-automated system that can extract information from naturally-occurring texts and represent who knows what in the text. It will also code information in terms of its likelihood of being included in the memory representations of readers. Based on the findings in the first two stages of the research, this could challenge traditional assumptions that all information may be found in the text itself, and could result in a more complete, and more accurate model of text processing.■

## GENETIC INTERACTIONS BETWEEN HOP1, RED1 AND MEK1 SUGGEST THAT MEK1 REGULATES ASSEMBLY OF AXIAL ELEMENT COMPONENTS DURING MEIOSIS IN THE YEAST SACCHAROMYCES CEREVISIAE

Hollingsworth NM. Ponte L.

*Genetics. 147(1):33-42, 1997 Sep.*

During meiosis, axial elements are generated by the condensation of sister chromatids along a protein core as precursors to the formation of the synaptonemal complex (SC). Functional axial elements are essential for wild-type levels of recombination and proper reductional segregation at meiosis I. Genetic and cytological data suggest that three meiosis-specific genes, HOP1, RED1 and MEK1, are involved in axial element formation in the yeast Saccharomyces cerevisiae. HOP1 and RED1 encode structural components of axial elements while MEK1 encodes a putative protein kinase. Using a partially functional allele of MEK1, new genetic interactions have been found between HOP1, RED1 and MEK1. Overexpression of HOP1 partially suppresses the spore inviability and recombination defects of mek1-974; in contrast, overexpression of RED1 exacerbates the mek1-974 spore inviability. Co-overexpression of HOP1 and RED1 in mek1-974 diploids alleviates the negative effect of overexpressing RED1 alone. Red1p/Red1p as well as Hop1p/Red1p interactions have been reconstituted in two hybrid experiments. Our results suggest a model whereby Mek1 kinase activity controls axial element assembly by regulating the affinity with which Hop1p and Red1p interact with each other.

---

## THE CAK1P PROTEIN KINASE IS REQUIRED AT G(1)/S AND G(2)/M IN THE BUDDING YEAST CELL CYCLE

Sutton A. Freiman R.

*Genetics. 147(1):57-71, 1997 Sep.*

The CAK1 gene encodes the major CDK-activating kinase (CAK) in budding yeast and is required for activation of Cdc28p for cell cycle progression from G(2) to M phase. Here we describe the isolation of a mutant allele of CAK1 in a synthetic lethal screen with the Sit4 protein phosphatase. Analysis of several different cak1 mutants shows that although the G(2) to M transition appears most sensitive to loss of Cak1p function, Cak1p is also required for activation of Cdc28p for progression from G(1) into S phase. Further characterization of these mutants suggests that, unlike the CAK identified from higher eukaryotes, Cak1p of budding yeast may not play a role in general transcription. Finally, although Cak1 protein levels and in vitro protein kinase activity do not fluctuate during the cell cycle, at least a fraction of Cak1p associates with higher molecular weight proteins, which may be important for its in vivo function.

---

## KINETICS OF ADSORPTION WITH GRANULAR, POWDERED, AND FIBROUS ACTIVATED CARBON

Shmidt JL. Pimenov AV. Lieberman AI. Cheh HY.

*Separation Science & Technology. 32(13):2105-2114, 1997.*

The properties of three different types of activated carbon, fibrous, powdered, and granular, were investigated theoretically and experimentally. The adsorption rate of the activated carbon fiber was found to be two orders of magnitude higher than that of the granular activated carbon, and one order of magnitude higher than that of the powdered activated carbon. Diffusion coefficients of methylene blue in the fibrous, powdered, and granular activated carbons were determined experimentally. A new method for estimating the meso- and macropore surface areas in these carbons was proposed.

---

## SIMPLE TESTS FOR DENSITY FUNCTIONAL METHODS

Csonka GI. Nguyen NA. Kolossvary I.

*Journal of Computational Chemistry. 18(12):1534-1545, 1997 Sep.*

The performance of the currently used generalized gradient approximation density functionals is analyzed using several simple, yet critical requirements. We analyze the effects of the self-interaction error, the inclusion of the exact exchange, and the parameter settings used in the popular three-parameter hybrid density functionals. The results show that the elimination of the self-interaction error from the current density functionals lead to very poor results for H-2. The inclusion of the exact exchange does not significantly influence the self-interaction corrected results. The variation of the A, B, and C parameters of a hybrid DFT method influences the H-H equilibrium bond length through a very simple Linear equation, and it is possible to reproduce the experimental H-H distance with appropriate selection of these parameters, although an infinite number of solutions exists. Similar results were obtained for the total energy and the electron density along the internuclear axis. The analysis of the exact KS potential at the bond critical point of the dissociating H-2 molecule shows that, for this property, the second order Moller-Plesset perturbation theory yields a better potential than the density functionals studied in this article.

---

## THE FEMR315 GENE FROM STAPHYLOCOCCUS AUREUS, THE INTERRUPTION OF WHICH RESULTS IN REDUCED METHICILLIN RESISTANCE, ENCODES A PHOSPHOGLUCOSAMINE MUTASE

Jolly L. Wu SW. Vanheijenoort J. Delencastre H. Menginlecreulx D. Tomasz A.

*Journal of Bacteriology. 179(17):5321-5325, 1997 Sep.*

The femR315 gene was recently identified by Tn551 insertional mutagenesis as one of the new auxiliary genes, the alteration of which resulted in a drastically reduced methicillin resistance of the Staphylococcus aureus strain COL. femR315 (also known as femI) theoretically encoded a protein of 451 amino acids showing significant amino acid sequence homology with phosphoglucomutases and similar enzymes catalyzing the isomerization of hexoses and hexosamine phosphates (S. Wu, H. de Lencastre, A. Sali, and A. Tomasz, Microb. Drug Resist, 2:277-286, 1996), We describe here the overproduction and purification of the FemR315 protein as well as its identification as the phosphoglucosamine mutase which catalyzes the formation of glucosamine-1-phosphate from glucosamine-6-phosphate, the first step in the reaction sequence leading to the essential peptidoglycan precursor UDP-N-acetylglucosamine. On the basis of these findings, we propose to change the names femR315 and femD to the functionally more appropriate name glmM.

---

## LONGITUDINAL WAKEFIELD FOR AN ELECTRON MOVING ON A CIRCULAR ORBIT

Murphy JB. Krinsky S. Gluckstern RL.

*Particle Accelerators. 57(1):9-64, 1997.*

Using a time-domain analysis, we determine the longitudinal wakefield of an electron moving on a circular orbit in both free space, and between a pair of symmetrically placed infinitely conducting plates. Our calculation is restricted to points on the circular orbit. We obtain an analytic expression for the short-range wakefield of a highly relativistic electron in free space. For an electron circulating midway between parallel plates, the method of image charges is used to derive the wakefield, exhibit a scaling property and evaluate the scaling functions. As a complement to the time-domain analysis of the wakefield, we discuss its frequency-domain counterpart, the longitudinal coupling impedance. Beginning with a review of the seminar work of Schott from the early part of the century, our presentation continues to the frontier where many new results are provided.

---

## GENETIC CONTROL OF PROGRAMMED CELL DEATH AND AGING IN THE NEMATODE CAENORHABDITIS ELEGANS

Hengartner MO.

*Experimental Gerontology. 32(4-5):363-374, 1997 Jul-Oct.*

The nematode Caenorhabditis elegans has been used extensively as a model system for the study of basic biological processes. In this species, apoptosis and aging are both under genetic control. Molecular studies have shown that the death machinery that kills C. elegans cells has remained conserved through evolution and also functions to promote apoptotic death in mammalian cells. At least some of the genes that affect C. elegans life span are also evolutionarily conserved; whether the vertebrate homologs of these genes also influence life span remains to be determined. Although a large number of mutations have been isolated that affect either apoptosis or aging in C. elegans, there is so far no evidence that the genetic pathways that control these processes might overlap.

---

## THE CHEMICAL EVOLUTION OF PLANETARY NEBULAE

Bachiller R. Forveille T. Huggins PJ. Cox P.

*Astronomy & Astrophysics. 324(3):1123-1134, 1997 Aug.*

We report millimeter line observations of CO, (CO)-C-13, SiO, SiC2, CN, HCN, HNC, HCO+, CS, and HC3N to study the chemistry in planetary nebulae (PNe) with massive envelopes of molecular gas. The sample observed consists of representative objects at different stages of development in order to investigate evolutionary effects: the proto-PNe CRL 2688 and CRL 618, the young PN NGC 7027, and the evolved PNe NGC 6720 (the Ring), M4-9, NGC

6781, and NGC 7293 (the Helix). The observations confirm that the chemical composition of the molecular gas in PNe is radically different from that in interstellar clouds and the circumstellar envelopes of Asymptotic Giant Branch (AGE) stars. There are also clear trends in the chemical evolution of the envelopes. As a star evolves beyond the AGE, through the proto-PN and PN phases, the abundances of SiO, SiC2, CS, and HC3N decrease, and they are not detected in the PNe, while the abundances of CN, HNC, and HCO+ increase dramatically. Once a PN has formed, the observed abundances in the molecular clumps of the envelope remain relatively constant, although HNC is anomalously underabundant in NGC 7027. In the evolved PNe, CN is about an order of magnitude more abundant than HCN, HNC, and HCO+, and the average abundance ratios are CN/HCN = 9, HNC/HCN = 0.5, and HCO+/HCN = 0.5. These ratios are, respectively, one, two, and three orders of magnitude higher than in the prototypical AGE envelope IRC+10216. The C-12/C-13 ratios are approximate to 10-25, within the large range found in AGE envelopes. The chemical evolution of the envelopes likely occurs through the development of photon-dominated regions produced by the ultraviolet radiation field of the central star. The observations also provide important information on the physical conditions in the molecular gas. Multi-line observations of CN, CO, and HCO+ show that the clumps which form the envelopes .of the evolved PNe maintain remarkably high gas densities (similar to few x 10(5) Cm-3) and low temperatures (similar to 25 K). These values are consistent with the idea that the clumps are in rough pressure equilibrium with the more diffuse, ionized gas and can last for a significant part of the nebular lifetime, providing the environment needed for the survival of the molecules. Thus the clumping of the gas in these PNe is an essential aspect of both their physical and chemical evolution.

---

## CHARACTERIZATION OF THE EXON STRUCTURE OF THE POLYCYSTIC KIDNEY DISEASE 2 GENE (PKD2)

Hayashi T. Mochizuki T. Reynolds DM. Wu GQ. Cai YQ. Somlo S.

*Genomics. 44(1):131-136, 1997 Aug 15.*

PKD2, the gene defective in the second form of autosomal dominant polycystic kidney disease (ADPKD), has been identified by positional cloning and found to encode an integral membrane protein with similarity to the gene for the more common form of ADPKD and to calcium channels. We have determined the exon-intron structure of the PKD2 gene. PKD2 is encoded in at least 15 exons with the translation start site in exon 1. All the splice acceptor and donor sites conform to the AG/GT rule. We have designed a series of intronic oligonucleotide primers for amplifying the entire coding sequence from genomic DNA in segments well suited to mutation analysis using conventional screening strategies such as SSCA or heteroduplex analysis.

---

## TAPPING SCANNING FORCE MICROSCOPY IN AIR-THEORY AND EXPERIMENT

Spatz JP. Sheiko S. Moller M. Winkler RG. Reineker P. Marti O.

*Langmuir. 13(17):4699-4703, 1997 Aug 20.*

Ultrathin layers of micelles of a diblock copolymer with a polystyrene corona and a poly(2-vinylpyridine) core have been studied by tapping scanning force microscopy in air, probing the surface with varying forces depending on the setpoint of the probe and the tapping frequency. The compliance of the core of the micelles was varied by neutralization of the pyridine groups with HAuCl4 and incorporation of small particles. The apparent deformation of the globular micelles was compared with a simple model describing the probe as a forced oscillator which changes its effective spring constant depending on the direct contact with the surface. Consistent with the experiment, the model shows that the deformation and the shift in phase are minimized by tapping on the low-frequency side of the noncontact cantilever resonance.

---

## STUDIES ON THE STRUCTURE, REGULATION, AND PATHOGENIC POTENTIAL OF ANTI-DSDNA ANTIBODIES [Review]

Spatz L. Iliev A. Saenko V. Jones L. Irigoyen M. Manheimerlory A. Gaynor B. Putterman C. Bynoe M. Kowal C. Kuo P. Newman J. Diamond B.

*METHODS-A COMPANION TO METHODS IN ENZYMOLOGY. 11(1):70-78, 1997 Jan.*

Studies of anti-double-stranded (anti-ds)DNA antibodies have provided insights into how and why these antibodies arise in systemic lupus erythematosus. In this review we discuss the experimental approaches that have been used by our laboratory to study these autoantibodies. Structure/function analyses including site-directed mutagenesis have helped characterize the molecular genetics of anti-dsDNA antibodies, and more recently peptide libraries have been used to define molecular motifs that these antibodies bind. Most of the pathogenic anti-dsDNA antibodies observed in lupus are somatically mutated. We demonstrated in vitro and in vivo that antibacterial antibodies can mutate to acquire specificity for dsDNA. Furthermore, using a fusion partner constitutively expressing bcl-2, NSObcl-2, we have shown the existence of anergic or preapoptotic B cells making antibodies that cross-react with both bacterial antigen and dsDNA. Whether defects in the regulation of these antibodies might contribute to serum expression of anti-dsDNA antibodies in some individuals remains unknown. A major emphasis of this review is the regulation of anti-dsDNA antibodies in a transgenic mouse model harboring the gene for the heavy chain of a pathogenic anti-dsDNA antibody. Nonautoimmune transgenic mice effectively regulate autoreactive B cells by anergy and deletion, white their autoimmune counterparts do not, The vast majority of anergic B cells expressing high-affinity transgenic anti-dsDNA antibody fail to display allelic exclusion of the heavy chain. We postulate that this may be one mechanism that allows them to escape deletion. Comparative studies on light chain usage in both the autoimmune and the nonautoimmune transgenic mouse strains have demonstrated that within the autoreactive B-cell population, there are subsets that are differentially regulated. Ultimately transgenic animals making pathogenic autoantibodies may provide us with a system for testing novel therapies for autoimmune disease.

---

## EVIDENCE FOR INHIBITION OF MYEF-2 BINDING TO MBP PROMOTER BY MEF-1/PUR ALPHA

Muralidharan V. Tretiakova A. Steplewski A. Haas S. Amini S. Johnson E. Khalili K.

*Journal of Cellular Biochemistry. 66(4):524-531, 1997 Sep 15.*

Myelin basic protein (MBP) is a major component of the myelin sheath whose production is developmentally controlled during myelinogenesis. Earlier studies have indicated that programmed expression of the MBP gene is regulated at the level of transcription. Evidently, the MB1 regulatory motif located between nucleotides -14 to -50 plays an important role in transcription of the MBP promoter in both in vitro and in vivo systems. The MB1 element contains binding sites for the activator protein MEF-1/Pur alpha and the repressor protein MyEF-2. In this study we use bandshift assays with purified MEF-1/Pur alpha and MyEF-2 and demonstrate that binding of MyEF-2 to its target sequence is inhibited by MEF-1/Pur alpha. Under similar conditions, MyEF-2 enhances the association of MEF-1/Pur alpha with MB1 DNA. MEF-1/Pur alpha binds to MB1 in mono-and dimeric forms. Inclusion of MyEF-2 in the binding reaction increases the dimeric association of MEF-1/Pur alpha with the MB1 sequence. The use of MEF-1/Pur alpha variants in the bandshift assay suggests that two distinct regions of this protein may be involved in its binding to the MB1 sequences, and its ability to block MyEF-2 interaction with the MB1 sequence. Based on previous studies on the programmed expression of MEF-1/Pur alpha and MyEF-2 during myelination and the current findings on their interplay for binding to the MB1 motif, a model is proposed for their involvement in transcriptional regulation of the MBP gene during the course of brain development.

---

## TIME-DEPENDENT FULLY NONLINEAR GEOSTROPHIC ADJUSTMENT

Kuo AC. Polvani LM.

*Journal of Physical Oceanography. 27(8):1614-1634, 1997 Aug.*

Shock-capturing numerical methods are employed to integrate the fully nonlinear, rotating ID shallow-water equations starting from steplike nongeostrophic initial conditions (a Rossby adjustment problem). Such numerical methods allow one to observe the formation of multiple bores during the transient adjustment process as well as their decay due to rotation. It is demonstrated that increasing the rotation and/or the nonlinearity increases the rate of decay. Additionally, the time required for adjustment to be completed and its dependence on nonlinearity is examined; this time is found to be highly measure dependent. Lastly, the final adjusted state of the system is observed through long time integrations. Although the bores that form provide a mechanism for dissipation, their decay results in a final state in very good agreement with the one computed by well-known (dissipationless) conservation methods.

---

## IDENTIFICATION AND CHARACTERIZATION OF RAT ORBICULARIS OCULI

# NEW YORK REGIONAL CALENDAR OF

## SEP 29-OCT 2

Sept. 29: "Community-Level Consequence of Competition, Dr. Deborah Goldberg, Univer. Michigan, Dept. of Ecology & Evolution, 3:30, Rm.038 Life Scinces building, SUNY Stony Brook.

29: "Linear Fitting with Missing Data: Applications to Structure-from-motions and to Characterizing Intensity Images," David Jacobs, NECI, 3:30-4:30, Courant Inst. of Mathematical Sciences, Rm. 1302, Warren Weaver Hall, 251 Mercer St., NYU.

29: "New Bounds for k-sets and Some Related Identities," Boris Aronov, Polytechnic Univ., Brooklyn, 6:15, Courant Inst. of Mathematical Sciences, Rm . 613, Weaver Warren Hall, 251 Mercer St., NYU.

30: "Study of Driven Reconnection in Controlled Laboratory Experiments," M. Yamada, Princeton Plasma Physics Laboratory, 11:00 A.M., Courant Inst. of Mathematical Sciences, Rm. 1013, Warren Weaver Hall, 251 Mercer St., NYU.

29: "Uniqueness of Harmonic Maps to General Targets," Michael Struwe, ETH Zurich, 1:20 P.M., Courant Inst. of Mathematical, Rm. 1302, Warren Weaver Hall, 251 Mercer St., NYU.

30: "Molecular mechanisms involved in the polarization of MDCK cells and retinal pigment epithelium," Enrique Rodriques-Boulan, Cornell Univ., Physiology Dept., 12:00, Rover Physiology Conference Room, P&S 11-505, Columbia University.

30: "Molecular Neuroplasticity: Ca2+-activated K+ channels as targets for second messenger cascades," Dr. Peter Reinhart, Dept. Of Neurobiology, Duke University, 12:30, Dept. of Neurobiology & Behavior, Rm 038, Life Scienes Building, SUNY Stony Brook.

Oct 1: "Tropical Convection, Radiation, and Ocean Coupling in a Cloud-Resolving Model," Xiaoqing Wu, NCAR, 3:30-5:00, Inst. of Mathematical Sciences, Rm.1302, Warren Weaver Hall, 251 Mercer St., NYU.

2: "The Construction of Ergodic Twist Maps," Denis Kosygin, CIMS, 11:00A.M., Courant Inst. of Mathematical Sciences, Rm. 1302, Warren Weaver Hall, 251 Mercer St., NYU.

2: "Theta Rhythm, Synaptic Plasticity, and hte Chemistry of Memory, " Ursula Stubli, Ctr. for Neural Science, NYU, 12:00, 7th floor Conference room, N.Y. State Psychiatric Inst., 722 West 168th Street, Columiba Univ. Hospital.

## OCT 3-9

3: " Alfven Wave Experiments and Structures in Plasmas," Dr. Walter Gekelman, Univ. of California, Los Angeles, Plasma Physics Colloquia, 3:10, Rm 214 S.W. Mudd, Columbia University.

3: " The Manganese Cluster in Photosynthesis; Where Plants Oxidize Water to Dioxygen," Dr. Vittal Yachandra, Univ. of California/Berkeley, Dept. of Chemistry, 3:00, Rm. 1003 Main Building, 100 Washington Sq., NYU.

6: "Structural Studies of Intracellular Signal Transduction," Dr. David Cowburn, Rockefeller Univ., 1:00, Dept. of Biochemistry & Cell Biology, Rm. 038, Life Sciences Building, SUNY Stony Brook.

6: "Functional Organization and Neutral Codes in the Bird Song System," Dr. Dan Margoliash, Univer. of Chicago, Ctr. for Neural Science, 12:00, Rm. 122, Washington Sq., Meyer Bulding, NYU.

7; 'Motor Cortex and Sensorimotor Transformations," Dr. John Kalaska, Univ. Montreal, 4:00, Rm. 038, Life Sciences Building, SUNY Stony Brok,

8: "Satelite Data Integration Analysis for Air-Sea and Interaction and Upper Ocean Studies in the Tropical Pacific," Dr. Xiao-Hai Yan, Ctr for Remote Sensing, College of Marine Sciences, Unver. of Delaware, 12-1, Rm. 120, Endeavor Hall - South Campus, SUNY Stony Brook.

8: "Molecular and Morphological Evolution in the Grasses," Elizabeth Kellog, Harvard, grass Systematics, Dept. of Ecology & Evolution, 3:30, Rm 038, Life Sciences Bldg., SUNY Stony Brook.

9: "Flavins and 'Smart' materials. The Interplay of Recognition and Redox Process," Dr. Vincent M. Rotello, Dept. Chemistry, Univ. of Massachusetts at Amherst, 4:00, Rm 412, Chemistry Bldg., SUNY Stony Brook.

9: "Towards a Large Scale Insertional Mutagenesis Screen in Zebrafish,"Dr. Nancy Hopkins, MIT, 4:00, Dept. of Biochemistry & Cell Biology, Rm. 038, Life Sciences Building, SUNY Stony Brook.

9: "Neural Foundations of 3D Vision: Organization and Function of Depth-Selective Nerons in Extratriate Visual Cortex," Greg DeAngelis, Dept. of Neurobiology, Stanford, 12:00, Ctr. for Neurobiology & Behavior, 7th floor conference room, N.Y. State Psychiatric Inst, 722 West 168st., Columbia Hospital.

## OCT 10-16

10: "Enzymatic Degradation of Dissolved Organic Contaminants in the Great Lakes: Relevance to Urbanized Coastal Area - Host: Cindy Lee," Dr. Carol Arnosti, Dept. of Marine Sciences, University of North Carolina, 12:30, Rm. 120, Endeavor Hall - South Campus, SUNY Stony Brook.

13: "What Combinations of Cells and Factors Will Best Promote Axonal Regeneration in Adult Mammalian Spinal Cord," Dr. Mary B. Bunge, Univ. of Miami, 12:00, Ctr. for Neural Sciences, Mediacl Center, Jacob Bleibtreu Seminar Rm., Skirball Inst., 3rd Fl., NYU

13: "Evolving Nature of Pharmaceutical Research: Impact on Collaborations with Academia," Dr. Leon E. Rosenberg, Bristol-Myers Squibb Company, Physiology & Cellular Biophysics, 12:00, Rover Physiology Conference Room - P&S 11-505, College of Physians & Surgeons of Columbia University.

14: "Of Neuronal Weavings and Cognition," Dr. Rodolfo Llinas, Dept. Physiology, NY Medical Ctr., 4:00, Rm. 038, Life Sciences Building, SUNY Stony Brook.

14: "Regulation of Calcium Release Channels," Andrew Marks, Dept. of Molecular Cardiology, Columbia Univer., Physiology & Cellular Biophysics, 12:00, Rover Physiology Conference Room - P&S 11-505, College of Physians & Surgeons of Columbia University.

15: "Large-Scale Moist-Convective Coherency in the Tropical Atmosphere: A Short Reviews on Observations and Idealized Numerical Experiments," Jun-Ichi Yano, UCAR, Monash University, Courant Inst. of Mathematical Sciences, 3:30-5:00, Rm. 1302, Warren Weaver Hall, 251 Mercer St., NYU.

15: " TBA," Kerry Shaw, Harvard, Speciation in Hawaiian Crickets, Dept. of Ecology & Evolution, 3:30, Rm 038 , Life Sciences Bldg., SUNY Stony Brook.

15: "TBA,"Dr. Jon Kaufman, EXXON, 4:00, Geosciences Dept., 4:00, Rm. 123, ESS Building, SUNY Stony Brook.

16: "New Applications for Olefin Metathesis in Organic Synthesis," Dr. Marc L. Snapper, Dept. of Chemistry, Boston Univ., 4:00, Rm. 412, Chemistry Bldg. , SUNY Stony Brook.

# SEMINARS & EVENTS

## OCT 16-22

16: "Coordinating Cell Cycle Events: The Kinase Specificity Problem," Dr. Douglas Kellogg, Univr. of Cali at Santa Cruz, 4:00, Dept. of Biochemistry & Cell Biology, Rm. 038, Life Sciences Building, CUNY Stony Brook.

16: " Genetic Analysis of Neuronal Patterning in the Dorsal," Kein Lee, Lab of Dr. T Jessell, Neural, 12:00, Ctr. for Neurobiology& Behavior, 7th FLoor conference room, N.Y. State Psychiatric Inst., 722 West 168th st.,Columbia.

17: "Fessibility Study for a New Inlet in East Matagorda Bay, Texas - Host: Henry Bokuniewicz," Dr. Nicholas Kraus, Coastal and Hydraulics Lab., U.S. Army Engineer Waterways, 12:30, 120 Endeavor Hall - South Campus, SUNY Stony Brook.

17: "The envelope please - A role for direct determination of phases in macromolecular crystallography," Dr. Douglas Dorst, Head, Electron Diffraction Department, Hauptman-Woodward Medical Research Inst., 12:00-1:15, Annenberg 21-92, Dept. of Physiology & Biophysics, Mt. Sinai, School of Medicine.

17: "Genetic Analysis Using Structure Specific Nuceases," Dr. Vitor Lyamichev, Third Wave Technology, Inc., Dept. of Chemistry, 3:00 PM, Rm. 1003, Main Building, 100Washington Sq., NYU.

21: "K Channel Structure and Function Again: a Prokaryotic End-run?," Chris Miller, Dept. Biochemistry, Brandeis Univ., 12:00, Rover Physiology Conference Room, P&S 11-505 Columbia Univer.

21: "GABA: Excitatory Transmitter in Developing Neurons," Dr. Anthony van den Pol, Yale Univ., 4:00, Dept. of Neurobiology & Behavior, Rm 038, Life Sciences Building, SUNY Stonay Brook.

22: "Water Vapor and Climate: A New Perspective," Kerry Emanuel, MIT, Courant Inst. of Mathematical Sciences, 3:30-5:00, Rm. 1302, Warren Weaver Hall, 251 Mercer St., NYU.

22: "Peroxides in the Environment: Measurement Techniques and their Role in Atmosphereic Photochemistry," Dr. Judy Lloyd, SUNY Old Westbury, Inst. for Terrestiral & Planetary Atmospheres, 12-1, Rm. 120 Endeavor Hall, SUNY Stony Brook.

22: "TBA," Carl Schlichtin, Univ. of Connecticut, Plasticity, Dept. of Ecology & Evolution, 3:30, Rm. 038, Life Sciences Blidg., SUNY Stony Brook.

## OCT 23-31

23: "Agrobacterium and Host Genes Involved in Crown Gall Tumorigenesis," Dr. Stanton B. Gelvin, Perdu Univ., 4:00, Rm. 038, Life Sciences Building, SUNY Stony Brook

24: "Aedamers and Serpentercaltors: Large Synthetic Molecules that Fold and Bind DNA," Dr. Brent Iverson, Univ. of Texas/Austin, Dept. of Chemistry, 3:00 PM, Rm 1003 Main Building, 100 Washington Sq., NYU.

24: "New Approaches in Aquatic Microbial Ecology," Dr. Paul Kemp, Dept. of Marine Sciences, 12:30, 120 Endeavor Hall - South Campus, SUNY Stony Brook.

24: "Circadian organization in mammals and other vertebrates," Sr. Michael Menaker, Dept. of Biology& NSF Center for Biological Timing, Unversity of Virginia, 12:00-1:15, Annenberg 21-92, Dept. of Physiology& Biophysics, Mt. Sinai, School of Medicine.

29: "Stochastic Models of Storm Tracks," Isaac Held, GRDL, Princeton University, Courant Inst. of Mathematical Sciences, 3:30-5:00, Rm. 1302, Warren Weaver Hall, 251 Mercer St., NYU.

29: "TBA," Peter Turchin, Univ. of Connecticut, Ecological Theory, 3:30, Rm. 038, Dept. of Ecology & Evolution, Life Science Bldg., SUNY Stony Brook.

30: "Synthesis and Biological Charactization of Endothelin Receptor Antagonists: Applications for the Treatment of Cariovascular Disease," Dr. Joel Barrish, Bristol Myers Squibb, 4:00, Rm. 412, Chemistry Bldg., SUNY Stony Brook.

30: "Was there a Cambrian Explosion?," Dr. Jefferey Levinton, 4:00, Dept. of Ecology & Evolution, Rm 123, ESS BUilding, SUNY Stony Brook.

31: "G Protein-Mediated signal transduction: Lessons from modified moleculars and modified mice," Dr. Eva Neer, Dept. of Medicine/Cardiovascular Division, 12-1:15, Anneberg 21-92, Dept. of Physiology & Biophysics, Mt. Sinai School of Medicine.

31: "The Atmonospheric Centers of Action," Dr. Sultan Hameed, Institute of Terrestrial and Planetary Atmospheres/Marine Sciences Research Center, 12:30, 120 Endeavor Hall - South Campus, SUNY Stony Brook.

## MOTONEURONS USING CONFOCAL LASER SCANNING MICROSCOPY

Faulkner B. Brown TH. Evinger C.

*Experimental Brain Research. 116(1):10-19, 1997 Aug.*

The eyeblink reflex is one of the most extensively studied behaviors in mammals. The active downward force that causes lid closure is controlled by the orbicularis oculi (OO) muscle. To augment our studies on the neurophysiology and plasticity of the rat eyeblink circuit, here we present the first anatomical paper to focus exclusively on identifying and characterizing the OO motoneurons of the rat facial motor nucleus (FMN). One thousand and twenty-nine cells from four animals were retrogradely labeled by injecting the OO muscle with HRP and were imaged conventionally. One hundred and one cells from five animals were labeled by injecting the OO muscle with a 3000 mel. wt. fluorescent dextran and were imaged using confocal laser scanning microscopy (CLSM). The latter method resulted in little tissue shrinkage, bright labeling, and excellent resolution of the soma, dendrites, and axon. Furthermore, it is a histologically simple alternative to HRP for retrograde labeling from the neuromuscular junction. Both methods revealed that the OO motoneurons were distributed over the entire length of the FMN, that they were concentrated along the dorsal crest of the nucleus, and that they were less numerous in the extreme rostral and caudal regions. As measured using the CLSM method, cell body areas were highly variable, ranging from 317 to 1500 mu m(2), but there was no size gradient along the rostrocaudal extent of the FMN. The neurons exhibited seven primary dendrites on average, which gave rise to bifurcating and even trifurcating secondary dendrites. Using the HRP method, the estimated area of OO motoneurons ranged from 161 to 1381 mu m(2). The combined methods furnished a detailed characterization of the number, spatial distribution, and morphology of rat OO motoneurons. Moreover, these methods provide a useful way to analyze the circuitry that modulates the rat eyeblink.

---

## CARBOHYDRATES AND FERTILIZATION - AN OVERVIEW [Review]

Benoff S.

*Molecular Human Reproduction. 3(7):599-637, 1997 Jul.*

Initial sperm-egg binding in mammals involves recognition of glycosylated proteins of egg zonae by glycosylated proteins on sperm surfaces. Egg zona protein structure is relatively simple, and has been strongly conserved. Species specificity must reside in the carbohydrate modifications on the egg surface, and in the co-ordinated assembly of a unique cohort of sperm proteins at capacitation. Fruitful advances have been made along four lines, Oligosaccharide structures capable of binding spermatozoa have been dissected by in-vitro synthesis and binding experiments, informed by the general advance of knowledge of protein glycosylation processes. Site-specific mutagenesis of zona proteins and their expression in tissue culture have identified glycosylation sites involved in species-specific sperm binding. Antibody and lectin labelling studies show a continuing process of remodeling of glycosylated sperm surface epitopes within a set of stable compartments during epididymal transit and capacitation of spermatozoa, Characterization of sperm-egg binding proteins from a variety of mammalian species shows that a different set of effecters induce acrosome reactions in each species, with each set including one or more sugar-recognizing proteins. Sequencing of some of these effecters suggests that each group may form a supermolecular complex to induce a species-specific acrosome reaction, with the functional activities distributed in a species limited or non-limited manner among the individual proteins.

---

## LIMITS ON WWZ AND WW-GAMMA COUPLINGS FROM P(P)OVER-BAR-]E-NU-JJX EVENTS AT ROOT-S=1.8 TEV

Abbott B. Abolins M. Acharya BS. Adam I. Adams DL. Adams M. Ahn S. Aihara H. Alves GA. Amidi E. Amos N. Anderson EW. Astur R. Baarmand MM. Baden A. Balamurali V. Balderston J. Baldin B. Banerjee S. Bantly J. Bartlett JF. Bazizi K. Belyaev A. Beri SB. Bertram I. et al.

*Physical Review Letters. 79(8):1441-1446, 1997 Aug 25.*

We present limits on anomalous WWZ and WW gamma couplings from a search for WW and WZ production in p (p) over bar collisions at root s = 1.8 TeV. We use p (p) over bar --> evjjX events recorded with the DO detector at the Fermilab Tevatron Collider during the 1992-1995 run. The data sample corresponds to an integrated luminosity of 96.0 +/- 5.1 pb(-1). Assuming identical WWZ and WW gamma coupling parameters, the 95% C.L. limits on the CP-conserving couplings are -0.33 < lambda < 0.36 (Delta kappa = 0) and -0.43 < Delta kappa < 0.59 (lambda = 0), for a form factor scale Lambda = 2.0 TeV. Limits based on other assumptions are also presented.

---

## CONTRIBUTION OF VESTIBULAR COMMISSURAL PATHWAYS TO SPATIAL ORIENTATION OF THE ANGULAR VESTIBULOOCULAR REFLEX

Wearne S. Raphan T. Cohen B.

*Journal of Neurophysiology. 78(2):1193-1197, 1997 Aug.*

During nystagmus induced by the angular vestibuloocular reflex (aVOR), the axis of eye velocity tends to align with the direction of gravitoinertial acceleration (GIA), a process we term "spatial orientation of the aVOR." We studied spatial orientation of the aVOR in rhesus and cynomolgus monkeys before and after midline section of the rostral medulla abolished all oculomotor functions related to velocity storage, leaving the direct optokinetic and vestibular pathways intact. Optokinetic afternystagmus and the bias component of off-vertical-axis rotation were lost, and the aVOR time constant was reduced to a value commensurate with the time constants of primary semicircular canal afferents. Spatial orientation of the aVOR, induced either during optokinetic or vestibular stimulation, was also lost. Vertical and roll aVOR time constants could no longer be lengthened in side-down or supine/prone positions, and static and dynamic tilts of the GIA no longer produced cross-coupling from the yaw to pitch and yaw to roll axes. Consequently, the induced nystagmus remained entirely in head coordinates after the lesion, regardless of the direction of the resultant GIA vector. Gains of the aVOR and of optokinetic nystagmus to steps of velocity were unaffected or slightly increased. These results are consistent with a model in which the direct aVOR pathways are organized in semicircular canal coordinates and spatial orientation is restricted to the indirect (velocity storage) pathways.

---

## ANCIENT MISSENSE MUTATIONS IN A NEW MEMBER OF THE RORET GENE FAMILY ARE LIKELY TO CAUSE FAMILIAL MEDITERRANEAN FEVER

Aksentijevich I. Centola M. Deng ZM. Sood R. Balow JE. Wood G. Zaks N. Mansfield E. Chen X. Eisenberg S. Vedula A. Shafran N. Raben N. Pras E. Pras M. Kastner DL. Blake T. Baxevanis AD. Robbins C. Krizman D. Collins FS. Liu PP. Chen XG. Shohat M. Hamon M. Kahan T. et al.

*Cell. 90(4):797-807, 1997 Aug 22.*

Familial Mediterranean fever (FMF) is a recessively inherited disorder characterized by dramatic episodes of fever and serosal inflammation. This report describes the cloning of the gene likely to cause FMF from a 115-kb candidate interval on chromosome 16p. Three different missense mutations were identified in affected individuals, but not in normals. Haplotype and mutational analyses disclosed ancestral relationships among carrier chromosomes in populations that have been separated for centuries. The novel gene encodes a 3.7-kb transcript that is almost exclusively expressed in granulocytes. The predicted protein, pyrin, is a member of a family of nuclear factors homologous to the Ro52 autoantigen. The cloning of the FMF gene promises to shed light on the regulation of acute inflammatory responses.

---

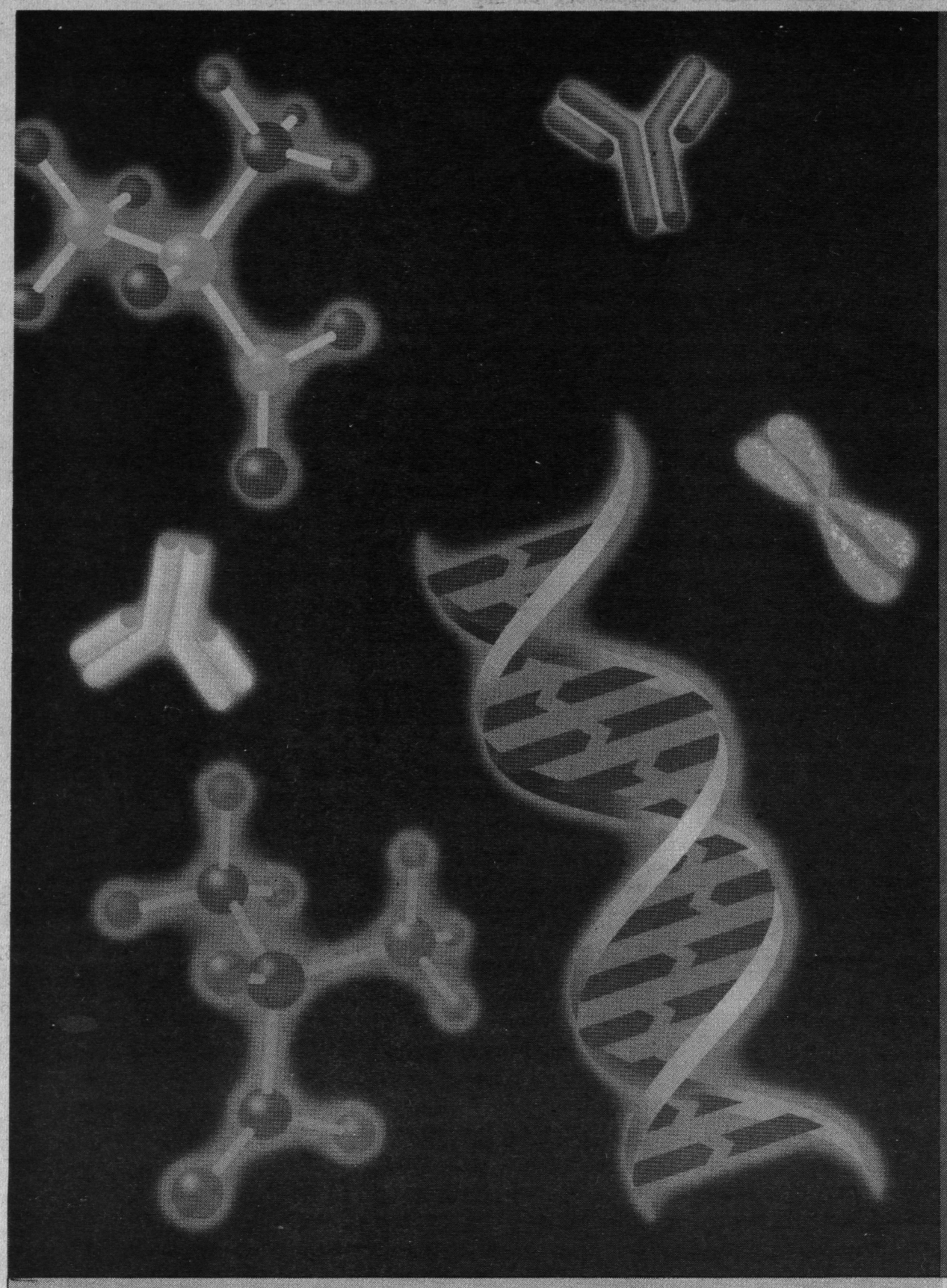
## POSTMORTEM STUDIES OF THE HIPPOCAMPAL FORMATION IN SCHIZOPHRENIA

Dwork AJ.

*Schizophrenia Bulletin. 23(3):385-402, 1997.*

Many postmortem studies report differences between the hippocampal formations of patients with schizophrenia and those of controls, These differences include volume changes, cell density changes, periventricular gliosis, senile degenerative changes, and abnormalities of neuronal size, position, or orientation, However, the findings are almost never common to all schizophrenia patients within a series. Furthermore, some well-designed studies are negative, and different positive reports are mutually contradictory, Some of the inconsistencies are methodological, The normal variation, over small distances, in the cytoarchitecture of the temporal allocortex creates particular difficulties when this region is studied with a limited number of sections, especially if the sample size is small, Other inconsistencies are probably the result of case selection. We review the methods and findings of some of these studies, stressing the dangers of eliminating (rather than evaluating) cases with definite neuropathologic changes, We conclude that the existing postmortem studies of temporal lobe morphology provide little conclusive evidence for the neural substrate of schizophrenia.

---



Your time is better spent researching science – we'll research the supplies.

Suppliers of enzymes, antibodies, lab equipment, and over 15,000 other biomedical research products can now all be found from one source: *The 1997 BioSupplyNet Source Book* or its World Wide Web counterpart, BioSupplyNet.

As a companion to Cold Spring Harbor Laboratory Press manuals, *The Source Book* has quickly become the authority on where to find anything you would need to outfit your lab.

Through our web site, you're able to search databases by product name or category. Need protease inhibitors? Click a button, and you have access to over a dozen suppliers. Click again, and you have access to protocols and specific product data for your comparison. Click again, and you have access to special offers and the latest products on the market.

Now you can find exactly what you need when you need it. Visit our web site at http://www.biosupplynet.com, and get *The Source Book* while you're there.

BIOSUPPLYNET
INCORPORATED

**http://www.biosupplynet.com**

# Selected Funding Updates

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

**NSF: 1998 Graduate Research Fellowships Program**

NSF will award approximately 1,000 new three-year **Graduate Fellowships** and **Minority Graduate Fellowships** in March 1998. Separate competitions are conducted for Graduate Fellowships and Minority Graduate Fellowships, each with additional awards offered for **Women in Engineering and Computer and Information Science.** Minority Graduate Fellowships are available to members of racial and ethnic minority groups that traditionally have been underrepresented in the advanced levels of the Nation's science and engineering talent pool. Fellowships are awarded for graduate study leading to research-based master's or doctoral degrees in the fields of science, mathematics, and engineering supported by the National Science Foundation.

Graduate and Minority Graduate Fellowships are open only to individuals who are, at the time of application, citizens or nationals of the United States or permanent resident aliens of the United States. Fellowships are intended for students at or near the beginning of their graduate study in science, mathematics, or engineering. In most cases an individual has two opportunities to apply: during the senior year of college and in the first year of graduate school. Specifically, eligibility is limited to those individuals who, by the beginning of the fall 1997 term, have completed no more than 20 semester hours, 30 quarter hours, or equivalent, of graduate study in the science and engineering fields supported by this program since completion of a baccalaureate degree in science or engineering.

All applicants are expected to take the GRE General Test (Verbal, Quantitative, and Analytical). In addition, all applicants should take a GRE Subject Test in the science or engineering field most closely related to their chosen area of graduate study.

The NSF Fellowship stipend during 1998-99 will be $15,000 for 12-month tenures, prorated monthly at $1,250 for lesser periods. In addition to the funds for stipend payments, the NSF provides the fellowship institution, on behalf of each Fellow, a cost-of-education allowance of $9,500 per tenure year. During tenure, Fellows will be exempt from paying tuition and fees normally charged to students of similar academic standing, unless such charges are optional or are refundable.

Printed application forms may be obtained by direct request: NSF Graduate Research Fellowship Program, Oak Ridge Associated Universities (ORAU), P.O.Box 3010, Oak Ridge, TN 37831-3010, or telephone: 423-241-4300, or fax: 423-241-4513, or Internet electronic mail to: nsfgrfp@orau.govb. Application materials may also be found at the NSF WWW-site. Deadline for entering the competition: **November 6, 1997.**

**EPA: 1998 Grants for Research**

The U.S. Environmental Protection Agency (EPA), Office of Research and Development (ORD), invites research grant applications in the following areas of special interest to its mission.

**Exploratory Research**

- environmental biology, due March 31,1998
- human health, due December 16, 1997
- environmental chemistry, due December 16, 1997
- physics, due March 12, 1998
- environmental engineering, due March 12, 1998

Contact: Clyde Bishop 202-564-6914
bishop.clyde@epamail.epa.gov

NCERQA is seeking grant applications to conduct exploratory environmental research based on investigator-initiated proposals in the broad areas listed above. Funding: Approximately $6 million is expected to be available in FY 98 for new exploratory research grants. The projected award range is $75,000 to $125,000/year for up to 3 years.

**Indicators of Global Climate Change,** due February 12, 1998
Contact: Barbara Levinson 202-564-6911
levinson.barbara@epamail.epa.gov

This competition requests proposals designed to distinguish, quantify, and evaluate local or regional ecological impacts of global climate change in the context of other environmental changes. The competition will focus on developing indicators of ecological impacts within the United States of changing (a) global climate and (b) greenhouse gas (GHG) concentrations. The indicators produced will necessarily involve ecological processes in ecosystems which are modeled and measured in several regions. Funding: Approximately $5 million, with a projected award range from $75,000 to $250,000 per award per year, and an approximate duration of 3 years, will be available.

**Interindividual Variation in Human Susceptibility to Environmentally-caused Disease,** due February 12, 1998
Contact: David Reese 202-564-6919
reese.david@epamail.epa.gov

Proposals are requested to evaluate the role that interindividual variation plays in the susceptibility of humans to disease caused by environmental agents. Susceptibility can be a function of intrinsic factors such as age, sex, race, and/or genetic polymorphisms; it may also be due to extrinsic factors such as unique patterns of exposure. Those factors which can have an effect on the susceptibility of individuals to specific disease need to be identified and quantitated in the general population. Although molecular epidemiological approaches are of interest, studies on experimental animal models which can be extrapolated to humans are also appropriate. Studies which incorporate data into the development of dose-response models for use in risk assessment are of particular interest. The most competitive proposals, in priority order, will be those which: (1) utilize hypothesis testing in defining cause and-effect relationships between changing climate and GHG concentrations and documented ecological impacts in the U.S.; and (2) document indicators which function as early-warning signals of significant ecological impacts in the U.S. from changing climate. Funding: Approximately $2 million is expected to be available in FY 98 for new research grants. The projected award range is $100,000 to $200,000/year for up to 3 years.

Additional general information on the grants program, forms used for applications, etc., may be obtained by exploring the EPA Web page at **<http://www.epa.gov/ncerqa>**.

**AFOSR: BAA 98-1**

The Air Force Office of Scientific Research (AFOSR) invites proposals for basic research in support of the Air Force Defense Research Sciences Program. This program is described in the document entitled "Research Interests and Broad Agency Announcement 98-1". This document will guide proposers through AFOSR's research program and facilitate their preparation of research proposals. It is available on the AFOSR web site at **http://www.afosr.af.mil**. The general areas of interest are:

**New World Vistas:** e.g. science and technology needed to support six future Air Force capability areas: Global Awareness, Dynamic Planning and Execution Control, Global Mobility in War and Peace, Projection of Lethal and Sublethal Power, Space Operations, and People.

**Aerospace and Materials Sciences:** structural mechanics; mechanics of materials; particulate mechanics; turbulence and internal flows; airbreathing combustion; space power and propulsion; metallic structural materials; ceramics and nonmetallic structural materials; and organic matrix composites.

**Physics and Electronics:** plasma physics; electromagnetic devices; novel electronic components; atomic and molecular physics; imaging physics; optoelectronic information processing: devices and systems; photonic physics; optics; quantum electronic solids; semiconductor materials; electromagnetic materials.

**Chemistry and Life Sciences:** polymer chemistry; surface science; theoretical chemistry; molecular dynamics; chronobiology and neural adaptation; perception and cognition; sensory systems; bioenvironmental sciences

**Mathematics and Geosciences:** dynamics and control; physical mathematics and applied analysis; computational mathematics; optimization and discrete mathematics; signal communication and surveillance; software and systems; artificial intelligence; electromagnetics; external aerodynamics and hypersonics; atmospheric physics; ionospheric research; and space sciences.

**Researcher Assistance Programs:** United States Air Force/National Research Council Resident Research Associateship Program; University Resident Research Program; Summer Faculty Research Program; Summer Research Extension Program; Graduate Student Research Program; and National Defense Science and Engineering Graduate Fellowship Program.

Contact persons, evaluation criteria, and details on specific areas of interest, is discussed in the AFOSR pamphlet entitled "Research Interests and Broad Agency Announcement, 98-1." Before sending a proposal, inquire if someone at AFOSR is interested in your field of work. That person can also provide guidance for preparing a proposal before you begin to develop the proposal. d. Additional information and guidance on format and proposal submittal may be found in AFOSR Pamphlet 64-11, "Proposer's Guide to AFOSR's Research Programs". This pamphlet is also available on the AFOSR web site.

AFOSR will physically move in the Spring of 1998 from Bolling Air Force Base, Washington DC to Arlington VA and all phone number will undoubtedly change. The document will be updated as soon as any new information regarding new phone numbers and points of contact changes become available.

**NSF: STC Integrative Partnerships**

The Science and Technology Centers (STC) Integrative Partnerships Program serves as an innovative vehicle to conduct world-class research by bringing together a critical mass of facilities and expertise from academia, national laboratories, industry, and other sectors of society. The program's mode of funding, which involves multiple partners, brings key strengths to national research enterprises and focuses on making research useful to society. The program will support basic research to study multidisciplinary problems of the type that NSF normally supports and the integration of this research with educational processes. The program will initiate a competition in early fiscal year 1998 and expects to make 8 to 10 awards in fiscal year 2000. Proposed annual budgets may range from $1.5 to $4.0 million of NSF support.

For updates or further information, visit the Office of Science and Technology Infrastructure (OSTI) Home Page (http://www.nsf.gov/od/osti) on the World Wide Web, or contact OSTI by phone, 703-306-1040, or by e-mail, sti@nsf.gov.

**US Army Medical Res. & Materiel Command: Prostate Cancer Research Program**

The United States Army Medical Research and Materiel Command (USAMRMC), through this Broad Agency Announcement (BAA), is soliciting applications for prostate cancer research. Proposals are sought across all areas of basic, clinical, behavioral, and epidemiological research. The objective of the USAMRMC Prostate Cancer Research Program (PCRP) is to

Continued on Page 22

# Two Physics Discoveries At BNL

## Exotic Meson, Rare Kaon Decay Both Reported in September

by Kathryn Gavin

A pair of physics discoveries were published in September by two separate international teams of scientists working at the Alternating Gradient Synchrotron particle accelerator at Brookhaven National Laboratory. Both papers were published in *Physical Review Letters.*

**Evidence for a New Particle: The Exotic Meson**

On September 1, a team of 51 researchers led by physicists from the University of Notre Dame and including scientists from Brookhaven and six other institutions announced they may have found evidence of a new and rare subatomic particle, called an "exotic meson."

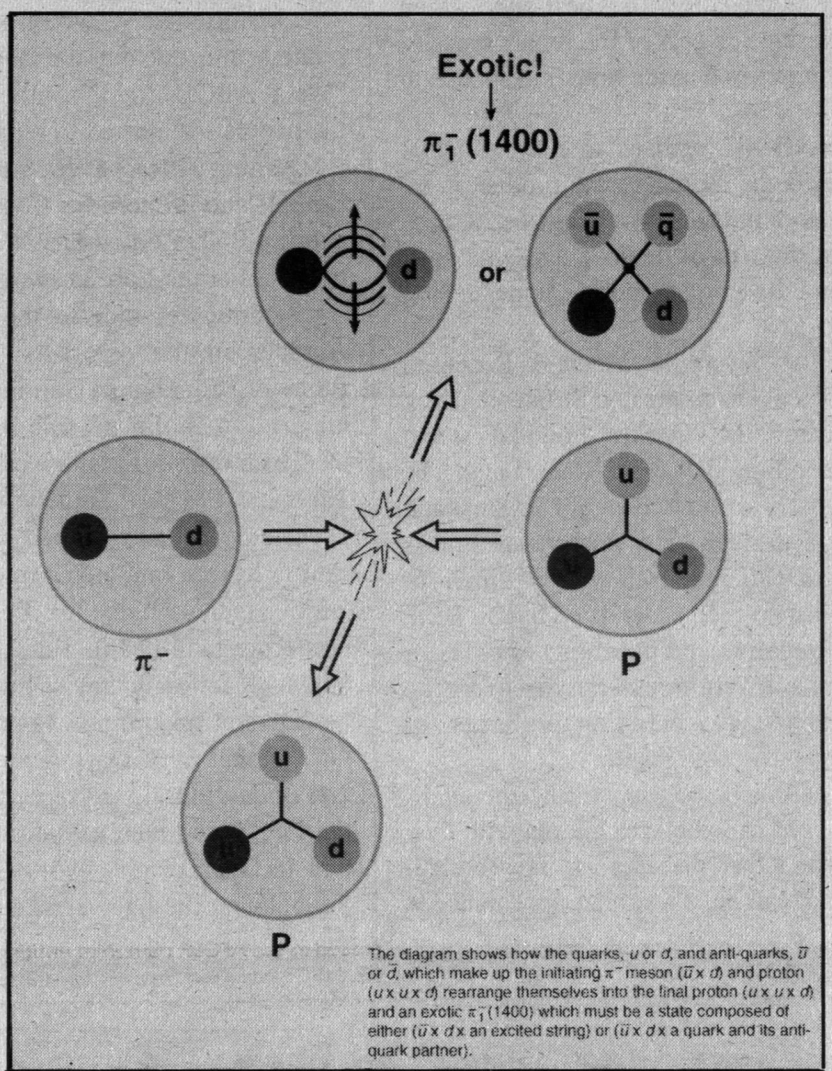
The finding, which helps validate the central theory of modern physics called the Standard Model, came after five years of needle-in-a-haystack searching through the reaction products of billions of particle collisions at the AGS.

The experiment, known as E852, closely examined each of the particles produced when an 18-billion-electron-volt AGS particle beam hit a target of liquid hydrogen in an instrument called the Multi-Particle Spectrometer. The physicists then weeded out possible exotic mesons from the billions of particles produced in the target, and analyzed their results using sophisticated statistical techniques.

Theorists hailed the reported find as a possible fulfillment of earlier predictions that hybrid mesons, containing both quarks and gluons, could exist.

Besides BNL and Notre Dame, the paper's authors included scientists from Northwestern University, Rensselaer Polytechnic Institute, the University of Massachusetts Dartmouth, and Russia's Institute for High Energy Physics and Moscow State University.

But missing from the paper were ten members of the E852 collaboration from Indiana University, who made public their disagreement with their colleagues' claim. The scientists said they were not convinced that the evidence pointed clearly to a new particle.




The diagram shows how the quarks, *u* or *d*, and anti-quarks, $\bar{u}$ or $\bar{d}$, which make up the initiating $\pi^-$ meson ($\bar{u} \times d$) and proton ($u \times u \times d$) rearrange themselves into the final proton ($u \times u \times d$) and an exotic $\pi_1^-(1400)$ which must be a state composed of either ($\bar{u} \times d$ x an excited string) or ($\bar{u} \times d$ x a quark and its anti-quark partner).

A depiction of the production of the exotic meson, from a collision between a normal meson and a proton. (Image courtesy BNL)

Meanwhile, the remaining members of the collaboration presented their findings at a conference held at BNL the week before the paper's publication. The conference also featured possible confirmation of the result, reported by the "Crystal Barrel" collaboration at CERN, the European particle physics laboratory.

**An Odd Bird in the Particle Zoo**

The exotic meson, like many of the elementary particles studied by physicists, is thought to have an internal structure. The building blocks of this structure are called quarks, anti-quarks (which are the anti-matter opposites of quarks), and gluons, named for their ability to hold quarks and anti-quarks together like glue.

Elementary particle physicists have divided these quark-and-gluon particles into two types, called baryons and mesons, depending on which building block combinations they are made of. Baryons (such as the familiar proton and neutron) contain three quarks, while mesons contain a quark and an anti-quark. The quarks in both baryons and mesons are bound together by gluons.

In one theoretical model of how a meson is structured, the gluon is pictured as a sort of string stretched between the quark and the anti-quark. The quark and anti-quark "pull" on opposited ends of the string, much like contestants in a tug-of-war.

In normal mesons, the gluon "string" is stretched tight, in what is called its ground state, and is not vibrating. But theorists have expected that mesons should also exist in states where the gluon string is oscillating, like a plucked violin string.

Some of those theoretical mesons have been predicted to have properties not allowed in normal mesons, making them "exotic." A meson could also have these exotic properties if it consisted of a pair of quarks and a pair of anti-quarks, instead of just one quark and one anti-quark.

Explained Suh-Urk Chung, a Brookhaven physicist and co-spokesman for the E852 collaboration, "Our new meson is exotic because it can't be a meson made of a quark and an anti-quark with a ground-state gluon string. It must be either a quark and an anti-quark with a "plucked" string, or a four-quark system bound by a ground-state string."

**A Rare Find: One-in-Ten-Billion Kaon Decay**

Just three weeks after the exotic meson paper was published, an entirely different team of scientists working at another huge AGS experiment reported their own discovery in the same journal. After ten years of searching, physicists working on the experiment called E787 reported finding the rarest decay of a subatomic particle ever detected.

The phenomenon is thought to happen only once or twice in every 10 billion self-destructions of an unstable particle known as a kaon. Instead of producing the usual breakdown products seen when a kaon decays, the rare kaon decay, as it is called, is thought to have released a positively charge pi meson, a neutrino and an anti-neutrino.

Not only is the proccess rare, it is also extremely elusive. The scientists report that to see even one such event, they had to sift through one trillion ordinary decays to achieve the one-in-ten-billion level of sensitivity required.

The team is made up of 50 researchers from Brookhaven, Canada's TRIUMF laboratory and University of Alberta, Japan's KEK laboratory and Osaka University, and Princeton University.

The spotting of the rare kaon decay sheds new light on the universe's most elemental forces and most basic building blocks, as explained by the extraordinarily successful theory of subatomic particles known as the Standard Model. It may also suggest new phenomena that cannot be explained by the Standard Model.

Said Brookhaven physicist and E787 co-spokesman Laurence Littenberg, "From here, it is up to us and others to test that belief through further exploration and experimentation. We plant to collect and analyze ten times more data in order to gauge its consistency with the Standard Model,

Continued on Page 19

## The AGS: A Workhorse of Physics

This month's pair of announcements from scientists working at the Alternating Gradient Synchrotron have focused new attention on the 37-year-old machine, the workhorse of Brookhaven's stable of scientific facilities.

Its power level and particle-beam intensity improved by recent upgrades, the AGS is not resting on the laurels won in earlier years, when three Nobel prizes in physics were given for discoveries made there, and several new particles were first glimpsed in bubble chambers and spark chambers in its cavernous experimental hall.

The accelerator has actually broadened its user base, expanding from purely high-energy physics to nuclear physics and radiation biology studies that use a heavy-ion beam produced by another BNL accelerator, the Tandem Van de Graaff and fed into the AGS.

Beginning in 1999, the AGS itself will inject heavy ion and polarized proton beams into the Relativistic Heavy Ion Collider (RHIC), BNL's newest accelerator, while keeping its own scientific programs going simultaneously.■

Dystonia.. Continued from Page 4

end of 1998.

What the team is presently finding however, is that the DYT1 protein has significant similarities to heat-shock proteins and proteases. Found in virtually all living organisms, the heat-shock proteins/proteases help cells recover from stresses including heat, traumatic injury, and chemical poisoning. Until now, no human disease has been associated with these proteins.

"The heat-shock proteins have a binding site for ATP which is the energy molecule in the cell. The heat-shock proteins appear to become more active or upregulated when the cell is stressed with heat, for example" says Dr. Brin. "The buzzword for these proteins is 'chaperone' — they chaperone energy from one part of the cell to the other — and if you stress the cell with a heat-shock, then the chaperoning process becomes more aggressive as part of the repair process. Our idea is that if you cripple a heat-shock protein, then the body's response to stress can become compromised."

"The disease needs a trigger," says Breakefield, "perhaps an environmental stress, infection or a change in another gene. If the mutated gene product is set off, there is no stopping it, but if the process does not start by the age of 28, people with the mutation are virtually free from the risk of developing symptoms. We now have an important clue to help us find that trigger and, we hope, to stop it."

Supporters of this research include the Dystonia Medical Research Foundation, the National Institute of Neurological Disorders and Stroke, the Jack Fasciana Fund for Support of Dystonia Research, the Histadrut Foundation and the Bachmann-Strauss Dystonia and Parkinson Foundation at Mount Sinai. The Bachmann-Strauss Foundation works very closely with Dr. Brin of Mt. Sinai and has raised over $3 million since its inception in 1995. The Bachmann-Strauss Foundation is led by Bonnie Strauss, a dystonic patient herself who was improperly diagnosed for years until her condition was correctly identified by Dr. Brin.

Present treatments include deep brain stimulation and injections of drugs or purified toxins to help ease dystonic symptoms. If future research discovers the triggers that set off dystonia in vulnerable individuals, identifying the carriers of the mutation could allow application of preventative treatments.

One of the most immediate application of this discovery will be the availability of a simple, inexpensive blood test to confirm whether children with dystonia symptoms have this disorder rather than other diseases — like cerebral palsy or early-onset Parkinson's disease — that can have a similar appearance.■

Reactor... Continued from Page 5

not respond kindly. On Sept. 17, representatives of many local civic organizations and community groups gathered at the BNL main gate to voice their distress at what they saw as an effort to derail the DOE's community-involvement process.

"DOE began a process two months ago wherein they were going to allow the community to have some input as to what the future of the HFBR would be, and then in December there would be a draft of the community's response," said Rich Johannessen, president of the Affiliated Brookhaven Civic Organization, or ABCO, an umbrella group for the numerous village and hamlet civic associations in Brookhaven Town.

"Unfortunately, two of our elected officials decided to circumvent that process and cut out the people's participation," Johannessen continued. "We at ABCO find that offensive. The process has been short-circuited by the people we elected to represent us."

Joining ABCO at the press conference were representatives from the Long Island Progressive Coalition, the Long Island Neighborhood Network and the BNL Community Work Group, which has monitored environmental issues at the Lab for two years.

Adding its voice to the chorus of disapproval was the Long Island Association, the largest local business organization. "The decision on the future of Brookhaven National Laboratory's reactor should be based on science, not on politics," said Matthew Crosson, the LIA's president.

Even former Presidential Science Advisor and current president of the American Physical Society Allan Bromley chimed in, writing in a letter to D'Amato, "I have learned recently that you and Representative Michael Forbes have submitted companion legislation that would permanently close Brookhaven's High Flux Beam Reactor, one of only four major neutron scattering facilities in our country. From a scientific standpoint, I believe that such action is unwise and unwarranted."

Several upcoming events should continue the debate over the HFBR. On October 6, at Dayton Ave. School in Manorville, from 6-8 p.m. DOE and BNL will hold the second in a series of public poster sessions to explain the HFBR and the evaluation process. And on October 9 at 7 p.m., ABCO and the Community Work Group will hold a forum at Longwood High School near the Lab, to take community comments.■

Continued from Page 17

and to test the possibility that the event we've seen could even involve entirely new particles or forces."

**Catching A Shooting Star**

Finding the rare kaon decay required an accelerator powerful enough to produce kaons in vast numbers, making the AGS, with the world's most intense kaon beam, an appropriate choice.

But equally important was the team's array of detectors sensitive enough to catch the particle equivalent of a shooting star: Kaons last only about 12 billionths of a second before decaying, and they can decay a multitude of different ways, creating showers of particles that can only be seen with specialized equipment.

The Standard Model predicts that the decay of a kaon to a pi meson and a neutrino pair sometimes involves the momentary creation of both a charged W boson and a neutral Z boson (which itself instantly decays into the two neutrinos), rather than the more easily produced exchange of a single W or Z. It can also involve the recently discovered massive top quark, and thus give a window into the relation between that exotic object and the normal quarks which make up our everyday world.

Understanding such complex forms of decay is especially important to physicists attempting to learn how matter behaves at the most fundamental level. The one-in-ten-billion probability of a kaon decaying to a pi meson and a neutrino pair is a remarkable prediction of the Standard Model - and one that the experimenters set out to test.

So, to catch a fleeting pi meson, the experimenters in 1995 built themselves a new "catcher's mitt," located in a strong magnetic field, which was made up of sophisticated particle detectors used to measure as much as possible about each pi meson that passed by. These detectors included scintillating fibers, a tracking chamber and a host of other device used to determine the energy and momentum of the pi meson and to observe its characteristic decay into other particles.

The improved equipment increased the chances of seeing a rare decay if it occurred, and vastly reduced the chances of confusing it with other phenomena that send out nearly the same signal but happen billions of times more often.■

# Resistance to Leptin Contributes to Obesity

## New Study of Leptin Intolerance Provides Clues to Protein's Action

by RU News Services

Insensitivity to the protein leptin, which helps the body regulate its fat stores, contributes to obesity in mice according to the first formal study of leptin intolerance, report scientists in the Aug. 5 *Proceedings of the National Academy of Sciences.* The findings also provide clues about leptin's action in the nervous system and may help to explain some forms of obesity that affect humans, including more than 50 million overweight adult Americans, the researchers note.

"We knew obese mice and humans generally have high levels of leptin in their blood, which suggested that the protein was not fully active. Our new research directly shows that resistance to leptin can cause obesity," explains senior author Jeffrey Friedman, M.D., Ph.D., professor at The Rockefeller University and an investigator with Howard Hughes Medical Institute (HHMI).

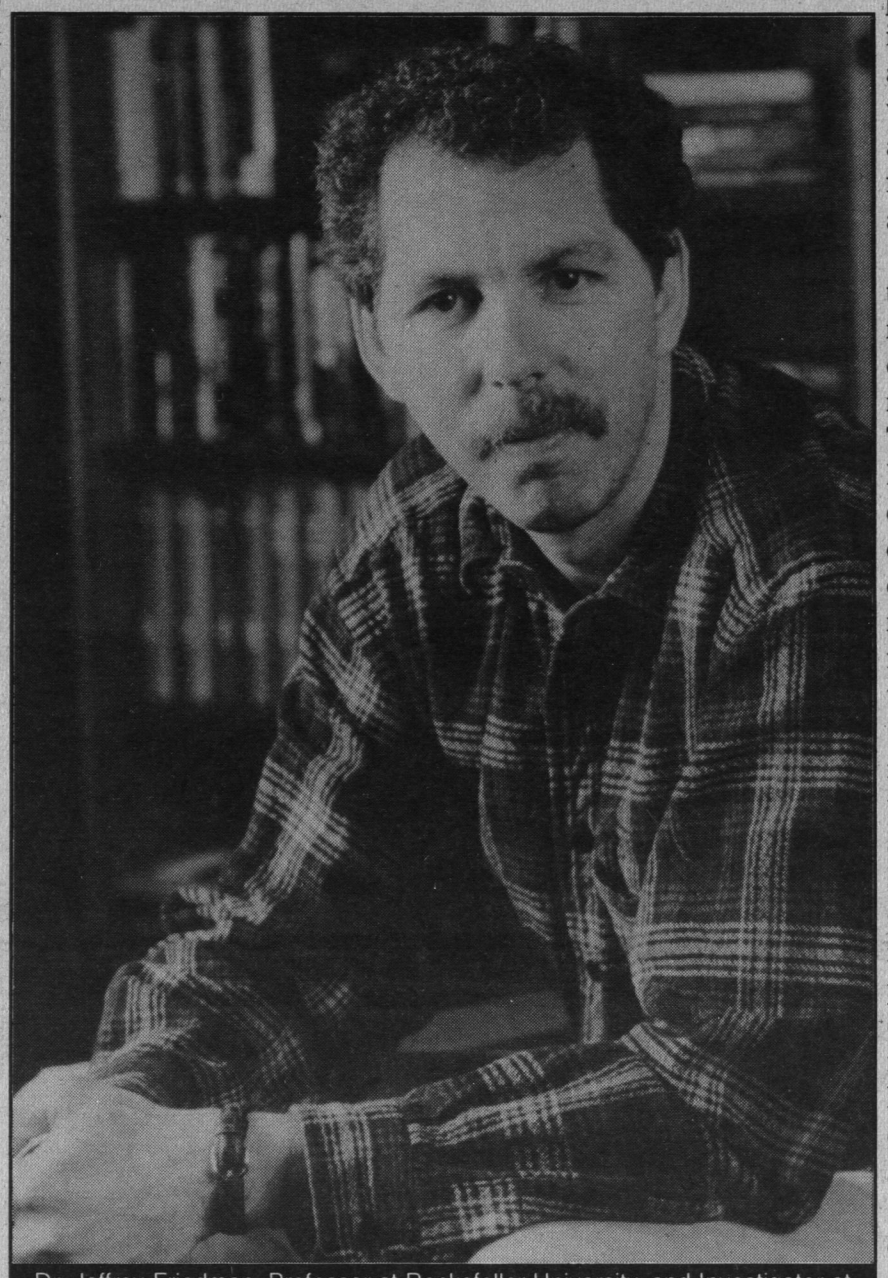
Some investigators have suggested that leptin's principal role is to suppress the body's response to starvation. The new study also suggests that receiving extra leptin adjusts a mouse's `set point' for the body weight to a lower — but stable level — by reducing food intake without an accompanying decrease in energy use.

"These data confirm that leptin plays an important role in the body's response to weight gain. This result suggests that lean animals increase their production of leptin to return their weight to the set point," explains first author Jeffrey L. Halaas, B.S., biomedical fellow at Rockefeller. "Also, leptin acts to blunt the reduction in energy use that typically follows a reduction in the number of calories eaten."

In previous studies, Friedman and his colleagues discovered leptin and documented weight loss in genetically obese and normal mice given daily injections of the protein for two weeks. These early studies required high dose injections of leptin. In the current study, much lower doses were effective in reducing weight when the hormone was delivered as a constant infusion. While receiving leptin, the mice ate less and had a relative increase in their energy use compared to fasted mice. Leptin, a product of the obese gene, is made in fat and then is released into the blood stream, by which it travels to the brain.

Obesity, defined as being more than 20 percent above a healthy weight, affects one in three Americans and is a major risk factor for diabetes, heart disease, high blood pressure, stroke, sleep apnea, gallstones, some cancers and forms of arthritis, according to the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), part of the federal government's National Institutes of Health. NIDDK supported the research, along with the Robert J. Jr. and Helen C. Kleberg Foundation.

In the new study, Friedman and his coinvestigators from Columbia University, St. Luke's-Roosevelt Hospital Center, University of Melbourne and the Howard Florey Institute of Experimental Physiology and Medicine, found that three strains of obese mice, all with normally high levels of leptin, are overweight because they have varying degrees of insensitivity to the protein. The team examined the effect of leptin given during a 30-day period as infusions either into the fat tissue under the skin or directly into the fluid that bathes the brain and spinal column. This innovative technique, called ICV infusion, was developed by coauthor Dr. Derek A. Denton of the Howard Florey Institute in Melbourne, Australia.



Dr. Jeffrey Friedman, Professor at Rockefeller University, and Investigator at Howard Hughes Medical Institute

Normal weight, lean mice receiving leptin by either method lost significant weight and fat, with low doses delivered via ICV infusion having the same effects as high doses given as subcutaneous infusions into the fat tissue. For example, during ICV infusion, at a constant rate of 8 nanograms (ng) per hour, lean mice lost 15 percent of their body weight, yet this dose had no effect when given to other lean mice by the subcutaneous injection.

"The difference between the increased potency of leptin in lean mice receiving the protein via ICV infusion and those receiving subcutaneous injections shows that the central nervous system, in particular the hypothalamus, is an important site of leptin action," says Friedman. "Indeed, chronic ICV infusions of very low doses of leptin replicate the weight-reducing effects of much higher doses of leptin given by injection. The basis for this apparent difference is not clear, but may suggest that the transport of leptin across the blood-brain barrier, which allows leptin to enter the brain from the body's blood stream, may be an important step in the body's processing of leptin's signal."

Specifically, in normal, lean mice, injecting leptin subcutaneously at an infusion rate of 200 ng per hour, for example, led to an increase in blood levels, from 5 to 7 ng/milliliter, and resulted in a 5 percent reduction in weight. A doubling of leptin levels led to a 9 percent reduction in weight, while a five-fold increase in leptin levels yielded a 15 percent weight loss.

Other lean mice receiving leptin through ICV infusion rapidly lost fat, reaching their lowest weight by the eighth day of treatment and maintained it for the remainder of the 30-day infusion period. The mice reduced their food intake to its lowest level, a drop of more than 50 percent, by the third day, but their food intake crept back to original levels by the eighth day. After the 30 days of ICV, the researchers replaced the cerebrospinal fluid and the mice quickly recovered their weight by eating more food.

To compare leptin's effects via injection and ICV infusion among overweight mice, the researchers selected strains of mice with different types of obesity. One type, the Diet Induced Obese (DIO) mouse, is lean when fed regular mouse chow, but has an inherited predisposition to develop obesity when fed a diet in which 45 percent of the calories are from fat. The second strain, the NewZealand Obese (NZO) mouse, is overweight because of the action of several genes. The third kind of mouse, called *Yellow Agouti* ($A^y$), is obese due to single copy of a mutant gene.

In the leptin injection study, NZO and $A^y$ mice did not respond to subcutaneous leptin doses of 5 micrograms per hour, a 10 times greater dose than required to achieve a maximum response in the lean mice. The DIO mice lost weight when give injections of leptin, but were less sensitive than the lean mice. Also, the DIO mice fed the regular diet had a greater response to high doses of injected leptin than DIO on high-fat diets: losses of 83 vs. 30.5 percent of body fat. In the ICV infusion studies, NZO mice responded to low doses of 5 ng per hour, but doses 100 times greater yielded modest weight loss in the $A^y$ mice.

"Because the $A^y$ mice required substantially higher doses than those needed in lean and NZO mice for weight loss, leptin resistance in the $A^y$ mice may result from a defect in the nerve pathway activated by leptin," Friedman says. "In NZO mice, a decrease in the transport of leptin into the cerebrospinal fluid may cause the obesity."

Friedman, Halaas and Denton's coauthors include: Naseem Fidahusein, B.S., at Rockefeller; Carol Boozer, D.Sc., at Columbia University School of Medicine and the Obesity Research Center at St. Luke's-Roosevelt Hospital Center; and John Blair-West, Ph.D., of the University of Melbourne.■

Huntington's... Continued from Page 3

study, which showed that the mutant huntingtin protein aggregates in the nucleus of mice made transgenic for the first exon from the human protein. These mice also displayed abnormalities in movement and brain size, comparable to what is seen in the human condition. The other paper reported an *in vivo* experiment that illustrated the insolubility of the portion of the protein that contained the poly-glutamine repeats. When expressed in a test tube the poly-glutamine stretch formed aggregates. Dr. Scott Zeitlin at Columbia University is enthusiastic about the importance of the publications; "The identification of the nuclear inclusion bodies opens up a new area of investigation in HD research and helps to unify the study of other triplet repeat disease. If the inclusion bodies cause neuronal degeneration, then finding a means of dissolving the aggregates may provide a potential therapy. In this case, the result that huntingtin aggregates form in the test tube is also very important. It is much easier to screen for potential therapeutic drugs using an in vitro assay than it is to use an animal model."

Dr. Zeitlin has been working in the field of Huntington research "...since 1993, very shortly after the gene was discovered. Nancy Wexler was interested in developing animal models for Huntington's and wanted more Columbia researchers to get involved in the field. I thought it was an interesting problem to work on and a nice change from my previous work in the field of RNA processing." Dr. Wexler was on the team of researchers involved in the gene's discovery and is a colleague of Dr. Zeitlin at Columbia.

He remained in the field and now is "interested in developing mouse models for Huntington's. This involves using gene targeting technology to replace a portion of the mouse gene with the homologous region of the human gene containing the mutation responsible for the disease."

Dr. Zeitlin's work, however, is different from that in last month's *Cell* journal authored by Gill Bates at Guy's Hospital in England and Erich Wanker at the Max-Planck Institute in Germany. "Unlike Gill Bates' mice, our animals express the entire protein. We are starting to analyze our mice now to look for the effects of the mutation. We are also continuing with our initial studies on the normal function of the huntingtin gene. Previous work from our laboratory and several others showed that the gene is essential for early embryonic development." As mentioned earlier, if both copies of the huntingtin gene are knocked out in embryonic mice, they die without ever being born.

Dr. Zeitlin's latest results, not yet published, suggests that "the gene's function is essential in the extra-embryonic visceral endoderm. This tissue is responsible for providing nutrients to the growing embryo during development. We are also developing a mouse model to conditionally inactivate the huntingtin gene at different times in development and in different tissues. These mice should help us find out what the normal function of the gene is in the adult. In addition, these mice may also be important for evaluating potential gene therapy approaches based on inactivating the huntingtin gene's function."

With the publication of these two papers more questions arise. For instance, why is it that the offspring of male sufferers are fated to suffer at an earlier age than their fathers? Furthermore, although it has been shown that the huntingtin protein is expressed in many tissues of the body, why does it seem only to affect nervous tissue, with particular areas like the striatum being especially hard hit? Dr. Zeitlin is quick to point out "that a recent study investigating huntingtin expression in the rat striatum showed that huntingtin is more abundant in those cells affected by the disease. Furthermore, cells in the striatum may be more sensitive to the effects of the mutant protein because they are under more metabolic stress to begin with, and the mutant protein might interact with proteins that are present only in those cells that will be affected".

Dr. Zeitlin remains hopeful about work on Huntington's. When asked what his motivation for studying the disease was, he replied, "In addition to providing a good research problem, work on Huntington's has a direct effect on the future of Huntington patients and their families. Knowing that your work will someday have a positive effect on peoples lives is a strong motivator for the long hours in the lab."■

## – Funding Updates –

Continued from Page 16

promote innovative ideas that will lead to better understanding and control of prostate cancer. As directed in the Congressional language, the PCRP encourages innovative, multi-institutional, multi-disciplinary, and regionally focused research that is directed toward eliminating prostate cancer.

USAMRMC is strongly encouraging the scientific community to undertake great strides in innovative research to conquer prostate cancer by calling for proposals that will foster new directions, breakthrough ideas, and approaches and will bring new investigators into the field of prostate cancer research. The central theme is innovation. Scientific ventures that represent under-investigated avenues of research or novel applications of existing technologies are highly sought. Proposals addressing the needs of minority, elderly, low-income, rural, and other under-represented populations are encouraged. Although the program wishes to encourage risk-taking research, such projects must nonetheless demonstrate solid scientific judgment and rationale.

The programmatic strategy is being implemented by a solicitation for proposals in two research award categories: **New Investigator Awards** and **Idea Development Awards**. The intent of the New Investigator Award is to promote and reward innovative ideas and technology from new investigators to conquer prostate cancer. In accordance with this challenge to be innovative, the USAMRMC invites the submission of New Investigator proposals that may lack pilot data. The Idea Development Awards, on the other hand, are intended to support innovative projects from established investigators that show promising preliminary data in prostate cancer. The USAMRMC is particularly interested in preparing new scientists for careers in prostate cancer research and presenting an opportunity to move established investigators into the prostate cancer field.

There is a total of $32M available for this program. The programmatic strategy features a change in emphasis from past Department of Defense (DOD) Congressionally Directed Medical Research Programs. The strategy is centered around a new Dual-Phase Research Award. After two years of research, the USAMRMC will challenge all funded PCRP investigators to compete for an additional two years of funding. Awards will be given after competitive evaluation to the prostate cancer investigators who (1) demonstrate the most productivity and innovation in Phase I and (2) submit the most scientifically promising Phase II research project. Proposals are due on **29 October 1997**.

For more information or to receive a copy of the Broad Agency Announcement: (1) Download the document from the world wide web — http://mrmc-rad6.army.mil/documents.html or (2) fax a request to 301-682-5521.

**Howard Hughes Medical Institute: Fellowship Programs**

**Predoctoral Fellowships in Biological Sciences:** the goal of this program is to promote excellence in biomedical research by helping prospective researchers with exceptional promise obtain high-quality graduate education. Predoctoral fellowships are intended for students at or near the beginning of their graduate study toward a PhD or an ScD degree in one of the designated fields. College seniors, college graduates with no or limited postbaccalaureate graduate study in the biological sciences, and first-year graduate students may apply. U.S. citizens may study in the United States or abroad; others must study in the United States. Deadline: **November 12.**

**Research Training Fellowships for Medical Students:** the goal of the Research Training Fellowships for Medical Students program is to strengthen and expand the pool of medically trained researchers. The program enables selected U.S. medical students with an interest in fundamental research to spend a year of intensive work in a research laboratory. Important opportunities for understanding and treating human diseases are rapidly emerging from basic biomedical research, and ways to bridge the gap between research and clinical medicine are needed. Traditionally, this has been the role of the physician-scientist. HHMI hopes to encourage medical students to pursue research careers.

**Postdoctoral Research Fellowships for Physicians:** this program is intended to help increase the supply of well-trained physician-scientists. These 3-year fellowships support physician-scientists who are seeking additional research training to become independent investigators. By the start of the fellowship, applicants must have completed at least 2 years of postgraduate clinical training and may have no more than 2 years of postdoctoral research experience. U.S. citizens may select mentors in the United States or abroad; others must select mentors at U.S. institutions. After the fellowship, those who proceed to independent faculty or research appointments should be able to prepare highly competitive research proposals.

Deadlines have usually been early November through December for these fellowships. Program announcements and applications (PDF files) are to be available in September for these fellowships. Materials can be found on the WWW at: http://www.hhmi.org/fellowships/

**HL-97-014: Endothelial Dysfunction in HIV Infection**

This solicitation invites research grants focused on how HIV infection alters the expression of endothelial cell genes thereby modifying the normal structure and function of the endothelium and exposing organs to HIV-infected cells and to circulatory factors that could cause damage. Ultimately, the goal of this solicitation is to contribute to knowledge that might lead to new approaches to prevent HIV associated dysfunction and degeneration caused by HIV to vital organs, including lungs, heart, bone marrow, and the vasculature. It is anticipated that for fiscal year 1998, approximately $2.0 million total costs will be available for the first year of support for this initiative. Applicants may request up to five years of support. For this RFA, funds must be requested in $25,000 direct cost modules and a maximum of eight modules ($200,000 direct costs) per year may be requested. Letter of Intent Receipt Date: January 5, 1998; Application Receipt Date: March 26, 1998.

**PA-97-098: Autoimmunity - Genetics, Mechanisms, and Signaling**

The National Institute of Allergy and Infectious Diseases, National Institute of Diabetes and Digestive and Kidney Diseases, National Institute of Arthritis, Musculoskeletal and Skin Diseases, National Institute on Aging, and the Office of Research on Women's Health, National Institutes of Health invite applications for new and innovative investigator-initiated basic and preclinical research into the immune responses underlying autoimmune disease and its regulation for preventive or therapeutic purposes. Three specific areas of emphasis are highlighted: 1) genetic susceptibility for autoimmune disease, including the MHC and other genetic loci; 2) role and regulation of co-stimulation of T cells in autoimmunity; and 3) signal transduction in the autoreactive response. The funding mechanisms to be used to support research under this PA are research project grants (R01) and First Independent Research Support and Transition (FIRST) (R29) awards.

**PAR-97-104: Centers for Behavioral Science Research in Mental Health**

NIMH invites centers grant (P50) applications for Centers for Behavioral Science Research in Mental Health (CBSR). The purpose of these Centers is to provide integrated multidisciplinary research environments in which to pursue focused questions in basic behavioral science related to mental health and mental disorder. This mechanism is intended to encourage investigators from a variety of disciplines and approaches to contribute the full range of expertise and advanced technologies available in basic behavioral science toward the understanding of mechanisms underlying mental health and mental illness, and to begin the translation of basic behavioral findings and techniques to relevant clinical issues.

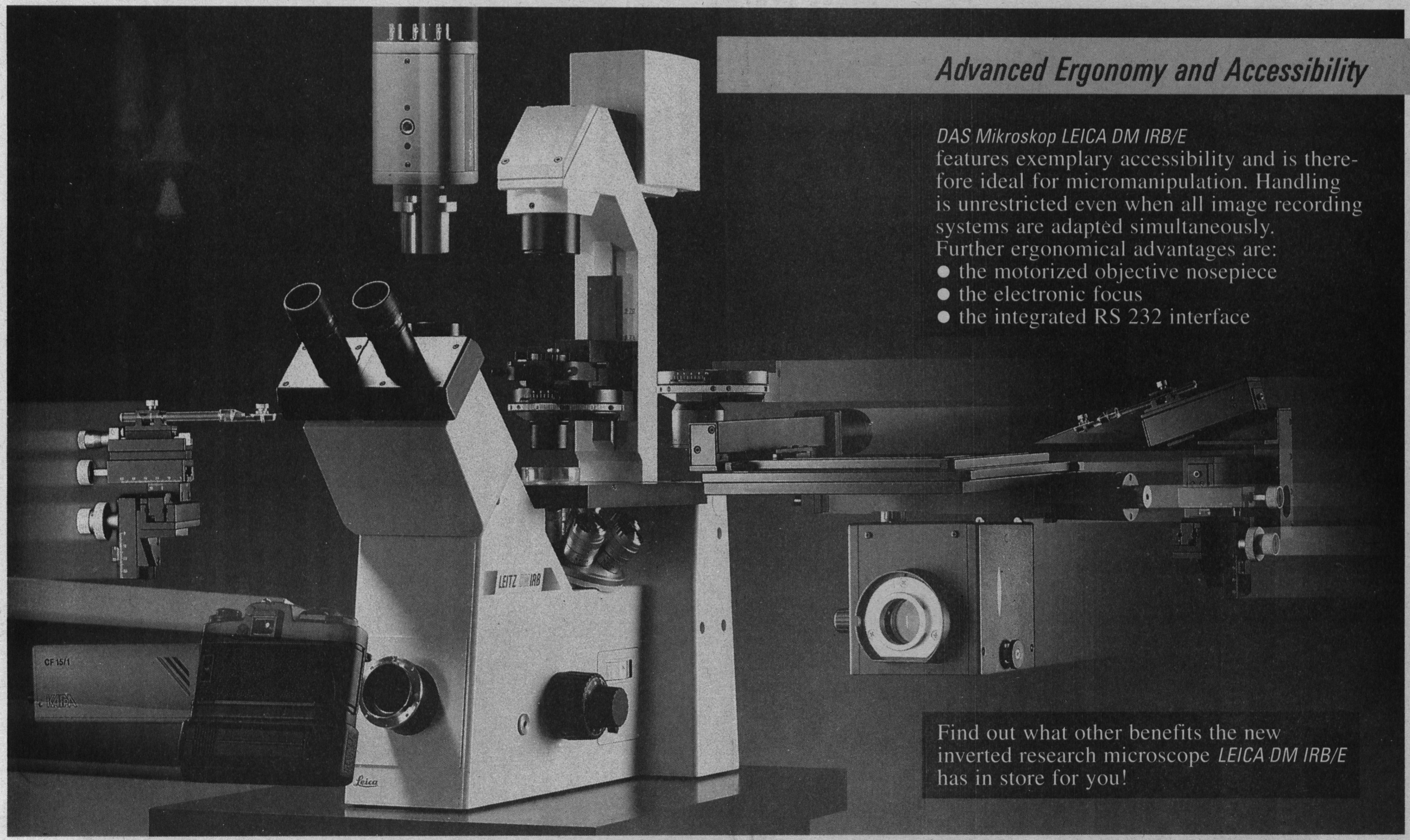
**PA-97-099: Genes and Mechanisms Underlying Primary Immunodeficiency**

The NIAID and NICHHD invite applications for research studies to: identify and characterize genes that cause primary immunodeficiency diseases; characterize the molecular mechanisms involved in primary immunodeficiency diseases which are not the result of a single defective gene; identify the immunologic role of defective gene products and their normal counterparts; and, based on this knowledge, develop more effective approaches for the diagnosis, treatment, and prevention of these disorders. The funding mechanisms to be used to support research under this PA are R01s and R29s.■

## Corrections

Last month's lead article, entitled "Boxers at Risk" contained two errors. The article stated that beta amyloid protein is deposited in neurofibrillary tangles. In fact, in Alzheimer's disease beta amyloid is deposited primarily in senile plaques, while neurofibrillary tangles are composed predominantly of paired helical filaments of the protein tau.

Also, one sentence was improperly capitalized; it should have read: The average age was 49, and boxers were either Black, White, or Hispanic.




## *Advanced Ergonomy and Accessibility*

*DAS Mikroskop LEICA DM IRB/E*
features exemplary accessibility and is therefore ideal for micromanipulation. Handling is unrestricted even when all image recording systems are adapted simultaneously.
Further ergonomical advantages are:

- the motorized objective nosepiece
- the electronic focus
- the integrated RS 232 interface

Find out what other benefits the new inverted research microscope *LEICA DM IRB/E* has in store for you!

*Leica Inc.*
*111 Deer Lake Road*
*Deerfield, Illinois 60015*
*800/248-0123 FAX 847/405-0147*

*Leica Canada Inc.*
*513 McNicoll Avenue*
*Willowdale, Ontario M2H 2C9*
*416/497-2460 FAX 416/497-2053*

Leica

# BIOMARKERS™

## dsDNA SIZING STANDARDS

## NEW 10KB MARKER


PROVIDES :

ACCURATE SIZING OF LINEAR dsDNA OVER THE 1-10KB RANGE

9 BANDS OF EQUAL ETHIDIUM BROMIDE INTENSITY

KINASE READY-REQUIRES NO DEPHOSPHORYLATION

STABLE AT AMBIENT TEMPERATURE

NO DRY ICE SHIPPING CHARGES

NEXT DAY DELIVERY

100 ASSAYS CATALOG NO. M-10KB $85.00

## BIOMARKER LOW


ACCURATE SIZING OF LINEAR dsDNA OF 50-1000BP

9 BANDS OF EQUAL ETHIDIUM BROMIDE INTENSITY

ACCURATE ESTIMATION OF PRODUCT YIELDS

KINASE READY-REQUIRES NO DEPHOSPHORYLATION

ALL MARKER BANDS INFORMATIVE

STABLE AT AMBIENT TEMPERATURE

NO DRY ICE SHIPPING CHARGES

NEXT DAY DELIVERY

50 ASSAYS CATALOG NO. M-1 $75.00

TO ORDER OR OBTAIN INFORMATION CALL

**BioVentures,Inc.**

Phone 800-235-8938 FAX 615-896-4837