

# IN VIVO

Newsletter of the University of Tennessee Division of Biology

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FEBRUARY - MARCH 2002

## From the Director

John Koontz, Ph.D.



Dear Alumni and Friends:

I wish all of you could be on campus to participate in our efforts to recruit new faculty to the

departments of the Division. This is such an exciting opportunity for the Division and the university. As mentioned in previous editions, we are trying to recruit eight new faculty into the departments in the Division

Each of the departments is involved in this process and many faculty members have already devoted considerable time to evaluating the applications, calling references, finding out as much as possible about those candidates whose qualifications stand out from the others.

The search committees had some concern in that the number of applicants was less than in previous searches. While this was troubling, the chair of one of the search committees inquired at other universities conducting searches for similar positions and

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## Your clock is ticking

We all know that we can sense various environmental stimuli. Most are tangible so that we can see, smell, and taste them. But are we able to sense the passage of time? The answer is yes.

The presence of time-sensing machinery in our bodies is demonstrated with troubles caused by jet lag and shift work. Since similar biological clock systems are present in most living organisms on earth, the study of fruit flies, an excellent model organism, helps scientists to better understand the mechanisms of how we can sense time.



**Dr. Park at home in his lab**

With a background in molecular biology and entomology, **Dr. Jae Hyeon Park**, Assistant Professor of Biochemistry and Cellular and Molecular Biology (BCMB), brings the genetic study of fruit flies to UT. He began his studies at Seoul National University in Korea in the 1980s and finished his education at Texas A&M University in 1996. Dr. Park conducted his postdoctoral fellowship at Brandeis

University in Massachusetts. He came to UT in January 2000 and teaches the Advanced Genetics Laboratory.

While at Brandeis University, Dr. Park began to study the genes that regulate the biological clock of the fruit fly, *Drosophila melanogaster*. The fruit fly lends itself well as a model organism to the study of genetics. It has a short generation time, is easily maintained in the lab, reproduces profusely and is easily mutated.

Earlier scientists thought that daily light:dark cycles gave the cues to the pacemakers. However, it has since been discovered that organisms sense

the passage of time and adjust to time changes even in the absence of environmental stimuli.

Normal flies show daily rest-activity rhythms, in which peak activities are observed at dawn and dusk when flies are placed under cyclic light:dark changes. Moreover, the flies can predict, by their behavior,

when the light will come on and go off.

Dr. Park said, "After a seven-day entrainment period, they will continue the same activity pattern in total darkness." Therefore, even though light:dark cycles trigger the entrainment process, the rhythm that is set appears to be innate. Humans also tend to operate on a fixed 24-hour schedule.

Over the past 30 years, seven

*Please see PARK on page 3*



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## A Word from the Head

**Bruce McKee, Ph.D.**



How do biological molecules combine and interact to form the complexes, structures, networks and

cells that underlie all the fascinating diversity in biological systems? And how are these processes regulated at the cellular, genetic and epigenetic levels? These are the types of questions that motivate the faculty and students of the Biochemistry and Cellular and Molecular Biology (BCMB) department.

A focus on molecular and cellular mechanisms of biological processes unites an otherwise highly diverse department. Research interests of BCMB faculty range from mechanisms of protein-protein interactions to calcium-based signaling in plant cells to the genetic and neural underpinnings of circadian rhythms in animals, among many others. However recent growth and development in BCMB has focused in three major areas: structural biology, neurobiology and genetics.

Structural biology deals with 3-dimensional structures of biological molecules and how those structures are related to biological functions. The primary methods for determination of such structures are X-ray crystallography and nuclear magnetic resonance (NMR), supplemented by a variety of other biochemical methods.

Two years ago, BCMB added an X-ray crystallography facility, housed in the basement of Walters Life Sciences Building, to its established NMR facility. This past year has also seen the addition of an analytical ultracentrifuge and a dynamic light scattering source to an equipment suite on the fourth floor of Walters.

Even more important has been the addition of two new faculty members in

X-ray crystallography. We have been joined by **Dr. Chris Dealwis** (see interview, p. 4), who arrived in August 1999, and **Dr. Elias Fernandez** (see interview, p. 5), our newest faculty member, who arrived in August 2001.

Further growth in structural biology in BCMB received strong impetus in the Fall of 2000 with the announcement of a multi-million dollar Center of Excellence in Structural Biology. It is one of nine new Research Centers on the Knoxville and Memphis campuses. Although the Structural Biology Center is an interdisciplinary center with members from various departments on the main campus and the medical center, its primary home is in the BCMB Department. The director is **Dr. Engin Serpersu**, an NMR spectroscopist in the BCMB department, and its membership includes approximately half of the BCMB faculty.

The Center has funded seven new pilot research projects so far aimed at generating exciting new research directions in structural biology. With support from the center, two additional BCMB faculty positions in experimental and/or computational structural biology were advertised in the late fall and eight candidates have been chosen. Interviewing and deciding among the eight candidates for these positions will be a major departmental preoccupation in March and April.

Two other areas of strength in BCMB are genetics and neurobiology. The addition of **Dr. Jae Park**, a neurogeneticist with interests in circadian rhythms of *Drosophila*, in January 2000 (see interview, p. 1), is helping to bridge these diverse areas.


In addition, BCMB is currently interviewing four candidates for an open faculty position in mammalian genetics. The successful candidate is expected to promote already strong interactions between the geneticists in our department and the mouse genetics group at ORNL as well as to

strengthen the statewide Tennessee Mouse Genetics Consortium.

Three recent programs highlight the growing importance of genomics within the genetics area, both locally and nationally. BCMB sponsored an invited-speaker seminar course in "Neurogenomics" last spring, and this spring is jointly sponsoring (with the Graduate School of Genome Science and Technology) a similar seminar series in "Mammalian Genetics and Genomics."

In addition, a highly successful workshop on microarray technology, sponsored by a focus group in "Functional genomics of animal and plant reproduction", headed by **Dr. Mary Ann Handel** of our department, drew participants from all over campus.

With three new faculty members in the process of initiating their research programs and interviews in progress or scheduled for three additional new faculty positions, it is evident that a youth movement is in progress in BCMB.

New emphases both locally and nationally in structural biology and genomics are pushing even us veteran researchers to explore new directions. We look forward with great anticipation to seeing the development of new research programs and emphases, but expect to maintain our overall focus on molecular and cellular mechanisms of biological processes. 

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### IN VIVO

An alumni newsletter published by the Division of Biology

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**Park, Continued from page 1**

rhythm genes have been isolated that contribute to the timing, or circadian rhythm, of the body. The “period,” “timeless,” “clock,” “cycle,” “double time,” “shaggy,” and “cryptochrome” genes work together in a pacemaker system to produce a messenger that causes the neurons in the brain to regulate various tissues in the body. In addition to sleep-wake cycles, there are other rhythms that take place in the bodies of various organisms, such as body temperature changes, heart rate fluctuations, and egg laying behavior.

***Studying these proteins can eventually lead to drug therapies engineered to battle insomnia, the side effects of shift work, jet lag, and seasonal depression.***

Dr. Park is currently studying the newly discovered “pdf” (pigment-dispersing factor) gene to see what role it has in the messenger system. When this gene is mutated, abnormal behavior related to the biological clock is observed. However, Dr. Park does not believe that the pdf gene is the master messenger for all rhythms of the body. By using fruit flies, he continues to study how the pdf gene regulates rest-activity rhythms in flies.

The clock genes in the pacemakers are switched on and off by the proteins they encode. Studying these proteins can eventually lead to drug therapies engineered to battle insomnia, the side effects of shift work, jet lag, and seasonal depression. In this respect, it is notable that all clock genes identified in flies are also discovered in mammals including human beings. This strongly demonstrates that the molecular time-keeping mechanisms are conserved in a wide array of organisms on earth. 

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**Director, Continued from page 1**

found that they also had fewer applications. This was reassuring in that I was concerned that the financial problems plaguing our state and higher education in the state may have been causing qualified potential applicants to look elsewhere.

We are offered an educational treat as we interview these candidates: as if each department is running a seminar series focusing on the research area of the candidates being interviewed. All of the candidates are working in excellent laboratories doing research at the forefront of their respective areas. In addition to providing an opportunity to evaluate their scholarly/research capabilities, we get an update on the most recent advances in these areas. It is particularly exciting for me because I get to meet each of the candidates and go to as many of the seminars as possible.

On another note, the actual process of renovating the Hesler Biology Building is now a reality. The old wing, the first to be renovated, is now sealed off to all except the contractors. We have removed everything of value for the faculty whose research labs were located there and the teaching laboratories that were taught there.

Following completion of the asbestos abatement the contractors will begin gutting the building and starting anew. Some of you who took classes there or did your research in one of the labs there might be thinking that it is about time. Others will miss the sense of history, the character of the building and all of its idiosyncrasies.

These past few weeks I took a number of walks through that wing and invariably came across another nook or cranny. Although we might miss the character of the original building, we are all looking forward to occupying the completely renovated structure. 

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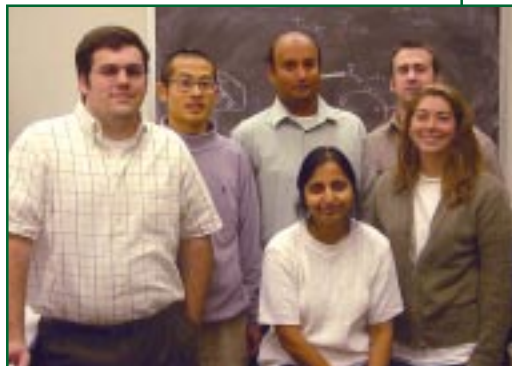
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*Please see FACULTY on page 6*

## A rational approach to drug design

Although he has only been with UT since 1999, Assistant Professor, **Dr. Chris Dealwis** has carved a nice niche for himself within the BCMB Department. His research centers on the study of rational drug design at UT.



**Front - Brad Bennett, Vibha Gupta and Lezlee Dye**

**Back - Tomaki Uchiki, Chris Dealwis and Matt Wilkerson**

To design therapeutics, Dr. Dealwis uses protein crystallography, a primary technique for solving the three-dimensional structure of biological molecules. He said, "let's say you have an enzyme that's a target enzyme like the HIV 1 protease and you can solve the structure of this protease and look where the drug molecule would be binding at the active site. Then you can design better drug molecules to bind even tighter by optimizing interactions at the active site. This technique is called rational drug design."

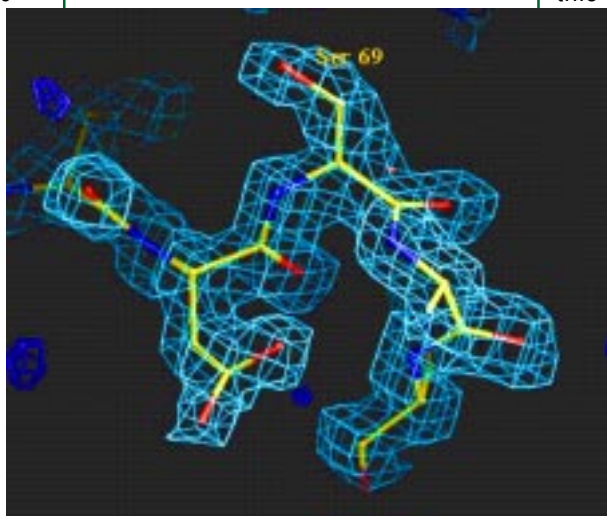
He began his molecular detective work at the University of London, where he received his Ph.D. in 1993 under the tutelage of **Sir Tom Blundell**. His target of study at that time was hypertension.

After graduation, he and his wife moved to the U.S. for him to take a post-doctoral position at the University of Chicago. It was during this time that he was recruited by Abbott Laboratories and began work in their Diagnostic and Pharmaceutical Divisions.

While in with the Diagnostic Division, he worked on ways to improve the detection systems against AIDS. While in the Pharmaceutical Division he worked on the HIV protease inhibitor that is now marketed as *Retinovir*.

After he left Abbott Labs, he joined Yale Medical School and took a post-doctoral position in the department of Pharmacology. He said, "During that time I solved structures that could be used as a template for making drug molecules to attack the HIV virus from another front, which is to stop its viral entry into cells."

Once at UT, Dr. Dealwis immediately established a structural biology laboratory. He has several projects taking place in the lab; one is an attempt to find therapeutics against Alzheimer's Disease. For this project he is collaborating with **Dr. Richard Lee** at UT Memphis' School of Pharmacy, **Dr. Ron Wetzel** and **Dr. Alan Solomon** of UT Hospital in Knoxville and **Dr. Xuemin Xu** at the College of Veterinary Medicine.



**Crystal structure of a light chain antibody involving Amyloid Disease**

Other areas of rational drug design research include searching for therapeutics to combat Amyloid


Disease and Acute Lymphoblastic Leukemia (ALU). ALU is the most common form of childhood leukemia.

Chemotherapy is the classical treatment for ALU and 20 percent of patients relapse, which eliminates the effectiveness of chemo treatments for them. He is hoping that his lab can find a way to combat this problem. Dr. Dealwis is also trying to understand how the cell is able to overcome DNA damage due to radiation. Several of these projects will lead to furthering the understanding of cellular signaling.

Outside his lab, Dr. Dealwis has been busy convincing an instrumentation committee for the Spallation Neutron Source in Oak Ridge, that the facility will be valuable to biological sciences. Currently, an exploration study is underway to build a single crystal diffraction meter that will help scientists like Dr. Dealwis use neutrons to observe hydrogen atoms.

He said, "it will be important for drug discovery, so we can look at where the hydrogen atoms are in a drug molecule and the way they interact with the target. We can use this as a guide to make a stronger, tighter binding, more potent drug." At this time Dr. Dealwis' lab uses a state of the art x-ray detector that is available to him and **Dr. Elias Fernandez** (see facing page).

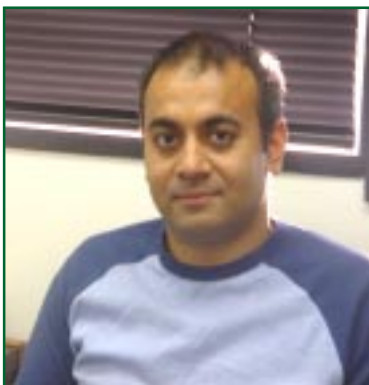
As an extension of his interest in drug discovery, Dr. Dealwis teaches biophysical chemistry to seniors and graduate students. He also teaches for the Graduate School of Genome Science and Technology (GST) and serves on the executive committee for the Center for Excellence in Structural Biology.

With an interest as focused as rational drug design, Dr. Dealwis is able to bring progress to the fight against many diseases. 

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## Finding the “how” in protein interactions

In the area of protein research, it's not the “what” questions that intrigue **Dr. Elias Fernandez**, it's the “how.” He said, “My principal interest is understanding what proteins look like and how the architecture of the proteins governs the way in which they function.”



Dr. Fernandez is BCMB's newest assistant professor. He has been setting up a lab that uses x-ray crystallography to determine highly detailed three-dimensional images of proteins. This will be an arduous process, using thousands of different conditions to get a proper crystal of each protein.

Once crystals are obtained and the initial structures determined, Dr. Fernandez can begin what he calls the “real science” of making changes biochemically to the proteins to determine how they interact with other proteins.

He makes a change to a specific site on the molecule and measures the resulting interactions. This technique, called site-specific mutagenesis, is used to validate his deduction of the image he has of the crystallized protein.

He said, “My education is in physical chemistry, but I've been training for the past few years in biology. So, I've been using the techniques of physical chemistry to understand problems in biology.”

There are three different proteins being studied in Dr. Fernandez's lab. The first protein is involved in the development of B-lymphocytes or B-cells, and is called Bruton's tyrosine kinase (Btk). He is interested in one particular event in the development of the Btk because when things go wrong in this process two different diseases can result.

One disease is B-cell lymphoma and the second is an immune disorder known as x-linked agammaglobulinemia (XLA). The latter mainly affects males because it is an x-chromosome-specific disease.

The second protein (hSK4/IK1) is the potassium ion channel in red blood cells. This protein funnels potassium ions from outside the cell to the inside. He is focusing on the transport mechanism of the process because when it fails, the results can be sickle-cell anemia or Diamond-Blackfan anemia.

**“I've been using the techniques of physical chemistry to understand problems in biology”**

The third protein (CARB) is regulated by a steroidal hormone and is present largely in the liver. He said, “we know it is involved in helping the body to get rid of toxic substances, medicative drugs in particular, but we don't know how it does this.” This recently discovered protein has generated great interest in both academic labs and pharmaceutical companies.

Dr. Fernandez said, “the functions of each of these three proteins are controlled by other proteins that interact with and turn them on or off. Disruptions in this process, either untimely turning on or shutting off their function, causes the problems that can result in a disease. That in itself is motivation enough to understand how this process works.”

He is currently working with three collaborators: **Dr. Xin-Yun Huang** at Cornell University, **Dr. Barry Foreman** at The Beckman Research Center in

San Diego, and with **Dr. Leonard Kaczmarek** at Yale University. He said, “biology is what they do, I do the physics part.”

Originally from India, Dr. Fernandez completed his undergraduate work at Bangalore University. He received his Ph.D. at Loyola University in Chicago in 1995 and did his post-doctoral work at Yale University.

Four staff members maintain his lab. His post-doctoral associate is **Dr. D. Prahadeeswaran**; undergraduate research student is **Dawn Ware**; graduate student is **Anton Mitsky**; and undergraduate technician is **Allison Wilkes**.

Dr. Fernandez said, “My main reason for study is purely from a scientific point of view. I like to know how things work. The second reason is that when things go wrong it can lead to disease. Once we know how these proteins work, we can find ways to fix them.”

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### BCMB Spring Seminars:

**Feb. 13-14** “Functional annotations of the mouse genome”, **Terry Magnuson, Ph.D.**, from the University of North Carolina at Chapel Hill.

**Feb. 27-28** “Mechanisms of genomic imprinting, with emphasis on Prader-Willi and Angelman Syndromes in man and mouse”, **Robert D. Nicholls, D.Phil.**, from the University of Pennsylvania.

**March 13-14** “Too much of a good thing: Mechanisms of gene action in Down Syndrome”, **Roger Reeves, Ph.D.**, from The Johns Hopkins School of Medicine.

**April 3-4** “The genetic dissection of complex multigenic traits: Focus on brain and behavior”, **Robert Williams, Ph.D.**, from the UT Health Science Center, Memphis.

**April 17-18** “The genetics of cancer: Using mouse models to probe susceptibility to mammary tumor initiation and dissemination”, **Kent Hunter, Ph.D.**, from the National Cancer Institute, NIH.

## Botany is her life

For 2,200 students, **Dr. Patricia Cox** holds the last word on their introduction to General Biology at UT. As an Adjunct Assistant Professor and the Core Biology Coordinator, Dr. Cox



**Dr. Cox in Sandhill Crane Wildlife Refuge, Gulfport, Miss.**

organizes six first and second level biology courses, including labs, for major and non-majors.

She is assisted by a staff of three including **Janet Hudson**, Lab Coordinator; **Russ Patterson**, Lab Preparator; and **Patricia Gantt**, secretary. All labs are conducted in the Neyland Biology Annex building, which is a temporary structure to be used until the Hesler Renovations are complete.

Her background and extra-curricular activities make Dr. Cox a well-rounded coordinator. She

received her undergraduate and graduate degrees in Biology from the University of Louisiana at Monroe (formerly Northeast Louisiana University) and her Ph.D. in Botany from Louisiana State University.

Her research interests are in the systematics of *Rudbeckia* and related composites, *Liatris* of the southeast, and field pteridology.

Her major professor at NELU was a student of **Dr. Jack Sharp**, so when she came to UT in 1990 to serve as a teaching postdoc, Dr. Sharp called her his "academic granddaughter." She has also been a research associate and an instructor.

From these diverse experiences, she was able to become coordinator of not only general biology, but also many other academic activities associated with the University and beyond.

Along with **Dr. Eugene Wofford** and **Dr. Ken McFarland** of Botany, Dr. Cox

is a co-coordinator of the Annual Wildflower Pilgrimage. This event takes place in the Great Smoky Mountains National Park and is sponsored by the Park, the Botany Department, the Southern Appalachian Botanical Society (SABS) and the National History Association. This is the 52<sup>nd</sup> year of the Pilgrimage and it will take place the week of April 22-28. On-line information and registration is available at [wildflowerpilgrimage.org](http://wildflowerpilgrimage.org).

In addition, Dr. Cox serves on the




**Volunteers for a summer Fern Foray in the Smokies**

Education Committee of Discover Life in America ([www.discoverlife.org](http://www.discoverlife.org)), which sponsors the annual All Taxa Biodiversity Inventory (ATBI) in the Smokies. She serves as coordinator of the Plant Twig (Taxonomy Working Group) and conducts six Fern Forays from June to September. The group is comprised of volunteers and graduate students who use GPS coordinates to map the distribution of ferns in the park.

She is the editor for the journal *Castanea*, for the SABS and is currently running for Vice President of that organization.

As if all of that were not enough, Dr. Cox also coordinates graduate student field trips twice a year. In the spring she takes students to the annual meeting of the SABS. During fall break she takes a group to either Florida or the Outer Banks to study local flora and fauna.

Dr. Cox immerses herself in the study of Botany, bringing knowledge and enthusiasm to the classroom to ensure that UT undergraduate students receive the education they need in General Biology. 

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## Alumni News

### 1960's

**Dr. James C. Sparks** received a B.S. from the Zoology program with a minor in Chemistry in 1966 and completed the Ph.D. program in Zoology with a minor in Biochemistry in 1971. He received additional clinical training in Clinical Chemistry at the University of Tennessee Memorial Research Center and Hospital and has pursued a career in Clinical Laboratory Science since that time.

He has also published over 30 original articles related to Clinical Laboratory Medicine. He is currently President and CEO of Alverno Clinical Laboratories, Inc., a core laboratory facility that also operates six hospital laboratories, two stat laboratories and 19 patient access facilities with over 500 employees in the south Chicagoland area.


### 1980's

**Andy Allison** received his undergraduate degree in Biology from UTK in 1980. He served in roles of primary sales, specialty sales, oncology sales, national sales trainer, district sales manager, specialty sales manager and regional sales manager with Stuart Pharmaceuticals, Zeneca Pharmaceuticals and AstraZeneca Pharmaceuticals over the past 20 years.

He was recently named Vice-President of Pharmaceutical Practice with The Benfield Group in Atlanta. As a consulting company, The Benfield Group, specializes in delivering pharmaceutical and employer services to major pharmaceutical companies. Allison is based in St. Louis.

### 1990's

**Michael Finley** completed his bachelor's degree in Botany at the age of 42 in 1995. He is now retired and living in San Francisco. He said, "I consider it one of my life accomplishments and have wonderful memories as a UTK student. **Dr. (James) Caponetti** was an inspiration to me, and I am honored that I was his student. Thank you, Dr. C!"

**Jean Brennan** completed her degree in Zoology in 1995. She is currently serving as a science and policy advisor for the U.S. Agency for International Development in Washington, DC. She provides technical assistance in the areas of forest biodiversity, conservation and climatic change. 

## Division Faculty News

### Where are they now?

With this issue we will start a new section that highlights former faculty members. If there is a certain faculty member you have been wondering about, let us know. We will do our best to track them down and give you an update.

Also, if you are a former faculty member and would like to be featured so that your colleagues will know where you are now and what you are doing, please contact us.


**Dr. Karen Hughes** from the Botany Department provided the following update on **Dr. Patricia Walne**.

"Pat, Benwood Distinguished Professor of Botany (Emerita), recently retired to Bloomington, Indiana. While at UT, Pat's research focused on the euglenoid flagellates and involved the isolation and characterization of subcellular components important in the

photobehavior and evolution of these enigmatic protists.

Of particular importance are the identification and localization of the main photoreceptor pigment and ongoing evaluations of the evolutionary significance of certain subcellular structures. She continues to pursue these interests with colleagues in Italy, Poland, and Denmark.

Pat is also enjoying the intellectual and cultural activities associated with nearby Indiana University and has just finished a course on the architecture and architectural history of Bloomington.

Pat is a former UTK Macebearer, a Fulbright Research Scholar in Denmark, and a recipient of the prestigious Darbaker Prize for meritorious research from the Botanical Society of America." 

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### Graduate Student News

Congratulations to GST student **Nathan VerBerkmoes**, who recently received two prestigious awards.

He received an award of \$500 from the Cambridge Healthtech Institute for his outstanding poster presented at the Second Annual Human Proteome Conference "Pep Talk", January 9-11, 2002, in San Diego, Calif.

Even more impressive, Nathan has been selected from a large pool of applicants for support by the Department of Energy Office of Science to attend a meeting of Nobel Laureates in Lindau, Germany in July. This will provide Nathan an opportunity to meet with fellow students and Nobel Laureates from around the world.

Congratulations Nathan!



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# IN VIVO

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## 5<sup>th</sup> Annual Friends of Biology Golf Tournament

Date: April 30, 2002

Time: Shotgun start at 9:00 am

Location: Centennial Golf Course

A spike-less facility, proper attire is required

Cost: \$60 entry fee that includes greens fee, cart and lunch

Hole Sponsorship: Individual \$50

Corporate \$100

Deadline for fees is **March 15, 2002**

For more information contact:

Janet Hudson (865) 974-8761 or [jlhudson@utk.edu](mailto:jlhudson@utk.edu)

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