



# SCRIPPS DISCOVERS

*Improving Lives Through Research*

A Newsletter for Philanthropists Published Quarterly by The Scripps Research Institute

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## INSTITUTE UPDATE

### John J. Moores to chair Scripps Research Institute Board of Trustees

> John J. Moores, a San Diego business leader and philanthropist, was unanimously selected by his fellow board members recently to serve as chairman of The Scripps Research Institute's board of trustees.

Moores will succeed Alice D. Sullivan, a retired California Superior Court judge who has served as chairwoman for the past three years. Sullivan will continue serving on the 31-member board.

Moores, a native of Texas, has owned the San Diego Padres since 1994. He has served as a Scripps Research trustee since 1997.

## Inside:

- 2... Fragile X Honors
- 3... *News & Views*: Microsoft alliance to accelerate drug discovery
- 4... Research on Cancer & Aging
- 5... Alcohol Treatment Study
- 6... Summer Teacher Internship Program
- 6... Tax-Wise Retirement Planning
- 7... PKU Research

### BACK COVER:

Scripps Council of 100, Contact Us

"John's leadership abilities in so many areas are well known to all—in business, technology, finance, philanthropy and professional sports," said Scripps Research President Richard Lerner. "He will bring

enormous skill and energy as head of our board. We are lucky to have Alice staying on. We are fortunate to have John taking over."

Moores has contributed more than \$22 million to help further research efforts at Scripps Research and is a founder of Scripps Research's Institute for Childhood and Neglected Diseases. He also founded the River Blindness Foundation in 1989 to distribute treatments in developing countries.

Moores founded BMC Software in 1980 and continues to help start-up software companies develop software.

### Meeting with President Jimmy Carter energizes research team

It's not often that you get to present your work to a former president of the United States, but that's what a team from The Scripps Research Institute did this summer.

The session, in which individuals from the Worm Institute for Research and Medicine (WIRM) at Scripps Research met with President Jimmy Carter and members of The Carter

Center, brought together individuals working on parasitic diseases in the lab with those fighting diseases in the field. These parasitic diseases, while rare in the United States, afflict hundreds of millions of people in many other parts of the world with painful, disfiguring, and debilitating conditions.

*continued on page 2*



Chairman of the Scripps Research Institute Board of Trustees, John J. Moores and President Jimmy Carter

## Peter Vanderklish honored at Fragile X Awareness Day

Scripps Research Assistant Professor **Peter Vanderklish, Ph.D.**, was among three researchers honored in ceremonies for the first California Fragile X Awareness Day, held this Spring on the University of California, San Diego campus.

“During the past three years, with funding from the FRAXA Research Foundation, Dr. Vanderklish has been studying neurons from the Fragile X knockout mouse in great depth,” said

Cindy de Grunchy, president of the Fragile X Center of San Diego whose 16-year-old son has fragile X syndrome, which is the leading cause of genetically inherited mental impairment. “[Dr. Vanderklish’s] results have been very promising. One of the most noteworthy aspects of this line of research is that it strongly suggests that some of the biochemical, and possibly structural, changes seen in Fragile X brains may be reversible.”



Dr. Peter Vanderklish

### Meeting with President Jimmy Carter, CONTINUED

“President Carter took a keen interest in our work and underlined the huge impact it could have in developing countries,” said **Kim Janda, Ph.D.**, director of the WIRM Institute who is also Ely R. Callaway, Jr. Professor of Chemistry at Scripps Research and a member of its Skaggs Institute for Chemical Biology. “The meeting was a tremendous energizer for our team.”

Janda presented the work of WIRM investigators aimed at laying the scientific foundation for developing efficient and effective diagnostic tools for the parasite that causes

onchocerciasis, which according to the World Health Organization affects 18 million people in 35 countries. Onchocerciasis is often referred to as “river blindness” because it occurs in areas close to fast-flowing water where the black flies transmitting the parasite, a tiny worm called *Onchocerca volvulus*, like to lay their eggs. In severe cases, the worms cause lesions and massive inflammation in the eyes of the infected person, leading to vision problems and blindness.

While river blindness can be effectively treated with the drug ivermectin, which is provided free of

charge by its manufacturer, Merck & Co., there is an urgent need to find ways to detect the presence of the adult parasite in the body. A rapid diagnostic test would greatly assist public health efforts to treat and potentially eliminate river blindness as a global health threat.

President Carter outlined the latest work of The Carter Center, a nonprofit, non-governmental organization he founded with his wife, Rosalynn, in 1982 to advance human rights and alleviate unnecessary human suffering. The work of the center, which partners with Emory University, includes multiple health programs targeting developing countries.

Who recognized the potential of such a meeting? None other than John Moores, who chairs the boards of both Scripps Research and The Carter Center.

Moores, a San Diego business leader, philanthropist, and long-time supporter of Scripps Research, launched the WIRM last year with a donation of \$4 million. Moores has had a strong interest in river blindness since founding the River Blindness Foundation in 1989. The foundation was formed to distribute the Merck-donated drug, ivermectin, in endemic countries worldwide. In 1995, the River Blindness Foundation merged into The Carter Center.

“I am optimistic that linking the people in the labs with the people in the field can only lead to good things in areas where there is tremendous need,” said Moores. “I am excited about the potential of this partnership between WIRM and The Carter Center, and am hopeful that this effort is the first of many.”

Others present at the gathering included Richard Lerner, president of Scripps Research; Edward Holmes, vice chancellor for health sciences and dean of the School of Medicine at the University of California, San Diego; and WIRM research team members Tobin Dickerson, Lisa Eubanks, Andy Brogan, Junguk Park, Suresh Mahajan, and Mark Hixon.

# Microsoft alliance to accelerate drug discovery

> Microsoft Corp. has announced the formation of BioIT Alliance, a cross-industry group working to integrate science and technology. The alliance unites members of the pharmaceutical, biotechnology, hardware and software industries to speed the pace of drug discovery and development.

Founding members of the alliance include Accelrys Software Inc., Amylin Pharmaceuticals Inc., Affymetrix Inc., Applied Biosystems and **The Scripps Research Institute**, among more than a dozen industry leaders.

*The alliance has announced its first project, called Collaborative Molecular Environment, a data management solution to help make research more efficient.*

“Advances in our understanding of the human genome promise to revolutionize medicine and open the door to therapies that are tailored to individuals,” said Bill Gates, chairman and chief software architect of Microsoft. “By bringing together people from innovative life sciences organizations that span the biomedical industry, the BioIT Alliance will play an important role in the development of solutions that transform today’s data into knowledge and improve the quality of millions of lives.”

The alliance has announced its first project, called Collaborative Molecular Environment, a data management solution to help make research more efficient. Collaborative Molecular Environment, which targets common

technology problems faced by life sciences companies, will provide a means for data capture, visualization, annotation and archiving using Microsoft® Office, Windows® Presentation Foundation, and SharePoint® Technologies. Microsoft is partnering with alliance member company InterKnowlogy LLC on the project, which is being tested by several other alliance members.

“Bringing research results to the bedside and patient response to

the research bench is at the core of translational medicine,” said **Peter Kuhn, Ph.D.**, professor of cell biology at The Scripps Research Institute, whose research includes cancer diagnostic and structure-based drug development that directly impacts human health. “The Collaborative Molecular Environment developed with InterKnowlogy and Microsoft through the BioIT Alliance is a response to the critical need for productivity tools at the laboratory bench that connect experimental data, support decision-making on the spot, and communicate the data in context to other members of our research groups and our collaborators.”

Most efforts to unite the life science and IT industries are focused on developing technology to enable the early-stage drug discovery process. By addressing the technology issues that companies face throughout the development cycle and by working with some of world’s top technology providers, the alliance will help the industry move closer to bringing personalized medicine to today’s patients.



Dr. Peter Kuhn

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# Unique protein aids research in cancer and aging

> A team of scientists from The Scripps Research Institute and Lawrence Berkeley National Laboratory has determined the crystal structure and molecular mechanisms of a key part of WRN, a protein that protects humans from premature aging and cancer.

When the gene for WRN is defective, the result is often Werner syndrome, a rare inherited disease causing rapid aging symptoms that start to appear after puberty.

Beginning in their twenties, victims may become afflicted with cataracts, hair loss, wrinkled skin, osteoporosis, arteriosclerosis, and type II diabetes; many patients contract cancer, and most die by their early fifties. Understanding how the WRN protein normally works to maintain genomic integrity could lead to new forms of treatment for cancer and age-related pathologies.

*“If we can understand how this unique protein works, we’ll have a key to how all these pathways work in human beings.”*



Dr. John Tainer

“One reason we are particularly interested in WRN is because Werner syndrome is unusual among premature-aging diseases in that children are born normal and show no signs of disease until early adulthood,” says Steven Yannone of Berkeley Lab’s Life Sciences Division. “This gives us a better chance of clearly separating defects in development from [those of] aging.”

“We wanted to study the protein itself because it is unique,” says **Jeff Perry, Ph.D.**, a research associate in the Scripps Research Institute’s Department of Molecular Biology and Skaggs Institute for Chemical Biology, formerly of Berkeley Lab, who led the research with Yannone. “WRN belongs to a family of enzymes called RecQ helicases”—of which there are five in the human genome, performing important functions in DNA replication, recombination, and repair—“but in this

family, only WRN has coupled a helicase function and a nuclease function within the same protein.”

Helicases open up the double helix of DNA, while nucleases degrade one or both of the DNA chains; both operations are critical to repairing errors and proofreading DNA sequences. One part of WRN is an exonuclease, which starts working from the end of a DNA strand. Perry and Yannone and their colleagues determined the structure of the WRN exonuclease domain (WRN-exo) and showed how the enzyme may function in a series of specific DNA repair events.

All the members of the research team were participants in the SBDR program (Structural Cell Biology of DNA Repair Machines) sponsored by the National Cancer Institute. **John Tainer, Ph.D.**, a professor at Scripps Research, member of the Skaggs Institute for Chemical Biology, and a visiting scientist at Berkeley Lab, is SBDR’s principal investigator.

Tainer says, “The exonuclease domain of the WRN protein is a prime example of what we in SBDR call ‘master keys,’ structures that open doors to lots of different repair pathways. Among other things, WRN is involved in repairing double-strand breaks, single-strand breaks, replication forks and junctions, even DNA-RNA duplexes. How does one protein know how to interact in so many different processes? If we can understand how this unique protein works, we’ll have a key to how all these pathways work in human beings.”

Berkeley Lab’s Judith Campisi, Ph.D., an expert in the molecular and cellular basis of aging, says it’s tempting to speculate that differences in the way people age, and how fast they age, could be partly due to variations in their WRN proteins. “Should this be the case, knowing the structure of WRN will be crucial for understanding how slight variations in the protein might alter its function,” she says. “Ultimately, scientists might be able to use the

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This research is published by Perry *et al.*, “WRN exonuclease structure and molecular mechanism imply an editing role in DNA end processing.” *Nat. Struct. Mol. Biol.* (2006) May; 13(5):414-22 and Epub 2006 Apr 23.

# Study results offer guidance in treatment of alcohol dependence

> What is the best way to treat alcohol dependence? The results of a new large-scale study of different treatment approaches have shed some light on the question, underlining that medication can play a key role in treatment.

“To me, the most compelling finding of the study is that those receiving any medication did much better than those who received no pills at all,” says The Scripps Research Institute’s Professor **Barbara Mason, Ph.D.**, an author of the paper. “This should be a wakeup call. With less than one percent of those seeking help for alcohol dependence receiving a prescription for an FDA-approved anti-relapse drug, medication to treat alcoholism is drastically underutilized in the U.S. Medication for alcoholism can offer patients an advantage in their recovery, especially in a real-world setting.”

Another important aspect of the study, says Mason, is that it offers new safety data on the prescription drugs used in the trial, naltrexone and acamprosate, which were administered at higher-than-standard doses. “We had no serious drug-related events during the course of the research,” she says. “That fact should offer prescribing physicians a high degree of comfort.”

About eight million individuals in the United States currently meet the diagnostic criteria for alcohol dependence, also called alcoholism, a leading preventable cause of morbidity

and mortality and a major contributor to health care costs, according to the paper’s background information. In primary care settings, the prevalence of alcohol use disorders ranges from 20 percent to 36 percent.



Dr. Barbara Mason

While several behavioral treatment programs and drugs now approved by the U.S. Food and Drug Administration had been shown effective for treating alcohol dependence in previous studies, no large-scale randomized controlled study had evaluated whether combined

drug treatment with or without behavioral therapy could improve outcome. In 2001, the National Institute on Alcohol Abuse and Alcoholism, part of the National Institutes of Health, launched “Combining Medications and Behavioral Interventions for Alcoholism” (COMBINE) to identify the most effective current treatments and treatment combinations.

The trial, conducted at 11 sites around the country from January 2001 to January 2004, recruited and randomly assigned 1,383 recently abstinent alcohol dependent patients to one of nine treatment groups. In eight of the nine groups, patients received what the paper called “medical management,” attending sessions with a physician, nurse, physician’s assistant, or pharmacist where these health care professionals reviewed the diagnosis, recommended abstinence and mutual-help participation, and reviewed patients’ progress.

Patients were assessed during the 16 weeks of active treatment and one year after treatment.

Mason, who is co-director of the Pearson Center for Alcoholism and Addiction Research at The Scripps Research Institute, and director of The Scripps Research Institute’s Laboratory of Clinical Psychopharmacology of the Molecular and Integrative Neurosciences Department — explores the physiological changes in the brain that drive excessive drinking and create vulnerability to relapse. She also investigates the viability of using new compounds to modulate the neurological effects of alcohol, reduce excessive intake, and prevent relapse.

## *Unique protein aids in research,* CONTINUED

structural data to design drugs to specifically optimize WRN function, leading to healthier life spans!”

Berkeley Lab’s Priscilla Cooper, Ph.D., co-Principal Investigator of the SBDR program project says, “SBDR

investigators and others have shown that WRN interacts directly with a number of other proteins that have been implicated in premature aging disorders, some of which probably constitute other hubs. Ongoing studies

of how these hubs connect should yield further noteworthy insights into the molecular bases of cancer predisposition and premature aging.”

# Biogen Idec Foundation funds summer teacher internship program

The Biogen Idec Foundation has donated \$25,000 to support three teachers from San Diego public schools in The Scripps Research Institute's Summer Internship Program for Teachers. The program, for middle and high school science teachers, exposes teachers to new laboratory techniques and procedures, and informs them about contemporary issues in biomedical research.

"Study after study has found that American schools fall short in helping students achieve scientific literacy. A critical element in improving science

education is effective teacher training," said Jeffery Kelly, Ph.D., Dean of Graduate and Postgraduate Studies. "We want to express our deep appreciation to the Biogen Idec Foundation for awarding a \$25,000 grant for the first time to the Scripps Research summer internship program for middle and high school teachers."

In addition to an intensive, hands-on, eight-week summer experience, teachers are expected to use the laboratory experience as a springboard to create and enhance their curriculum for their students and to become resources for other educators.



San Diego public high school teachers Victor J. Rodriguez and Stephanie H. Simmons participated in the Scripps Research Summer Internship Program for teachers this summer, supported by the Biogen Idec Foundation.

Scripps Research relies on the generosity of private donors and foundations, like the Biogen Idec Foundation, for program support.

"Our mission is to improve the quality of people's lives and contribute to the vitality of the communities where we operate, with a special emphasis on innovative ways to promote science literacy and encourage young people to consider science careers," said Kathryn R. Bloom, Director of the Biogen Idec Foundation.

"Providing teachers with up to date, real world science learning experiences fits nicely with this mission and we're pleased to be partnering with a first-rate program and world-class institution like Scripps Research — it seemed a logical fit."

"Local initiatives, such as this one, help develop and train the workforce of the future to help us achieve our mission of pioneering therapeutics for patients in need," said Jim Mullen, President and CEO of Biogen Idec.

Biogen Idec focuses on neurology, oncology, and immunology. They are leaders in the area of multiple sclerosis, discovered and co-market the leading therapy for non-Hodgkin's lymphoma, and are developing much-needed treatments for rheumatoid arthritis, lupus, and other inflammatory diseases. Biogen Idec has operations in Cambridge, Massachusetts; San Diego; and Research Triangle Park, North Carolina. The Biogen Idec Foundation was established in 2004.

## Tax-wise retirement planning — it's easy



> Your retirement plan is designed to benefit you during your retirement. However, you may name beneficiaries for your plan in case you pass away with funds still in your account. Along with family and friends, a charity may also be named as a beneficiary of a portion of your plan.

Retirement fund assets can be great charitable gifts because of the tax implications to your non-charitable beneficiaries. Most retirement plans are income tax-deferred, meaning you do not pay income tax on the funds

contributed to your plan or on the growth of the assets within the fund. However, you are responsible for paying the tax when the funds are distributed. Your beneficiaries are also

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Erica Burkharth, who organized the Pittsburgh PKU fundraising event, with Dr. Ray Stevens.

## On the front lines of PKU research

> Phenylketonuria (PKU) is an inherited metabolic disorder that affects almost 30,000 children and adults in the United States—approximately one out of every 10,000 births. Until recently, the only treatment available for the disorder was a strict, very difficult to maintain, low phenylalanine diet that had to be maintained for a lifetime.

**D**uring the past few years, the Ray Stevens laboratory at Scripps Research has worked with a number of non-profit organizations to raise several hundred thousand dollars for PKU research.

Fundraising activities, such as picnics and bicycle rides for this year's National PKU Month in May were held across the country each weekend, with Professor Stevens participating in several of the events.

Recent PKU research has led to one compound in Phase III trials for mild PKU and the development of another therapeutic in pre-clinical studies to treat severe or classical PKU.

For more information about PKU research in the Stevens Laboratory, <http://stevens.scripps.edu/pku-research.html>.

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### *Retirement planning, CONTINUED*

required to pay the income tax that has not been paid. Charitable organizations, like The Scripps Research Institute, are tax-exempt and not liable for the unpaid taxes. If you name The Scripps Research Institute as a beneficiary of your retirement plan, the full amount of your gift will be used for developing new treatments and cures to diseases.

Naming or changing your beneficiaries is easy. Simply contact your retirement plan administrator and request a designated beneficiary form.

Recently, Jeffery Kelly, Ph.D., Dean of Graduate and Postgraduate Studies and Lita Annenberg Hazen Professor of Chemistry at The Scripps Research Institute, decided to designate The

Scripps Research Institute as the beneficiary of his retirement plan.

“It’s pretty simple,” said Jeff. “The Scripps Research Institute has been very good to me. I have no dependents, and this is my way of giving something back in a way that will benefit society. The Scripps Research Institute needs philanthropic support for innovations in science, and it is one of the best charities around. I can’t think of a better gift than improving the quality of life for humankind and pushing forward the frontiers of science.”

To learn more about retirement plan designations or joining the Scripps Legacy Society, please contact Cheryl Dean, Planned Giving Counsel at (858) 784-2380 or [cdean@scripps.edu](mailto:cdean@scripps.edu).



Dr. Jeffery Kelly

# The Scripps Council of 100

> The Scripps Council of 100 consists of individuals, couples, and representatives of corporations or foundations that contribute \$100,000 annually or make a single contribution of \$1 million or more to The Scripps Research Institute.

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