Washington University Record, February 11, 2005

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New method makes genetic changes easier to identify

'Major technological breakthrough'

BY MICHAEL C. PEROV

It is now significantly easier to search long stretches of DNA for genetic changes associated with disease, thanks to a School of Medicine scientist.

WUSTL researchers have developed a method called "direct genomic selection" that accelerates the transition between family or population-based studies of disease inheritance patterns and identification of genetic variations that may contribute to disease.

That transition normally slows down dramatically when scientists sequence regions of interest in patients' DNA, determining the letter-by-letter genetic code found in those regions. With the base sequences from many patients' DNA, scientists can conduct comparisons that highlight the changes most commonly linked to disease, which provide the leads they need to better understand and treat a wide range of disorders.

Researchers reported in a recent issue of Nature Methods that they've already applied direct genomic selection to a region of DNA linked to psoriasis, a disfiguring and debilitating inherited skin condition.

"We quickly found 100 previously unidentified genetic variations with potential links to psoriasis," said senior author Michael Lovett, Ph.D., professor of genetics and of pediatrics. "It really is a much quicker and more affordable way of getting at these types of variations and has potential for applications in other areas, including cancer research."

Lovett is working with his colleagues at the Genome Sequencing Center to make direct genomic selection available to a much wider group of researchers. The approach will further empower the University's BioMed 21 initiative, which is dedicated to harnessing genetic studies and other basic research for improved patient diagnosis and treatment.

"This is a major technological breakthrough," said Mark Johnston, Ph.D., professor and chair of the Department of Genetics. "It's clearly an enabling technology that will let us extract the region of interest from each individual's DNA and sequence it."

Direct genomic selection answers a growing need for what geneticists call resequencing — sequencing the same genetic region in many individuals.

Scientists measure DNA by its individual units of code, which are known as base pairs. Current automated DNA sequencing technology can process pieces of DNA 700-1,000 base pairs long, but inheritance studies can leave researchers searching for changes in segments of DNA hundreds of times longer.

Scientists formerly had only two unsatisfactory options for overcoming this disparity and sequencing such large regions. One, which reproduces patients' entire genomes, can take up to a year and costs tens of thousands of dollars and discards most of the genetic material produced. The other uses a process that focuses more directly on the region of interest in patients' DNA but leaves the genetic material in other species.

See Gene, Page 6

Cardiac cell model sheds light on irregular heartbeats

BY TONY FITZPATRICK

University scientists have developed the first mathematical model of a canine cardiac cell that incorporates a vital calcium regulatory pathway that has implications in life-threatening cardiac arrhythmias, or irregular heartbeats.

The work was done by Thomas J. Hourl, Ph.D., a postdoctoral researcher in the laboratory of Jeffrey K. Safrit, Ph.D., M.D., the Paul E. Lacy and Ellen Lacy Professor in pathology and immunology in the School of Medicine, and Stanton Rudy, Ph.D., the Fred Singh Distinguished Professor of Engineering.

They have incorporated the Calcium/Calmodulin-dependent Protein Kinase II (CaMKII) regulatory pathway into their model, improving the understanding of the relationship between calcium handling in cardiac cells and the cell's electrical activity.

Normal contraction of the heart relies on normal generation of electrical signals, called action potentials, and their organized spread through cardiac tissue. The normal conduction of action potentials is reliant upon sodium channels.

But slow conduction of action potentials that can lead to heart arrhythmias depends on calcium channels, which, in turn, are modulated by cell calcium.

"CaMKII mediates an important regulatory pathway that influences calcium cycling in the cell and modulates many processes involving calcium, including activities of calcium channels," Rudy said. "Having this pathway modeled is a valuable research tool because there is a strong link between abnormalities of calcium handling and cardiac arrhythmias."

In addition, being a first mathematical model of a regulatory pathway involved in cell electrophysiology, it can serve as a paradigm for modeling effects of other regulatory pathways on cell function.

Rudy and Hund published their findings in a recent issue of Circulation, a journal of the American Heart Association. The work was funded by grants from the National Institutes of Health's National Heart, Lung, and Blood Institute and a Whizzer Foundation Development Award.

Throughout all living cells, there is a broad array of charged atoms called ions interacting in a

See Model, Page 6
Upgraded bike locks available through WUSTL police

By ANDY CLENDENNEN

In an effort to stay one step ahead of would-be bad guys, the University Police Department has upgraded bike locks. Bike clubs have been informed and Kryptonite bike locks that were purchased from Radio Shack in the fall of 2004 will be upgraded to those with the cylinder style lock, which is more resistant to being picked than prior styles.

The rate remains $20 for the lock, and members of the University community can either receive their full money back when they leave the University, or they may keep the lock.

For owners of KryptoLoc bike locks, the police department is encouraging direct contact with Kryptonite to receive this free upgrade. Individuals who have questions or wish to report a compromised lock should contact Glenn at 935-5084. Inquires to receive this free upgrade, including postage.

Wearable computer also

At the urging of a wearables research group at MIT, researchers have developed a computer that can be worn like a watch, as a bracelet or as a necklace.

The device, called the "Luminator," is a battery-powered, wireless computer that can be used to access the Internet, take digital photos, send text messages and play music.

The computer is about the size of a deck of cards and has a small screen that can display text or images. It is controlled by a small keypad that can be either a touch screen or a numeric keypad.

The device is connected to a network via a wireless radio frequency signal, and it can communicate with other devices using a wireless protocol called ZigBee.

The Luminator is currently being developed by a team of researchers at MIT, including professor of computer science and electrical engineering David W. Irwin.

The device is expected to be available in the next year at a cost of about $200.

Ethnicity's complexities examined

By NEIL SCHNEIDER

Reid M. Kennedy, Ph.D., associate professor of classics in Arts & Sciences, has been awarded a $95,275 grant from the Fogarty Foundation for a working group on "Ethnolinguistics: Bridging the Pedagogy of Ethnicity." This collaborative research project will involve faculty members from WUSTL, Ohio Wesleyan University, and Luther, Midland and Union colleges, with the goal of examining the role of ethnicity in the teaching of foreign language and the classroom's contribution to the promotion and practice of ethnicity in the curricula of diverse institutions.

The ultimate goals are to help institutions fulfill the civic mission of educating students in multicultural student communities and to help students grapple with the complexities of ethnicity.

"I'm very excited about this opportunity to work with colleagues who are looking forward to working with colleagues who are looking forward to this project," said Kennedy.

"Ethnicity is a subject of central importance for higher education because, given the role of other, nationalistic, and multicultural dimensions of demotic political cultures.

"How can we help students understand the role of ethnicity in their own lives and the role of ethnicity in their own lives in the world?"

Balot said it related to "historical context, solidarity, genealogy and culture.

"How can we help students understand the role of ethnicity in their own lives and the role of ethnicity in their own lives in the world?"
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Improved stem cell procedure offers superior results

BY GWEN ERICSON

The pilot study of the procedure was recently reported in the journal Bone Marrow Transplant.

The regimen was administered to 11 pediatric and five adult patients who had normalizing bone marrow or metabolic disorders, such as sickle cell anemia, thalassemia or Hunter's syndrome. The patients were at St. Louis Children's and Barnes-Jewish hospitals and the Children's Hospital of New Orleans.

Several and disease parameters improved or improved in patients who underwent successful transplants.

In a successful stem cell transplant, the donor stem cells become permanently established, or engrafted, in the patient's bone marrow and continually produce healthy blood cells.

To prevent the host immune system from destroying the foreign stems, physicians administer a pretransplant immunosuppressing treatment.

We wanted an approach that would effectively knock out the patient's immune system to let the transplanted cells engraft, but then allow immune function to return, said study leader Shrinu Shenoy, M.D., assistant professor of pediatrics and a Siteman Cancer Center faculty member.

A key innovation in this study changes the timing of administering a powerful pretransplant conditioning drug, called Campath-1H, which destroys only one experienced late-graft rejection, an unusually high rate of success, according to Shenoy.

Furthermore, the grafts took hold quickly.

Donor stem cells had established in the bone marrow completely at one month, protecting from other reduced-intensity protocols, in which donor engraftment is gradual and often takes many months.

The protocol also reduced the incidence and severity of graft versus host disease. For the majority of patients who experienced graft versus host disease, the symptoms were limited to the skin and were controlled with treatments that were later temporarily withdrawn.

To minimize damage to growing tissues like the brain and reproductive organs, the procedure allows early recovery of immune function. It also nearly eliminates transplant rejection and decreases the incidence and severity of graft versus host disease, which occurs when transplanted immune cells attack various cells in the body and is a common complication in transplants.

Termed a "reduced-intensity" protocol, in pediatric patients it may minimize damage to sensitive growing organs like the brain and reproductive organs.

A safe haven

Chebbie Smith and Alvin Lucious, social worker Kelly Nolan for fun and games at the January support meeting of Project ARK (ADVANCES Resources and Knowledge).

The School of Medicine program coordinates medical care, social support and prevention services for children, young adults, women and families that are infected, affected or at risk for HIV. The program also hosts special events throughout the year to help families develop support systems.

"We all consider each other family," says Nolan, who manages more than 45 pediatric cases for the program. "Project ARK offers a safe place for the kids to have fun and network with each other."

Passion for social justice, medical education earns Mathews award

BY GWEN ERICSON

Faith, formal education and life experiences have shaped the character of Katherine Jahinge Mathews, M.D., assistant professor of obstetrics and gynecology. But she feels fate played a part in bringing her to St. Louis in 1998, where she found a way to fulfill her passion for pursuing social justice through medicine.

A faculty member at the Siteman Cancer Center and the School of Medicine program coordinates medical care, social support and prevention services for children, young adults, women and families that are infected, affected or at risk for HIV. The program also hosts special events throughout the year to help families develop support systems.

"We all consider each other family," says Nolan, who manages more than 45 pediatric cases for the program. "Project ARK offers a safe place for the kids to have fun and network with each other."

Jost named chairman of radiological society

BY MICHAEL C. POOTY

Ralph Jost, M.D., the Elizabeth Mallinckrodt Professor and head of radiology, has been named chairman of the board of directors of the Radiological Society of North America (RSNA).

The society comprises more than 57,000 radiologists, radiation oncologists and related scientists committed to promoting excellence in radiology through education and research, with the ultimate goal of improving patient care.

Jost, 65, earned his bachelor's degree in chemical engineering at MIT in 1962. He received his medical degree from the University of California School of Medicine in 1966.

Before moving to WUSTL, Jost interned at Cleveland Metropolitan General Hospital and was a radiology fellow at the National Institutes of Health. He has been active with the RSNA since 1991 and recently held the second year of the WUSTL presidency.

Jost also is the director of the Mallinckrodt Radiology Laboratories at the School of Medicine and an affiliate professor of computer science.

"When the opportunity came, I was very excited, especially for the potential for diagnostic radiology, the use of information technology in the practice of diagnostic radiology," Jost said.

"I feel the RSNA speaks to the future of medicine," he added.

Mathews

The RSNA's scientific meeting is one of the largest annual medical meetings in the world with approximately 60,000 attendees from 70 countries.

"We've had our first pregnancy in that first year. Then he will serve successive one-year terms as president-elect and president of the RSNA." He has been active with the RSNA since 1991 and recently held the second year of the WUSTL presidency.

"I feel the RSNA speaks to the future of medicine," he added.

"We've had our first pregnancy in that first year. Then he will serve successive one-year terms as president-elect and president of the RSNA," he said. "I feel the RSNA speaks to the future of medicine," he added. 

The Nickel's Fellowship includes a $15,000 grant to support the recipient's academic efforts in the area of radiology.

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in the summer of 1816, Romantic poets Percy Bysshe Shelley and Lord George Gordon Byron were both fleeing scandal in their native England, met in Switzerland, sparking one of literature’s most storied, passionate and tumultuous friendships. This month, the Performing Arts Department in Arts & Sciences will revisit those days with Howard Brenton’s Bloody Poetry, a swirling tale of two 19th-century literary luminaries who spent their lives squabbling over legendary encounters and its political, emotional and artistic consequences. Performances will begin at 8 p.m. Feb. 17-19 and at 2 p.m. Feb. 20 in the A.C. Hutcher Studio Theatre in Mallinckrodt Student Center.

WASHINGTON UNIVERSITY IN ST. LOUIS

University Events

PAD to present Howard Brenton’s Bloody Poetry

BY KURT MUELLER

The celebrated spoken-word poet Saul Williams will give a presentation on “The Connection Between Hip-Hop and Poetry” at 11 a.m. Feb. 16 in Grobe Chapel. The Assembly Series event will serve as the Social Justice Center Lecture.

His poetry, as renowned spoken-word artist Williams observes in fast words that have an innate rhythm to them, like hip-hop, is a movement and is about bringing poetry back to the public.

Spoken-word artists often compete in “slams,” where their best sound off against one another. Audience members choose among random judges the winner.

Williams became the Grand Slam Champion in 1996 at the Nuyorican’s Poet’s Cafe in New York City. The competition is for the most captivating written and spoken word, music, hip-hop, visual arts, comedy and dance.

In 1998, Williams appeared in Slum, a film that details the life of a young man in prison who discovers the power of poetry and uses it to regain his sense of self. The film won awards at both the Sundance and San Francisco film festivals.

RECORD 1 p.m. French Film Series.

Spoken-word artist Williams to talk Feb. 16

Raja.

expanded calendars for the Hilltop Campus

PAD to present Howard Brenton’s Cannes and Sundance film festivals.

sense of self. The film won awards at both the

ers the power of poetry and uses it to regain his

where one poet sounds off against another. Audience

Lighting and sound design are by senior

Les Karpas and freshman Andrew Renard,

respectively. Dramaturge is senior Amy Soil.

Tickets — $12 for the general public; $8

for senior citizens and WUSTL faculty, staff,

and students — are available through the

Education Office, 935-9543, and all MetroTix outlets.

For more information, call 935-6433.

East Asian Religions • Victory Songs • Monsieur Ibrahim

Lectures

Friday, Feb. 11


4 p.m. Dept. of Music Lecture. "Parents Forever in the Novelette" Reading of Meaning of "Victory Songs and jams" by Howard Brenton. Washington University. 935-8541.

Saturday, Feb. 12

8 a.m.-1:15 p.m. Center for the Application of Information Technology Two-Week Workshop. "Workshop's single-minded search for the English of Medicine" (www.cait.org/). 935-4668.

Monday, Feb. 14

8:30 a.m.-4:30 p.m. Center for the Application of Information Technology Two-Week Workshop. "Workshop's single-minded search for the English of Medicine" (www.cait.org/). 935-4668.

4:30 p.m. 13th. Cost $195, reduced to $135 for WUSTL students, faculty, and staff. Byers, Brown Hall, Room 200. 935-4841. 362-9368.

Monday, Feb. 14


Tuesday, Feb. 15


5 p.m. College of Arts and Sciences Contingent of the "New Play Reading Festival." "Mephisto" by Howard Brenton (character). Leon Schartel Auditorium, 510 S. Scarpellino. 362-2763.

6 p.m. College of Arts and Sciences Contingent of the "New Play Reading Festival." "Mephisto" by Howard Brenton (character). Leon Schartel Auditorium, 510 S. Scarpellino. 362-2763.

Wednesday, Feb. 16


Thursday, Feb. 17

3 p.m. College of Arts and Sciences Contingent of the "New Play Reading Festival." "Mephisto" by Howard Brenton (character). Leon Schartel Auditorium, 510 S. Scarpellino. 362-2763.

5 p.m. College of Arts and Sciences Contingent of the "New Play Reading Festival." "Mephisto" by Howard Brenton (character). Leon Schartel Auditorium, 510 S. Scarpellino. 362-2763.

Friday, Feb. 18


3 p.m. Joint Center for East Asian Studies Assembly Series. "The Iranian Revolution: 25 Years Later." Karim Siavashi, assoc. prof. of political science at the University of Tehran & director of the Institute of Iranian Studies. 4444 Forest Park Blvd., St. Louis, Mo. 63108. 362-4017.

Monday, Feb. 21


Tuesday, Feb. 22

4:30 p.m. College of Arts and Sciences Contingent of the "New Play Reading Festival." "Mephisto" by Howard Brenton (character). Leon Schartel Auditorium, 510 S. Scarpellino. 362-2763.

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`Maximizing Civic Engagement of Older Adults' forum Feb. 15

BY JENNIFER MARTIN

With the first wave of baby boomers preparing for retirement, the 2005 White House Conference on Aging (WCHA) Oct 23-26 in Washington, D.C., will be an important opportunity to assess aging in America and improve the lives of older Americans.

The WCHA will play a significant role in shaping the discussion at the conference through "Maximizing Civic Engagement of Older Adults:" outreach to State and Local government officials, the private sector, and the public at large.

We are proud that Washington University was selected as a site for a WCHA event because of our work on productive aging and Civic Engagement in Older Adults, a priority of the White House Conference on Aging.

We have been studying ways to increase the engagement of older adults in volunteerism, a form of civic engagement that can make a difference in our communities. At the forums, we will present our research findings to local leaders and volunteers and will be discussing innovative volunteer programs in the local community.

During the forum, which will be conducted in a style of legalese, professionals will discuss:

**Fiction writing by Kathryn Davis to read**

**BY LEAH OTTEN**

"Kathryn Davis' fiction defies all the same fictional territory. No one else writes a sentence like Davis or even comes close."

"She is one of the most interesting and original American fiction writers."

Davis has received a Kafka Prize for fiction by an American woman: the Albertine Prize sponsored by Albertine Editions.

Davis is being held in Orlando, Phoebe Siegel, and Boston.

On Feb. 18, 2005

9:15 p.m. Career Center Event. Student Advisory Board Meeting, West Hall, Rm. 117. Cost: $35-$40

**WCHA**

The following incidents were reported to University Police Feb. 2-8. Readers with information and data-gathering assistance in investigating these incidents are urged to call 935-5555. This information is provided as a public service to promote safety awareness and is available to the general public at www.police.wustl.edu.

**Crime alert**

On Feb. 4, the residents of an apartment in the 6100 block of Washington University Avenue reported that a burglary in their apartment at about 10 p.m. On observing the suspect in the apartment, the suspect fled and no property was stolen.

The suspect is described as an African American male in his mid- to late-30s, wearing dark pants, a maroon jacket and a black skull cap.

**Crimes reported to University Police**

8 a.m. 11:00 a.m. 3:00 p.m. Career Center Event. Student Advisory Board Meeting, West Hall, Rm. 117. Cost: $35-$40

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**Crimes reported to University Police**
Was there a football game, too? More than 100 students, faculty and staff from the Olin School of Business gathered Feb. 8 at the Charles F. Knight Executive Education Center for the annual "Super Ad Bowl," an opportunity to watch and evaluate the advertisements broadcast during the Super Bowl. The event included presentations by area advertising associates such as Todd Crombecke (above), senior vice president and account director at Leo Burnett, who spoke about what makes an effective advertisement. Students voted for their favorite spot by casting ballots on the criteria laid out by Crombecke. The hands-down winner: Diet Pepsi's ad in which musician P. Diddy unexpectedly creates a fist for the soft drink's truck.

Model
Method provides tool for diagnosis, treatment — from Page 1

dynamic environment. Ion channels along cell membranes open or close to allow these interactions.

In heart cells, for instance, many different kinds of ion channels interact to generate the action potentials that go through the heart and cause a synchronous contraction.

In a normal heart, action potentials form very organized waves of activity and contraction. In arrhythmias, though, normal wave of action potentials can be disrupted, either by a focal activity or a continuous group of heart cells or by electrical waves that break the heart's rhythm in a number of different manners.

The largest killer of Americans is heart disease, claiming 1 million Americans annually. More than 300,000 of these deaths are attributed to arrhythmia, 7 million worldwide.

Researchers used a computation-al biology approach to study arrhythmic heart tissues (ion channels, cell, multicellular tissue) of the cardiac system, and researchers in his laboratory have also developed detailed computer models of the workings of cardiac cells and their alteration by genetic mutations.

Until recently, heart specialists have had no functional tool like MRI and CT to better understand the heart's electrical function. In work supported by a Merit Award from the NIH, Ford has pioneered a novel, non-invasive imaging modality for cardiac electrophysiology and arrhythmias.

The new method, electrocar-diography imaging (ECCI), adds a much-needed clinical tool for the diagnosis and treatment of cardiac rhythms. It also provides a noninvasive method for

spending region from a patient's DNA for sequencing. Lovett also developed modifications to the steps used to prepare patient DNA specimens and ensure that the material stored by the fishing rods can easily be processed.

The challenge now is that we have to face questions that are not all-or-nothing factors — they can be a complex mix of risk of disease, but not to guaranteed development of the disease," Lovett said. "If we have enough instan-

tences, there's concern that another gene or bit of genetic code string somewhere near it, in the same approximate region, might be able to more completely explain what happens in the disease.

Genetic selection should also be helpful to cancer research, according to Lovett. "In many cancer cases, we know that the DNA of cancer cells — deletions, additions or substitutions," Lovett said. "We've gained great deal of understanding in narrowing those differences down through genetic selection could help scientists go in, grab the appropriate region of DNA, sequence it and start to learn what's going on."
Faculty members receive promotions, tenure

By Tony Fitzpatrick

Jennifer Neswald, a doctoral student in the Olin School of Business, has joined other American and Canadian doctoral students as 2004 Canon National Parks Science Scholars.

This is the largest corporate-supported science program for doctoral students in the world. From 1990-2004, more than $8 million has been appropriated to support 388 national parks for the promotion of science in the promotion of scientific freedom and responsibility.

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The Canon National Parks Science Scholars Program helps develop the next generation of scientists and conservationists in the field of science and technology. The program is designed to support research and education in the fields of science and technology.
Taking things to a personal level

Nanette Tarbouni gets to know potential students as well as possible

BY ANDY CLENDENNEN

Nanette Tarbouni and her husband, Younasse, hope to take a trip to Morocco this year to visit his family. They know that she is a person of integrity, I have learned about a great deal about her. She is a terrific colleague and friend. The friendship extends beyond just colleagues, through. Her personality is just part of what makes her an effective recruiter, which quite an impact on prospective students.

She’s been wonderful to work with,” says Kathleen Jaspert, a graduate adviser at Parkview Central High School in Chesterfield, Mo. “She’s great with the kids, she’s an outstanding representative for Washington University and she’s never too busy to return a call or answer questions.”

“Everyone knows how professional and well-organized the admissions staff is,” said one prospect. “They look at you like ‘Who the heck are you?’ It’s sort of awe-inspiring how you can get from the 10-12 pieces of paper you get from them. It’s fascinating.”

Each year, Tarbouni has more and more friends to make through the application process. About 20 years ago, the University received approximately 4,500 applications, and approximately 50 percent of them were admitted. This year, the University received well over 31,000 applications and only 20 percent will be admitted. That’s a huge step for a school once known as a “streetcar campus,” but according to Tarbouni, it is that they have raised the consciousness of parents and students in just thinking about college — thinking about going to college for some, and thinking about which college for others.

Regardless of the reasons, admissions this year — is an absolute joy,” Tarbouni said. “I immediately applied and came to interview. I had done advising for 3-4 years, I thought I would do admissions for a couple of years and did that. As well be to go to student services for a couple of years and then settle on what I liked best.

But this admissions thing just got in my blood, and I cannot leave it.”

Which might sound odd to some, but her colleagues in the admissions office, Tarbouni has stayed, and her efforts — and loyalty — are appreciated.

“It is so rare in the world of admissions that a person of Nanette’s talent would remain at one place for more than 20 years,” said John Berg, associate vice chancellor — are appreciated.

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