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Brain activity in youth could give rise to Alzheimer's disease

Using five different medical imaging techniques to study the brain activity of 274 people, including those with Alzheimer's disease, those on the brink of the disease and healthy individuals, University researchers have found that the areas of the brain that young, healthy people use when daydreaming are the same areas that fail in people who have Alzheimer's disease.

On the basis of their data, the researchers are proposing a hypothesis that Alzheimer's disease may be due to abnormalities in the regions of the brain that operate the "default state." This is the term used to describe the cognitive state people default to when resting, daydreaming or thinking to themselves.

The regions of the brain we use in our default state when we are young are very similar to the regions where plaques tend to form in people with Alzheimer's disease, said the study's lead author, Dr. Shin-ichiro Imai, a professor of molecular biology and pharmacology.

"Researchers such as myself who study aging are expectedly observing that the regions of the brain that light up when humans slip into comfortable patterns of thought are the same as those that, later in life, exhibit the disabling clumps of plaque characteristic of Alzheimer's.

That remarkable correlation, Buckner says, suggests that default activity may be a remnant of the everyday function of the brain.

"It may be the normal cognitive function of the brain that leads to Alzheimer's later in life," said Buckner, who also holds joint appointments with the departments of radiology, pediatrics and psychiatry.

See Alzheimer's, Page 6

La Russa appointed vice chancellor for fall Assembly Series

By Barbara Rea

The Assembly Series will have an unusual start to its fall schedule with a talk by Cardinals manager Tony La Russa at 11 a.m. Sept. 7 in Graham Chapel.

The rest of the series will feature speakers on a wide range of topics such as politics, economics, writing, history, religion, medicine, science, exploration, space, exploration and the Holocaust.

Assembly Series lectures are held at 11 a.m. Wednesday in Graham Chapel, unless otherwise noted. They are free and open to the public; however, due to the popularity of some speakers, there may be a limited seating available for the public.

For the most current information, go online to assemblies.wustl.edu or call 935-5287.

La Russa is one of baseball's greatest managers, ranking third on the all-time Major League Baseball managerial wins list.

Now in his 30th season at the Cardinals' helm, he has taken them to five postseason appearances, including last year's World Series. He is the leader in career winning percentage among active managers and ranks third all-time on the Cardinals' managerial wins list.

In 2002, he was named National League Manager of the Year. La Russa began his managing career in 1978 with Knoxville, Tenn., in the Class AA Southern League. He took his first major-league managing job in 1979 with the Chicago White Sox.

In 1983, he led Chicago to the American League West title and finished with the best record in the major leagues that year. He has also received honors from the Sporting News, The Associated Press and the Baseball Writers' Association of America.

In 1986 he took over the Oakland Athletics, won the Manager of the Year award in 1988 and guided the A's to the 1989 World Series title. In 1992, he earned another Manager of the Year award.

Considered by many to be the shrewdest mind in the game today, La Russa's intellectual, strategically adept style of managing flows through his Busch Biscuit's current best-seller, Three Nights in August: Strategy, Heartbreak, and Joy Inside the Mind of a Manager, which takes readers into the minds and hearts of La Russa and his team during a three-game series in 2003 between the Cards and the Cubs.

A book-signing will be held at 9:45 a.m. at the Campus Store in Mallinckrodt Student Center.

Before his managerial career, See Assembly, Page 6

Protein may provide new diabetes therapies

By Gregory Erichson

Opening the possibility of new therapies for type 2 diabetes, School of Medicine researchers have found that a protein called Sirtl enhances the secretion of insulin in mice and allows them to better control blood glucose levels.

The study was published in the Aug. 17 issue of Nature and Metabolism.

According to senior author Shin-ichiro Imai, M.D., the finding suggests therapies that increase the activity of Sirtl could be of benefit in type 2 diabetes.

"We are especially interested in how we can activate Sirtl in a natural way," said Imai, assistant professor of molecular biology and pharmacology. "One option we are investigating is increasing the body's synthesis of NAD, a necessary cofactor for Sirtl's function. Because vitamin B3, often called niacin, is a building block of NAD, it has interesting potential."

Sirtl is referred to as Sir2 in lower organisms, in which it has previously proven to be a key to aging and longevity. Increasing the amount of Sir2 dramatically extends life spans in experimental worms, yeast and flies.

"Researchers such as myself who study aging are enthusiastically investigating Sir2," Imai said. "In 2000, I found that Sir2 responds to the level of energy in the form of NAD available in cells. Further research has shown that Sir2 connects nutrient status and longevity."

In mammals, scientists have shown that restricting calories can extend life span and also leads to an increase in Sir2, the mammalian version of Sir2. Sir2 reacts to changes in nutrient availability in a wide variety of tissues.

Uptake of the basic nutrient glucose is controlled by insulin, and Imai's research group found that the protein appears to be well conserved among animals.

"This study is a remarkable convergence that we did not expect," Imai said.

The findings are important because they could help scientists and clinicians identify and understand the beginnings of what is probably a cascade of events that ultimately leads to Alzheimer's.

The most common form of dementia among older people, Alzheimer's is characterized outwards by the erosion of language, thought and memory, within the brains of people with Alzheimer's, abnormal clumps of plaque and tangled bundles of fibers form and characterize the physical manifestation of the disease, which may affect as many as 4.5 million Americans.

The disease most frequently manifests itself after age 65, but its causes are unknown.

"The availability of powerful imaging techniques and the ability to merge different sets of imaging data through bio-informatics and statistical methods enabled Buckner and Imai to construct a picture of Alzheimer's from molecular changes to the structural and functional manifestations of the disease.

In the process, the team unexpectedly observed that the regions of the brain that light up when humans slip into comfortable patterns of thought are the same as those that, later in life, exhibit the disabling clumps of plaque characteristic of Alzheimer's.

That remarkable correlation, Buckner says, suggests that default activity may be a remnant of the everyday function of the brain.

"It may be the normal cognitive function of the brain that leads to Alzheimer's later in life," said Buckner, who also holds joint appointments with theSee Alzheimer's, Page 6

Lokken appointed vice chancellor for government and community relations

By Andy Clegenhin

Pamela S. Lokken has been appointed vice chancellor for government and community relations, Chancellor Mark S. Wrighton announced. Lokken has served as director of government and community relations since 1993.

"Pam Lokken is a leader in the country in strengthening relations between higher education and the federal government, and it is wonderful to have her in an expanded leadership role here at Washington University," Wrighton said. "We face many issues at the local, state and federal levels, and Pam will be a key contributor to the growing impact of our university at all levels."
Vice chancellor for research

12-member committee to identify candidates named by Wrighton

**By Jim Draper**

Chancellor Mark S. Wrighton appointed a 12-member advisory committee to identify candidates for the vice chancellor for research position. The committee will be chaired by Martin H. Israel, Ph.D., professor of Arts & Sciences.

"I want to thank Marty Israel for agreeing to serve the University in this capacity," said Wrighton. "Professor Israel has a broad, valuable perspective as the dean of the Washington University community since joining the faculty in 1965. In addition to his excellence as a researcher, he is a former dean of the faculty of Arts & Sciences and vice chancellor. He is well suited to lead our mission and research and our research infrastructure, which should drive the committee well in the task ahead."

During Israel's tenure, the University's research enterprise expanded greatly. In fiscal year 1996, total research funding was $220 million. Today that funding has more than doubled, with research support reaching almost $535 million in fiscal year 2004.

The committee will recommend a list of five candidates for the vice chancellor for research in the next few months.

In addition to Israel, the other members of the committee are:

- Ellinor F. Lokken, Ph.D., professor of psychology in Arts & Sciences;
- William E. Schoff, Ph.D., professor of chemistry in Arts & Sciences;
- Christopher I. Byrnes, Ph.D., dean of the School of Engineering & Applied Science and the Edward H. and Florence G. Wilson Professor of Systems Science and Mathematics;
- Michael R. Cannon, J.D., executive vice chancellor and general counsel;
- Elliott L. Lieben, Ph.D., the Alumni Endowed Professor Biochemistry and Molecular Biophysics in the School of Medicine;
- Sally A. Goldman, Ph.D., professor and assistant chair of the Department of Computer Science and Engineering;
- Edward E. Lawler, Ph.D., dean of the George Warren Brown School of Social Work and the William E. Gordon Professor; and
- Edward S. Macian, Ph.D., executive vice chancellor, dean of Arts & Sciences and Barbara and William E. Gordon Professor.

**Chemistry faculty connected with Manhattan Project to be honored**

**By Tony Fitzpatrick**

A special feature honoring WUSTL chemistry faculty in Arts & Sciences who were connected in the Manhattan Project and an exhibit honoring women in chemistry will be included in the 46th Joseph W. Kennedy Memorial Lecture on Monday, Sept. 24. The lecture, "A Few Months: The Manhattan Project," will begin at 7 p.m. in the Science Building, Room 300.

Robert J. Cavers, Ph.D., professor and chair of the Department of Chemistry's chemistry department, will present a talk on "Water, Trigonal, and Cubic: The Mystery of Cobalt Oxides" on 4 p.m. in the Arts & Sciences Building. The lecture is free and open to the public.

The following incident was reported to University Police. Readers with information may contact University Police at 314-935-5555.

On Aug. 29, University Police issued the following alert:

A person wearing a hooded sweatshirt and a sweatshirt with a hooded sweatshirt was walking toward Lindbergh Boulevard on the sidewalk in the 6100 block of Waterman Avenue about 1 p.m. on Aug. 28 and observed two people seated on some steps.

She reported the subjects started to follow her and then one grabbed her bag. She initially resisted — however, one of the subjects ran ahead of her in the face with his hand. She fled to the ground and the subjects took her bag and cell phone. The subjects ran away. Her cell phone was not damaged.

**For more information:**
- Avoid walking or jogging alone and never walk or jog alone after dark.
- Carry a whistle to summon help.
- Be alert to your surroundings. If you suspect you are being followed, run in a different direction; go to the other side of the street and yell or whistle for help; or quickly to a business or a group of people or business.
- If you are confronted by a thief, submit to his demands, don't chase them as they leave. Report suspicious persons or activity immediately to the police.
- Be extra cautious if someone approaches your car and asks for information.

**Campus Watch**

The following incident was reported to University Police. Readers with information that could assist in investigating this incident are urged to call 314-935-5555. This information is provided to alert students, faculty, and staff to apparent safety issues and is available on the University Police Web site at police.wustl.edu.

On Aug. 29, University Police received the following alert:

A person was reported to be walking toward Lindbergh Boulevard on the sidewalk in the 6100 block of Waterman Avenue about 1 p.m. on Aug. 28. She fled to the other side of the street and yelled for help just ahead of her. She initially resisted — however, one of the subjects ran ahead of her in the face with his hand. She fled to the ground and the subjects took her bag and cell phone. The subject ran away and her cell phone was not damaged.

**For more information:**
- Avoid walking or jogging alone and never walk or jog alone after dark.
- Carry a whistle to summon help.
- Be alert to your surroundings. If you suspect you are being followed, run in a different direction; go to the other side of the street and yell or whistle for help; or quickly to a business or a group of people or business.
- If you are confronted by a thief, submit to his demands, don't chase them as they leave. Report suspicious persons or activity immediately to the police.
- Be extra cautious if someone approaches your car and asks for information.

**Students learn systems biology techniques**

**By Tony Fitzpatrick**

Our undergraduate students — who also come from the School of Arts & Sciences; and WUSTL graduate students — will participate in the biology summer program this year on the Hilltop Campus.

The students participated in four week-long courses in systems biology concepts and methods, while working in a systems biology summer program last year on the Hilltop Campus.

The WUSTL graduate school is one of the three from Colgate University and the WUSTL graduate school is one of the two undergraduate programs that have received the award.

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promising new anti-cancer drug now in a newly opened clinical trial at the Siteman Cancer Center. Previous research showed that the compound, known as 17AAG, has the unusual ability to simultaneously target multiple proteins implicated in human cancers.

Administered by the Phase II Consortium at the Mayo Clinic — which carries out trials of new anti-cancer drugs and is funded through the National Cancer Institute (NCI) — the trial will be conducted at several centers around the country. Study head Jeffrey E. Molley, M.D., associate director of clinical investigations at the Siteman Cancer and professor of surgery, initiated the clinical trial of 17AAG (17-allylamino, 17-deoxygeldanamycin) after tests in his laboratory demonstrated that the drug inhibited growth of thyroid tumor cells in culture. "We contacted the Phase II Consortium and the NCI with our initial results, and they quickly agreed to set up this trial," said Molley, who is well-known for developing pioneering surgical techniques for management of recurrent and inoperable thyroid cancer. "This is the first and only NCI-funded therapeutic clinical trial for thyroid cancer that I know of."

The clinical trial will have two arms. One will test the ability of 17AAG to reduce metastatic tumors in different types of cancers that were not cured by surgery and radiotherapy.

The other arm will examine the drug's effect on metastatic, mediastinal thyroid cancer (MTC), a form that's much harder to treat. Physicians treat MTC typically through removal of primary and secondary tumors. More than half of MTC patients treated with surgery will experience a recurrence of the cancer.

"MTC currently has no effective chemotherapy," Molley said. "Unlike other forms of thyroid cancer, MTC tumors don't absorb iodine, so standard therapy with radioactive iodine is of no use against the disease. Similarly, there's no effective chemotherapy for other forms of thyroid cancer once they advance to a stage where they don't take up iodine anymore."

Many thyroid tumors arise from mutations in a gene called RET. The mutation causes cancerous cell growth by turning up the RET protein's activity, so the RET protein is potentially a key target for treating thyroid cancer.

The activity of the RET protein was decreased by 17AAG in studies by Molley's laboratory. Interestingly, 17AAG doesn't directly affect the RET protein. Instead, it interferes with abundant chaperone protein that stabilizes the RET protein through its formative stages. The fact that the drug influences this important chaperone protein, called heat shock protein 90, has focused much scientific attention on 17AAG.

17AAG targets one of the few compounds known to specifically inhibit heat shock protein 90, a protein that was decreased by 17AAG in thyroid tumor cells in culture. "This is an important target for drug development," Molley said. "Scientists have linked these changes to many different disorders."

"In the case of NF-KappaB, there were also mechanisms to affect multiple cellular pathways," Molley said. "Scientists have used a glowing protein from fireflies to observe the activity of a molecule that is an important target for new drugs to treat cancer, autoimmune diseases and several other disorders."

"IKK'stands at a pivot point in the middle of an hourglass-like shape, fanning out from its start to many different receptors on cell surfaces; its finish changes the activity levels of many genes," Piwnica-Worms said. "Establishing that normally this enzyme is altered in cancerous cell cultures is a major step toward tackling and crippling cancer cells."

Scientists have used the glowing protein from fireflies to observe the activity of a molecule that is an important target for new drugs to treat cancer, autoimmune diseases and several other disorders.

PIWNIKA-WORMS AND LEAD AUTHOR SHIMON GROSS, PH.D., A POSTDOCTORAL FELLOW, MEASURED LIGHT FROM THE FIREFLY PROTEIN, LUCIFERASE, TO MONITOR IKK ACTIVITY IN TUMOR CELLS AND INFUSED LIVER CELLS IN LIVE MICE. THEY ALSO SHOWED THE TECHNIQUE CAN GREATLY REDUCE THE COSTS OF TESTS THAT ESTABLISH THE BEST DOSAGES FOR DRUGS THAT TARGET IKK.

The results appeared in the August issue of Nature Medicine and were also published in Nature and in the journal Cell. IKK stands at a pivot point in the middle of an important set of linked chain reactions known as the NF-KappaB pathway. The pathway can start at many different receptors on cell surfaces; its finish changes the activity levels of many genes.

The result, according to Piwnica-Worms, is that the potential reactions patterns in the NF-KappaB pathway form an hourglass-like shape, fanning out among many options at the start, narrowing in the middle, and again fanning out among many options at the end.

"At the waist of that hourglass is IKK," he said. "This appears to put it in a position to be the key regulator of NF-KappaB activity. When we make sure it's intact, that has made it a subject of great interest both from the perspective of understanding how this pathway works and from that of developing drugs to affect conditions in this pathway."

"Researchers around the world are trying to develop techniques that use luciferase to monitor protein-protein interactions," Piwnica-Worms said. "Researchers can employ an instrument known as an in-vivo bioluminescence camera to take real-time measurements of light from luciferase in cell culture and in cells within live animals."

"To use the firefly protein to monitor IKK, Gross altered cell lines to genetically fuse the luciferase protein to IKK (IKK-KappaB), the protein that comes immediately after IKK as the NF-KappaB pathway," Piwnica-Worms said. "Using this approach, they were able to develop a line of mice with genetically altered IKK. The attached luciferase is broken down too, meaning scientists can detect increased IKK activity via decreased light from the cells."

"This is like doing in-vivo pharmacodynamics and pharmacokinetics," Piwnica-Worms said. "With the pathway enabled, IKK triggers reactions that lead to the degradation of IKK. In cells with genetically altered IKK, the attached luciferase is broken down too, measuring scientists can detect increased IKK activity via decreased light from the cells."

"In the case of NF-KappaB, they were also able to develop a line of mice that monitored IKK activity via changes in the levels of gene activation at the end of the pathway," he said. "But those took hours to days to deliver results, and our approach works continuously and in real-time."

In an in-vivo study, Gross and Piwnica-Worms tested the technique in live mice by transplanting genetically altered tumor cells and using a technique that inserted the fused IKK-luciferase protein into liver cells only.

They are working to develop a line of mice with the IKK-luciferase fusion built into its genetic code. In addition, they showed that the system is not only helpful for learning if a drug is having the desired effect, but it can also be used to fine-tune drug dosage from the start. "One of the reviewers of our paper suggested that we use the system to produce a full dose-response curve, which helps establish how best to use a drug," Piwnica-Worms said. "Establishing that normally takes six months and 300 mice. With our monitoring technique, Shimon did it in a five-day period using 50 mice. That's a 90 percent cost savings."
Volleyball again ranked preseason No. 1
For the third straight year, the WUSTL team was named preseason No. 1 in the 2005 CSTV/AmVerCave Volleyball Coaches Association (AVCA) Preseason Coaches Poll, as announced by the AVCA.
It marks the fifth straight year the Bears have finished first. In the previous 10 years WUSTL has finished No. 1 ranking at some point in seven of those years. The 2004 season was the Bears’ third consecutive year as No. 1 and the fourth No. 1 ranking in five years.
WUSTL tallied 584 total points in the poll, including eight first-place votes, putting it five points ahead of Juniata College (579), the 2004 national champion. University Athletic Association rivals New York University (319 points) and Emory University (281 points) and Emory University (272 points) also finished in the top five.

WUSTL, which is scheduled to play eight of the nine other pre- season top-10 teams, opens its season Friday against the Loyola Dominican at 5:15 p.m. today at the Field House to kick off a season-opening stretch of 11 straight home matches.

Kara Liefer is one of three seniors returning to lead the top-ranked volleyball squad this year. Last season, Liefer posted 1,055 assists, good for second in the University Athletic Association.

By JESSICA MARTIN
The lead counsel for Vice President Al Gore in the 2000 election litigation and the director of the Southern Center for Human Rights are part of the full lineup for the School of Law’s eighth annual Public Interest Law Symposium.

Titled "Access to Justice: The Social Responsibility of Lawyers," the series brings to the University outstanding academics and practitioners in areas such as tort, constitutional human rights, the economics of poverty, civil liberties, social justice, capital punishment, clinical legal education, and government accountability.

This popular series provides a forum for the School of Law and the wider University community to engage in a discussion of the legal, social and ethical issues that bear upon access to justice.

All of the full presentations will be held in Anheuser-Busch Hall and are free and open to the public.

The schedule is:

• 11 a.m. Sept. 14 — Marc Galanter, the John and Rylla Bosshard Professor of Law and South Asian Studies at the University of Wisconsin and the LSE Centre for Law, Economics and Policy, will present "Fewer Trials, More Law, More Justice: A Legal Overview of India."

Galanter is author of a number of highly regarded studies about litigation, torts and lawyers and legal culture, such as "When the Game Comes on the Court: Speculation on the Limits of Legal Legitimacy" and "Thinking Trial: An Examination of Trials and Related Matters in State and Federal Courts." He is also the co-author of the book, Tournament of Law: The Transformation of the Big Law Firm, which attempts to explain the growth and transformation of large law firms in the United States.

Galanter’s lecture is co-sponsored by the School of Law Alternative Dispute Resolution Program.

• 4 p.m. Nov. 2 — Stephen Breyer, a nationally recognized expert on criminal law and capital punishment, will speak about "Crime, Prison and the Death Penalty: The Influence of Race and Poverty." Breyer is a member of the Commission on Safety and Abuse in America’s Prisons and is the director of the Southern Center for Human Rights in Atlanta, a public-interest legal project that provides representation to prisoners in challenges to cruel and unusual conditions of confinement and to persons facing the death penalty.

Breyer is a former staff attorney for the Appalachian Research and Defense Fund, and a former trial attorney for the Public Defender Service in Washington, D.C. He has been a visiting lecturer and clinical teacher at several law schools, including Yale, Harvard, Georgetown and Emory universities.

His address is co-sponsored by the Assembly Series and Student Union in conjunction with the Commission on Safety and Abuse in America’s Prisons hearings at the School of Law Nov. 1-2.

• 11 a.m. Nov. 15 — David Boies, Esq, the lead counsel during the 2000 election litigation, will present "Judicial Independence and the Rule of Law." Special counsel for the U.S. Department of Justice in the Microsoft anti-trust lawsuit, Boies is former chief counsel and staff director for the U.S. Senate Antitrust Subcom- mittee and the U.S. Senate Judiciary Committee.

Boies is the chairman of the law firm Boies, Schiller and Flexner LLP, and author of Courting Justice and Public Control of Business. He will serve as the annual School of Law Tyrrell Williams Lecturer.

Boies will participate in a panel of law professors on the topic of technology.

For more information, call 935-9598.

Tuesdays, Sept. 6


Lectures, 8:30 a.m.-4:30 p.m.

8 a.m.-1 p.m. Critical Care CME Course.

Saturday, Sept. 3

11 a.m. Critical Care CME Course — "An Introduction of Critical Care Topics," Cooling & heating.

Saturday, Sept. 10

5:30-8:30 p.m. Medical Ophthalmology CME Course — "Retinal Detachment." Cost: $25; $35 after Sept. 3. Hilton St. Louis.

Monday, Sept. 12

6:30-8:30 p.m. Center for the Application of Information Technology New-selected Lecture — "The Vicissitudes of the Information Technology Industry." Sponsored by CITP, memSec/IT, 935-4705.

Tuesday, Sept. 13


Saturday, Sept. 17

11 a.m. Medical Ophthalmology CME Course — "An Introduction of Critical Care Topics," Cooling & heating.

Saturday, Sept. 24

11 a.m. Medical Ophthalmology CME Course — "An Introduction of Critical Care Topics," Cooling & heating.

Tuesday, Sept. 27

7 p.m. Women’s Soccer vs. Maryville U.

Wednesday, Sept. 28

7 p.m. Men’s Soccer vs. Fontbonne U.

Friday, Sept. 9


Saturday, Sept. 10

8:00 a.m. - 4:00 p.m. Medical Ophthalmology CME Course — "Retinal Detachment." Cost: $25; $35 after Sept. 3. Hilton St. Louis.

Saturday, Sept. 17

11 a.m. Medical Ophthalmology CME Course — "An Introduction of Critical Care Topics," Cooling & heating.

Saturday, Sept. 24

11 a.m. Medical Ophthalmology CME Course — "An Introduction of Critical Care Topics," Cooling & heating.

Friday, Sept. 9

3 p.m. Volleyball vs. Wittenberg U.

Saturday, Sept. 10

3 p.m. Volleyball vs. Ohio Northern U.

Wednesday, Sept. 7

7 p.m. Men’s Soccer vs. Westminster College, 935-4705.

Wednesday, Sept. 7

7 p.m. Men’s Soccer vs. Fontbonne U.

Wednesday, Sept. 14


Wednesday, Sept. 14


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Wednesday, Sept. 14

Researchers continue to track mice's progress

From Page 1

cells responsible for secreting insulin — beta cells in the pancreas — also produce Sirt1. So the researchers investigated the effects of increasing the amount of Sirt1 in pancreatic beta cells in mice to better understand the link between Sirt1 and glucose metabolism.

They designed transgenic mice with a genetic switch that turned up the gene that makes Sirt1 in beta cells.

"We confirmed that the mice overexpress Sirt1 proteins specifically in pancreatic beta cells, not in other kinds of pancreatic cells, and not in brain, liver, kidneys, fat or muscle," said Kathryn Moynihan, a graduate research assistant.

Compared with wild-type mice, the transgenic mice had the same levels of blood glucose and insulin both when well-fed and during fasting. They were of similar weights and their pancreatic cells looked very similar in size and structure. But when the two sets of mice were given a large dose of glucose, a difference became apparent.

The transgenic mice produced more insulin and cleared glucose from their blood streams significantly faster than did wild-type mice.

Challenging the mice's systems with glucose in this manner mimics the glucose tolerance tests used to check for diabetes in human patients. Diabetic patients clear glucose more slowly than do non-diabetics in these tests.

"If your system reacted like that of these transgenic mice, you could process sugar more quickly and much more efficiently after eating sweets," Imai said.

The research group found that the transgenic mice retained their unique beta cell function as they aged from 3 months to 8 months, the equivalent of middle age in human patients. The researchers are continuing to track the progress of the mice, which are now about 20 months old.

An analysis of the activity of genes in the beta cells showed that several genes linked to insulin secretion were affected by the increased expression of Sirt1.

Most prominently, Sirt1 turned down the activity of a gene that decreases insulin secretion.

"The gene makes uncoupling protein 2, which is intimately connected to ATP production," Imai said. "ATP is a fundamental source of energy for metabolism, and by down-regulating uncoupling protein 2, Sirt1 not only enhances insulin secretion, but also increases ATP energy."

"This is a further indication of the connection between Sirt1 and energy status," Imai feels that Sirt1 is probably a very important regulator that integrates cellular response to different types of nutrients, such as glucose, amino acids and fatty acids.

Continued research in the lab will use the transgenic mice to further investigate Sirt1's role in this response.

"By down-regulating uncoupling protein 2, Sirt1 not only enhances insulin secretion, but also increases ATP energy. This is a further indication of the connection between Sirt1 and energy status."

SHEN-SHIRO IMAI
Interdisciplinary collaboration fosters Alzheimer’s insight

RANDY L. BUCKNER, PH.D., lead author of the potential Nature paper on Alzheimer’s disease in the Aug. 24 issue of the Journal of Neuroscience, credits the breakthrough to the close-knit and creative collaboration of researchers in array of cognitive and psychiatric specialties at Washington University. Buckner, an associate professor of psychology in Arts & Sciences, also holds joint appointments, with the Mallinckrodt Institute of Radiology and the Department of Anatomy and Neurobiology in the School of Medicine.

The work stems from major involvement of the Alzheimer’s Disease Research Center, in the Department of Neurology, to analyze the fMRI of novel imaging methods spearheaded by Mark Minn in radiology and visualized using methods and software developed by David Van Essen in neurobiology.

Buckner’s School of Medicine collaborators on this study include:
- Anthony P. Fotenos, a doctoral student in the Medical School Training Program and the Division of Biology and Biomedical Science.
- Gina LaRossa, a medical student.
- Minut, M.D., professor of radiology and with the Mallinckrodt Institute of Radiology.
- Michael C. Morris, the Harvey A. and Dominique Hack Perelman Distinguished Professor of Neurology of pathology and of immunology.

Stages, said John William F. Klemm, M.D., Ph.D., professor of psychiatry at the University of Pittsburgh and a co-author of the Journal of Neuroscience paper. “We have to get this pathology before it has its biggest effect, before it has done its damage,” said Klemm, who has developed techniques for imaging the brain.”

Butter and its findings suggest that there is now the potential to obtain those observations of the disease and to develop methods to detect it before the clinical symptoms begin. Be "broadly useful," he says.

Buckner emphasized that the notion of a causative relationship between everyday metabolic functions of the brain and Alzheimer’s disease has a hypothesis. Hoover, said, may also help explain why panic attacks are high for Alzheimer’s patients.

"We are very interested in exploring the Level observation to understand who is at risk and who is protected from Alzheimer’s disease," he said.

In addition to Buckner and Klemm, the study’s co-authors include Abraham Z. Snyder, Benjamin J. Shuval, Gina LaRossa, rimson Sachs, Anthony F. Fotenos, Yvette L. Sheline, John C. Morris and Mark A. Minn, all of Washington University; and Chester Mathis of the University of Pittsburgh.

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Notables

The Community Service Program, the Richard A. Gephardt Institute for Public Service and the Campus Division will hold a meeting for representatives of student groups and offices.

HURRICANE RELIEF MEETING TODAY

The University Community Service Program, the Richard A. Gephardt Institute for Public Service and the Campus Division will host a meeting for representatives of student groups and offices.

Social work service day

Second-year master of social work student Kelly Miller paints a fence at the Grace Hill Settlement House as part of Community Service Day, an annual event during the George Warren Brown School of Social Work’s orientation. More than 60 social work students participated in service projects Aug. 27 at 27 of a number of sites throughout St. Louis.

Campus Authors

America’s Game: The Epic Story of How Pro Football Captured a Nation

(Random House, 2004)

Michael MacCambridge, adjunct professor in University College in Arts & Sciences

Medicine

MacCambridge tracks the rise in popularity of the NFL since that title game in 1958. He realized that pro football had been America’s unchallenged most popular sport for more than a generation, yet he never read a good account of how it got to be that way, how it eclipsed baseball, the unchallenged champion prior to that time. He set out to tell the story of football, for which he has a lifelong love and admiration.

The epic story of how pro football captured a nation

Pro football has survived a number of transgressions in America’s past; the NFL’s championship game has never read a good account of how it got to be that way, how it eclipsed baseball, the unchallenged champion prior to that time. He set out to tell the story of football, for which he has a lifelong love and admiration.

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James B. Lowe III, M.D., chief of the Section of Cosmetic Surgery, admits he's obsessed with detail. "When I'm in the operating room, every millimeter and every second counts," he says. "It's so important to be 100 percent focused in the OR, I go into this zone and nothing can distract me."

With every procedure — whether it's extensive facial plastic surgery, Botox injections or traumatic hand reconstruction — the field of plastic and reconstructive surgery offers Lowe an amazing artistic opportunity to rejuvenate patients and make a profound difference in their lives.

"Plastic and reconstructive surgery is an art," Lowe explains. "My goal is to achieve a harmonious balance between form and function. It offers me a chance to drastically improve my patients' lives by using my artistic abilities and creative problem-solving skills."

For the past three years, Jennifer Smith has been coming to Lowe for minor cosmetic procedures, so when she decided to undergo more extensive plastic surgery, she knew she was in good hands.

"Dr. Lowe is so talented — he aims for perfection," says Smith, who thoroughly researched the region's top plastic surgeons via news stories, medical journals and online patient experiences before choosing a doctor.

"Two of those aspects are a perfect match for an aesthetic surgeon," Lowe explains. "Jim has very high standards for himself and his practice, which benefits both his patients and the residents who train with him."

Lowe adds that his primary goal with all his patients is to provide them with the individual care and attention of a small practice. "I look as great as I feel," he says. "I want to be the best cosmetic surgeon that I can be for my patients."

Lowe's study includes African-Americans and Hispanic-Americans, along with a break-down of Asian subcultures. Lowe aims to define "a standard of beauty" for major ethnic groups. "The goal is to establish a clear reference for each group," he says. "We aim to probe the depths of what is aesthetically pleasing for each group."

A recent study by the American Academy of Plastic and Reconstructive Surgery reveals that Reconstructive Surgery on African-Americans increased exponentially among minority groups from 1999 to 2001 — more than quadrupling among African-Americans and African-Americans and tripling among Hispanics.

As the number of ethnic patients seeking plastic surgery continues to rise, understanding how to preserve ethnicity is critical to creating an attractive and natural look. "Caucasian beauty is pretty well defined in our culture, so we know what's acceptable," Lowe says. "We also ought to know what's acceptable for each ethnic group. What's attractive for Caucasians isn't necessarily beautiful for everyone."

For the past three years, Lowe and his team have been researching aesthetic attractiveness for different ethnic groups. By measuring the position of facial features, such as the lips, brow line and nose, of people from different ethnicities, researchers are determining attractive facial features for each group. Lowe's study includes African-Americans, Middle Easterners, Hispanics and Native Americans, along with a break-down of Asian subcultures. Lowe aims to define "a standard of beauty" for major ethnic groups. "The goal is to achieve a natural look that brings out the best in each individual's facial harmony while maintaining ethnic traits."

"Jim's skills are exemplary as he develops advanced techniques," Mackinnon says. "He's a dynamic asset to the University and an excellent academician. He has been the driving force in creating an outstanding cosmetic surgery section at the University."

Lowe and his team also publish New Horizons, an educational newsletter — found on drjlowe.com — that informs patients about the latest developments in plastic and reconstructive surgery and provides patients cutting-edge treatment options and procedures.

"My philosophy is simple: Cosmetic surgery is creative problem solving," Lowe says. "I analyze all the options, explain the risks involved and then strive for the optimal aesthetic result."

"With every procedure, I have the chance to dramatically improve my patients' lives — and that's incredibly rewarding."