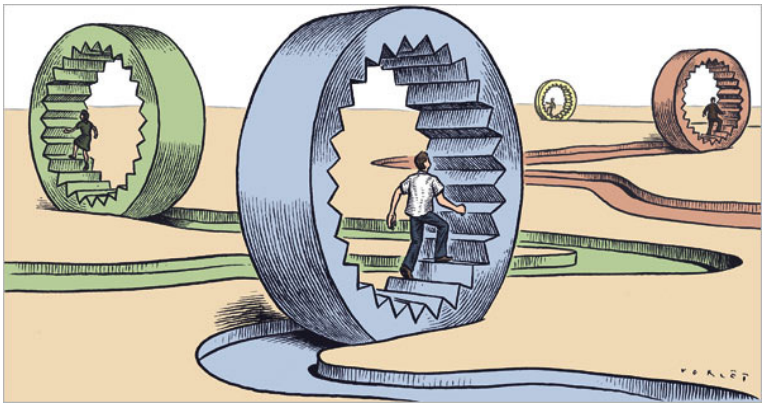
Unboxed

Can You Become a Creature of New Habits?

By JANET RAE-DUPREE

HABITS are a funny thing. We reach for them mindlessly, setting our brains on auto-pilot and relaxing into the unconscious comfort of familiar routine. “Not choice, but habit rules the unreflecting herd,” William Wordsworth said in the 19th century. In the ever-changing 21st century, even the word “habit” carries a negative connotation.



Christophe Vorlet

So it seems antithetical to talk about habits in the same context as creativity and innovation. But brain researchers have discovered that when we consciously develop new habits, we create parallel synaptic paths, and even entirely new brain cells, that can jump our trains of thought onto new, innovative tracks.

Rather than dismissing ourselves as unchangeable creatures of habit, we can instead direct our own change by consciously developing new habits. In fact, the more new things we try - the more we step outside our comfort zone - the more inherently creative we become, both in the workplace and in our personal lives.

But don’t bother trying to kill off old habits; once those ruts of procedure are worn into the hippocampus, they’re there to stay. Instead, the new habits we deliberately ingrain into ourselves create parallel pathways that can bypass those old roads.

“The first thing needed for innovation is a fascination with wonder,” says Dawna Markova, author of “The Open Mind” and an executive change consultant for Professional Thinking Partners. “But we are taught instead to ‘decide,’ just as our president calls himself ‘the Decider.’ “ She adds, however, that “to decide is to kill off all possibilities but one. A good innovational thinker is always exploring the many other possibilities.”

All of us work through problems in ways of which we’re unaware, she says. Researchers in the late 1960s discovered that humans are born with the capacity to approach challenges in four primary ways: analytically, procedurally, relationally (or collaboratively) and innovatively. At puberty, however, the brain shuts down half of that capacity, preserving only those modes of thought that have seemed most valuable during the first decade or so of life.

The current emphasis on standardized testing highlights analysis and procedure, meaning that few of us inherently use our innovative and collaborative modes of thought. “This breaks the major rule in the American belief system - that anyone can do anything,” explains M. J. Ryan, author of the 2006 book “This Year I Will...” and Ms. Markova’s business partner. “That’s a lie that we have perpetuated, and it fosters mediocrity. Knowing what you’re good at and doing even more of it creates excellence.”

This is where developing new habits comes in. If you’re an analytical or procedural thinker, you learn in different ways than someone who is inherently innovative or collaborative. Figure out what has worked for you when you’ve learned in the past, and you can draw your own map for developing additional skills and behaviors for the future.

“I apprentice myself to someone when I want to learn something new or develop a new habit,” Ms. Ryan says. “Other people read a book about it or take a course. If you have a pathway to learning, use it because that’s going to be easier than creating an entirely new pathway in your brain.”

Ms. Ryan and Ms. Markova have found what they call three zones of existence: comfort, stretch and stress. Comfort is the realm of existing habit. Stress occurs when a challenge is so far beyond current experience as to be overwhelming. It’s that stretch zone in the middle - activities that feel a bit awkward and unfamiliar - where true change occurs.

“Getting into the stretch zone is good for you,” Ms. Ryan says in “This Year I Will... .” “It helps keep your brain healthy. It turns out that unless we continue to learn new things, which challenges our brains to create new pathways, they literally begin to atrophy, which may result in dementia, Alzheimer’s and other brain diseases. Continuously stretching ourselves will even help us lose weight, according to one study. Researchers who asked folks to do something different every day - listen to a new radio station, for instance - found that they lost and kept off weight. No one is sure why, but scientists speculate that getting out of routines makes us more aware in general.”

She recommends practicing a Japanese technique called kaizen, which calls for tiny, continuous improvements.

"Whenever we initiate change, even a positive one, we activate fear in our emotional brain," Ms. Ryan notes in her book. "If the fear is big enough, the fight-or-flight response will go off and we'll run from what we're trying to do. The small steps in kaizen don't set off fight or flight, but rather keep us in the thinking brain, where we have access to our creativity and playfulness."

Simultaneously, take a look at how colleagues approach challenges, Ms. Markova suggests. We tend to believe that those who think the way we do are smarter than those who don't. That can be fatal in business, particularly for executives who surround themselves with like-thinkers. If seniority and promotion are based on similarity to those at the top, chances are strong that the company lacks intellectual diversity.

"Try lacing your hands together," Ms. Markova says. "You habitually do it one way. Now try doing it with the other thumb on top. Feels awkward, doesn't it? That's the valuable moment we call confusion, when we fuse the old with the new."

AFTER the churn of confusion, she says, the brain begins organizing the new input, ultimately creating new synaptic connections if the process is repeated enough.

But if, during creation of that new habit, the "Great Decider" steps in to protest against taking the unfamiliar path, "you get convergence and we keep doing the same thing over and over again," she says.

"You cannot have innovation," she adds, "unless you are willing and able to move through the unknown and go from curiosity to wonder." *Janet Rae-Dupree writes about science and emerging technology in Silicon Valley.*

Ibuprofen linked to reduced risk of Alzheimer's disease

ST. PAUL, Minn. – Long-term use of ibuprofen and other drugs commonly used for aches and pains was associated with a lower risk of Alzheimer's disease, according to a study published in the May 6, 2008, issue of Neurology®, the medical journal of the American Academy of Neurology. Previous studies have shown conflicting results, but this is the longest study of its kind.

For the study, researchers identified 49,349 US veterans age 55 and older who developed Alzheimer's disease and 196,850 veterans without dementia. The study examined over five years of data and looked at the use of several non-steroidal anti-inflammatory drugs (NSAIDs). The veterans received medical care and prescriptions through the VA Health Care system.

The study found people who specifically used ibuprofen for more than five years were more than 40 percent less likely to develop Alzheimer's disease. Results also showed that the longer ibuprofen was used, the lower the risk for dementia. In addition, people who used certain types of NSAIDs for more than five years were 25 percent less likely to develop Alzheimer's disease than non-users.

While other NSAIDs such as indomethacin may also have been associated with lower risks, others such as celecoxib did not show any impact on dementia risk. "These results suggest that the effect may be due to specific NSAIDs rather than all NSAIDs as a class," said study author Steven Vlad, MD, with Boston University School of Medicine.

"Some of these medications taken long term decrease the risk of Alzheimer's disease, but it's very dependent on the exact drugs used. It doesn't appear that all NSAIDs decrease the risk at the same rate," said Vlad. "One reason ibuprofen may have come out so far ahead is that it is by far the most commonly used."

Observational studies such as this one must be interpreted with the understanding that they do not prove that an NSAID has a therapeutic effect. The study is subject to what is called "indication bias." That means that it might not be the NSAID use that drove the lower risk of dementia, but rather something about the people who chose to use the NSAIDs that was responsible. These findings should not be taken to mean that NSAIDs should be administered to prevent dementia.

The most common side effects of NSAIDs are nausea, vomiting, diarrhea, dizziness, constipation and headache.
The study was supported by grants from the National Institutes of Health.

Short arms and legs linked to risk of dementia

ST. PAUL, Minn. – People with shorter arms and legs may be at a higher risk for developing dementia later in life compared to people with longer arms and legs, according to a study published in the May 6, 2008, bonus issue of Neurology®, the medical journal of the American Academy of Neurology. Researchers say the association between short limbs and dementia risk may be due to poor nutrition in early life, which can affect limb growth.

Several studies have shown that early life environment plays an important role in susceptibility to chronic disease later in life. "Body measures such as knee height and arm span are often used as biological indicators of early life deficits, such as a lack of nutrients," said Tina L. Huang, PhD, who was with Johns Hopkins University in Baltimore, MD, when the study started. Huang is now with the Jean Mayer USDA Human Nutrition Research Center on Aging at Tufts University in Boston, MA. "Because the development of the brain

region most severely affected by Alzheimer's disease coincides with the greatest change in limb length, we thought it was possible that men and women with shorter limbs could be at greater risk for developing dementia and Alzheimer's disease."

Researchers from the Cardiovascular Health Cognition Study followed 2,798 people for an average of five years and took knee height and arm span measurements. Most participants were white with an average age of 72. By the end of the study, 480 developed dementia.

Researchers found women with the shortest arm spans were 1.5 times more likely to develop dementia and Alzheimer's disease than women with longer arm spans. For every inch longer a woman's leg, the risk of dementia and Alzheimer's disease was reduced by 16 percent.

In men, only arm span was associated with a lower risk of dementia. With every increased inch in arm span, men had a six-percent decrease in risk of dementia. The associations with such measures in men and women were stronger toward Alzheimer's disease compared to other types of dementia.

Huang says there is a strong correlation between height and socioeconomic background, and trends are reflected as early as the first two years of life. "Reduced height for age, or stunting, is thought to be most closely tied to environment and the quality of diet in early life, which corresponds with periods of the fastest leg growth," said Huang. "As a result, environment in the first years of life may play an important role in determining future dementia risk."

"Our findings are consistent with other studies that have been done in Korean populations, where shorter limb length was associated with greater risk of dementia," said Huang.

The study was supported by grants from the National Institute on Aging, the National Heart, Lung and Blood Institute and the National Institutes of Health.

Mental disorders in parents linked to autism in children

CHAPEL HILL – Parents of children with autism were roughly twice as likely to have been hospitalized for a mental disorder, such as schizophrenia, than parents of other children, according to an analysis of Swedish birth and hospital records by a University of North Carolina at Chapel Hill researcher and colleagues in the U.S. and Europe.

The study, "Parental psychiatric disorders associated with autism spectrum disorders in the offspring," appears in the May 5, 2008, issue of the journal Pediatrics.

"We are trying to determine whether autism is more common among families with other psychiatric disorders. Establishing an association between autism and other psychiatric disorders might enable future investigators to better focus on genetic and environmental factors that might be shared among these disorders," said study author Julie Daniels, Ph.D., an assistant professor in the UNC School of Public Health's epidemiology and maternal and child health departments.

"Earlier studies have shown a higher rate of psychiatric disorders in families of autistic children than in the general population," she said. "We wanted to see if the parents of autistic children were more likely to be diagnosed with mental disorders.

"Our research shows that mothers and fathers diagnosed with schizophrenia were about twice as likely to have a child diagnosed with autism. We also saw higher rates of depression and personality disorders among mothers, but not fathers," Daniels said.

This information will help researchers look among related diseases, such as psychiatric disorders, for causes of autism, Daniels said. "It may eventually help identify opportunities to prevent or treat the disorder."

The study examined 1,237 children born between 1977 and 2003 who were diagnosed with autism before age 10, and compared them with 30,925 control subjects matched for gender, year of birth and hospital. The large sample size enabled researchers to distinguish between psychiatric histories of mothers versus fathers in relation to autism. The association was present regardless of the timing of the parent's diagnosis relative to the child's diagnosis.

Coauthors of the study include Ulla Forssen, Ph.D., GlaxoSmithKline epidemiologist, Collegeville, Pa.; Christina Hultman, Ph.D., Sven Cnattingius, M.D., Ph.D. and Par Sparen, Ph.D., all of the department of medical epidemiology and biostatistics at the Karolinska Institutet, Stockholm, Sweden; David Savitz, Ph.D., director of the Center of Excellence in Epidemiology, Biostatistics and Disease Prevention, Mt. Sinai School of Medicine, New York; and Maria Feychting, Ph.D., Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden.

Low blood levels of vitamin D may be associated with depression in older adults

Older adults with low blood levels of vitamin D and high blood levels of a hormone secreted by the parathyroid glands may have a higher risk of depression, according to a report in the May issue of Archives of General Psychiatry, one of the JAMA/Archives journals.

About 13 percent of older individuals have symptoms of depression, and other researchers have speculated that vitamin D may be linked to depression and other psychiatric illnesses, according to background information in the article. “Underlying causes of vitamin D deficiency such as less sun exposure as a result of decreased outdoor activity, different housing or clothing habits and decreased vitamin intake may be secondary to depression, but depression may also be the consequence of poor vitamin D status,” the authors write. “Moreover, poor vitamin D status causes an increase in serum parathyroid hormone levels.” Overactive parathyroid glands are frequently accompanied by symptoms of depression that disappear after treatment of the condition.

Witte J. G. Hoogendijk, M.D., Ph.D., and colleagues at VU University Medical Center, Vrije Universiteit Amsterdam, the Netherlands, measured blood levels of vitamin D and parathyroid hormone and assessed symptoms of depression among 1,282 community residents age 65 to 95. Of those individuals, 26 had a diagnosis of major depressive disorder, 169 had minor depression and 1,087 were not depressed. The average blood vitamin D level was 21 nanograms per milliliter and the average parathyroid hormone level was 3.6 picograms per milliliter.

Blood vitamin D levels were 14 percent lower in individuals with major and minor depression (average, 19 nanograms per milliliter) compared with non-depressed participants (average, 22 nanograms per milliliter). In addition, parathyroid hormone thyroid levels were an average of 5 percent higher in those with minor depression (average, 3.72 picograms per milliliter) and 33 percent higher in those with major depressive disorder (average, 4.69 picograms per milliliter) than in those who were not depressed (average, 3.53 picograms per milliliter).

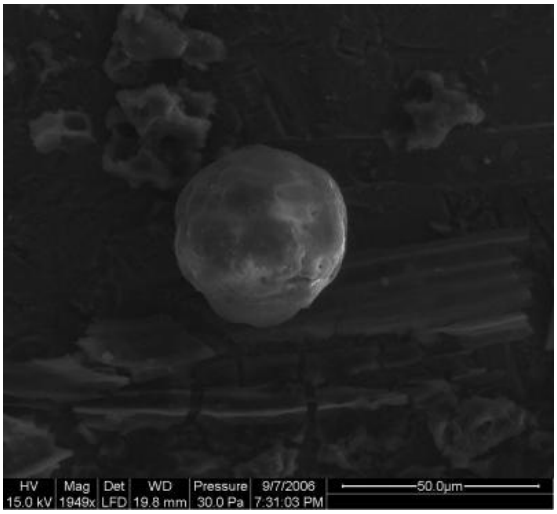
The findings may be important to patients because both low blood vitamin D levels and high parathyroid hormone levels can be treated with higher dietary intake of vitamin D or calcium and increased sunlight exposure. “Moreover, the clinical relevance of the present study is underscored by our finding that 38.8 percent of men and 56.9 percent of women in our community-based cohort had an insufficient vitamin D status,” they conclude. Additional studies are needed to determine whether changes in levels of vitamin D and parathyroid hormone precede depression or follow it.

(Arch Gen Psychiatry. 2008;65[5]:508-512. Available pre-embargo to the media at www.jamamedia.org.)

Editor’s Note: *This study was supported by a clinical fellow grant from the Netherlands Organisation for Scientific Research. Please see the article for additional information, including other authors, author contributions and affiliations, financial disclosures, funding and support, etc.*

65-million-year-old asteroid impact triggered a global hail of carbon beads

BLOOMINGTON, Ind. -- The asteroid presumed to have wiped out the dinosaurs struck the Earth with such force that carbon deep in the Earth's crust liquefied, rocketed skyward, and formed tiny airborne beads that blanketed the planet, say scientists from the U.S., U.K., Italy, and New Zealand in this month's Geology.



The beads, known to geologists as carbon cenospheres, cannot be formed through the combustion of plant matter, contradicting a hypothesis that the cenospheres are the charred remains of an Earth on fire. If confirmed, the discovery suggests environmental circumstances accompanying the 65-million-year-old extinction event were slightly less dramatic than previously thought.

"Carbon embedded in the rocks was vaporized by the impact, eventually forming new carbon structures in the atmosphere," said Indiana University Bloomington geologist Simon Brassell, study coauthor and former adviser to the paper's lead author, Mark Harvey.

Carbon cenospheres are tiny, carbon-rich particles that form when coal and heavy fuel are heated intensely. Scientists have now learned that cenospheres can form in the wake of asteroid impacts, too. **Mark Harvey**

The carbon cenospheres were deposited 65 million years ago next to a thin layer of the element iridium -- an element more likely to be found in Solar System asteroids than in the Earth's crust. The iridium-laden dust is believed to be the shattered remains of the 200-km-wide asteroid's impact. Like the iridium layer, the carbon cenospheres are apparently common. They've been found in Canada, Spain, Denmark and New Zealand.

But the cenospheres' origin presented a double mystery. The cenospheres had been known to geologists only as a sign of modern times -- they form during the intense combustion of coal and crude oil. Equally baffling, there were no power plants burning coal or crude oil 65 million years ago, and natural burial processes affecting

organic matter from even older ages -- such as coals from the 300-million-year-old Carboniferous Period -- had simply not been cooked long or hot enough.

"Carbon cenospheres are a classic indicator of industrial activity," Harvey said. "The first appearance of the carbon cenospheres defines the onset of the industrial revolution."

The scientists concluded the cenospheres could have been created by a new process, the violent pulverization of the Earth's carbon-rich crust.

Geologists do believe the Earth burned in spots as molten rock and super-hot ash fell out of the sky and onto flammable plant matter. But the charcoal-ized products of these fires only appear in some places on Earth, and are more often found near the asteroid impact site of Chicxulub Crater, just west of Mexico's Yucatan Peninsula. Some geologists had thought all carbon particles resulting from the impact was ash from global scale forest fires, but the present research strongly contradicts that assumption.

The scientists examined rock samples from eight marine locations in New Zealand, Italy, Denmark and Spain. They also examined carbon-rich particles from five non-marine locations in the U.S. and Canada. Following chemical and microscopic analysis, the researchers concluded the particles were carbon cenospheres, similar to the ones produced by industrial combustion.

The scientists also found that the farther the sample site was from the Chicxulub Crater, the smaller the cenospheres tended to be. That observation is consistent with the expectation that particles were produced by the asteroid impact, since once the particles are ejected, heavier particles should fall back to Earth sooner (and travel shorter distances) than lighter particles.

Last, the scientists estimated the total mass of carbon cenospheres ejected by the asteroid collision, assuming a global distribution, to be perhaps as much as 900 quadrillion kilograms. Whether or not the carbon cenospheres are truly ubiquitous, however, needs further corroboration.

"There are still clues to unravel about the events occurring around the time of the impact," Brassell said. "And there are aspects of the Earth's natural carbon cycle that we didn't previously consider."

Harvey is interested in the unique properties of the cenospheres themselves. "Perhaps we can generate and study carbon cenospheres to better understand them," he said. "We also need to look for the cenospheres in other parts of the world and also around the time of other extinction events."

Harvey conducted the research while he was a master's student at IU Bloomington. He is now a geoscientist for Sinclair Knight Merz in New Zealand. Claire Belcher (University of London) and Alessandro Montanari (Coldigioco Geological Observatory) also contributed to the study. It was funded by the Geological Society of America, the Indiana University Department of Geological Sciences, and the Society for Organic Petrology.

MGH researchers report successful new laser treatment for vocal-cord cancer

Technique targets blood vessels to remove tumor while preserving and restoring vocal quality

An innovative laser treatment for early vocal-cord cancer, developed at Massachusetts General Hospital (MGH), successfully restores patients' voices without radiotherapy or traditional surgery, which can permanently damage vocal quality. This new option for patients, which has now been used in more than 25 patients, was reported on May 1 at the annual meeting of the American Broncho-Esophagological Association, and the data will soon be published as a supplement to the Annals of Otology, Rhinology, & Laryngology.

"We had previously adapted lasers that target blood vessels to treat precancerous vocal-cord dysplasia and a variety of benign vascular lesions. We have now applied that experience to treat vocal-cord cancer, which is diagnosed in several thousand American patients each year," says Steven Zeitels, MD, director of the MGH Voice Center.

Zeitels' team began applying pulsed lasers to the treatment of early vocal-cord cancer more than five years ago. After successfully treating the first eight patients with the pulsed-dye laser, Zeitels' group switched to the more precise pulsed Potassium-Titanyl-Phosphate (KTP) laser, which is even less likely to damage delicate vocal-cord tissue. The use of specific wavelengths of laser light to target blood vessels was originally applied to the removal of vascular skin lesions like port-wine stains by Rox Anderson, MD, now director of the MGH Wellman Center of Photomedicine. In a close collaboration with Anderson, Zeitels previously developed application of these angiolytic lasers to benign and precancerous vocal-cord lesions.

As Zeitels reported at the ABEA meeting, the first 22 patients receiving pulsed laser treatment for vocal-cord cancer are cancer-free up to 5 years after treatment, without removal of vocal-cord tissue or loss of voice quality. Some have required second or third laser treatments to remove residual disease, but another benefit of the therapy is that it does not rule out future therapeutic options. Zeitels notes that this treatment has become a standard management approach at MGH and should soon spread to other institutions in the US and abroad. He estimates that 90 percent of patients with early vocal-cord cancer would be candidates for pulsed-KTP laser treatment.

"Currently the optimal angiolytic laser for vocal-cord problems, the pulsed-KTP laser is a critical innovation in the instrumentation arsenal of the laryngeal surgeon," says Zeitels. "It has greatly enhanced the precision by which we can perform many procedures for chronic laryngeal diseases, both in the operating room, accompanied by the surgical microscope, and in the office." Zeitels is the Eugene B. Casey Professor of Laryngeal Surgery at Harvard Medical School (HMS).

The MGH Voice Center team has created a number of groundbreaking procedures and was the first in the world to treat vocal cords and other structures in the larynx with controlled pulses of the green KTP laser light. Zeitels has been recognized for his 2006 use of pulsed-KTP laser to treat Steven Tyler of the rock band Aerosmith for vocal-cord hemorrhage. With his unique perspective on voice restoration and preservation resulting from years of treating elite singers, Zeitels was called on to work with Julie Andrews after she lost her singing voice due to a failed surgical procedure. He subsequently has collaborated with Miss Andrews to increase awareness of voice problems and spearhead a research project investigating new voice restoration surgical procedures.

The MGH and HMS instituted one of the first academic programs in Laryngology in the United States in 1870. The MGH program was discontinued in the 1920s and was reestablished in 2004 with the philanthropic assistance of the Eugene B. Casey Foundation and the Institute of Laryngology and Voice Restoration (ILVR – website at http://ilvr.org/), a patient-based organization with the mission to further research, clinical care and education in laryngeal and voice disorders. Miss Andrews is the honorary chairwoman of the ILVR, and the organization's president is John Ward, PhD, a Northwestern University professor who was the first patient to receive the new laser treatment for vocal-cord cancer.

The cooperative view: New evidence suggests a symbiogenetic origin for the centrosome

MBL, WOODS HOLE, MA - There are two ways in which cooperation is the theme of a paper published this week by Mark Alliegro and Mary Anne Alliegro, scientists at the Marine Biological Laboratory's (MBL) Josephine Bay Paul Center. One is revealed in the paper's acknowledgements, where the Alliegros thank those who helped them after Hurricane Katrina completely disrupted their laboratory at Louisiana State University (LSU) in New Orleans – and their lives – in 2005.

The second is the paper's scientific theme: the origin of the centrosome, a component of animal cells that functions in cell division. In their paper, published in Proceedings of the National Academy of Sciences, the Alliegros give evidence that the centrosome evolved through symbiogenesis – in which previously independent organisms fuse, become mutually dependent, and over time, become a single composite organism - rather than by the evolutionary process of random, heritable mutations and natural selection.

The Alliegros moved to the MBL permanently in September 2007, after two years of attempting to forge on in a devastated New Orleans. "We realized, if we stayed there, our research program would not survive," says Mark Alliegro, who was a professor at LSU Health Sciences Center.

The origin of the centrosome, their paper points out, has been controversial for many years. The theory of symbiogenesis as a mechanism of evolution has also stirred debate since it was introduced in the 1920s and subsequently elaborated in the 1960s by Lynn Margulis of University of Massachusetts, Amherst. Today, only two cellular components – the mitochondria and the chloroplasts – are generally accepted by evolutionary biologists as having a symbiogenetic origin. The Alliegros' paper suggests that centrosomes are another likely candidate. They base their argument on evidence that the centrosomes, which they obtained from the eggs of the surf clam Spisula, contain RNA that is likely a remnant of a once-independent, simpler genome that was incorporated by symbiosis.

"Most animal genes have introns, regions that are transcribed into RNA but then spliced out," says Alliegro. "But if you look at viral genes or bacterial genes, they have little or no introns. It turns out the genes for Spisula centrosomal RNAs have few or no introns. They are a special set of RNAs that derived from intron-poor or intron-less genes, which may very well support the idea that they come from a simpler organism, like a virus or bacteria."

The Alliegros lost their RNA library due to Katrina, and in their paper they acknowledge Gloria Giarratano of LSU Health Sciences Center, who helped them re-clone the library from DNA they recovered in the hurricane's aftermath. They also thank Bruce and Sharon Waddell of Slidell, Louisiana, in whose home they lived after Katrina, and where "our laboratory was resurrected in part from the dining room table"; as well as Carol Burdsal and other colleagues at Tulane University, where they temporarily set up a new lab. Robert Palazzo of Rensselaer Polytechnic Institute, a longtime visiting investigator at the MBL, is acknowledged for providing the centrosome preparation for the original RNA extractions as well as advice and encouragement.

This work was supported by the National Institutes of Health as well as post-Katrina emergency recovery funds from the Society for Developmental Biology.

Researchers Find Quick Way to Make Human Monoclonal Antibodies against Flu

Human monoclonal antibodies (mAbs) - highly specific, identical, infection-fighting proteins produced in large quantities in the lab in cell lines that are derived from a single antibody-producing cell - against influenza can be rapidly produced in the lab, according to a new report from scientists supported by the National Institutes of Health (NIH). Using cells drawn from volunteers inoculated with seasonal influenza vaccine, the investigators made influenza-specific mAbs in just a few weeks rather than the typical two to three months. The new technique could potentially be used to rapidly create mAbs for a range of uses, the team says.

Rafi Ahmed, Ph.D., and Jens Wrammert, Ph.D., of Emory Vaccine Center of the School of Medicine, Atlanta, and their coworkers collaborated with Patrick Wilson, Ph.D., and J. Donald Capra, M.D., and others from the Oklahoma Medical Research Foundation, Oklahoma City. They describe their new method in an advance online publication in Nature. The research was supported by the NIH's National Institute of Allergy and Infectious Diseases (NIAID) and National Center for Research Resources (NCRR).

The first therapeutic mAb was approved for human use in 1986 and there are now more than 20 Food and Drug Administration-approved mAbs, including two human mAbs, most of which are used to treat certain cancers or immunological diseases. Human mAbs have long been envisioned as possible treatments for acute or chronic infections, but various technical barriers have slowed their development.

"With this new technique for making human monoclonal antibodies efficiently and quickly, Drs. Wilson and Ahmed and their colleagues have made a significant advance," says NIAID Director Anthony S. Fauci, M.D. "Their accomplishment opens the way to producing mAbs that potentially could be used diagnostically or therapeutically not only for influenza but for other infectious diseases as well."

In addition to being relatively quick to make, the influenza mAbs also bound tightly to virus strains in the seasonal influenza vaccine, the scientists determined. Such high affinity for the vaccine's viruses suggests that the mAbs would also bind well to the circulating viruses targeted by the vaccine and thus could be used either as a therapy or as a way to diagnose the strain of influenza virus an individual is infected with, say the investigators.

The mAbs made in this study were not tested on influenza virus strains with pandemic potential, such as the H5N1 subtype that causes so-called bird flu. Nevertheless, notes Dr. Ahmed, the ability to make high-affinity influenza mAbs quickly raises the possibility of deploying them in combination with other disease control strategies in the event of a global influenza pandemic. According to Dr. Ahmed, the group is now planning to use their technique to generate mAbs against H5N1.

To make the new influenza mAbs, the researchers first inoculated volunteers with seasonal influenza vaccine. The scientists wanted to know if a subset of immune system cells called antibody-secreting plasma cells (ASCs) could serve as a source of mAbs. ASCs are the body's first responders, churning out a surge of antibodies as part of the initial reaction to infection or vaccination. ASC activity is swift but brief. In this study, ASC responses peaked at one week after vaccination, then dropped sharply and were barely detectable after two weeks. The Emory University researchers found a way to capture the fleeting ASCs that produce the initial wave of influenza-specific antibodies. Importantly, says Dr. Ahmed, as many as 80 percent of the purified ASCs produced influenza-specific antibodies.

Dr. Wilson and his coworkers at the Oklahoma Medical Research Foundation used the vaccine-generated, influenza-specific ASCs to create the mAbs. Only a few weeks elapsed between vaccination of the volunteers and purification of human mAbs with a high affinity for influenza virus. "With just a few tablespoons of blood, we can now rapidly generate human monoclonal antibodies that potentially could be used for diagnosis and treatment of newly emerging strains of influenza," says Dr. Wilson. "In the face of a disease outbreak, the ability to produce infection-fighting human mAbs swiftly would be invaluable."

The technique developed by the Emory University and Oklahoma Medical Research Foundation scientists is not limited to the production of mAbs for influenza, and the team is currently working to make mAbs for other disease agents. "This research holds clinical potential for a host of infectious diseases including anthrax, respiratory syncytial virus and pneumococcal pneumonia," says Dr. Capra.

For more information on information about influenza, visit
http://www3.niaid.nih.gov/healthscience/healthtopics/Flu/default.htm.

Redefining Disease, Genes and All

By ANDREW POLLACK

Duchenne muscular dystrophy may not seem to have much in common with heart attacks. One is a rare inherited disease that primarily strikes boys. The other is a common cause of death in both men and women. To Atul J. Butte, they are surprisingly similar.

Dr. Butte, an assistant professor of medicine at Stanford, is among a growing band of researchers trying to redefine how diseases are classified - by looking not at their symptoms or physiological measurements, but at their genetic underpinnings. It turns out that a similar set of genes is active in boys with Duchenne and adults who have heart attacks.

The research is already starting to change nosology, as the field of disease classification is known. Seemingly dissimilar diseases are being lumped together. What were thought to be single diseases are being split into separate ailments. Just as they once mapped the human genome, scientists are trying to map the "diseasome," the collection of all diseases and the genes associated with them.

"We are now in a unique position in the history of medicine to define human disease precisely, uniquely and unequivocally," three scientists wrote of the new approach last year in the journal Molecular Systems Biology. Such research aims to do more than just satisfy some basic intellectual urge to organize and categorize. It also promises to improve treatments and public health.

Scientists are finding that two tumors that arise in the same part of the body and look the same on a pathologist's slide might be quite different in terms of what is occurring at the gene and protein level. Certain breast cancers are already being treated differently from others because of genetic markers like estrogen receptor and Her2, and also more complicated patterns of genetic activity.

"In the not too distant future, we will think about these diseases based on the molecular pathways that are aberrant, rather than the anatomical origin of the tumor," said Dr. Todd Golub, director of the cancer program at the Broad Institute in Cambridge, Mass.

The reclassification may also help find drugs. "There are 40 drugs to treat heart attacks, but none to treat muscular dystrophy," Dr. Butte said. If the diseases are similar in some molecular pathways, perhaps the heart attack drugs should be tested against muscular dystrophy.

Dr. Golub and colleagues at the Broad Institute have developed a "Connectivity Map," which profiles drugs by the genes they activate as a way to find new uses for existing drugs.

The research will also improve understanding of the causes of disease and of the functions of particular genes. For instance, two genes have recently been found to influence the risk of both diabetes and prostate cancer.

"I'm shaking my head with disbelief that two genes would pop up in these two diseases that have absolutely nothing in common," said Dr. Francis S. Collins, the director of the National Human Genome Research Institute. He said another gene, cyclin-dependent kinase inhibitor 2A, seemed to be involved in cancer, diabetes and heart disease.

A consistent way to classify diseases is also essential for tracking public health and detecting epidemics. The World Health Organization takes pains to periodically revise its International Classification of Diseases, which is used, among other ways, to tally the causes of death throughout the world. The classification is also the basis of the ICD-9 codes used for medical billing in the United States.

The first international classification, in the 1850s, had about 140 categories of disease, according to Dr. Christopher G. Chute, chairman of biomedical informatics at the Mayo Clinic. The 10th edition, in 1993, had 12,000 categories, said Dr. Chute, chairman of the committee developing the 11th version, due in 2015.

The increase stems mainly from better knowledge and diagnostic techniques that allow diseases to be distinguished from one another. For most of human history, diseases were named and classified by symptoms, which was all people could observe.

Linnaeus, the 18th-century Swedish scientist known for categorizing creatures into genus and species, also developed a taxonomy of disease. He had 11 classes - painful disease, motor diseases, blemishes and so on - that were further broken down into orders and species. But not knowing about viruses, for instance, he classified rabies as a mental disease, Dr. Chute said.

In the 19th century, a big shift occurred. Doctors began learning how to peer inside the body. And diseases began to be classified by their anatomic or physiological features.

The stethoscope let doctors realize that what had been thought of as 17 conditions - like coughing up blood and shortness of breath - could all be different symptoms of the same disease, tuberculosis.

"The advent of the stethoscope made it possible to unify tuberculosis," said Dr. Jacalyn Duffin, a professor of the history of medicine at Queen's University in Ontario.

The shift from symptoms to anatomical measurements had big implications for patients, said Dr. Duffin, who is also a hematologist.

"Up until the 18th century, you had to feel sick to be sick," she said. But now people can be considered sick based on measurements like high blood pressure without feeling ill at all.

Indeed, Dr. Duffin said, people who feel sick nowadays "don't get to have a disease unless the doctor can find something" and instead might be told that it's all in their head. Doctors argue, for instance, about whether fibromyalgia or chronic fatigue syndrome, which have no obvious anatomical causes, are really diseases.

Genes might allow the study of diseases at a finer level than even physiological tests. Genes are the instructions for the production of proteins, which interact in complex ways to carry out functions in the body. Disruptions in these molecular pathways can cause disease.

"It gives you a direct connection to what the root causes are," said Dr. David Altshuler, a professor of medicine and genetics at Harvard and Massachusetts General Hospital, and a researcher at the Broad Institute. "That is different from listening to a stethoscope."

Some of the earliest work has until now been with inherited diseases caused by mutations in a single gene. Diseases have been subdivided by the type of mutation. Hemophilia was divided into hemophilia A and B, caused by mutations in different genes for different clotting factors. And what was once considered a mild form of hemophilia was later identified as a variant of a different clotting disorder, von Willebrand disease, caused by mutations in a different gene and requiring a different clotting factor as treatment.

Diseases are being lumped, as well as split. Researchers at Johns Hopkins reported in the April issue of Nature Genetics that two rare syndromes with different symptoms might represent a continuum of one disease. One syndrome, Meckel-Gruber, is tied to neural defects and death in babies. The other, Bardet-Biedl, is marked by vision loss, obesity, diabetes and extra fingers and toes.

The techniques are being applied to diseases for which the genetic cause is not as clearly known and which might be a result of multiple genes.

Dr. Butte uses data from gene chips that measure which genes are active, or expressed, in a cell. Amid thousands of studies using such chips, many compared the gene activity patterns in diseased tissue with that of healthy tissue. Much of the raw data from such studies are deposited in a database. So Dr. Butte can gather data on gene activity for scores of diseases without leaving his desk. He then performs statistical analyses to map diseases based on similarities in their patterns of gene activity.

Other scientists use data on which genes appear to cause disease or contribute to the risk of contracting it.

Using such data, Marc Vidal, a biologist at Harvard, and Albert-Laszlo Barabasi, now a physicist at Northeastern University, created a map of what they called the "diseasome" that was published last year in The Proceedings of the National Academy of Sciences.

Diseases were represented by circles, or nodes, and linked to other diseases by lines that represent genes they have in common - something like the charts linking actors to one another (and ultimately to Kevin Bacon) based on the movies they appeared in together.

The number of genes associated with diseases is expanding rapidly because of so-called whole genome association studies. In these studies, gene chips are used to look for differences between the genomes of people with a disease and those without. Multiple techniques can be combined. In a paper published online in Nature in March, scientists at Merck reconstructed the network of genes involved in obesity.

One area that might benefit from genetic disease classification is psychiatry. Because of the difficulty of measuring the brain, psychiatric diagnoses are still mainly based on symptoms. The Diagnostic and Statistical Manual of Mental Disorders contains descriptions of conditions as diverse as acute stress disorder and voyeurism.

Scientists have found that certain genes appear to be associated with both schizophrenia and bipolar disorder. Those links, and the fact that some drugs work for both diseases, have prompted a debate over whether they are truly distinct disorders. "The way we categorize these into two separate entities is almost certainly not correct," said Dr. Wade H. Berrettini, a professor of psychiatry at the University of Pennsylvania.

But Dr. Kenneth S. Kendler, a professor of psychiatry and human genetics at Virginia Commonwealth University, said that even if the two diseases shared genes, the diseases remained distinct. Schizophrenia is marked by hallucinations and impaired social functioning, and bipolar disorder by mood swings.

"It's extremely naïve to think that psychiatric illnesses will collapse into categories defined by a gene," he said. "Each gene at most has a quite modest effect on the illness."

Some experts say that such limitations may hold true for other diseases, as well, and that genetics will not be able to unequivocally define and distinguish diseases. "We shouldn't expect, nor will we get, this decisive clarity," said Fiona A. Miller, associate professor of health policy, management and evaluation at the University of Toronto.

She and others said genetic classification could bring its own ambiguities. Newborns are now often screened for cystic fibrosis with the idea that they can be treated early to help avoid complications. But some infants with

a mutation in the gene responsible for the disease are unlikely ever to have symptoms. Do they have the disease?

"We don't know what to call these infants," said Dr. Frank J. Accurso, a professor of pediatrics at the University of Colorado. "We don't even have a good language for it yet."

Still, Dr. Butte said nosology based on genes would one day make today's classifications look as quaint as ones from 100 years ago look now. One category in the 1909 listing of the causes of death, for instance, was "visitation of God."

"Imagine how they are going to be laughing at us," he said. "Not 100 years from now, but even 50 or 20 years from now."

Some Diabetics Don't Have What They Thought They Had

By ANDREW POLLACK

Ryan Collins of Aldie, Va., was only 10 weeks old when doctors made the diagnosis: Type 1 diabetes. That meant up to eight insulin shots per day, a big burden on him and his family.

"He couldn't be anywhere unless there was someone around to give a shot," said his mother, Dana Collins. "Everything had to be planned. There was no impromptu anything."

Until last month, that is, when Ryan, now almost 7, stopped needing shots.

Ryan, it turns out, does not have Type 1 diabetes after all. He has a rare form of diabetes, not yet discovered when he was born, that is caused by a genetic mutation. And it is treatable by a pill.

Ryan's story is the latest case of how research is changing doctors' understanding of diabetes.

Diabetes is named, from the Greek, for its symptoms of heavy thirst and frequent urination. But for hundreds of years, it has been possible to make a further breakdown. Diabetes mellitus, from the Latin for honeyed, was the form with sweet urine. Diabetes insipidus was marked by bland or insipid urine.

This may have been the first time two diseases with similar symptoms were distinguished by a "molecular" test. "We had receptors for one molecule and could figure it out," said Dr. Yves A. Lussier, director of the center for biomedical informatics at the University of Chicago, referring to taste buds.

Today these are considered completely different diseases. Mellitus is the one commonly called diabetes. It involves high blood sugar and insulin. Insipidus is related to a different hormone, vasopressin.

In the 1930s, after it became possible to treat diabetes with insulin derived from animals, diabetes mellitus itself began to be subdivided into what would come to be called Type 1, marked by lack of insulin, and Type 2, marked by insensitivity to insulin. The distinction became stronger in the 1970s with the development of blood tests to tell them apart better, though there is still no definitive test.

Now, in just the last few years, scientists have found about 35 genes that influence the risk of getting diabetes, said Dr. David Altshuler, a professor of medicine and genetics at Harvard. But so far, there is no overlap at all between the genes that help cause Type 1 and those that help cause Type 2, he said.

"In that regard, it's held up that they are separate diseases at the genetic level," Dr. Altshuler said.

Some scientists think genetic analysis will further subdivide Type 2. While there is yet no major new class (a Type 3 or Type 4), scientists are discovering the genetic causes of several rare types of diabetes that are caused by single mutations.

The most common such "monogenic" diabetes is maturity-onset diabetes of the young, or MODY. Dr. Andrew Hattersley of the University of Exeter in England, a leading researcher, said 1 percent to 2 percent of diabetics might have MODY. But most do not know it. "There were a whole lot of people misdiagnosed as Type 1 or Type 2," Dr. Hattersley said. But now there are genetic tests for MODY, and people with MODY might need less treatment, he said.

Dr. Hattersley has also helped show that diabetes diagnosed in the first six months of life is monogenic. And about half those cases are caused by a particular mutation that can be overcome by sulfonylurea pills, an old and inexpensive class of diabetes drugs.

After he tested positive for that mutation, Ryan Collins spent five days last month in the University of Chicago Medical Center, where doctors gradually substituted the pills for the insulin.

Thirty-five or so American children with that mutation have now been weaned off insulin, according to the Chicago medical center, which has been involved in many of the cases. It says there may be 1,000 to 2,000 such children who have not been identified.

Ryan now takes three small pills with breakfast and three with dinner. His body is making insulin again, and his blood sugar is better controlled than when he was taking all those shots.

"He's ecstatic," Ms. Collins said. "For this summer, I'm signing him up for summer camp, which he's never been able to do before."

Evidence a High-Fat Diet Works to Treat Epilepsy

By ALIYAH BARUCHIN

A formerly controversial high-fat diet has proved highly effective in reducing seizures in children whose epilepsy does not respond to medication, British researchers are reporting.

As the first randomized trial of the diet, the new study lends legitimacy to a treatment that has been used since the 1920s but has until recently been dismissed by many doctors as a marginal alternative therapy.

"This is the first time that we've really got Class 1 evidence that this diet works for treatment of epilepsy," said Dr. J. Helen Cross, professor of pediatric neurology at University College London and Great Ormond Street Hospital. She is a principal investigator on the study, which will appear in the June issue of The Lancet Neurology.

Though its exact mechanism is uncertain, the diet appears to work by throwing the body into ketosis, forcing it to burn fat rather than sugar for energy. Breakfast on the diet might consist of bacon, eggs with cheese, and a cup of heavy cream diluted with water; some children drink oil to obtain the fats that they need. Every gram of food is weighed, and carbohydrates are almost entirely restricted. Breaking the diet with so much as a few cookies can cause seizures to flare up.

For the British trial, the researchers enrolled 145 children ages 2 to 16 who had never tried the diet, who were having at least seven seizures a week and who had failed to respond to at least two anticonvulsant drugs.

One group began the ketogenic diet immediately. The control group waited three months before starting it. In the first group, 38 percent of the children had seizure rates reduced by half, compared with 6 percent in the control group. Five children in the diet group had reductions exceeding 90 percent.

Perceptions of the diet have changed sharply in the last decade. In 1993, a Hollywood producer, Jim Abrahams, took his 1-year-old son, Charlie, to Dr. John M. Freeman at the Pediatric Epilepsy Center at Johns Hopkins, which was one of the few centers championing the diet. Within three days of starting the diet, Charlie's incapacitating seizures, which had resisted multiple medications and surgery, stopped entirely.

With his wife, Nancy, Mr. Abrahams founded the Charlie Foundation to Help Cure Pediatric Epilepsy to promote education about the diet. He produced an instructional video for parents and a made-for-television movie, "First Do No Harm," starring Meryl Streep as a mother who seeks out the diet for her child.

As a result of the Johns Hopkins work, research on the diet blossomed and it became a standard treatment at hospitals and epilepsy centers in the United States and abroad.

Dr. Shlomo Shinnar, director of the Comprehensive Epilepsy Management Center at the Montefiore Medical Center in the Bronx, called the new study "an important trial that lays to rest the issue of 'Does it really work or not?' "

Although the diet has to be medically supervised, Dr. Shinnar said, it is a mistake to believe that it requires extensive hospital resources and a staff's constant attention. "Here they don't have this," he said of the British trial. "This study makes it clear that this actually can be made to work in a community setting."

Mind

I'm Not Lying, I'm Telling a Future Truth. Really.

By BENEDICT CAREY

John Cuneo

Some tales are so tall that they trip over their own improbable feats, narrative cracks and melodrama. That one-on-one playground victory over Kobe Bryant back in the day; the 34 hours in labor without painkillers; the former girlfriend or boyfriend who spoke eight languages and was a secret agent besides.

Yes, uh-huh, really. Is it closing time yet?

Yet in milder doses, self-serving exaggeration can be nearly impossible to detect, experts say, and there are several explanations.

A series of recent studies, focusing on students who inflate their grade-point average, suggests that such exaggeration is very different psychologically from other forms of truth twisting. Touching up scenes or past performances induces none of the anxiety that lying or keeping secrets does, these studies find; and embroiderers often work to live up to the enhanced self-images they project. The findings imply that some kinds of deception are aimed more at the deceiver than at the audience, and they may help in distinguishing braggarts and posers from those who are expressing personal aspirations, however clumsily.

"It's important to emphasize that the motives driving academic exaggeration seem to be personal and 'intrapsychic' rather than public or interpersonal," said Richard H. Gramzow, a psychologist at the University

of Southampton in England who has led much of the research. “Basically, exaggeration here reflects positive goals for the future, and we have found that those goals tend to be realized.”

Psychologists have studied deception from all sides and have found that it usually puts a psychological or physical strain on the person doing the dissembling. People with guilty knowledge - of a detail from a crime scene, for example - tend to show signs of stress, as measured by heart and skin sensors, under pointed questioning.

Trying to hold onto an inflammatory secret is mentally exhausting, studies have found, and the act of suppressing the information can cause thoughts of it to flood the consciousness. When telling outright lies, people tend to look and sound tenser than usual.

“Specifically, people are especially more tense when lying, compared to telling the truth, when they are highly motivated to get away with their lies and when they are lying about a transgression,” said Bella DePaulo, a visiting professor of psychology at the University of California, Santa Barbara.

But a study published in February in the journal Emotion found that exactly the opposite was true for students who exaggerated their grades. The researchers had 62 Northeastern University students fill out a computerized form asking, among other things, for cumulative grade point average. The students were then interviewed while hooked up to an array of sensitive electrodes measuring nervous system activation. The scripted interview covered academic history, goals and grades.

The researchers then pulled the students’ records, with permission, and found that almost half had exaggerated their average by as much as six-tenths of a point. Yet the electrode readings showed that oddly enough, the exaggerators became significantly more relaxed while discussing their grades.

“It was a robust effect, the sort of readings you see when people are engaged in a positive social encounter, or when they’re meditating,” said Wendy Berry Mendes, an associate professor of psychology at Harvard and senior author of the study. Dr. Gramzow and Greg Willard, then at Northeastern and now at Harvard, were co-authors.

The researchers videotaped the interviews, and independent observers rated how students looked and behaved. “The ones who exaggerated the most appeared the most calm and confident” on the ratings, Dr. Mendes said.

The grade inflation was less an attempt to deceive, the authors concluded, than a reflection of healthy overconfidence and a statement of aspirations. “It’s basically an exercise in projecting the self toward one’s goals,” Dr. Gramzow said.

In earlier studies, Dr. Gramzow and Dr. Willard found that students who bumped up their averages in interviews subsequently improved their grades - often by the very amount they had exaggerated.

The findings provide another lens through which to view claims, from Senator Hillary Rodham Clinton’s story of sniper fire in Bosnia to exaggerations of income, charitable contributions and SAT scores. As much as these are embroideries, they are also expressions of yearning, and for reachable goals.

In that sense, fibs can reflect something close to the opposite of the frustration, insecurity and secretiveness that often fuel big lies. That may be why they can come so easily, add up so fast and for some people - especially around closing time - become indistinguishable from the truth.

Researchers Seek to Demystify the Metabolic Magic of Sled Dogs

By DOUGLAS ROBSON

When humans engage in highly strenuous exercise day after day, they start to metabolize the body’s reserves, depleting glycogen and fat stores. When cells run out of energy, a result is fatigue, and exercise grinds to a halt until those sources are replenished.

Dogs are different, in particular the sled dogs that run the annual Iditarod Trail Sled Dog Race in Alaska. This is a grueling 1,100-mile race, and studies show that the dogs somehow change their metabolism during the race.

Dr. Michael S. Davis, an associate professor of veterinary physiology at Oklahoma State University and an animal exercise researcher, said: “Before the race, the dogs’ metabolic makeup is similar to humans. Then suddenly they throw a switch - we don’t know what it is yet - that reverses all of that. In a 24-hour period, they go back to the same type of metabolic baseline you see in resting subjects. But it’s while they are running 100 miles a day.”

Dr. Davis, who studied the sled dogs, found they did not chew up their reserves and avoided the worst aspects of fatigue. He is pursuing the research for the Defense Advanced Research Projects Agency, which gave him a $1.4 million grant in 2003 to study the physiology of fatigue resistance of sled dogs.

Dr. Davis, who is teaming with researchers at Texas A&M in a $300,000 Darpa grant, awarded last fall, has been traveling to Alaska for years to learn why the sled dogs are “fatigue-proof.”

"They have a hidden strategy that they can turn on," he said. "We are confident that humans have the capacity for that strategy. We have to figure out how dogs are turning it on to turn it on in humans."

Researchers have not demonstrated that ability in other species, but Dr. Davis said migratory mammals or birds could have it. Nor is it similar to the mammalian diving reflex that lets aquatic mammals like seals, otters and dolphins stay under water for long periods of time by slowing metabolic rates.

"The level of metabolism is staying the same," Dr. Davis said. "It's not slowing down their calorie burn rate."

In fact, sled dogs in long-distance racing typically burn 240 calories a pound per day for one to two weeks nonstop. The average Tour de France cyclist burns 100 calories a pound of weight daily, researchers say.

How the dogs maintain such a high level of caloric burn for an extended period without tapping into their reserves of fat and glycogen (and thus grinding to a halt like the rest of us) is what makes them "magical," Davis says. If Dr. Davis and the Texas A&M researchers identify the biomarker, or "switch," that could help the military understand and develop ways to control and prevent the physiological effects of fatigue in strenuous cases like combat.

"Soldiers' duties often require extreme exertion, which causes them to become fatigued," Jan Walker of Darpa wrote in an e-mail message. "Severe fatigue can result in a compromised immune system, making soldiers more susceptible to illness or injury."

Hunger hormone: makes food look more attractive

A new brain-imaging study by researchers at the Montreal Neurological Institute, McGill University reveals that ghrelin - a stomach hormone, acts on specific regions of the brain to enhance our response to food related cues and eating for pleasure. This study, published in the May 7 issue of Cell Metabolism, is critical to advance understanding and treating obesity, a condition affecting millions world-wide.

Appetite was previously thought of as being controlled by two separate mechanisms: homeostatic and non-homeostatic or hedonic food consumption. Homeostatic feeding is controlled by hormones such as ghrelin, that act on the brain to tell the body when to eat in an attempt to keep a constant body weight. Hedonic consumption is triggered by visual or smell cues. For example, wanting to eat a piece of cake just because it looks good and will bring pleasure when eaten. This study demonstrates that both food consumption behaviours are inter-connected and a key player in their regulation is the stomach hormone ghrelin.

"Our study demonstrates that ghrelin actually activates certain regions of the brain to be more responsive to visual food cues, thereby enhancing the hedonic and incentive responses to food-related cues,' says Dr. Alain Dagher, neurologist at the Montreal Neurological Institute, McGill University and principal investigator in the study. "Ghrelin is a hormone that triggers hunger, and is secreted by the stomach [when it is empty]. An easy analogy would be to think about when you go shopping on an empty stomach, you tend to buy more food and products higher in calories. The reason is that your brain views the food as more appealing, largely due to the action of ghrelin on the brain."

The study supports the view that obesity must be understood as a brain disease and that hunger should also be looked at as a kind of food addiction. Obese individuals may eat too much largely due to excess hunger. Dr. Dagher and colleagues found that ghrelin worked on regions of the brain known to be involved with reward and motivation, the same regions implicated in drug addiction – the amygdala, insula, the orbitofrontal cortex (OFC) and striatum. "These areas work together to assign incentive value to objects in the world and to actions, and exert very powerful control over our behavior. They are all targets of addictive drugs (like cocaine and nicotine), and are also targets of feeding signals like ghrelin," explains Dr. Dagher.

Participants in the study were shown images of food and scenery [as a control] before and after receiving ghrelin intravenously during functional magnetic resonance imaging (fMRI). In addition to analyzing the activation of different brain regions, subjects also answered questions about their mood and appetite before and after seeing sets of images. The effects of ghrelin on the amygdala and OFC correlated with the self-rated hunger ratings.

This study has shown that ghrelin action is more complex than previously thought and furthers our understanding of how drug treatment might be used to combat obesity. This research may also inform public policy. If food is thought of as potentially 'addictive,' this would support action to limit or ban fast food from schools and junk food advertisements geared towards children, in the same way that results proving nicotine to be addictive spurred the current public policy towards nicotine.

Naturally-occurring protein may be effective in limiting heart attack injury and restoring function

Medical College of Wisconsin researchers in Milwaukee have shown for the first time that thrombopoietin (TPO), a naturally occurring protein being developed as a pharmaceutical to increase platelet count in cancer patients during chemotherapy, can also protect the heart against injury during a heart attack.

The study, led by John E. Baker PhD, professor of pediatric surgery in the division of cardiothoracic surgery, was published in the January 2008 issue of Cardiovascular Research. The importance of these findings was underscored in an accompanying editorial.

Currently there are no therapies available to directly protect the heart against the damaging effects of a heart attack. Dr. Baker's team has shown that administering a single dose of TPO to rats during a heart attack decreased the extent of permanent muscle damage to the heart and increased the ability of the heart to function afterwards, when compared with no drug treatment. Additionally, they found that a single cardioprotective treatment with TPO did not increase platelet count. This novel finding suggests the cardioprotective actions of TPO are separate from its ability to increase platelet count.

Dr. Baker has submitted a US and worldwide patent application on the tissue protective properties of TPO. Dr. Baker's discovery is licensed to Cardiopoietis, a Wisconsin LLC, formed to develop drugs for the treatment of heart attacks.

TPO is a hormone which is naturally produced by the liver and kidney. Dr. Baker's investigative team had previously shown that erythropoietin, a protein and pharmaceutical currently in clinical use to treat anemia in end-stage kidney disease, protects the rat heart against injury during a heart attack. They found that although erythropoietin and TPO have separate functional roles, there were similarities in the structures of the two proteins that suggested TPO may have protective properties similar to erythropoietin.

"We hypothesized that a single treatment with TPO during a heart attack would be sufficient to protect the heart from injury," says Dr. Baker. "Our results suggest that TPO directly protects the heart and may represent a novel approach for the treatment of acute heart attack."

The study was supported by a grant from the National Institutes of Health, National Heart, Lung and Blood Institute.
Co-authors of the study included Jidong Su, research associate of cardiothoracic surgery at the Medical College of Wisconsin; Anna Hsu, research associate of pharmacology and toxicology; Yang Shi, Ph.D., assistant professor of surgery; Ming Zhao, Ph.D., assistant professor of biophysics; Jennifer Strande, M.D., PhD instructor in Cardiovascular Medicine; Xiangping Fu, Research Technologist of surgery; Hao Xu, research scientist of surgery; Annie Eis, research associate of pediatrics; Richard Komorowski, M.D., professor of pathology; Eric Jensen, D.V.M., staff veterinarian at the Biomedical Resource Center; James Tweddell, M.D., professor and chief of cardiothoracic surgery; Parvaneh Rafiee, Ph.D., associate professor of surgery; and Garrett Gross, Ph.D., professor of pharmacology and toxicology.

Killer competition: Neurons duke it out for survival

The developing nervous system makes far more nerve cells than are needed to ensure target organs and tissues are properly connected to the nervous system. As nerves connect to target organs, they somehow compete with each other resulting in some living and some dying. Now, using a combination of computer modeling and molecular biology, neuroscientists at Johns Hopkins have discovered how the target tissue helps newly connected peripheral nerve cells strengthen their connections and kill neighboring nerves. The study was published in the April 18th issue of Science.

"It was hard to imagine how this competition happens because the signal that leads cells to their targets also is responsible for keeping them alive, which begs the question: How do half of them die?" says David Ginty, Ph.D., a professor of neuroscience and investigator of the Howard Hughes Medical Institute.

Target tissues innervated by so-called peripheral neurons coax nerves to grow toward them by releasing nerve growth factor protein, or NGF. Once the nerve reaches its target, NGF changes from a growth cue to a survival factor. In fact, when some populations of nerve cells are deprived of NGF they die. To further investigate how this NGF-dependent survival effect works the researchers looked for genes that are turned on by NGF in developing nerve cells.

They found hundreds of genes that respond to NGF genes, some of which are involved in enhancing NGF's effect. With the observation that NGF seems to control genes that improve NGF effectiveness, Ginty's team hypothesized that this could be the way in which nerve cells compete with one another for survival. To test this idea the team turned to colleagues at the Mind/Brain Institute at Hopkins who specialize in computer modeling of such problems.

The computer model they built assigns each nerve cell its own mathematical equation that take into account how much NGF the cell encounters or how effective NGF can be to simulate a cell's drive to survive. When

they plugged in the model, it showed that over time-about 100 days or so-about half of the cells manage to survive, while the other half die.

But, in the developing mouse embryo, nerve cells that die do so over the course of two to three days just before birth. "So then we considered whether these nerves compete like other systems in the body, where those with stronger connections punish the weaker ones," says Ginty. The team turned their attention to other genes they found to be NGF dependent; two of which code for proteins that kill neighboring nerve cells and another is the receptor for these death proteins.

According to Ginty, nerves that connect to muscles undergo a similar process called synapse elimination where stronger connections stay connected and weaker ones are eliminated. The team wondered if this is also true of peripheral nerve cells competing for NGF availability and ultimate cell survival. To test this idea they plugged these three additional genes into their computer model, assuming that the stronger connected nerve cell punishes its neighbors by releasing the two proteins capable of killing. The computer model showed again, that half the nerve cells die over time, but this time the death occurred over two to three days rather than 100 days, just as in living animals.

To confirm that the model is accurate, the team went back to genetically altered mice. They predicted that removal of the punishment signals should delay cell death as observed in their early computer simulations. Indeed, nerve cells in mice lacking the receptor protein for the death signals died much slower than in mice with the receptor protein intact.

"I never would have believed that these three genes could speed up competition so much," says Ginty. "But there it was in front of us-it was amazing."

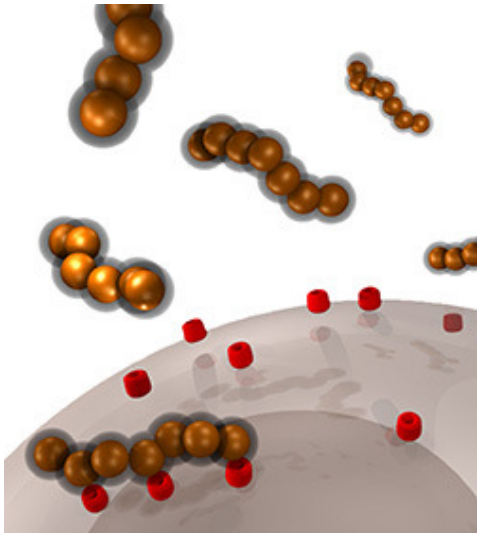
The research was funded by the National Institutes of Health, a Woodrow Wilson Undergraduate Research Fellowship, and the Howard Hughes Medical Institute.

Authors on the paper are Christopher Deppmann, Stefan Mihalas, Nikhil Sharma, Bonnie Lonze, Ernst Niebur and Ginty, all of Hopkins.

On the Web: *http://neuroscience.jhu.edu/ http://www.mb.jhu.edu/ http://www.sciencemag.org/magazine.dtl*

UC San Diego Researchers Target Tumors with Tiny 'Nanoworms'

By Kim McDonald



Segmented "nanoworms" composed of magnetic iron oxide and coated with a polymer are able to find and attach to tumors. **Ji-Ho Park, UCSD**

Scientists at UC San Diego, UC Santa Barbara and MIT have developed nanometer-sized "nanoworms" that can cruise through the bloodstream without significant interference from the body's immune defense system and—like tiny anti-cancer missiles—home in on tumors.

Their discovery, detailed in this week's issue of the journal Advanced Materials, is reminiscent of the 1966 science fiction movie, the Fantastic Voyage, in which a submarine is shrunken to microscopic dimensions, then injected into the bloodstream to remove a blood clot from a diplomat's brain.

Using nanoworms, doctors should eventually be able to target and reveal the location of developing tumors that are too small to detect by conventional methods. Carrying payloads targeted to specific features on tumors, these microscopic vehicles could also one day provide the means to more effectively deliver toxic anti-cancer drugs to these tumors in high concentrations without negatively impacting other parts of the body.

"Most nanoparticles are recognized by the body's protective mechanisms, which capture and remove them from the bloodstream within a few minutes," said Michael Sailor, a professor of chemistry and biochemistry at UC San Diego who headed the research team. "The reason these worms work so well is due to a combination of their shape and to a polymer coating on their surfaces that allows the nanoworms to evade these natural elimination processes. As a result, our nanoworms can circulate in the body of a mouse for many hours."

"When attached to drugs, these nanoworms could offer physicians the ability to increase the efficacy of drugs by allowing them to deliver them directly to the tumors," said Sangeeta Bhatia, a physician, bioengineer and a professor of Health Sciences and Technology at MIT who was part of the team. "They could decrease the side effects of toxic anti-cancer drugs by limiting their exposure of normal tissues and provide a better diagnosis of tumors and abnormal lymph nodes."

The scientists constructed their nanoworms from spherical iron oxide nanoparticles that join together, like segments of an earthworm, to produce tiny gummy worm-like structures about 30 nanometers long—or about 3

million times smaller than an earthworm. Their iron-oxide composition allows the nanoworms to show up brightly in diagnostic devices, specifically the MRI, or magnetic resonance imaging, machines that are used to find tumors.

"The iron oxide used in the nanoworms has a property of superparamagnetism, which makes them show up very brightly in MRI," said Sailor. "The magnetism of the individual iron oxide segments, typically eight per nanoworm, combine to provide a much larger signal than can be observed if the segments are separated. This translates to a better ability to see smaller tumors, hopefully enabling physicians to make their diagnosis of cancer at earlier stages of development."

In addition to the polymer coating, which is derived from the biopolymer dextran, the scientists coated their nanoworms with a tumor-specific targeting molecule, a peptide called F3, developed in the laboratory of Erkki Ruoslahti, a cell biologist and professor at the Burnham Institute for Medical Research at UC Santa Barbara. This peptide allows the nanoworms to target and home in on tumors.

"Because of its elongated shape, the nanoworm can carry many F3 molecules that can simultaneously bind to the tumor surface," said Sailor. "And this cooperative effect significantly improves the ability of the nanoworm to attach to a tumor."

The scientists were able to verify in their experiments that their nanoworms homed in on tumor sites by injecting them into the bloodstream of mice with tumors and following the aggregation of the nanoworms on the tumors. They found that the nanoworms, unlike the spherical nanoparticles of similar size that were shuttled out of the blood by the immune system, remained in the bloodstream for hours.

"This is an important property because the longer these nanoworms can stay in the bloodstream, the more chances they have to hit their targets, the tumors," said Ji-Ho Park, a UC San Diego graduate student in materials science and engineering working in Sailor's laboratory.

Park was the motivating force behind the discovery when he found by accident that the gummy worm aggregates of nanoparticles stayed for hours in the bloodstream despite their relatively large size.

While it's not clear yet to the researchers why, Park notes that "the nanoworm's flexibly moving, one dimensional structure may be one the reasons for its long life in the bloodstream."

The researchers are now working on developing ways to attach drugs to the nanoworms and chemically treating their exteriors with specific chemical "zip codes," that will allow them to be delivered to specific tumors, organs and other sites in the body.

"We are now using nanoworms to construct the next generation of smart tumor-targeting nanodevices," said Ruoslahti. We hope that these devices will improve the diagnostic imaging of cancer and allow pinpoint targeting of treatments into cancerous tumors."

Other researchers involved in the development were Michael Schwartz of UC San Diego, Geoffrey von Maltzahn of MIT, and Lianglin Zhang of UC Santa Barbara. The project was funded by grants from the National Cancer Institute of the National Institutes of Health.

Media Contact: Kim McDonald, 858-534-7572 Comment: Michael Sailor 858-534-8188

Platypus Looks Strange on the Inside, Too

By JOHN NOBLE WILFORD

If it has a bill and webbed feet like a duck, lays eggs like a bird or a reptile but also produces milk and has a coat of fur like a mammal, what could the genetics of the duck-billed platypus possibly be like? Well, just as peculiar: an amalgam of genes reflecting significant branching and transitions in evolution.

A swimming platypus. **Peter Arnold/BIOS**

An international scientific team, which announced the first decoding of the platypus genome on Wednesday, said the findings provided "many clues to the function and evolution of all mammalian genomes," including that of humans, and should "inspire rapid advances in other investigations of mammalian biology and evolution."

The research is described in Thursday's issue of the journal Nature by a group of almost 100 scientists led by Wesley C. Warren, a geneticist at Washington University School of Medicine in St. Louis. The single subject of

the study was a female platypus named Glennie, a resident of Glenrock Station in New South Wales, Australia, whose DNA was collected and analyzed.

The platypus, native to Australia, is so odd that when the first specimens were sent to Europe in the 19th century, scientists suspected a hoax. It was classified as a mammal, one of only two monotremes (echidna is the other) living today that are offshoots of the main mammalian lineage. The divergence occurred some 166 million years ago from primitive ancestors combining features of both mammals and reptiles.

"What is unique about the platypus is that it has retained a large overlap between two very different classifications, while later mammals lost the features of reptiles," Dr. Warren said in an interview.

In their investigation of the platypus genetic blueprint, the scientists found that its genome contains about 18,500 genes, similar to other vertebrates and about two-thirds the size of the human genome. The platypus shares 82 percent of its genes with the human, mouse, dog, opossum and chicken. Some repeated elements in the genome, the scientists noted, hold hints as to the chronology of changes in the platypus.

Of particular interest, the researchers reported, the analysis identified families of genes that link the platypus to reptiles (like those for egg-laying, vision and venom production), as well as to mammals (antibacterial proteins and lactation). The platypus lacks nipples; the young nurse through the abdominal skin.

One surprise was finding genes responsible for sensitive odor receptors. As a primarily aquatic animal, the platypus was already known to rely on electrosensory receptors in its bill to detect faint electric fields emitted by underwater prey. So why the considerable ability to sense odors? The scientists speculate that it may involve sexual communication or the use of water-soluble odorants in navigating and hunting underwater.

Richard K. Wilson, director of the Genome Sequencing Center at Washington University, said that the comparison of the platypus genes with those of other mammals was the beginning of an examination of how "genes have been conserved throughout evolution."

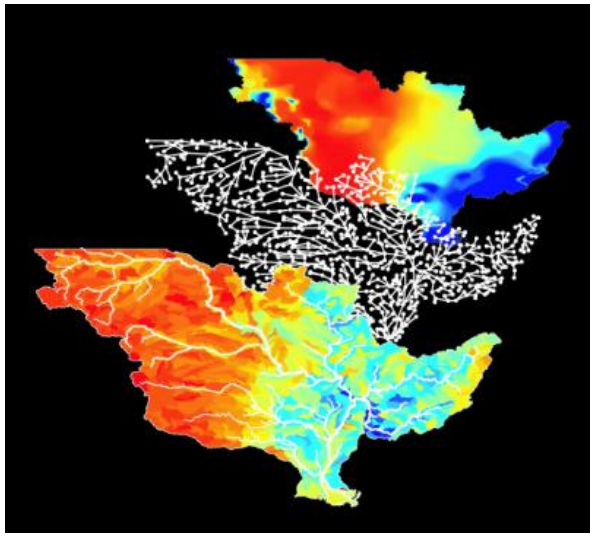
A platypus baby, or puggle, being held before being transferred back to its burrow at Taronga Zoo in Sydney, Australia. **Greg Wood/Agence France-Presse - Getty Images**

The project, involving scientists from eight countries, was primarily financed by the National Human Genome Research Institute in the United States. Its director, Francis S. Collins, said, "As weird as this animal looks, its genome sequence is priceless for understanding how mammalian biological processes evolved."

Biodiversity -- it's in the water

What if hydrology is more important for predicting biodiversity than biology" Research published in the May 8th issue of the journal Nature challenges current thinking about biodiversity and opens up new avenues for predicting how climate change or human activity may affect biodiversity patterns.

In the article, an international group of researchers demonstrates that the biodiversity of fish species in a river system can be accurately predicted with a simple method that uses only the geomorphology of the river network and rainfall measurements for the river system.



The 3,225,000 km2 Mississippi-Missouri river basin covers all or part of 31 US states, spanning diverse habitat types and encompassing very different environmental conditions. The one thing linking all these habitats is the river network. Using geomorphological data from the US Geological Survey, the researchers – hydrologists from Princeton University and the EPFL in Lausanne, Switzerland, and biologists from the University of Maryland -- identified 824 sub-basins in the network. In these, the simple presence (or not) of 433 species of fish was established from a database of US freshwater fish populations. Data on the average runoff production –the amount of rainfall that ends up in the river system and not evaporated back into the air – was then used to calculate the habitat capacity of each sub-basin.

Top: runoff distribution; Middle: sub-basin locations; Bottom: fish species distribution **Nature**

With just four parameters, it's "an almost ridiculously simple model," explains EPFL professor Andrea Rinaldo. The model results were compared to extensive data on actual fish species distributions. Various different measures of biodiversity were analyzed, and the researchers were surprised to find that the model

captured these complex patterns quite accurately. The model is all the more remarkable for what it does not contain – any reference, anywhere, to the biological properties of individual fish species.

It is a formulation that could be applied to any river system, or in fact, any network at all. All that's needed are the geomorphology of the landscape and an estimate of average dispersal behavior and habitat capacity. This model is general enough that it could be used to explore population migrations or epidemics of water-borne diseases in addition to biodiversity patterns. The researchers plan to extend their work to explore the extent to which simple hydrology can act as the determining factor in a wide range of biodiversity patterns.

"These results are a powerful reminder of the overarching importance of water, and the water-defined landscape, in determining patterns of life," notes Princeton professor Ignacio Rodriguez-Iturbe. It provides a framework that could be used to connect large scale environmental changes to biodiversity. Changes in precipitation patterns, perhaps due to global climate change, could be mapped to changes in habitat capacities in the model, ultimately providing a way to estimate how climate change would alter large-scale patterns of biodiversity. It could also be used for an assessment of the impact of specific, local human activities, such as flow re-routing or damming, on the biodiversity patterns in a river network.

Neutral Metacommunity Models Predict Fish Diversity Patterns in Mississippi-Missouri Basin: Rachata Muneepeerakul, Enrico Bertuzzo, Heather J. Lynch, William F. Fagan, Andrea Rinaldo, and Ignacio Rodriguez-Iturbe; Nature, May 8, 2008

First-of-its-kind 14-country study ranks consumers according to environmental behavior

Consumers in India, Brazil top index; US consumers rank last

WASHINGTON—The National Geographic Society and the international polling firm GlobeScan today unveiled a new mechanism for measuring and comparing individual consumer behavior as it relates to the environment. "Greendex™ 2008: Consumer Choice and the Environment - A Worldwide Tracking Survey" looks at environmentally sustainable consumption and behavior among consumers in 14 countries. This first-of-its-kind study reveals surprising differences between consumers in developed and developing countries in terms of environmentally friendly actions. This year's results are a baseline against which results of future annual surveys will be compared, in order to monitor improvements or declines in environmentally sustainable consumption at both the global level and within countries.

The Greendex survey was conducted online earlier this year among 14,000 consumers in Australia, Brazil, Canada, China, France, Germany, Great Britain, Hungary, India, Japan, Mexico, Russia, Spain and the United States. A panel of 27 international experts in global sustainability helped identify which consumer behaviors were most crucial to investigate. One thousand people in each country answered questions that measured their behavior in the areas of housing, transportation, food and consumption of goods; each respondent earned a score that reflected the environmental impact of his or her consumption patterns, which included size and energy-efficiency of residence, commuting mode and distance and use of fresh water, among dozens of other measures. Consumers were then assigned a Greendex score (a measure of the relative environmental sustainability of their consumption patterns) out of 100. Consumers in Brazil and India scored highest; U.S. consumers scored lowest.

Greendex vs. Other Environmental Studies

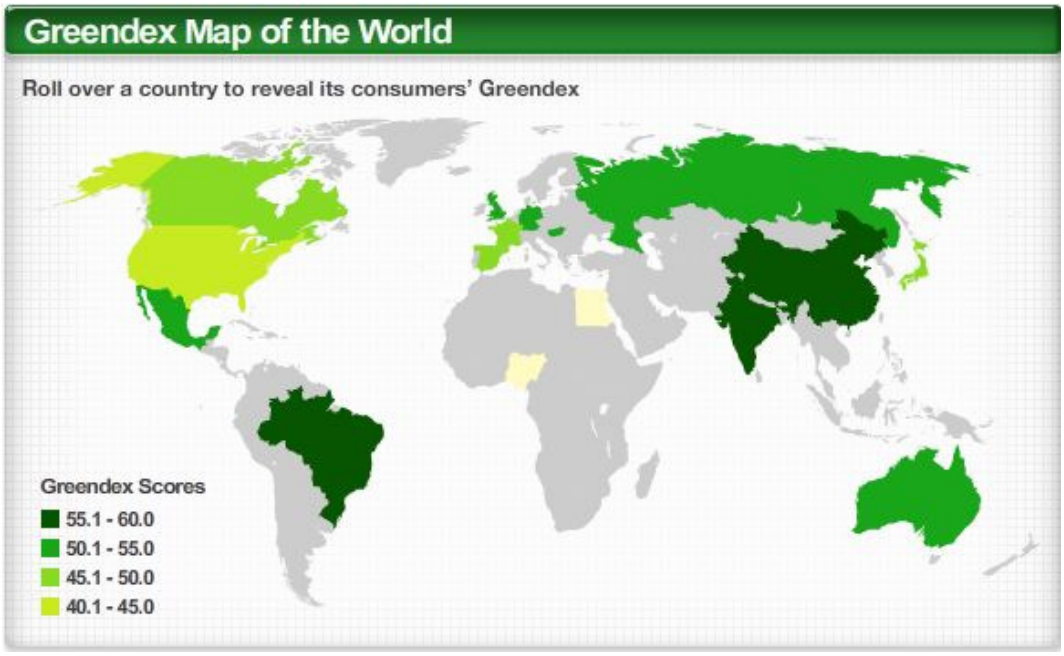
Unlike other measures that rank countries according to the environmental performance of their governments, businesses and other factors, the Greendex is the first to rank the performance of individual consumers, rather than countries as a whole. The results are strikingly different from existing performance rankings like the Environmental Performance Index, the Environmental Sustainability Index or Ecological Footprint.

"The Greendex gives us an unprecedented, meaningful look at how consumers across the globe are behaving," said Terry Garcia, National Geographic's executive vice president of Mission Programs. "It will allow us over time to assess the progress that people are making to conserve, minimize waste and protect natural resources for the future. Consumers who score highest have a responsibility to maintain their behavior and provide an example to those who need to improve. We hope the study inspires all consumers, particularly those in countries where consumers scored lowest, to adopt the best behaviors of those who scored well, and that consumers in countries with expanding economies, who may consume more in the future, will do so responsibly."

Determining Consumption

Consumption as measured by the Greendex is determined both by the choices consumers actively make - such as repairing rather than replacing items, using cold water to wash laundry, choosing green products rather than environmentally unfriendly ones - and choices that are controlled more by their circumstances - such as the climate they live in or the availability of green products or public transport. The initiative considered both of these factors, with 60 percent of the 65-variable index based on choice or discretionary behavior.

"The Greendex shows us that consumers' choices play a large role in their environmental footprint. Governments and businesses, therefore, have a responsibility to ensure that environmentally friendly options are available and affordable to all consumers, especially those in the developing countries, whose index rankings may fall as economies grow and consumption patterns change," said Thomas Lovejoy, president of the Heinz Center for Science, Economics and the Environment, chairman of National Geographic's Conservation Trust and an adviser to the Greendex project.



GlobeScan President Doug Miller added, "The Greendex initiative is ground-breaking. Never before has such a comprehensive survey been applied across a wide range of countries to scientifically track consumer behaviors related to the environment. While other surveys look at attitudes and intentions, the Greendex tracks actions that matter."

Consumer Greendex Rankings by Country

The findings show that consumers in Brazil and India tie for the highest Greendex score for environmentally sustainable consumption at 60 points each. They are followed by consumers in China (56.1), Mexico (54.3), Hungary (53.2) and Russia (52.4). Among consumers in wealthy countries, those in Great Britain, Germany and Australia each have a Greendex score of 50.2, those in Spain register a score of 50.0 and Japanese respondents, 49.1. U.S. consumers have the lowest Greendex score at 44.9. The other lowest-scoring consumers are Canadians with 48.5 and the French with 48.7.

There are signs that index rankings are set to change as people in developing countries become more economically successful and adopt more consumptive behaviors. Findings show that consumers in countries with emerging economies aspire to higher material standards of living and believe people in all countries should have the same living standards as those in the wealthiest countries.

Consumers in Developing vs. Developed Countries

While the survey found encouraging signs that individuals in all the surveyed countries feel empowered when it comes to the environment and are taking some action in their daily lives to reduce consumption and waste, it found that those in developing countries are the most concerned and that the behavior and personal choices of consumers in developing countries were more environmentally friendly than those in developed countries.

Consumers in developing countries feel more responsible for environmental problems than those in developed countries, and six in 10 people in developing countries report that environmental problems are negatively affecting their health - twice as many as in most developed countries. Moreover, consumers in developing countries feel strongest that global warming will worsen their way of life in their lifetime, are the most engaged when it comes to talking and listening about the environment, feel the most guilt about their environmental impact and are willing to do the most to minimize that impact. Their behavior reflects their concern. People in developing countries are more likely to:

* Live in smaller residences;
* Prefer green products and own relatively few appliances or expensive electronic devices;
* Walk, cycle, or use public transportation, and choose to live close to their most common destination.

By contrast, consumers in developed countries, who have more environmentally friendly options to choose from, often don't make those choices.

* They have larger homes and are more likely to have air-conditioning.
* They generally own more cars, drive alone most frequently and use public transport infrequently.
* They are least likely to buy environmentally friendly products and to avoid environmentally unfriendly products.

U.S. consumers scored worse than those in any other country, developing or developed, on housing, transportation and goods. They are by far the least likely to use public transportation, to walk or bike to their destinations or to eat locally grown foods. They have among the largest average residence size in the survey. Only 15 percent say they minimize their use of fresh water.

Discover Your Greendex Score

Individuals around the world can find out where they rank on the Greendex scale by visiting http://event.nationalgeographic.com/greendex/ and taking an abbreviated survey. They can also examine the Greendex survey results by country, measure their knowledge of some basic green issues against what others around the world know, and get tips on living a more environmentally friendly lifestyle. “National Geographic has been committed to caring for the environment for many years, and part of our mission is to help people understand how they can reduce their impact on the planet. We hope people will be inspired to look at how their own behavior is affecting the environment and take steps to minimize their environmental footprint,” the Society’s Terry Garcia said.

Market Basket

To provide context for the Greendex results, National Geographic and GlobeScan also developed a “Market Basket,” a set of national macroeconomic indicators of consumption in four areas important to environmentally sustainable behavior - energy, transportation, travel and consumer goods. The data, gathered by the Economist Intelligence Unit, mirrors in part the consumer behavior measured by the Greendex survey. The purpose of the Market Basket is to provide an external estimate of changes in consumer behavior over time, while acknowledging that industry and government also play a critical role. The Greendex, for example, measures things consumers are doing to save energy in a country; the Market Basket measures whether total energy consumption in the country is actually going up or down. The Market Basket will also establish a framework for comparing the relative environmental impact of each country’s size and rate of growth, over time.

Current Market Basket data validate the 2008 Greendex rankings, with actual energy consumption aligned with each country's Greendex score. More importantly, however, the Market Basket data suggest that if current growth rates are sustained in certain countries in 2008, Greendex rankings may change considerably in the near future.

Socrates in the classroom develops students' thinking and changes the distribution of power

When students have the opportunity to participate in “Socratic seminars” on a regular basis, a different classroom culture evolves. The students collaborate more and more voices are heard. The students develop their thinking skills in a cooperative and investigative atmosphere. This is shown in a new dissertation in Pedagogy by Ann S Pihlgren at the Stockholm University in Sweden.

The Socratic dialogue is a particular way of developing children’s, as well as adults’, thinking skills through cooperative dialogue where significant human ideas and values are discussed. By participating in Socratic seminars regularly every other week, preschool children and older students develop their thinking skills. The seminars address literature and art work, with questions such as these: is Pippi Longstocking is a good friend, is Jack is stupid or smart when he sells his mother’s cow for some beans or are we born good or evil. In the beginning the students have difficulty expressing their thoughts, but with time their ability to express themselves and to examine ideas critically and logically develops.

The study included seven groups of children, five to sixteen years old. The groups were filmed during three years of philosophizing in the classroom and the films were analyzed. The interaction in the classroom was positively influenced, according to Ann S Pihlgren. The teacher dominated less, more students spoke and the students gradually took over the responsibilities of the teacher to promote exploration in the dialogue. The ability to use the Socratic seminar is learned by students and teachers through practice and by testing the rules of the seminar. The students construct a supportive group culture through their silent interaction, where gestures, glances, and body language are used to show not only support or sympathy for each other, but also cooperation with each other when someone attempts to disturb or to provoke the dialogue. The teacher role changes to one of support, ensuring that the analysis is fruitful and that the dialogue is respectful.

Socratic methods have developed independently in various countries. They all describe a set of methodological steps to attain similar objectives. An opening question is answered by all participants and followed by cooperative, critical analysis. Finally, the new ideas are connected to the everyday life experience of the participants.

It seems as if this ritualized structure and the nurturing culture of the seminar provide a safe circle, helping the participants to try new, bold ideas that they might otherwise not have tested, Ann S Pihlgren says. By

cooperating when examining the ideas they also seem to learn a way to address problems on their own without teacher intervention.

To work with methods connected to the ancient philosopher Socrates may seem out-of-date in a modern school, but that is absolutely not the case, Ann S Pihlgren states.

The Socratic seminars have been seen as a complement to traditional classroom teaching for hundreds of years. But it is not easy to learn how to stage them to get positive effects. It is especially hard for teachers, who often fall back to their traditional, controlling "teacher" roles. The dissertation offers excellent tools for teachers who want to develop students' thinking and to foster cooperative group dialogue.

The name of the dissertation: Socrates in the Classroom. Rationales and Effects of Philosophizing with Children. The dissertation could be downloaded as pdf at http://www.diva-portal.org/su/theses/abstract.xsql?dbid=7392 .

Additional facts

Socrates (470-399 BC) Greek philosopher assumed in his dialogues that human reason has a right to impartially explore all subjects. He left no written work, we know him mostly through Plato's (427-347 BC) dialogues. Plato was Socrates disciple and a prominent figure within the idealistic tradition of Western philosophy. Socrates worked through what he called maieutics, midwifery. Through elenchus (Greek for inquiring, refuting), exploring questioning the questioner will help the participants to give birth to their thoughts. Similar methods was developed and practiced in the beginning of 20th century by the Swedish popular educators Hans Larsson and Oscar Olsson, in Germany in the 1920s by Leonard Nelson and in the USA during the later 20th century by Mortimer J Adler. In Sweden the dialogues were introduced by Lars Lindström. The seminars are practiced as a pedagogical method at the Freinet Academy in Norrtälje, Sweden www.mimer.org.
The students in the study are 5 to 16 years old (grade 9).

Power from Formic Acid

Room temperature is warm enough: hydrogen for fuel cells from formic acid

One of the central challenges of our time is the supply of enough environmentally friendly and resource-efficient energy to our society. In this context, hydrogen technology has taken on increased importance. Björn Loges, Albert Boddien, Henrik Junge, and Matthias Beller at the Leibniz Institute of Catalysis in Rostock have now succeeded in the controlled extraction of hydrogen from formic acid—without the need for the high-temperature reforming process usually involved in other hydrogen generation systems. As they report in the journal Angewandte Chemie, this hydrogen source, generated at room temperature, can be directly introduced into fuel cells.

Hydrogen-powered fuel cells are the cleanest source of energy because they only produce one type of exhaust gas: water vapor. However, it is not yet practicable to transport and store hydrogen, which is a gas and cannot be pumped into a tank as easily as gasoline. Storage systems currently in use are large and heavy, expensive, and complex. It would thus be better to couple the fuel cell directly to a hydrogen-producing material, which would supply the fuel cell on demand. Aside from methane and methanol, renewable resources such as biomass and its fermentation products (e.g. bioethanol) are the most promising starting materials for this technology. The serious disadvantage is that their conversion only works at temperatures above 200 °C, which consumes a significant portion of the energy produced.

The researchers from Rostock have now developed a feasible process for the on-demand release of hydrogen; they produce hydrogen from formic acid (HCO2H). In the presence of an amine (e.g. N,N-dimethylhexylamine) and with a suitable catalyst (e.g. the commercially available ruthenium phosphine complex [RuCl2(PPH3)2]), formic acid is selectively converted into carbon dioxide and hydrogen at room temperature. A simple activated charcoal filter is enough to purify the hydrogen gas for use in a fuel cell. The use of formic acid for "hydrogen storage" allows the advantages of established hydrogen/oxygen fuel cell technology to be combined with those of liquid fuels. Formic acid is nontoxic and easy to store. Because formic acid can be generated catalytically from CO2 and biomass-derived hydrogen, the cycle is CO2 neutral in principle.

Will we be replacing gasoline with formic acid in the future? It is not inconceivable, but initial applications requiring smaller amounts of energy are more probable. "For the use of fuel cells in portable electrical devices," says Beller, "this nascent formic acid technology opens up new possibilities in the short term."

Nitrates in vegetables protect against gastric ulcers

Fruits and vegetables that are rich in nitrates protect the stomach from damage. This takes place through conversion of nitrates into nitrites by the bacteria in the oral cavity and subsequent transformation into biologically active nitric oxide in the stomach. The Swedish researcher Joel Petersson has described the process, which also means that antibacterial mouthwashes can be harmful for the stomach.

"Nitrates in food have long been erroneously linked to an increased risk of cancer," says Joel Petersson of Uppsala University's Department of Medical Cell Biology.

He instead thinks that nitrate-rich vegetables such as spinach, lettuce, radishes and beetroot have a positive affect on the stomach by activating the mucous membranes' own protective mechanisms, thus reducing the risk of problems such as gastric ulcers.

In the body the blood circulation transports nitrates to the salivary glands, where they are concentrated. When we have eaten nitrate-rich food our saliva thus contains large amounts of nitrates, which the bacteria of the oral cavity partially convert into nitrites. When we swallow the nitrites they come into contact with acid gastric juice, and are then converted into the biologically active substance nitric oxide. This results in our developing high levels of nitric oxide in the stomach after eating vegetables.

It has long been known that nitric oxide is produced by various enzymes in the human body, but the fact that nitric oxide can also be formed in the stomach from nitrites in the saliva, entirely without the involvement of enzymes, is a relatively new discovery. Researchers still have very little idea of how the stomach is affected by these high levels of nitric oxide. Joel Petersson's thesis shows that the nitric oxide that is formed in the stomach stimulates the protective mechanisms of the mucous membrane – because the stomach constantly has to protect itself so as not to be broken down together with the food ingested. Two such important defence mechanisms are the stomach's constant renewal of the mucous layer that covers the mucous membrane and its maintenance of a stable blood flow in the mucous membrane. The nitric oxide widens the blood vessels in the mucous membrane, thus increasing the blood flow and regulating elimination of the important mucus. Together, these factors lead to a more resistant mucous membrane.

Using animal models Joel Petersson and his colleagues have shown that nitrate additives in food protect against both gastric ulcers and the minor damage that often occurs in the gastrointestinal tract as a result of ingestion of anti-inflammatory drugs.

"These sorts of drugs are very common in the event of pain and inflammation. They have the major disadvantage of causing a large number of serious side effects in the form of bleeding and ulcers in the gastrointestinal tract. With the aid of a nitrate-rich diet you can thus avoid such damage," he explains.

The thesis also shows that the bacteria in the oral cavity are very important to the process of nitrates in food protecting the stomach's mucous membrane. This has been examined in that rats have been given nitrate-rich feed, whereby some of them have also simultaneously received an antibacterial oral spray. When these rats were then given anti inflammatory drugs, damage to the mucous membrane only occurred in the ones that had received the oral spray. In the latter the nitrates no longer had a protective effect on the mucous membrane, as the oral spray had killed the important bacteria that normally convert nitrates into nitrites.

"This shows how important our oral flora is. The fact that these bacteria are not just involved in our oral hygiene but also play an important role in the normal functions of the gastrointestinal tract is not entirely new. It is currently an important issue, as antibacterial mouthwashes have become more and more common. If a mouthwash eliminates the bacterial flora in the mouth this may be important to the normal functioning of the stomach, as the protective levels of nitric oxide greatly decrease," says Joel Petersson.

In his opinion the research results also provide a new approach to the importance of fruit and vegetables in our diet.

"If we followed the National Swedish Food Administration's recommendation and ate 500 g of fruit and vegetables per person per day it would definitely be better for our stomachs.

Archaeologists uncover caveman bling

RABAT - Archaeologists have uncovered shells used for finery by prehistoric man 85,000 years ago in a cave in eastern Morocco, the country's heritage institute said today. A research team led by archaeology and heritage institute (INSAP) member Abdeljalil Bouzouggar and Nick Barton from Oxford University found the 20 perforated shells in a cave near Taforalt between March and April this year.

The Nassarius gibbosulus shells are the type prehistoric man would have worn, according to a statement from the Moroccan Ministry for Culture.

In 2007, Bouzouggar and Barton discovered 14 perforated shells in the same cave.

"This discovery shows that the making and use of objects of finery is very anchored in the traditions of Morocco's prehistoric people," said Bouzouggar, in whose opinion the country is the original centre of artistic and symbolic creation.

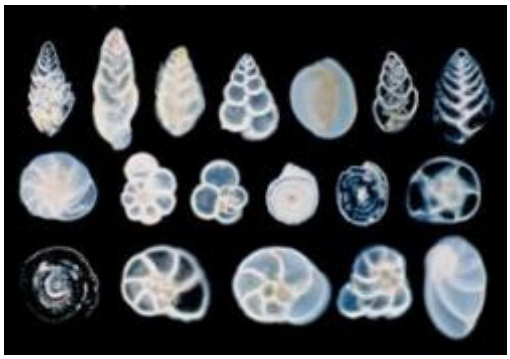
Objects of finery discovered in Morocco are "now considered to be even more ancient than those discovered in Algeria, South Africa and in Palestine", said the culture ministry. Known as the "cave of pigeons", the 30-metre deep and 10-metre high cave is situated 50km from Morocco's Mediterranean coast.

Sea creatures had a thing for bling

*** Lewis Dartnell**

Call it extraterrestrial bling. Fossilised sea creatures have been found that coated themselves in tiny diamonds created in the asteroid impact that killed off the dinosaurs.

The fossils were discovered by a team led by Michael Kaminski, a geologist at University College London. They went to the Umbria-Marche basin of eastern Italy in search of the fossilised remains of deep-ocean creatures called agglutinated foraminifera. These amoeba-like single-celled organisms build protective "tests" around themselves by sticking together sediment grains from the sea floor. Curiously, they seem to prefer heavy grains, presumably to help them sink to the bottom of the ocean.



(Image: E.R. Degginger/SPL)

Kaminski's team looked for fossils in rock samples taken just above and below the sediment layer created by the huge asteroid impact at the end of the Cretaceous period, 65 million years ago. The foraminifera tests they found were mainly composed of common minerals such as quartz, but some of the component grains were unusually rich in metals such as nickel and cobalt, indicating that they had originated in outer space.

Even more surprising were microscopic granules of carbon, no more than 10 micrometres across, which were subsequently identified as diamonds. "The foraminifera were deliberately using extraterrestrial diamonds in their shells," says Kaminski.

The majority of these microdiamonds were formed from terrestrial graphite rock that was altered by the extreme pressure and temperature of the asteroid impact, but a small proportion was truly extraterrestrial, derived from carbon in the asteroid itself.

It seems the main reason the foraminifera chose grains containing diamonds and metals for their tests was the lack of other grains of a similar density at this particular site. What remains a mystery is how these ancient foraminifera were able to pick out the densest grains, an ability they share with their latter-day descendants (pictured).

Kaminski's results were published last month in the Proceedings of the Seventh International Workshop on Agglutinated Foraminifera.

Flowers 'wave' at passing insects

By Matt Walker BBC

Flowers "wave" at insects to get their attention, scientists have discovered.

The finding helps explain why many flowers waft in the breeze, and reveals a hitherto unknown trick used to attract pollinators.

Scientists made the discovery while studying common wildflowers known as sea campion on the Welsh coast.

Mobile flowers are visited more often by insects and also produce more seeds, they report in the Journal of Evolutionary Biology.

Moving flowers also attract a wider variety of insect species than more static blooms.

For years, biologists have known that flowers use striking colours, fragrances, elaborately shaped petals and nectar to attract pollinating insects such as bees and flies.

Mobile flowers are visited by more insects, scientists discovered

Yet no-one had ever seriously considered whether wafting in the wind acted as a similar signal.

Beachside inspiration

"I was lying on the beach watching flowers wave in the wind at my daughter's birthday party, and I wondered why they have stalks and risked getting damaged in such an exposed habitat," recounted John Warren from the University of Aberystwyth.

So he looked at what research had previously been done, and found very few answers.

"The only reference I found to motion in attracting pollinators says it's unlikely to be important, because insects are not good at detecting movement; which is clearly rubbish."

To find out more, Dr Warren and colleague Penri James experimented with sea campion (Silene maritima) growing on an exposed coast within a Site of Special Scientific Interest in Cardigan Bay in west Wales.

They observed 300 specially grown flowers of varying stem lengths, recording how much each flower moved in the wind, how often it was visited by insects and for how long, and how many seeds it went on to produce.

Scientists investigate how sea campion attracts insects

Their experiments reveal that flowers mounted on long, thin stalks move around more in the wind.

This acts as a powerful signal to passing pollinators, allowing the plant to attract more insects than less mobile flowers growing atop short, thick stems.

"We found wavy flowers are more visible to insects, and thus attract more pollinators and set more seeds," said John Warren.

But flowers ultimately face an evolutionary trade-off, he believes.

"Short, fat-stalked flowers don't wobble enough and are less attractive to pollinators; yet very wobbly flowers are just too wobbly for the insects to handle, as the insects cannot land on them.

"Only flowers that wobble the right amount are successful in setting seeds."

New evidence from earliest known human settlement in the Americas

Provides support for coastal migration theories

New evidence from the Monte Verde archaeological site in southern Chile confirms its status as the earliest known human settlement in the Americas and provides additional support for the theory that one early migration route followed the Pacific Coast more than 14,000 years ago.

The study was conducted by a team of anthropologists, geologists and botanists headed by Vanderbilt University's Distinguished Professor of Anthropology Tom Dillehay and was reported in the May 9 issue of the journal Science.

The paper, which includes the first new data reported from the site in 10 years, includes the identification of nine species of seaweed and marine algae recovered from hearths and other areas in the ancient settlement. The seaweed samples were directly dated between 14,220 to 13,980 years ago, confirming that the upper layer of the site, labeled Monte Verde II, was occupied more than 1,000 years earlier than any other reliably dated human settlements in the Americas.

The Monte Verde site was discovered in 1976. It is located in a peat bog about 500 miles south of Santiago and has revealed well-preserved ruins of a small settlement of 20 to 30 people living in a dozen huts along a small creek. A wide variety of food has been found at the site, including extinct species of llama and an elephant-like animal called a gomphothere, shellfish, vegetables and nuts.

In 1979, when Dillehay and his colleagues first reported that the radiocarbon dating of the bones and charcoal found at Monte Verde returned dates of more than 14,000 years before the present, it stirred up a major controversy because the early dates appeared to conflict with other archaeological evidence of the settlement of North America.

Since at least 1900, the prevailing theory had been that human colonization began at the end of the last Ice Age about 13,000 years ago, when groups of big game hunters, called the Clovis culture, followed herds from Siberia to Alaska over a land bridge across the Bering Strait and then gradually spread southward. None of the Clovis artifacts were dated earlier than 13,000 years ago. So having a substantially older human settlement in southern Chile was difficult to reconcile with this view.

It wasn't until 1997 that the controversy was resolved by a prominent group of archaeologists who reviewed the evidence, visited the Monte Verde site and unanimously approved the dating.

Most scholars now believe that people first entered the new world through the Bering land bridge more than 16,000 years ago. After entering Alaska, it is not known whether they colonized the hemisphere by moving down the Pacific coast, by inland routes or both. The general view is that the early immigrants would have spread down the coast much faster than they could move inland because they could exploit familiar coastal resources more readily and get much of their food from the sea. However, evidence to support the coastal migration theory has been particularly hard to find because sea levels at the time were about 200 feet lower than today: As the sea level rose, it would have covered most of the early coastal settlements.

According to Dillehay, the new Monte Verde findings provide additional support for the coastal migration theory but, at the same time, raise the possibility that the process may have been considerably slower than currently envisioned.

At the time it was inhabited, Monte Verde was situated on a small tributary of a large river. It was about 400 feet above sea level and located more than 50 miles from the coast and about 10 miles from a large marine bay. Despite its inland location, the researchers identified a total of nine different species of seaweed and algae in the material collected at the site - material that the Monte Verdeans must have brought from the coast and the bay. The researchers have also found a variety of other beach or coastal resources, including flat beach pebbles, water plants from brackish estuaries and bitumen.

"Finding seaweed wasn't a surprise, but finding five new species in the abundance that we found them was a surprise," said Dillehay. "There are other coastal resources at the site. The Monte Verdeans were really like

beachcombers: The number and frequency of these items suggests very frequent contact with the coast, as if they had a tradition of exploiting coastal resources."

In addition, the scientists have found a number of inland resources, such as the gomphothere meat, in the ancient village. This suggests that the group was moving back and forth between different ecological zones, a process called transhumance.

"It takes time to adapt to these inland resources and then come back out to the coast. The other coastal sites that we have found also show inland contacts. If all the early American groups were following a similar pattern of moving back and forth between inland and coastal areas, then the peopling of the Americas may not have been the blitzkrieg movement to the south that people have presumed, but a much slower and more deliberate process," Dillehay observed.

Members of the research team included Carlos Remirez, Mario Pino and Daniela Pino-Navarro from the Universidad Austral de Chile; Michael B. Collins from the University of Texas, Austin; and Jack Rossen from Ithaca College.

The research was funded by the National Science Foundation, the Fondo Nacional de Desarrollo Cientifico y Tecnológica, the National Geographic Society and the Universidad de Chile.

Previously unseen switch regulates breast cancer response to estrogen

A tiny modification called methylation on estrogen receptors prolongs the life of these growth-driving molecules in breast cancer cells, according to research by scientists at Emory University's Winship Cancer Institute.

The results are published in the May 9, 2008 issue of the journal Molecular Cell.

Most breast cancers contain estrogen receptors, which enable them to grow in the presence of the hormone estrogen. Their presence can determine whether tumors will respond to the estrogen-blocking drug tamoxifen.

The finding will help researchers sort out how mutations change the estrogen receptor's function and allow some breast cancers to resist tamoxifen, says Paula Vertino, PhD, associate professor of radiation oncology at Emory University School of Medicine.

"The problem is that a significant fraction of estrogen receptor positive tumors don't respond to tamoxifen," Vertino says. "Development of new drugs that interfere with the methylation of the estrogen receptor may be an alternative way to treat those tumors."

Until recently, scientists thought methylation enzymes acted only on DNA molecules or on histones, proteins that bundle DNA into spool-like packages. Methylation enzymes add tags called methyl groups to other molecules, influencing their ability to turn genes on or off.

Vertino and her colleagues found that one of the modification enzymes, called SET7, methylates a flexible part of the estrogen receptor. When they created breast cancer cells with reduced levels of SET7, the estrogen receptor molecules lasted only half as long and were less effective in turning on genes.

Vertino's team showed that a mutation in the estrogen receptor found in more aggressive breast tumors interferes with methylation in cells. Also, the methylation appears in exactly the same spot where another protein called BRCA1 adds a different kind of regulatory marking, and may block BRCA1's restrictive effects on the estrogen receptor.

Women who inherit a mutation in the gene that encodes BRCA1 have up to an 80 percent lifetime risk of developing breast cancer, several times the risk of those who don't have it, according to the National Cancer Institute. BRCA1 mutations are estimated to account for about a third of all inherited breast cancers and roughly 2-3 percent of all breast cancers.

Scientists are beginning to look for drugs that could modulate methylation enzymes. Vertino says that methylation probably affects several other proteins similar to the estrogen receptor.

"I expect this will be just the tip of the iceberg," she says. "Methylation may be just as common as other protein modifications, and even more complicated."

The first author was postdoctoral fellow Krithika Subramanian, PhD. A separate paper recently published by co-author Xiaodong Cheng, PhD, professor of biochemistry at Emory University School of Medicine and a Georgia Research Alliance Eminent Scholar, also discusses protein methylation.

http://whsc.emory.edu/press_releases2.cfm?announcement_id_seq=13984

The research was supported by the National Institutes of Health and the American Cancer Society.

Do antidepressants enhance immune function?

Ex vivo results from HIV positive individuals with and without depression

Philadelphia, PA, May 8, 2008 – Infection with human immunodeficiency virus (HIV), which leads to acquired immunodeficiency syndrome (AIDS), is an epidemic of global concern. According to the most recent estimates, released in November 2007, by the Joint United Nations Programme on HIV/AIDS (UNAIDS) and the World Health Organization (WHO), an estimated 33.2 million worldwide are living with HIV infection currently.

Although the rates of infection appear to be decreasing, there are obviously immense implications for achieving improvements in HIV/AIDS treatment.

The functioning of natural killer (NK) cells, which are a major element of the innate immunity system and are involved in the body's first line of defense against infections such as HIV, is decreased in both HIV and depression. A group of researchers who have previously found that stress and depression impair NK cell function and accelerate the course of HIV/AIDS are now publishing a new report in the May 1st issue of Biological Psychiatry.

In this study, they recruited both depressed and non-depressed HIV-infected women and studied the ex vivo effects of three drugs, a selective serotonin reuptake inhibitor (SSRI), a substance P antagonist, and a glucocorticoid antagonist, on their NK cell activity. These drugs were selected because, as the authors state, each "affect[s] underlying regulatory systems that have been extensively investigated in both stress and depression research as well as immune and viral research." The scientists found that the SSRI citalopram, and the substance P antagonist CP 96,345, but not the glucocorticoid receptor antagonist RU486, increased NK cell activity. According to Dr. Dwight Evans, corresponding author of the article: "The present findings provide evidence that natural killer cell function in HIV infection may be enhanced by selective serotonin reuptake inhibition and also by substance P antagonism in both depressed and non-depressed individuals."

John H. Krystal, M.D., Editor of Biological Psychiatry and affiliated with both Yale University School of Medicine and the VA Connecticut Healthcare System, comments: "There has been growing evidence that the compromise of immune function associated with depression influences the outcomes of infectious diseases and cancer. Antidepressant treatments are beginning to be studied for their potential positive effects on immune function." He adds that "the paper by Evans et al. suggests that antidepressant treatment may have positive effects on natural killer cell activity in cells isolated from individuals infected with HIV with and without depression. This type of bridge between the brain and the rest of the body deserves further attention." Dr. Evans agrees, noting that "these findings begin to pave the way towards initiating clinical studies addressing the potential role of serotonergic agents and substance P antagonists in improving natural killer cell innate immunity, possibly delaying HIV disease progression and extending survival with HIV infection."

Notes to Editors:

The article is "Selective Serotonin Reuptake Inhibitor and Substance P Antagonist Enhancement of Natural Killer Cell Innate Immunity in Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome" by Dwight L. Evans, Kevin G. Lynch, Tami Benton, Benoit Dubé, David R. Gettes, Nancy B. Tustin, Jian Ping Lai, David Metzger and Steven D. Douglas. Drs. Evans, Lynch, Benton, Dubé, and Metzger and Mr. Gettes are affiliated with the Department of Psychiatry, with Dr. Evans also with the Departments of Medicine and Neuroscience, and Dr. Douglas is with the Department of Pediatrics, all at the University of Pennsylvania School of Medicine in Philadelphia, Pennsylvania. Ms. Tustin and Drs. Lai and Douglas are with the Division of Allergy and Immunology, Joseph J. Stokes Research Institute of The Children's Hospital of Philadelphia, in Philadelphia, Pennsylvania. The article appears in Biological Psychiatry, Volume 63, Issue 9 (May 1, 2008), published by Elsevier.
Full text of the article mentioned above is available upon request. Contact Jayne M. Dawkins at (215) 239-3674 or ja.dawkins@elsevier.com to obtain a copy or to schedule an interview.

New Cancer Gene Discovered

Researchers reduce protein; stop cancer growth – Plan to develop new cancer therapy target

OU Public Affairs

Oklahoma City, OK -- Researchers at the OU Cancer Institute have identified a new gene that causes cancer. The ground-breaking research appears Monday in Nature's cancer journal Oncogene.

The gene and its protein, both called RBM3, are vital for cell division in normal cells. In cancers, low oxygen levels in the tumors cause the amount of this protein to go up dramatically. This causes cancer cells to divide uncontrollably, leading to increased tumor formation.

Researchers used new powerful technology to genetically "silence" the protein and reduce the level of RBM3 in cancerous cells. The approach stopped cancer from growing and led to cell death. The new technique has been tested successfully on several types of cancers – breast, pancreas, colon, lung, ovarian and prostate.

"We are excited about this discovery because most cancers are thought to come from mutations in genes, and our studies, for the first time, have shown that too much of this type of protein actually causes normal cells to turn into cancer cells," said Shrikant Anant, Ph.D., a cancer biologist at the OU Cancer Institute and principal investigator on the project.

Anant said they found RBM3 protein in every stage of many cancers, and the amount of protein increased as the cancer grew. The protein helped the cancer grow faster, avoid cell death and was part of the process that formed new blood vessels to feed the tumor.

"This process, called angiogenesis, is essential for tumor growth and suggests that targeting RBM3 may be an extremely powerful tool against many and perhaps all solid tumors," Anant said.

A quarter of the funding for the cancer research comes from an $800,000 grant from the National Institutes of Health with remaining funds from the University of Oklahoma College of Medicine. The next step for Anant, Dr. Courtney Houchen and their research team at the OU Health Sciences Center is to develop agents that block the protein function in a variety of cancers. Researchers expect to start clinical trials at OU in about five years.

Hopkins researchers discover new link to schizophrenia

Mouse model mimics clinical features

Neuroscientists at Johns Hopkins have discovered that mice lacking an enzyme that contributes to Alzheimer disease exhibit a number of schizophrenia-like behaviors. The finding raises the possibility that this enzyme may participate in the development of schizophrenia and related psychiatric disorders and therefore may provide a new target for developing therapies.

The BACE1 enzyme, for beta-site amyloid precursor protein cleaving enzyme, generates the amyloid proteins that lead to Alzheimer's disease. The research team years ago suspected that removing BACE1 might prevent Alzheimer.

"We knew at the time that in addition to amyloid precursor protein, BACE1 interacts with other proteins but we didn't know how those interactions might affect behavior," says Alena Savonenko, M.D., Ph.D., an assistant professor in neuropathology at Hopkins.

Reporting in the Proceedings of the National Academies of Sciences, the research team describes how mice lacking the BACE1 enzyme show deficits in social recognition among other behaviors classically linked to schizophrenia.

A normal mouse, when introduced to another mouse, shows a lot of interest the first time they meet. If the mice are separated then reintroduced, their interest drops because they remember having met before, a phenomenon the researchers call habituation. If they then introduce a completely different mouse, interest piques again at the newbie.

The researchers introduced mice lacking BACE1 to another mouse. The first time they met, the BACE1 mouse showed interest, the second time meeting the same mouse the BACE1 mouse showed less interest and even less interest the third time. The researchers then introduced the BACE1 mouse to a totally different mouse of a different strain and the BACE1 mouse showed no interest at all. "These mice were totally disinterested, normal mice just don't behave like this," says Savonenko.

Additionally, the researchers found that these BACE1-lacking mice also displayed many other schizophrenia-like traits. Most importantly, according to Savonenko, some of the deficits improved after treatment with the antipsychotic drug clozapine.

Because schizophrenia is a disorder likely caused by many different factors, Savonenko explains that BACE1 might contribute to an increased risk of schizophrenia in certain patients and the BACE1 mice will be a useful animal model. "We never thought we would see one mouse that closely mimics so many of the clinical features of schizophrenia," says Alena Savonenko, M.D., Ph.D., an assistant professor of neuropathology at Hopkins. "This could be a really useful model to study and understand the molecular contributions to the disease."

The research was funded by the National Institutes of Health, the National Institute on Aging, the Alzheimer's Association, the Adler Foundation, the Ilanna Starr Scholar Fund and the Bristol-Myers Squibb Foundation.
Authors on the paper are Savonenko, T. Melnikova, F. Laird, K.-A. Stewart, D. Price and P. Wong, all of Hopkins.
On the Web: http://www.pnas.org

What's bugging locusts? It could be they're hungry -- for each other

by Kitta MacPherson · Posted May 8, 2008; 12:17 p.m.

Since ancient times, locust plagues have been viewed as one of the most spectacular events in nature. In seemingly spontaneous fashion, as many as 10 billion critters can suddenly swarm the air and carpet the ground, blazing destructive paths that bring starvation and economic ruin.

What makes them do it?

A team of scientists led by Iain Couzin of Princeton University and including colleagues at the University of Oxford and the University of Sydney believes it may finally have an answer to this enduring mystery.

"Cannibalism," said Couzin, an assistant professor of ecology and evolutionary biology at Princeton.

Writing in the May 8 online edition of Current Biology, Couzin and colleagues say that the collective motion of locusts is driven by "cannibalistic interactions."

"Cannibalism is rife within marching bands of locusts," said Couzin. Desert locusts usually feed on vegetation, but individual locusts have been observed to feed on other live locusts or cadavers. This behavior and its effect upon the group, however, have not previously been studied.

"No one knew until now that cannibalistic interactions are directly responsible for the collective motion exhibited by these bands," added Couzin, whose graduate student, Sepideh Bazazi, is the lead author on the paper.

In zoology, cannibalism is defined as occurring when any species consumes members of its own kind.

Young locusts are pressed to eat others when the food supply necessary for supporting the population starts to dwindle. Starved for essential nutrients such as protein and salt, young locust "nymphs" will nip at each other. Those under siege react by running from the aggressors. Others get jittery and simply seek to put space between them and any locust approaching from behind. That's how one aggressive interaction can lead to another and collectively start a vast migration, Couzin said.

And the activity intensifies, as the biting and ominous approach of others increases both the propensity to move and the forward momentum of individual locusts.

The researchers reached their conclusion by studying immature, flightless locusts. They developed computerized motion analysis to automatically track the insects marching in an enclosed arena.

In nature, Couzin said, these locust nymphs can gather in large mobile groups called bands. They can stretch over tens of miles, devouring vegetation as they march. They inevitably precede the flying swarms of adult locusts.

"Once they take flight, locust control is extremely expensive and ineffective," Couzin said. "So understanding when, where and why the bands of juvenile locusts form is crucial for controlling locust populations."

Through history, locusts have invaded up to one-fifth of the Earth's surface, he said. They have contributed to major humanitarian crises in areas such as Darfur and Niger.

Besides having practical applications, understanding the movement of locusts also is part of a growing inquiry by scientists into an area known as group dynamics. With locusts, researchers have been seeking to understand how the group seems to move with the synchronized perfection of the Rockettes when there is no centralized leader and individuals can barely see beyond a few neighbors on either side.

Animal groups such as flocks of birds, schools of fish and swarms of insects frequently exhibit such complex and coordinated collective motion and present a great opportunity to understand how local interactions can lead to vast collective behavior, the scientists said.

The research was supported by Princeton University, the Royal Society of London, the Engineering and Physical Sciences Research Council, and the Australian Research Council.

Cane Use May Reduce Risk of Knee Osteoarthritis Progression

Arthritis Care & Research Research News Alert Wiley-Blackwell May 07, 2008

A common, incurable joint disease, osteoarthritis (OA) is the leading cause of disability in elderly people. While nearly any joint can be affected, OA most often strikes the knee, particularly the inner aspect of the tibiofemoral joint. One source of stress on this vulnerable joint compartment is the knee adduction moment, an indication of weight placement while walking. A 20 percent increase in the peak knee adduction moment is associated with a 6-fold or greater increase in the risk of knee OA progression over 6 years. To reduce knee load, pain and damage in knee OA patients, physicians often prescribe two inexpensive interventions: footwear and cane use. While these simple strategies have the potential to alter the knee adduction moment, there is little research attesting to their specific benefits for knee OA sufferers.

To assess the immediate effects of walking shoes and a walking cane on the peak knee adduction moment in people with knee OA, researchers at the University of Melbourne turned to 3-dimensional (3-D) gait analysis. Their findings, featured in the May 2008 issue of Arthritis Care & Research, strongly support using a cane on a regular basis to reduce the load borne across the knee, while underscoring the urgent need for studies into which aspects of shoe design best support the treatment of knee OA patients.

Led by Dr. Rana S. Hinman, the team recruited 40 volunteers—16 men and 24 women—from the Victoria, Australia, community who met the clinical and radiographic criteria for knee OA. All had medial tibiofemoral osteophytes, as well as knee OA symptoms such as persistent knee pain and loss of physical function. None had a history of joint replacement. The group’s mean body mass index was 29.6 and mean age was 65 years.

Each subject underwent 3-D gait analysis, focusing on the knee most affected by OA, using a state-of-the-art Vicon 6-camera motion analysis system. Embedded in the test area walkway, and unknown to participants, two force plates captured ground impact. Reflective markers, strategically placed on the pelvis, thigh, knee joint, and foot, captured limb movement.

All participants were tested first in bare feet, followed immediately by testing in their own shoes—a comfortable pair typically used for walking. 20 of the participants were further tested wearing their own shoes and using a cane in the opposite hand to the study knee, after a brief instruction in ideal cane use by a

physiotherapist. Data from 5 successful trials were collected for each test. A mean score was used to calculate changes in gait parameters and determine the peak knee adduction moment.

Overall, the peak knee adduction moment when walking in shoes was significantly higher—7.4 percent—than when walking barefoot. The effect of footwear, however, varied considerably among individuals. While most demonstrated an increased knee adduction moment while wearing shoes, 6 of the 40 subjects actually demonstrated a beneficial decrease. The use of a cane resulted in a striking 10 percent average decrease in the knee adduction moment. What's more, a quarter of the participants demonstrated a reduction of more than 20 percent. While individuals tended to walk more slowly with the cane than unaided, they exhibited greater stride length and improved pelvis control, alleviating the destructive load on the affected knee.

Though canes are widely recommended to knee OA patients, this study validates their therapeutic value, at least in the short-term. "Further studies are required to establish whether knee loading remains lower with ongoing use of a cane," notes Dr. Hinman, "and whether the reductions in loading translate to a reduced risk of disease progression." Additional studies should also focus on men with knee OA, since 90 percent of the participants in this cane trial were women, and examine changes in knee pain, an issue which the team did not address.

On the other critical matter of footwear, Dr. Hinman admits lack of a clear explanation for why wearing shoes increased the peak knee adduction moment. Heel height, sole thickness, and arch supports may all play a contributing role. "Because it is potentially dangerous as well as impractical to advise patients with knee OA to walk about in bare feet, further research is needed to determine which types of shoes least increase the knee adduction moment or, ideally, reduce it," Dr. Hinman observes. "The shoe type optimal for knee OA with regard to its effects on symptoms and disease progression must be determined."

Article: "Reducing Joint Loading in Medial Knee Osteoarthritis: Shoes and Canes," Georgina Kemp, Kay M. Crossley, Tim V. Wrigley, Ben R. Metcalf, and Rana S. Hinman, Arthritis & Rheumatism (Arthritis Care & Research) , May 15, 2008; 59:5, pp. 609-614.

Early whales got the bends

* 18:08 08 May 2008
* NewScientist.com news service
*** Ewen Callaway**

Ancient whales were not master divers like their modern descendents. Biologists have discovered signs of decompression syndrome – the bends – in several different whale fossils, a finding that could revise the evolutionary history of deep diving.

A team of paleobiologists surveyed hundreds of modern and ancient whale skeletons for decompression syndrome, which occurs when quick pressure changes force air or fat bubbles out of blood vessels.

Such damage would have been common when whales first began plunging into the depths of the ocean, says Brian Beatty, of New York College of Osteopathic Medicine in Old Westbury, US, who led the study. However, whales eventually evolved to cope with frequent visits to their new world.

"Playing around in the shallows with Flipper is one thing," he says. "But going out in the open ocean and diving hundreds and thousand of meters to go and get a fish or a squid, is like going up in space in terms of changes in pressure."

Dive tactics

Scientists classify whales into two groups, both intrepid explorers of the deep sea.

Baleens, such as the gargantuan blue whale, take huge gulps of sea water, and then filter out their meals. While toothed whales like orcas and sperm whales prey on sharks and giant squid in the ocean's bowels. The two lineages split apart roughly 45 million years ago.

Modern whales of both branches have evolved exquisite adaptations to fight the bends. Some exhale before they dive to clear their lungs of nitrogen gas that could form bubbles, and many whales allow ample time between dives.

Some researchers have suggested that military sonar can startle whales into changing their diving behaviour, causing decompression syndrome.

To determine when the anti-bends adaptations first arose, Beatty and colleague Bruce Rothschild, of University of Kansas Natural History Museum in Lawrence, examined samples of ancient and modern whale vertebrae.

Minor damage

When gas or fat bubbles form in the blood vessels that feed bone cells, the vessels can burst and seal off the oxygen supply to the cells, resulting in tiny lesions that can be detected by X-ray.

"It's a measure of small regular damage and not necessarily something traumatic," Beatty says.

None of the 331 modern whale vertebrae showed signs of decompression syndrome, while a handful of the thousand ancient whale bones contained such marks.

Beatty views the damage as flirtations with the deep ocean, before more modern whales overcame decompression syndrome.

But baleen and toothed whales may have evolved such changes independently. Signs of decompression were found only in very ancient specimens of toothed whales, while more recent baleen whale fossils showed damage, suggesting tha**t baleen whales only evolved their defences much later.**

Tagging evidence

"Maybe baleen whales and toothed whales independently arrived at the same conclusion – that going out into the open water and going deep was a good idea," Beatty says.

Most researchers have assumed that the common ancestor of toothed and baleen whales was a deep diver.

"They have come up with quite a surprising story," says Erich Fitzgerald, a palaeontologist at Museum Victoria, in Melbourne, Australia.

Beatty's hypothesis is in accord with "our long-standing understanding of the different diving habits between baleen and toothed whales", says Nick Pyenson, a paleontologist at the University of California, Berkeley, US.

Tagging modern whales as they dive will help researchers understand how their ancestors evolved to cope, Pyenson adds. "As our sampling of living species gets better, these data will better inform our expectations of what to find in the fossil record," he says. *Journal reference: Naturwissenschaften (DOI: 10.1007/s00114-008-0385-9)*

Shift From Savannah to Sahara Was Gradual, Research Suggests

By KENNETH CHANG

Six thousand years ago, northern Africa was a place of trees, grasslands, lakes and people. Today, it is the Sahara - a desolate area larger area than Australia.

Lake Yoa, in northeastern Chad, has remained a lake through the millennia and is still a lake today, surrounded by hot desert. Although little rain falls, Lake Yoa's water is replenished from an underground aquifer.

By analyzing thousands of layers sediment in a core drilled from the bottom of this lake, an international team of scientists has reconstructed the region's climate as the savannah changed to Sahara.

In Friday's issue of the journal Science, the researchers, led by Stefan Kröpelin, a geologist with the Institute of Prehistoric Archaeology at the University of Cologne in Germany, report that the climate transition occurred gradually. In particular, the changing types of pollen that fell on the water and drifted to the bottom tell a story of how the surrounding terrain shifted from trees to shrubs to grasses to sand - "where today you don't find a single piece of grass," Dr. Kröpelin said.

The findings run counter to a prevailing view that the change happened abruptly, within a few centuries, about 5,500 years ago, marking the end of the "African Humid Period" when monsoon rains poured down on the region. That view arises from ocean sediment cores drilled off the coast of Africa, to the west of Mauritania. In 2000, analysis of the cores by researchers led by Peter B. deMenocal of Columbia University's Lamont-Doherty Earth Observatory showed a sudden rise in the dust blown off Africa at that time.

Dr. Kröpelin did not dispute the ocean core data, but said it had been "overinterpreted."

Data about what was happening on land is sparse, because sands blow around and do not preserve a clear geological record the way lake sediments do. But at Lake Yoa, the water that filled underground aquifers during the humid period, which began 14,800 years ago, is still flowing out into the 80-foot-deep lake. The groundwater is enough to offset the six meters of water that evaporates out of the lake every year, Dr. Kröpelin said. Only a few millimeters of rain fall a year.

Dr. Kröpelin said he hoped to return to Lake Yoa next year to drill a deeper core that could trace the climate history back 12,000 years.

Dr. deMenocal praised Dr. Kröpelin's research. "I think it's a very good body of work," he said. "It's really the only thing of its kind from the arid interior." But he wondered, he said, whether the pollen might have come from the area just around immediately surrounding the lake and not the larger Sahara.

"On the face of it, it's puzzling," said Jonathan A. Holmes, director of the Environmental Change Research Center at University College London in England. Dr. Holmes said both sets of research had been carefully done, and the challenge will be to put together a more complex history of the Sahara's climate.

"I don't think either record is somehow wrong," said Dr. Holmes, who wrote a commentary accompanying the article in Science. "I think what they are representing are slightly different things."

Dr. Holmes said one possibility was that the offshore dust might reflect a drop in water levels around Lake Chad, revealing more dust-producing soil, rather than a large-scale change in climate.

However fast the drying occurred, it pushed people out of north-central Africa, Dr. deMenocal said, and that climatically forced migrations might have led to the rise of the pharaohs and Egyptian civilization.

Researchers uncover mechanism of action of antibiotic able to reduce neuronal cell death in brain

Research Highlights:

**** Mechanism of action of compound found to induce neurotransmitter activity in brain cells***

**** The findings may lead researchers to develop potential novel therapies to treat Alzheimer's disease, amyotrophic lateral sclerosis, Huntington's disease, epilepsy, stroke/ischemia, dementia and malignant gliomas***

RICHMOND, Va. (May 9, 2008) – Virginia Commonwealth University researchers have discovered how an antibiotic works to modulate the activity of a neurotransmitter that regulates brain functions, which eventually could lead to therapies to treat Alzheimer's disease, Huntington's disease, epilepsy, stroke, dementia and malignant gliomas.

Neurodegenerative diseases are caused by the deterioration of neurons in the brain and spine resulting in problems related to either movement or memory. For most patients, it may be months or years before symptoms are evident because a large number of neurons die or stop functioning over a period of time. Currently, there are few treatment options for stopping this degeneration, and those currently being evaluated have shown minimal or no beneficial activity.

Paul B. Fisher, M.Ph., Ph.D., a professor and interim chair of the Department of Human and Molecular Genetics, and director of the VCU Institute of Molecular Medicine, in the VCU School of Medicine, and colleagues recently reported on the mechanism of action of ceftriaxone, a third-generation antibiotic with neuroprotective properties, in glutamate transport. The findings, published in the May 9 issue of the Journal of Biological Chemistry, suggest that this antibiotic or a similar drug may serve as a potential therapy against neurodegenerative disease caused by glutamate toxicity.

Glutamate is an amino acid that is important in nerve transmission and the synapse - the region that connects one neuron to another in the brain. When an excess of glutamate collects in the synapse, the result is glutamate toxicity or excitotoxicity. Ultimately, if glutamate is not cleared out of the synapse, neurons become damaged and die by a process called excitotoxicity. In previous studies, Fisher's team identified ceftriaxone as a potent physiological stimulator of glutamate transport both in cell culture and in animal models.

"Glutamate excitotoxicity is a very important and fundamental process in neurodegeneration," said Fisher. "Finding molecules, such as ceftriaxone, that may correct this problem can lead to preservation and increased survival of neurons in the brain and it may have direct implications in the therapy of many neurodegenerative diseases, such as in Alzheimer's disease, stroke, ALS and epilepsy."

In this study, Fisher and his colleagues were interested in identifying how the promoter region of the EAAT2 gene controlled the expression of glutamate in a group of brain cells called astrocytes. Using molecular biological approaches, the team examined all the regions and sequences in the promoter region and systematically eliminated them to then define which region was necessary to respond to ceftriaxone.

According to Fisher, this led the team to a critical transcription factor called nuclear factor kappaB, NF-kappaB, which regulates many functions in the brain and other parts of the body. This is a central molecule involved in regulation of genes controlling cell growth and survival. Once they identified critical regions in the EAAT2 promoter that might regulate activity, they found that alteration of one specific NF-kappaB site by mutation in the promoter was responsible for up-regulation of EAAT2 expression and consequently glutamate transport by ceftriaxone.

"This work not only has implications for the field of neurodegeneration and neurobiology, but may also help us more clearly understand brain cancer, including malignant glioma, an invariably fatal tumor, and how it impacts brain function," said Fisher, who is the first incumbent of the Thelma Newmeyer Corman Endowed Chair in Cancer Research and researcher with the VCU Massey Cancer Center.

Future studies will examine ways to modify the structure of ceftriaxone through medicinal chemistry to create molecules that are pharmacologically improved. Currently, ceftriaxone needs to be injected, which is not the ideal for patient therapy, however, the development of an oral form would be a more preferential way to treat patients.

This work was supported by a program project grant from the National Institutes of Health, Neurology and Stroke, and the Samuel Waxman Cancer Research Foundation.

Fisher worked with a team that included: Seok-Geun Lee, Ph.D., lead author of the paper and assistant professor, and Zaozhong Su, Ph.D., associate professor, both in the VCU Department of Human and Molecular Genetics; Devanand Sarkar, MBBS, Ph.D., assistant professor and Harrison Endowed Scholar in Cancer Research at the VCU Massey Cancer Center and Department of Human and Molecular Genetics; and David J. Volsky, Ph.D., professor, St. Luke's Roosevelt Hospital Center, Columbia University in New York.

Treatment hope for killer pregnancy condition

*** 18:00 11 May 2008**
*** NewScientist.com news service**
*** Ewen Callaway**

Pre-eclampsia – a condition that strikes 5% of pregnancies and kills over 60,000 women and hundreds of thousands of babies every year – was once so mysterious that doctors dubbed it the "disease of theories". Now, a team of researchers says that a single gene could explain most cases.

If their work in mice pans out for human childbirth, pre-eclampsia could be diagnosed earlier and even prevented by giving expecting mums a naturally occurring breakdown product, says Raghu Kalluri, a researcher at Beth Israel Deaconess Medical Center in Boston, who led the study.

His team showed that mice without a gene that makes a compound broken-down from oestrogen called 2-methoxyestradiol (2-ME) develop many of the signs of pre-eclampsia, including pre-term birth, high blood pressure and problems forming blood vessels.

"The difference sets the ball rolling and a million other things downstream go wrong," Kalluri says.

Medical mystery

A major cause of premature deliveries, pre-eclampsia strikes suddenly and often severely. After 20 weeks or longer, women develop high blood pressure and high levels of protein in their urine – a sign of kidney failure. Currently the only way to treat the disease is to deliver the child – often weeks early.

Previous studies pointed to abnormal blood vessel growth that starves a developing placenta of oxygen, but researchers had little clue what set off those changes.

"Nobody really knows what cause pre-eclampsia," says Kalluri "It has been one of the biggest mysteries in medicine."

Kalluri's team noticed that mice missing a gene that makes 2-ME had one of the hallmarks of pre-eclampsia – protein in their urine. The mutant mice also showed elevated levels of two blood vessel proteins that have turned up in pre-eclampsia patients.

Giving the pregnant rodents an extra dose of 2-ME reversed many of the symptoms.

His team also found that 13 women who had suffered from pre-eclampsia had slightly lower levels of 2-ME in their blood before birth than women who went through a normal pregnancy.

'Always present'

If researchers verify 2-ME's role in pre-eclampsia in humans, the metabolite could help predict and treat the disease, Kalluri says.

"The wonderful thing about this metabolite is that it is always present in high levels" during pregnancy, he says. "It's not like we are giving anything that the baby and the mother are not exposed to."

To strengthen the case, Kalluri's team plans to study pregnant women with mutations that hamper cells from making 2-ME.

"In some patients with pre-eclampsia, this may well be important," says James Roberts, a researcher at the University of Pittsburgh. However, one gene alone is unlikely to cause all of the cases, he says.

Treatments may be also premature, says Richard Levine, an epidemiologist and pre-eclampsia expert at the National Institute of Child Health and Human Development in Bethesda, Maryland.

"It is a provocative and potentially important paper – if it is confirmed by other labs," he says.

Journal reference: Nature (DOI: 10.1038/nature06951)

Why Superstition Is Logical

By John Tierney

Are you superstitious? I like to think I'm not, but I'm reconsidering after seeing the research of Jane Risen and the other psychologists mentioned in my Findings column. Dr. Risen, a professor at the University of Chicago, knows better than anyone how irrational superstition is. But consider what she does on plane trips.

"I don't turn my watch to the new time zone until my plane lands," she told me. "I know that it has nothing to do with whether or not we get to the location without difficulties and on time, but I just feel like it's presumptuous to assume that everything will work smoothly - and that by engaging in that presumptuous behavior it somehow makes it more likely that things won't go smoothly."

Her reluctance to tempt fate is irrational in one way, but there's also a certain logic to it, as Dr. Risen and a colleague, Thomas Gilovich of Cornell, found by monitoring the reaction times of college students who read a series of stories on a computer and then had to indicate as quickly as possible whether a one-sentence ending made sense or not. Some students, for instance, read a story about a woman named Julie who heard a forecast of rain and carried an umbrella; other students read that she didn't carry an umbrella. Then both groups of students would be asked if this conclusion made sense:

"As Julie is walking to class later that afternoon, it suddenly starts to rain."

The correct answer for either group was "yes" - rain was a logical outcome considering that it had been forecast. But the students who read about Julie not bringing her umbrella were quicker than the other group to recognize that it made sense. Dr. Risen and Dr. Gilovich argue that an action that tempts fate reflexively calls a negative outcome to mind, which, in turn, makes it seem especially likely to occur.

How does this reflexive thinking work? The researchers did another experiment in which a subliminal message - the word "rain" - was flashed on the screen just before the students read the final sentence of the story. This time there wasn't a difference in reaction time: The students who read about Julie carrying an umbrella were just as quick to realize that a rainy ending made sense as were the students who read about her not carrying the umbrella. The subliminal priming, just like a story about tempting fate, made the subjects reflexively think that a rainy outcome was more likely.

This reflexive thinking may be irrational, but there's a logic in the way the brain makes this instant calculation of probability. An outcome that's instantly accessible - rain - seems more likely than an outcome that isn't accessible. And negative images tend to be more vivid and accessible. We're more likely to remember the time we got drenched than the many days we stayed dry. While cultural conditioning may play some role - we've been told the old adage about not carrying an umbrella causing rain - Dr. Risen and Dr. Gilovich say that their series of experiments shows this reluctance to tempt fate isn't just the result of hearing about superstitions:

> Although some societies and cultures stress the role of supernatural agents more than others, we want to emphasize that the beliefs we have investigated are by no means absent in populations in which notions of fate and the intervention of supernatural agents are not well articulated. The present data, involving the responses of Western-educated college students, make that clear. People in different cultures, regardless of their explicit beliefs, do not much differ in the tendency for negative outcomes to jump to mind and in the use of accessibility as a cue for judging likelihood. Instead, cultures are more likely to differ in their access to and reliance on abstract rules that over-ride such automatic associations

Thus, even those of who don't think we're superstitious have a reflexive fear of tempting fate. In other experiments, Dr. Risen and Dr. Gilovich found that students think that not doing their reading makes them more likely to be called on in class; that trading away a lottery ticket makes that ticket more likely to win; that an applicant to Stanford graduate school is less likely to get in if he goes around wearing a Stanford T-shirt. The researchers conclude:

> The studies presented here document a widespread belief that it is bad luck to tempt fate, even among those who would deny the existence of fate. So what happens when people believe things they know are false? They do their class reading, bring their umbrellas, hold onto their lottery tickets, and (try to) avoid boasting or presuming anything too soon. And when they don't follow their intuition, they think about how they might be punished. All the while, they shake their heads and roll their eyes, knowing that their behavior and worries are unwarranted.

Is that what you do? Do you, like Dr. Risen, refrain from resetting your watch until you land safely? So far I've always reset my watch as soon as I get on a plane, but now that Dr. Risen has drawn attention to it, maybe I'll be more reluctant to tempt the gods on my next trip. Are there any other ways that you avoid tempting fate? Here's your chance to confess.