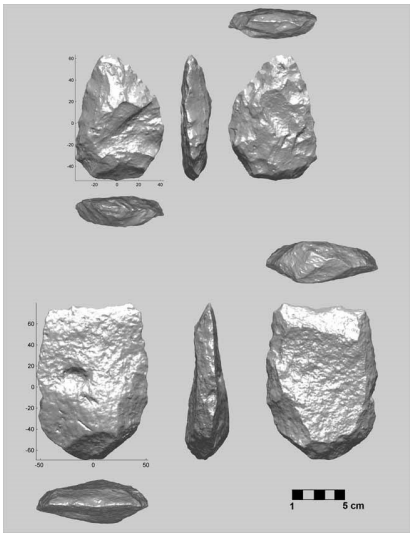
Human Ancestors Were Homemakers

By Clara Moskowitz, LiveScience Staff Writer



In a stone-age version of "Iron Chef," early humans were dividing their living spaces into kitchens and work areas much earlier than previously thought, a new study found.

So rather than cooking and eating in the same area where they snoozed, early humans demarcated such living quarters.

Archaeologists discovered evidence of this coordinated living at a hominid site at Gesher Benot Ya'aqov, Israel from about 800,000 years ago. Scientists aren't sure exactly who lived there, but it predates the appearance of modern humans, so it was likely a human ancestor such as Homo erectus.

Yet this advanced organizational skill was thought to be a marker of modern human intelligence. Before now, the only concrete proof for divided living spaces dated back to only 100,000 years ago.

"Seeing this at such an early site was surprising," said archaeozoologist Rivka Rabinovich of the Hebrew University of Jerusalem. "This means there was some ability or some need or requirement of organization."

***A basalt handaxe (top) and basalt cleaver (bottom), found at an archaeological site in Israel demonstrating the earliest known living area organization*. Credit: Leore Grosman, Computerized Archaeology Laboratory, The Hebrew University**

Rabinovich and her colleagues, led by Nira Alperson-Afil, also of the University of Jerusalem, published their findings in the Dec. 18 issue of the journal Science.

The researchers excavated the remains of an early human encampment on the shores of an ancient lake. They found used pieces of flint, rock tools, crab shells, fish bones, and bits of fruits, seeds, nuts, bark and wood.

The excavation proved that the hominids living there were hunting not just land mammals, but sea creatures like fish, crabs and turtles. And these remains were not scattered randomly, but instead concentrated in certain areas. The food remains and stone-tool bits were found in one area, while the flint scraps (likely from cooking tools) were clustered in another region.

The scientists think the camp's hearth was located in the southeast area of the site, and that food-making and eating took place mostly near there. In addition, most of the stone-tool remains - bits of basalt and limestone rocks that had been shaped into usable instruments - were also clustered near the hearth.

In contrast, the northwestern region held most of the flint remains and evidence of fish preparation. The archaeologists think this could have been a working area for the early human inhabitants.

"The designation of different areas for different activities indicates a formalized conceptualization of living space, often considered to reflect sophisticated cognition and thought to be unique to Homo sapiens," the researchers wrote in the Science paper. This skill also indicates the inhabitants had some kind of social organization and coordination between individuals.

"It clearly shows that they're much more advanced than we previously thought," co-author Irit Zohar of the University of Haifa told LiveScience.

Stone Age Pantry: Archaeologist Unearths Earliest Evidence of Modern Humans Using Wild Grains and Tubers for Food

ScienceDaily - The consumption of wild cereals among prehistoric hunters and gatherers appears to be far more ancient than previously thought, according to a University of Calgary archaeologist who has found the oldest example of extensive reliance on cereal and root staples in the diet of early Homo sapiens more than 100,000 years ago.

Julio Mercader, holder of the Canada Research Chair in Tropical Archaeology in the U of C's Department of Archaeology, recovered dozens of stone tools from a deep cave in Mozambique showing that wild sorghum, the ancestor of the chief cereal consumed today in sub-Saharan Africa for flours, breads, porridges and alcoholic beverages, was in Homo sapiens' pantry along with the African wine palm, the false banana, pigeon peas, wild oranges and the African "potato." This is the earliest direct evidence of humans using pre-domesticated cereals anywhere in the world. Mercader's findings are published in the December 18 issue of the research journal Science.

***These are Middle Stone Age food processing tools recovered from the Ngalue cave site, Mozambique*. (Credit: Grady Semmens, University of Calgary)**

"This broadens the timeline for the use of grass seeds by our species, and is proof of an expanded and sophisticated diet much earlier than we believed," Mercader said. "This happened during the Middle Stone Age, a time when the collecting of wild grains has conventionally been perceived as an irrelevant activity and not as important as that of roots, fruits and nuts."

In 2007, Mercader and colleagues from Mozambique's University of Eduardo Mondlane excavated a limestone cave near Lake Niassa that was used intermittently by ancient foragers over the course of more than 60,000 years. Deep in this cave, they uncovered dozens of stone tools, animal bones and plant remains indicative of prehistoric dietary practices. The discovery of several thousand starch grains on the excavated plant grinders and scrapers showed that wild sorghum was being brought to the cave and processed systematically.

"It has been hypothesized that starch use represents a critical step in human evolution by improving the quality of the diet in the African savannas and woodlands where the modern human line first evolved. This could be considered one of the earliest examples of this dietary transformation," Mercader said. "The inclusion of cereals in our diet is considered an important step in human evolution because of the technical complexity and the culinary manipulation that are required to turn grains into staples."

Mercader said the evidence is on par with grass seed use by hunter-gatherers in many parts of the world during the closing stages of the last Ice Age, approximately 12,000 years ago. In this case, the trend dates back to the beginnings of the Ice Age, some 90,000 years earlier.

Mercader's work was supported by the Canada Research Chairs program, Canada Foundation for Innovation, the Social Sciences and Humanities Research Council of Canada, the U of C's Faculty of Social Science and the National Geographic Society. ***Journal Reference:***

1. Julio Mercader et al. Mozambican grass seed consumption during the Middle Stone Age. Science, December 18, 2009

Meddling in mosquitoes' sex lives could help stop the spread of malaria, says study

Stopping male mosquitoes from sealing their sperm inside females with a 'mating plug' could prevent mosquitoes from reproducing, and offer a potential new way to combat malaria, say scientists publishing new results in PLoS Biology on 22 December.

The new study focuses on the species of mosquito primarily responsible for the transmission of malaria in Africa, known as Anopheles gambiae. These mosquitoes mate only once in their lifetime, which means that disrupting the reproductive process offers a good way of dramatically reducing populations of them in Africa.

When they mate, the male transfers sperm to the female and then afterwards transfers a coagulated mass of proteins and seminal fluids known as a mating plug. This plug is not found in any other species of mosquito and until now, very little has been known about what it is for and the role it plays in An. gambiae reproduction.

The authors of today's study, led by Imperial College London, have shown for the first time that the mating plug is essential for ensuring that sperm is correctly retained in the female's sperm storage organ, from where she can fertilise eggs over the course of her lifetime. Without the mating plug, sperm is not stored correctly, and fertilisation cannot occur.

In Imperial's mosquito labs, the scientists showed it was possible to prevent the formation of the plug in males, and that this stopped them successfully reproducing with females. Lead author Dr Flaminia Catteruccia, from Imperial's Department of Life Sciences, explains the significance of their discovery:

"We have shown that the male mating plug is not a simple barrier to insemination from rival males, as has been previously suggested. Instead, we discovered that the plug plays an important role in allowing the female to successfully store sperm in the correct way inside her, and as such is vital for successful reproduction.

"Removing or interfering with the mating plug renders copulation ineffective. This discovery could be used to develop new ways of controlling populations of An. gambiae mosquitoes, to limit the spread of malaria."

Dr Catteruccia and her colleagues analysed the composition of the protein-rich mating plug and discovered that it is formed when an enzyme called Transglutaminase interacts with other proteins in the male mosquito's seminal fluid. This interaction causes the seminal fluids to coagulate into a gelatinous solid mass.

When the research team knocked out this enzyme in male mosquitoes in the lab, the fluids failed to coagulate and form the plug. Furthermore, when these males, lacking the key protein and therefore the plug, mated with females, reproduction was not successful.

Dr Catteruccia concludes: "If in the future we can develop an inhibitor that prevents the coagulating enzyme doing its job inside male An. gambiae mosquitoes in such a way that can be deployed easily in the field – for example in the form of a spray as it is done with insecticides – then we could effectively induce sterility in female mosquitoes in the wild. This could provide a new way of limiting the population of this species of mosquito, and could be one more weapon in the arsenal against malaria."

The study was carried out in collaboration with Universita' degli Studi di Perugia in Italy, and was funded by the Medical Research Council and the European Union.

Poisonous prehistoric 'raptor' discovered by research team from Kansas and China

This is the first report of venom in the lineage that leads to modern birds

LAWRENCE, Kan. - A group of University of Kansas researchers working with Chinese colleagues have discovered a venomous, birdlike raptor that thrived some 128 million years ago in China. This is the first report of venom in the lineage that leads to modern birds.

"This thing is a venomous bird for all intents and purposes," said Larry Martin, KU professor and curator of vertebrate paleontology at the Natural History Museum and Biodiversity Institute. "It was a real shock to us and we made a special trip to China to work on this."

The KU-China team's findings will be published in the early edition of the Proceedings of the National Academy of Sciences during the week of Dec. 21. "We think it's going to make a big splash," said Martin.

This image of fossilized Sinornithosaurus shows the raptor's long, grooved fangs. It lived in prehistoric forests of northeastern China that were filled with a diverse assemblage of animals including other primitive birds and dinosaurs.

David A. Burnham, PhD University of Kansas Biodiversity Institute

The article's authors are Enpu Gong, geology department at Northeastern University in Shenyang, China, and researchers Martin, David Burnham and Amanda Falk at the KU Natural History Museum and Biodiversity Institute. The dromaeosaur or raptor, Sinornithosaurus (Chinese-bird-lizard), is a close relative to Velociraptor. It lived in prehistoric forests of northeastern China that were filled with a diverse assemblage of animals including other primitive birds and dinosaurs.

"This is an animal about the size of a turkey," said Martin. "It's a specialized predator of small dinosaurs and birds. It was almost certainly feathered. It's a very close relative of the four-winged glider called Microraptor."

The venom most likely sent the victim into rapid shock, shrinking the odds of retaliation, escape or piracy from other predators while the raptor manipulated its prey.

"You wouldn't have seen it coming," said Burnham. "It would have swooped down behind you from a low-hanging tree branch and attacked from the back. It wanted to get its jaws around you. Once the teeth were embedded in your skin the venom could seep into the wound. The prey would rapidly go into shock, but it would still be living, and it might have seen itself being slowly devoured by this raptor."

The genus had special depressions on the side of its face thought by the investigators to have housed a poison gland, connected by a long lateral depression above the tooth row that delivered venom to a series of long, grooved teeth on the upper jaw. This arrangement is similar to the venom-delivery system in modern rear-fanged snakes and lizards. The researchers believe it to be specialized for predation on birds.

"When we were looking at Sinornithosaurus, we realized that its teeth were unusual, and then we began to look at the whole structure of the teeth and jaw, and at that point, we realized it was similar to modern-day snakes," Martin said.

Sinornithosaurus is represented by at least two species. These specimens have features consistent with a primitive venom-delivery system. The KU-China research team said it was a low-pressure system similar to the modern Beaded lizard, Heloderma, however the prehistoric Sinornithosaurus had longer teeth to break through layers of feathers on its bird victims.

The discovery of features thought to be associated with a venom-delivery system in Sinornithosaurus stemmed from a study of the anatomy and ecology of Microraptor by the joint Chinese-KU team. They now are seeking to discover if Microraptor may have possessed a similar poison-delivery system.

Urinary tract cancer associated with Chinese herbal products containing aristolochic acid

The carcinogen aristolochic acid, which was found in many prescribed Chinese herbal products including Guan Mu Tong, is associated with an increased risk of urinary tract cancer, according to a new study published online December 21 in the Journal of the National Cancer Institute.

Many countries, such as Taiwan, have banned products containing aristolochic acid (Taiwan did in 2003), because of clinical cases of urothelial cancer in association with aristolochic acid use. However, no such associations, to the authors' knowledge, have been documented in herbal products containing aristolochic acid.

To examine this association, Jung-Der Wang, M.D., ScD, of the Institute of Occupational Medicine and Industrial Hygiene, College of Public Health, at the National Taiwan University, and colleagues conducted a population-based case–control study of Taiwanese patients newly diagnosed with urinary tract cancer from January 1, 2001, to December 31, 2002. They also looked at a random sample of the entire insured population

from January 1, 1997, to December 31, 2002. There were 4,594 case patients and 174,701 control subjects in the final analysis. The authors examined the association between having been prescribed Mu Tong, an herb that contains aristolochic acid, and urinary tract cancer using data from the National Health Insurance reimbursement database.

Having been prescribed more than 60 g of Mu Tong (possibly adulterated by Guan Mu Tong before banned), or consumption of an estimated amount of more than 150 mg of aristolochic acid was associated with an increased risk of urinary tract cancer in a dose–dependent manner. The increased risk was independent of arsenic exposure (another risk factor for urinary tract cancer).

"In addition to a ban on products that contain any amount of aristolochic acid, we also recommend continued surveillance of herbs or Chinese herbal products that might be adulterated with aristolochic acid–containing herbs," the authors write. "Finally, patients with a history of aristolochic acid nephropathy or consumption of Mu Tong or Fangchi before they were banned should be monitored regularly for urinary cancer."

Study limitations: Not all of the diagnoses were confirmed by histopathology reports. Subjects may have taken additional nephrotoxic herbs or agents that were not prescribed. Actual intakes of the prescribed herbal products recorded in the National Health Insurance reimbursement database were not validated. Smoking history was not taken into account.

Depression saps endurance of the brain's reward circuitry

MADISON - A new study at the University of Wisconsin-Madison suggests that depressed patients are unable to sustain activity in brain areas related to positive emotion.

The study challenges previous notions that individuals with depression show less brain activity in areas associated with positive emotion. Instead, the new data suggest similar initial levels of activity, but an inability to sustain them over time. The new work was reported online this week (Dec. 21) in the Proceedings of the National Academy of Sciences.

"Anhedonia, the inability to experience pleasure in things normally rewarding, is a cardinal symptom of depression," explains UW-Madison graduate student Aaron Heller, who led the project. "Scientists have generally thought that anhedonia is associated with a general reduction of activity in brain areas thought to be important for positive emotion and reward. In fact, we found that depressed patients showed normal levels of activity early on in the experiment. However, towards the end of the experiment, those levels of activity dropped off precipitously.

"Those depressed subjects who were better able to sustain activity in brain regions related to positive emotion and reward also reported higher levels of positive emotion in their everyday experience," Heller continues.

"Being able to sustain and even enhance one's own positive emotional experience is a critical component of health and well-being," notes the study's senior author, Richard Davidson, professor of psychology and psychiatry and director of both the UW-Madison Center for Investigating Healthy Minds, and the Waisman Laboratory for Brain Imaging and Behavior. "These findings may lead to therapeutic interventions that enable depressed individuals to better sustain positive emotion in their daily lives."

During the study, 27 depressed patients and 19 control participants were presented with visual images intended to evoke either a positive or a negative emotional response. While viewing these images, participants were instructed to use cognitive strategies to increase, decrease or maintain their emotional responses to the images by imagining themselves in similar scenarios. Heller and colleagues used functional magnetic resonance imaging (fMRI) to measure brain activity in the target areas. The scientists examined the extent to which activation in the brain's reward centers to positive pictures was sustained over time.

The work was funded by grants from the National Institute of Mental Health, Wyeth-Ayerst Pharmaceuticals, Fetzer Institute and Impact Foundation, and by gifts from the John W. Kluge Foundation, Bryant Wangard, Ralph Robinson and Keith and Arlene Bronstein.

Compound found to safely counter deadly bird flu

MADISON - The specter of a drug-resistant form of the deadly H5N1 avian influenza is a nightmare to keep public health officials awake at night.

Now, however, a study published this week (Dec. 21) in the Proceedings of the National Academy of Sciences (PNAS) suggests that a new compound, one on the threshold of final testing in humans, may be more potent and safer for treating "bird flu" than the antiviral drug best known by the trade name Tamiflu.

Known as T-705, the compound even works several days after infection, according to Yoshihiro Kawaoka, a University of Wisconsin-Madison virologist and the senior author of the new PNAS study.

"H5N1 virus is so pathogenic even Tamiflu doesn't protect all the infected animals," explains Kawaoka, a professor of pathobiological sciences at the UW-Madison School of Veterinary Medicine and a world authority on influenza. "This compound works much better, even three days after infection."

The Wisconsin research was conducted in mice and demonstrated that the compound was effective and safe against H5N1 virus, the highly pathogenic bird flu virus, which some scientists fear could spark a global epidemic of deadly influenza. The compound is also effective against seasonal flu and more worrisome varieties such as the H1N1 virus, and has already been tested against circulating seasonal influenza in humans in Japan where it is on the brink of Phase III clinical trials in people.

The prospect of a new front-line drug for influenza, in particular highly pathogenic strains such as H5N1 virus, is important as there are few drugs capable of checking the shifty influenza virus. The new study showing the efficacy and safety of T-705 assumes more importance as instances of Tamiflu-resistant strains of H5N1 virus have recently been reported, raising concerns about the ability of current antiviral drugs to blunt a pandemic of deadly avian flu.

Antiviral drugs are viewed as a readily available first line of defense against pandemic flu and are especially important for protecting health workers and others during an outbreak of disease. Vaccines, which utilize inactivated or weakened viruses to confer immunity, are the primary line of defense for influenza, but require months to formulate and mass-produce.

Aside from its safety and basic efficacy, another key trait of the T-705 compound is the fact that it is effective even after an infection is acquired. Bird flu, notes Kawaoka, is almost always diagnosed in the hospital after symptoms of the disease manifest themselves: "This compound has a chance to save people who have gone into the disease course," he says.

T-705 targets a critical viral molecule, polymerase, an enzyme that enables the virus to copy its genetic material, RNA. By disabling polymerase, the virus is unable to make new virus particles and maintain the chain of infection. Tamiflu, which remains an effective drug for blocking influenza virus, targets and regulates the enzyme neuraminidase, a protein found on the surface of the flu virus particle and that is essential for spreading the virus throughout the respiratory system.

"The activity of this agent is considerably higher than Tamiflu," says Kawaoka, adding, "the compound is very specific to viral polymerase. It doesn't affect host polymerase, which is important for safety and reducing side effects."

The new Wisconsin study was funded through the Program of Founding Research Centers for Emerging and Reemerging Infectious Diseases; the Japan Science and Technology Agency; the Ministry of Education, Culture, Sports, Science and Technology of Japan; and by the U.S. National Institutes of Health.

Heart transplant patients appear to have elevated risk for multiple skin cancers

Many heart transplant patients develop multiple skin cancers, with increased risk for some skin cancers among patients with other cancers and with increasing age, according to a report in the December issue of Archives of Dermatology, one of the JAMA/Archives journals.

"Solid organ transplant recipients are at increased risk for skin cancers," the authors write as background information in the article. "Incidence, tumor burden and risk factors for skin cancer are well documented in renal transplant recipients. However, these characteristics are documented to a lesser extent in heart transplant patients, who are at least twice as likely to have skin cancer compared with renal transplant recipients." Reasons for this could include the greater use of immunosuppressive medications and an older average age at the time of transplant.

Jerry D. Brewer, M.D., of Mayo Clinic, Rochester, Minn., and colleagues reviewed the records of 312 patients who had received heart transplants between 1988 and 2006. Patients had an average age of 47.4 years at the time of their transplant and information was extracted from their charts regarding overall characteristics, cancers, risk factors and death.

The patients developed a total of 1,395 skin cancers; overall, 46.4 percent of the patients had developed skin cancer during the 19 years of follow-up. This included 1,236 squamous cell carcinomas and 151 basal cell carcinomas (the non-melanoma skin cancers), five malignant melanomas and three other types.

When evaluating the tumor burden of the 312 patients, 76 (24.4 percent) had at least one squamous cell carcinoma, 24 (7.7 percent) had only one squamous cell carcinoma and 19 (6.1 percent) had 10 or more; in addition, 54 (17.3 percent) had at least one basal cell carcinoma, 23 (7.4 percent) had only one and two (0.6 percent) had 10 or more.

Patients were more likely to develop squamous cell carcinoma if they had other types of cancer after their transplant, were older or had a known cause for their heart failure. Infection with the herpes simplex virus, being older and using a medication known as mycophenolate to suppress the immune system were associated with an increased risk of basal cell carcinoma.

"Although a considerable tumor burden was found in this study, the rate of death due to skin cancer was surprisingly low. Only one patient died of skin cancer, of a melanoma," the authors write. "Health care

providers and patients at our center have been educated for more than 10 years about the risk, early detection and treatment of skin cancer, which is apparent from the low mortality rate seen in the patients of this study."

"Vigilant sun protection practices, skin cancer education, regular skin examinations and daily vitamin D supplementation are appropriate interventions in these high-risk heart transplant patients," they conclude.

(Arch Dermatol. 2009;145[12]:1391-1396. Available pre-embargo to the media at www.jamamedia.org.)

Enhanced sweet taste: This is your tongue on pot

Endocannabinoid modulation of tongue sweet taste receptors may help control feeding behavior

PHILADELPHIA - New findings from the Monell Center and Kyushu University in Japan report that endocannabinoids act directly on taste receptors on the tongue to enhance sweet taste. "Our taste cells may be more involved in regulating our appetites than we had previously known," said study author Robert Margolskee, M.D., Ph.D., a Monell molecular biologist. "Better understanding of the driving forces for eating and overeating could lead to interventions to stem the burgeoning rise in obesity and related diseases."

Endocannabinoids are substances similar to THC, the active ingredient in marijuana. Produced in the brain and body, they bind with cannabinoid receptors to help regulate appetite and many other processes involved in health and disease.

"Endocannabinoids both act in the brain to increase appetite and also modulate taste receptors on the tongue to increase the response to sweets," said study senior author Yuzo Ninomiya, Ph.D., Professor of Oral Neuroscience in the Graduate School of Dental Sciences at Kyushu University in Japan.

In the study, published online in the Proceedings of the National Academy of Sciences, the researchers conducted a series of experiments in mice to determine the behavioral, neural and cellular responses to sweet taste stimuli before and after the administration of endocannabinoids.

Sweet taste responses were enhanced by endocannabinoids in every case. The effect was specific for sweet taste, as endocannabinoids had no effect on responses to sour, salty, bitter or umami taste stimuli.

The effects were abolished when the experiments were repeated using knockout mice lacking the CB1 cannabinoid receptor. Additional studies revealed that the CB1 receptor and the T1R3 sweet taste receptor are present in the same taste cells.

Together, the experiments demonstrate that endocannabinoids selectively enhance sweet taste by acting on tongue taste cells and that the effect is mediated by the endocannabinoid receptor.

"Modulation of sweet taste responses may be an important component of the endocannabinoid system's role in regulating feeding behavior," said Margolskee. He parenthetically noted that the well-known "marijuana munchies" may depend at least in part on endocannabinoid stimulation of tongue taste cells.

Sweet taste receptors also are found in the intestine and pancreas, where they help regulate nutrient absorption, insulin secretion and energy metabolism. If endocannabinoids also modulate the responses of pancreatic and intestinal sweet receptors, the findings may open doors to the development of novel therapeutic compounds to combat metabolic diseases such as obesity and diabetes.

Also contributing to the study were Ryusuke Yoshida, Tadahiro Ohkuri, Masafumi Jyotaki, Toshiaki Yasuo, Nao Horio, Keiko Yasumatsu, Keisuke Sanematsu, Noriatsu Shigemura, Yuzo Ninomiya from Kyushu University and Tsuneyuki Yamamoto from Nagasaki International University.

The research was funded by grants from the Japan Society for the Promotion of Science and the National Institute on Deafness and Other Communication Disorders, National Institutes of Health.

Surgery recognized as effective treatment

Doha – A first-of-its-kind consensus statement by 50 medical experts from around the world has pronounced surgery to be a legitimate and effective treatment for type 2 diabetes, bringing the procedure a significant step closer to wider use and acceptance.

The report, recently published in the Annals of Surgery, illustrates the findings of the first Diabetes Surgery Summit (DSS), an international conference held at the Catholic University of Rome, Italy, where more than 50 scientific and medical experts agreed on a set of guidelines and definitions to guide the use and study of gastrointestinal surgery to treat type 2 diabetes.

"This is very good news for people in Qatar and other Gulf countries where diabetes continues to be a major health concern," says Bakr Nour, MD, professor of surgery at Weill Cornell Medical College in Qatar and vice chair of surgery at Weill Cornell Medical College in New York. "It is estimated that 15 to 20% of GCC nationals suffer from diabetes, though many may be unaware that they have it. The disease rates continue to rise both in adults and children, and prevalence among Qatari children has doubled in the past 10 years."

"While more study has been recommended, consensus about surgery as an effective treatment for select patients with type 2 diabetes means that many more patients will be considered as candidates for the

procedure," says Dr. Nour. "It could mean a dramatic improvement in the quality of life for those patients for whom lifestyle changes and less invasive therapies prove insufficient."

"The recommendations from the DSS are an opportunity to improve access to surgical options supported by sound evidence, while also preventing harm from inappropriate use of unproven procedures," says the consensus paper's lead author Dr. Francesco Rubino, director of the gastrointestinal metabolic surgery program at New York-Presbyterian Hospital/Weill Cornell Medical Center and associate professor of surgery at Weill Cornell Medical College.

The article in the Annals of Surgery summarizes the mounting body of evidence showing that bariatric surgery effectively reverses type 2 diabetes in a high proportion of morbidly obese patients, sometimes within weeks or even days, well before the patients have lost a significant amount of body weight.

Currently, bariatric surgery is only available as a treatment for severe obesity, defined as a body mass index of 35 kg/m2 or more, according to National Institutes of Health guidelines established in 1991. The consensus statement acknowledged that the cutoff is arbitrary and not supported by scientific evidence. "With an emphasis on caution and patient safety, the statement boldly advances a revolutionary concept, the legitimacy of gastrointestinal surgery as a dedicated treatment for type 2 diabetes in carefully selected patients," explains Dr. Rubino.

Based on earlier studies and on clinical experience in other countries, Dr. Rubino and his colleagues have found that removing portions of the jejunum or duodenum - the upper part of the small intestine right below the stomach - leads to spontaneous improvement or even resolution of diabetes. The same holds true when the surgeon simply inserts a tube in that part of the intestine, allowing food to pass through without coming into contact with the area. These findings suggest that when food normally passes from the stomach into the upper end of the small bowel, it triggers a cascade of hormonal reactions that cause diabetes.

"Prevention will always be the best strategy to approach the global epidemic of diabetes," says Dr. Rubino. "But gastrointestinal surgery promises to be an important addition to the treatments available, and its study may also allow us to understand the disease mechanism in depth. We can only prevent what we truly understand."

Scientists take important step toward the proverbial fountain of youth

New research in the FASEB Journal shows for the first time that reducing caloric intake, specifically in the form of glucose, extends the lifespan of human cells

Going back for a second dessert after your holiday meal might not be the best strategy for living a long, cancer-free life say researchers from the University of Alabama at Birmingham. That's because they've shown exactly how restricted calorie diets - specifically in the form of restricted glucose - help human cells live longer. This discovery, published online in The FASEB Journal (http://www.fasebj.org) could help lead to drugs and treatments that slow human aging and prevent cancer.

"Our hope is that the discovery that reduced calories extends the lifespan of normal human cells will lead to further discoveries of the causes for these effects in different cell types and facilitate the development of novel approaches to extend the lifespan of humans," said Trygve Tollefsbol, Ph.D., a researcher involved in the work from the Center for Aging and Comprehensive Cancer Center at the University of Alabama at Birmingham. "We would also hope for these studies to lead to improved prevention of cancer as well as many other age-related diseases through controlling calorie intake of specific cell types."

To make this discovery, Tollefsbol and colleagues used normal human lung cells and precancerous human lung cells that were at the beginning stages of cancer formation. Both sets of cells were grown in the laboratory and received either normal or reduced levels of glucose (sugar). As the cells grew over a period of a few weeks, the researchers monitored their ability to divide, and kept track of how many cells survived over this period.

They found that the normal cells lived longer, and many of the precancerous cells died, when given less glucose. Gene activity was also measured under these same conditions. The reduced glucose caused normal cells to have a higher activity of the gene that dictates the level of telomerase, an enzyme that extends their lifespan and lower activity of a gene (p16) that slows their growth. Epigenetic effects (effects not due to gene mutations) were found to be a major cause in changing the activity of these genes as they reacted to decreased glucose levels.

"Western science is on the cusp of developing a pharmaceutical fountain of youth" said Gerald Weissmann, M.D., Editor-in-Chief of The FASEB Journal. "This study confirms that we are on the path to persuading human cells to let us to live longer, and perhaps cancer-free, lives."

Fossil shelved for a century reworks carnivore family tree

A new look at limbs changes understanding of early carnivore locomotion

More than a hundred years after its discovery, the limbs and vertebrae of a fossil have been pulled off the shelf at the American Museum of Natural History to revise the view of early carnivore lifestyles. Carnivores - currently a diverse group of mostly meat-eating mammals like bears, cats, raccoons, seals, and hyenas - had been considered arboreal in their early evolutionary history. But now that the skeleton of 'Miacis' uintensis has been unpacked from its matrix of sandstone, it is clear that some early carnivores were built to walk on the ground at least part of the time. The new research is published this month in the Journal of Vertebrate Paleontology.

"Carnivores are highly varied today, and they were also very diverse in the past," says lead author Michelle Spaulding, a doctoral candidate at Columbia University and the Museum. "Examination of this fossil tells us that they were not all sitting in trees, looking down. 'M.' uintensis did not have a lot of adaptations for an arboreal lifestyle."

An early carnivore that was a close relative of Miacis uintensis, Vulpavus, is about to climb on a tree trunk. This illustrates the varied locomotor adaptations seen across even the earliest relatives of living carnivorans. **Marlene Donnelly and The Field Museum**

"It is typically thought that the miacoids of the Eocene - the basal fossil relatives of modern Carnivora that root the family tree - were arboreal," concurs co-author John Flynn, Frick Curator of Fossil Mammals at the Museum. "But we now are beginning to see that there was a greater diversity of locomotor styles in early carnivores."

'M.' uintensis was discovered on an American Museum of Natural History expedition in 1894 among the brown and red sandstones of the White River beds in Utah. Paleontologist Henry Fairfield Osborn, who first named the iconic dinosaurs Tyrannosaurus rex and Velociraptor mongoliensis, described the teeth of the newly discovered mammal carnivore species in a Museum monograph the following year. The specimen dates to 39-42 million years ago.

But the species is more than teeth and a jaw. Another specimen found in 1896 is more complete, represented by much of the skull, shoulder bones, limb bones, and even some tiny foot and finger bones. This specimen remained on a shelf in the Museum, largely ignored, because its teeth were badly crushed.

"When I examined the femur, I immediately knew this was a terrestrial animal because of the shape of its knee. It has a long and deep groove where the patella, or kneecap, would go," says Spaulding. If the early carnivore had been exclusively arboreal, the end of the femur would have had a flatter surface so that the joint would have a greater range of motion. Spaulding and Flynn found other indicators of terrestrial locomotion on bones like the radius, one of the two lower arm bones. The distal part of the radius, or the portion of the bone that would be in contact with the wrist, of 'M.' uintensis has an oval shape with a projection above the rim. These features also reduce the range of motion, making limbs more stable for walking on the ground. Other features, however, indicate that 'M.' uintensis had some adaptations for climbing, so this early carnivore was most likely flexible in locomotion style, active mostly on the ground but also capable of climbing bushes and trees.

This analysis is the fifth time that early carnivore postcrania have been carefully described in detail. Adding the information from this long-neglected fossil to the previously known data, though, does point researchers into new directions. An analysis of 99 traits among 29 fossils and 15 living taxa resulted in a new evolutionary tree that shows that 'M.' uintensis is distantly related to the type specimens from the Miacis genus, suggesting that an extensive revision of the current understanding of the evolutionary relationships among early carnivore fossils may be needed. But more significantly, the structure of the evolutionary tree suggests that adaptations to terrestrial or semi-terrestrial locomotion were more common than previously suspected in early fossil carnivores, preceding the split between the two major groups of living Carnivora, the Caniformia (a group that includes dogs, weasels, bears, seals and their relatives) and Feliformia (cats, hyenas, mongooses and civets).

"The fossil that we re-describe was thought to be in poor condition and had been ignored," says Flynn. "But now we are beginning to gain a better understanding of the ancestral conditions near the base of the carnivore tree. A lot of skeletons have been found over the years, and we think that intensively studying additional fossils will help build a more comprehensive view of the habitat-specializations of the early relatives of the living Carnivora."

This research was partially funded by several grants from the National Science Foundation and was supported by the American Museum of Natural History and Columbia University.

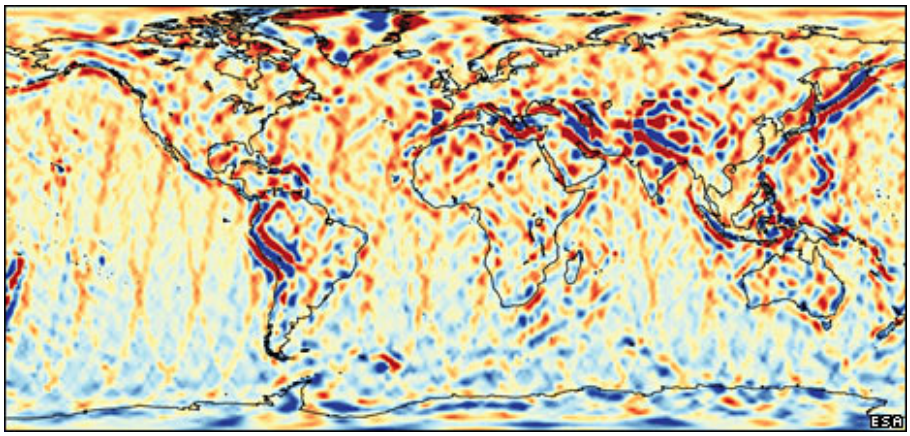
Esa satellite senses Earth's pull

By Jonathan Amos Science correspondent, BBC News

Europe's Goce satellite is returning remarkable new data on the way the pull of gravity varies across the Earth.

Scientists say its first maps clearly show details not seen in previous space and ground measurements.

Goce was launched by the European Space Agency (Esa) in March from the Plesetsk Cosmodrome in north-west Russia. Its information is expected to bring new insights into how the oceans move, and to frame a universal system to measure height anywhere on the planet. Researchers who study geological processes, such as earthquakes and volcanoes, will also make use of the data.



Goce's gradiometer senses the gravity field in three directions. The data above was recorded by accelerometers positioned across the direction of travel. This is completely new information to come from a space-borne instrument.

The first maps built from Goce observations were presented at the American Geophysical Union's (AGU) recent Fall Meeting, the world's largest annual gathering of Earth scientists.

More or less

Although they represent just 47 days of operation following the start of the satellite's science campaign on 30 September, the maps prove Goce is attaining an exceptional level of performance.

"There is a tremendous amount of geophysics in these plots," explained Rune Floberghagen, Esa's Goce mission manager. "You see where there are big variations, for example in the mountain range of the Andes, or the Mariana Trench, or the Indonesian Arc, or the Himalayas. In fact, on most of the continents, you see a lot of variation," he told BBC News. The maps reproduced on this page illustrate "gravity gradients".

The red colours indicate a positive variation in gravity moving from one place to another - i.e. places where Earth's tug becomes greater. The blue colours indicate a negative variation in gravity - places where Earth's tug is a little less. Simply put, if you were to take some bathroom scales to these locations you would weigh fractionally more in red places and weigh less in blue ones.

Most people are taught at school that the acceleration due to gravity at the Earth's surface - known as g - is about 9.8m per second squared. But, in truth, this figure varies around the planet depending on the nature of the material underfoot.

The planet is far from a smooth sphere; the radius of the globe at the equator is about 20km longer than at the poles. This ellipsoid is then marked by tall mountain ranges and cut by deep ocean trenches.

The Earth's interior layers are also not composed of perfect shells of homogenous rock - some regions are thicker or denser. Such factors will cause g to deviate from place to place by very small but significant amounts.

The Gravity Field and Steady-State Ocean Circulation Explorer (Goce) maps these differences with a state-of-the-art gradiometer produced by the French Onera company. The instrument is sensitive to accelerations of about one-tenth of a millionth of a millionth of g . And the gradiometer measures these accelerations across all three axes of the spacecraft to obtain a multi-dimensional view of the Earth's gravity field.

"These are by far the smallest accelerations ever measured from orbit," said Dr Floberghagen.

Ocean shape

The first maps not only record the three components but also compare their signals to the best available gravity field models assembled from existing space- and ground-acquired data-sets.

GRAVITY - A MOVING TARGET
The 'standard' acceleration due to gravity at the Earth's surface is 9.8m per second squared
In reality the figure varies from 9.78 (minimum) at the equator to 9.83 (maximum) at the poles

Again, in this challenge to the existing models the Goce gradients appear most pronounced in high latitude and continental regions. The gradients seem less marked over the oceans where a lot of gravity field information has already been determined by spacecraft that measure sea-surface topography.

The Goce team stresses that its data is not yet fully homogenous; some areas of the Earth are currently covered better than others. This is evident in the diagonal stripes that can be seen in a number of the maps. The scientists say that some work also remains to be done in understanding how best to process the data.

Nonetheless, it is hoped that sufficient high-quality information will have been gathered in the opening months of the science campaign to construct what geophysicists call a geoid.

This is a special type of Earth model which traces its idealised "horizontal" surface - the plane on which, at any point, the pull of gravity is perpendicular to it. If you could put a ball on this hypothetical surface, it would not roll - even though it appears to have slopes.

The geoid is of paramount interest to oceanographers who study the causes of the "hills" and "valleys" on the sea surface. If local gravity differences are not pulling water about to create these features, then other factors such as currents, winds and tides must be responsible.

Extended mission

The mission team also announced at the AGU meeting that Goce is likely to keep flying far longer than anyone had envisaged at launch.

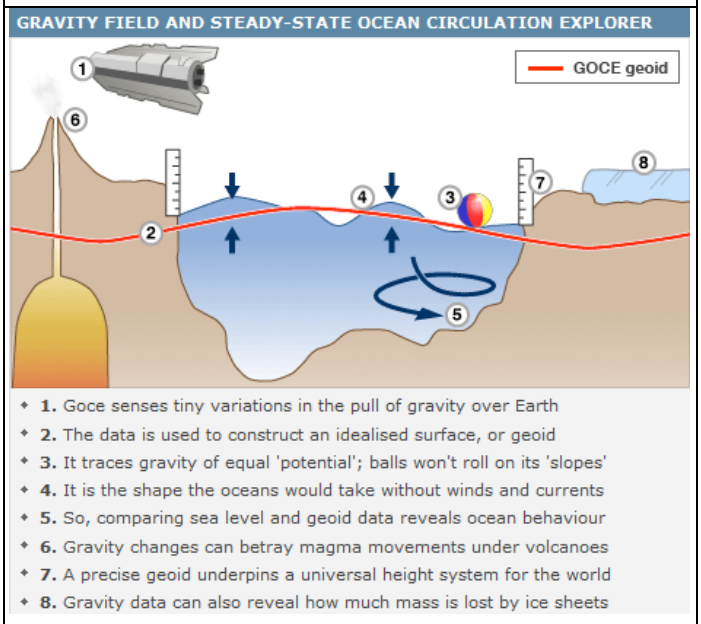
This increase in lifetime is a result of the unusually quiet behaviour of the Sun at the moment. In periods of reduced solar activity, the Earth's atmosphere is less extensive and this means satellites do not experience quite so much drag.

Even at its ultra-low altitude of just 254.9km, Goce requires little effort from its propulsion system to maintain a steady orbit and keep itself from falling out of the sky.

Esa had been expecting the satellite to stay aloft for about two years. Current solar conditions suggest Goce will still be orbiting and gathering science data in five years' time.

"The air drag that we have experienced on orbit after launching has been very different from what any model was able to predict pre-launch," said Dr Floberghagen.

GRAVITY FIELD AND STEADY-STATE OCEAN CIRCULATION EXPLORER



1. The 1,100kg Goce is built from rigid materials and carries fixed solar wings. The gravity data must be clear of spacecraft 'noise'
2. Solar cells produce 1,300W and cover the Sun-facing side of Goce; the near side (as shown) radiates heat to keep it cool
3. The 5m-by-1m frame incorporates fins to stabilise the spacecraft as it flies through the residual air in the thermosphere
4. Goce's accelerometers measure accelerations that are as small as 1 part in 10,000,000,000,000 of the gravity experienced on Earth
5. The UK-built engine ejects xenon ions at velocities exceeding 40,000m/s; the engine throttles up and down to keep Goce at a steady altitude
6. S Band antenna: Data downloads to the Kiruna (Sweden) ground station. Processing, archiving is done at Esa's centre in Frascati, Italy
7. GPS antennas: Precise positioning of Goce is required, but GPS data in itself can also provide some gravity field information

"And that in turn means there is a lot of new science not only in the gravity field measurements but also in the measurements of the surface forces acting on the spacecraft.

"So we plan to generate another product from this mission which will serve modellers of the thermosphere, people who model the air density in the upper layers of the atmosphere."

Researchers Identify Tuberculosis Strain That Thrives on Antibiotic

Scientists have identified a strain of antibiotic-resistant tuberculosis that thrives in the presence of rifampin, a front-line drug in the treatment of tuberculosis. The bacterium was identified in a patient in China and is described in a study by researchers at the Johns Hopkins Bloomberg School of Public Health, Chongqing Pulmonary Hospital, Lanzhou University and Fudan University. The researchers determined that the bacteria grew poorly in the absence of the antibiotic rifampin and better in the presence of the drug. They also observed that the patient's condition grew worse with treatment regimens containing rifampin, before being cured with rifampin-free regimens. The study, which will appear in the January 2010 issue of The International Journal of Tuberculosis and Lung Disease, is among the first to document the treatment of a patient with rifampin-dependent infection.

The World Health Organization (WHO) estimates that tuberculosis kills approximately 2 million people worldwide each year. Multidrug-resistant tuberculosis (MDR-TB) is becoming an increasing problem in many

parts of the world, largely due to poor patient adherence to the six-month tuberculosis chemotherapy. About 5 percent of all TB cases are MDR-TB that is resistant to isoniazid and rifampin, two main drugs used to treat the disease.

"Rifampin-dependent tuberculosis is an unrecognized and potentially serious treatment issue," said Ying Zhang, MD, PhD, senior author of the study and professor in the Bloomberg School's W. Harry Feinstone Department of Molecular Microbiology and Immunology. "Rifampin resistance is ominous. Our study highlights the potential dangers of continued treatment of MDR-TB with rifamycins that occur frequently due to delayed or absent drug susceptibility testing in the field. Further studies are urgently needed to determine how common such rifampin-dependent MDR-TB is in field conditions and if it contributes to the worsening of the disease in MDR patients and treatment failures."

Zhang adds that rifampin-dependent tuberculosis is difficult to detect and may be a bigger problem than we currently realize, since the bacteria do not grow well in the culture medium unless rifampin is added. The study authors urge timely detection of rifampin-dependent or -enhanced bacteria in patients with treatment failure by including rifampin in culture media and removing of rifampin from the treatment regimen once rifampin dependency or enhancement are detected. However, the researchers note that drug susceptibility testing is time-consuming and not easily performed in resource-poor settings where tuberculosis is frequently more common.

For the study, the research team documented the treatment of a 35-year-old Chinese man with tuberculosis. The man failed to respond to the WHO's thrice-weekly treatment regimen, which includes rifampin and other first-line tuberculosis drugs. The patient's condition worsened following an additional treatment regimen with rifampin and other second-line agents. Further testing detected the rifampin-dependency/enhancement. The patient fully recovered once rifampin was removed from his treatment regimen.

Additional authors of "An interesting case of rifampicin-dependent/enhanced multidrug-resistant tuberculosis" are M. Zhong, X. Zhang, Y. Wang, C. Zhang, G. Chen, M. Li, B. Zhu, and W. Zhang. The study is available online here.

The research was supported by the National Basic Research Program of China, the National Institutes of Health and the Changjiang Scholars Program.

Wild chimps have near human understanding of fire, says study by ISU's Pruetz

AMES, Iowa -- The use and control of fire are behavioral characteristics that distinguish humans from other animals. Now, a new study by Iowa State University anthropologist Jill Pruetz reports that savanna chimpanzees in Senegal have a near human understanding of wildfires and change their behavior in anticipation of the fire's movement.

An ISU associate professor of anthropology, Pruetz and Thomas LaDuke, an associate professor of biological sciences at East Stroudsburg (Pa.) University, co-authored the paper, which will be posted online Friday by the American Journal of Physical Anthropology. It will be published in a 2010 edition of the journal.

Data on the chimps' behavior with seasonal fires was collected by Pruetz during two specific encounters in March and April 2006. She reports that wildfires are set yearly by humans for land clearing and hunting, and most areas within the chimpanzees' home range experience burning to some degree.

Chimps have calm understanding of wildfires

The researchers interpret the chimpanzees' behavior to the wildfires as being predictive, rather than responsive, in that they showed no signals of stress or fear -- other than avoiding the fire as it approached them.

"It was the end of the dry season, so the fires burn so hot and burn up trees really fast, and they [the chimps] were so calm about it. They were a lot better than I was, that's for sure," said Pruetz, who was selected a 2008 National Geographic Emerging Explorer for her previous research on the savanna chimpanzees at the Fongoli research site in Senegal.

"They [the chimps] were experts at predicting where it was going to go," she continued. "I could predict it, sort of, but if it were just me, I would have left. At one time, I actually had to push through them because I could feel the heat from the fire that was on the side of me and I just wasn't that comfortable with it."

Pruetz says it was hard to find previous research on how other animals interacted with fire. But the few examples that she and LaDuke found -- such as elephants' encounters with similar wildfires -- reported that those animals were highly stressed and experienced high mortality rates.

In their paper, the researchers wrote that the control of fire by humans involves the acquisition of these three cognitive stages:

1. Conceptualization of fire. An understanding of the behavior under varying conditions that would allow one to predict its movement, thus permitting activity in close proximity to the fire.

2. The ability to control fire. Involving containment, providing or depriving the fire of fuel and perhaps the ability to put it out.

3. The ability to start a fire.

According to Pruetz, the Fongoli chimpanzees have mastered the first stage, which is the prerequisite to the other two. But she doesn't see them figuring out how to start a fire anytime soon -- at least, not without help.

"I think they could learn. It might be difficult only because of their dexterity, since they're less dexterous than us," she said. "But naturally, I can't ever see them making fire. I think cognitively they are able to control it (stage 2)."

Displaying a new "fire dance"

Yet they are very aware of fire and its power. In fact, Pruetz reports that the chimps have developed a unique "fire dance."

"Chimps everywhere have what is called a 'rain dance' -- Jane Goodall (a famed primatologist) coined that term -- and it's just a big male display (to show dominance)," she said. "Males display all the time for a number of different reasons, but when there's a big thunderstorm approaching, they do this real exaggerated display -- it's almost like slow motion. And when I was with this one party of chimps, the dominant male did the same sort of thing, but it was towards the fire, so I call it the fire dance.

"The other interesting thing was that I heard a vocalization that I never heard before [the fire dance] and I've never heard since," Pruetz continued.

She says the study provides insight into how the earliest human ancestors first developed the ability to control fire. "If chimps can understand and predict the movement of fire, then maybe that's the thing that allowed some of the very earliest bipedal apes [human ancestors] to eventually be able to control fire," she said.

Pruetz will be continuing her research in Senegal during the spring semester. It is sponsored, in part, by the National Geographic Society, in addition to Iowa State.

Up a little on the left ... Now, over to the right ...

-Johns Hopkins Scientists Find a Source of Nonallergic Itch

Scratching below the surface of a troublesome sensation that's equal parts tingle-tickle-prickle, sensory scientists from Johns Hopkins have discovered in mice a molecular basis for nonallergic itch.

Using the itch-inducing compound chloroquine, an antimalarial drug, the team identified that a family of proteins called Mrgprs, found only in a rare subset of nerve cells, functions as itch receptors. A report on the research appears Dec. 24 in Cell.

Itch research - and the sweet relief it may one day afford - has remained at a relative crawl, lagging well behind pain research, says Xinzhong Dong, Ph.D., an assistant professor in the Solomon H. Snyder Department of Neuroscience at the Johns Hopkins University School of Medicine. Most studies so far have focused on allergy-related itch, a reaction involving an itch mediator known as histamine and accounting for about one-third of all itch. Allergic itch often responds to antihistamines, but most kinds of itch do not, including the kind that's induced by chloroquine.

"The majority of itch is not associated with histamine and therefore antihistamines won't work," Dong says. "We're not saying that our discovery solves all other histamine-independent itch, but this research makes significant strides in getting to the root of a sensation that's poorly understood and about which there's heated debate."

Some researchers believe there are specific nerve cells dedicated for itch, different ones for pain, and still others for pleasant touch. Some contend that different firing patterns from the same nerve call deliver the different sensations. Both mice and men detect stimuli from the outside world via nerve cells called primary sensory neurons, which reside in clusters along the vertebrae known as dorsal root ganglia (DRG).

In his quest for the origins of nonallergic itch, Dong first engineered mice lacking each of 12 members of the family of Mrgpr genes.

The team studied the behavioral responses of the Mrgpr "knockout" mice and compared them to mice that still had the gene. In tests assessing their reactions to thermal, mechanical and chemical pain, all the knock-out and wild-type (normal) mice responded in kind, leading the research team to conclude that the Mrgpr gene is probably not important for detecting acute, painful stimuli.

Next, they injected histamine into the mice to induce itch; again, the knock-outs and the wild types behaved similarly, scratching at the same rates during five-minute intervals over the course of 30 minutes.

Finally, they injected chloroquine into the mice to induce itch and were surprised, Dong says, to find that over the course of 30 minutes, the wild-type mice used their hind paws to scratch their necks 270 times v. the 100 scratches by mice lacking Mrgpr genes.

"The behavioral study showed us that the Mrgpr-knockout mice responded specifically to chloroquine, and since we know that Mrgpr only expresses its protein in dorsal root ganglia, our hypothesis was that the deficit must happen in the DRG neuron," Dong says.

The team then focused on DRG neurons to see if it really is Mrgpr proteins that facilitate itch response in those cells. They first added chloroquine directly to individual DRG neurons from both knockout and wild-type animals and used a fluorescent dye to see if the cells responded. About 4 percent of wild-type neurons responded by glowing, while none of the knock-out neurons did.

Then the team measured chloroquine-induced electrical activity in the neurons, noting that the wild-type responded but that the knock-outs remained completely "silent."

To figure out which of the 12 Mrgprs actually controls chloroquine itch, the team tested each one individually, found that only one of the genes - MrgprA3 - responded significantly to chloroquine, and concluded that MrgprA3 is a major itch receptor for chloroquine.

"The reason we are excited about this family of genes is that they are located in this primary sensing neuron in the dorsal root ganglia and not anywhere else," Dong says, "so if you can develop a drug that targets a small subset of these neurons - those that manufacture the protein/receptor Mrgpr - you can specifically treat itch and probably without much side effect."

This research was supported by an Alfred P. Sloan Neuroscience grant, a Whitehall Foundation grant, a Blaustein Pain Research Fund award, and grants from the National Institutes of Health. Authors of the paper, in addition to Dong, are Qin Liu, Zongxiang Tang, Kush N. Patel, Andrew Kim, Fei Ru, Hao-Jui Weng, Yixun Geng, Bradley J. Undem, Marian Kollarik, Yun Gaun and Lenka Surdenikova, all of Johns Hopkins; Seungil Kim and Zhou-Feng Chen of the Washington University School of Medicine; and David J. Anderson of the California Institute of Technology.

Chicago Cancer Genome Project studies genetics of 1,000 tumors

No two tumors are alike, but analyzing the genetics of cancers from different parts of the body may reveal surprising details useful for treatment and prevention.

That process is already gaining traction at the University of Chicago's Institute for Genomics and Systems Biology (IGSB), where researchers are one year into a three-year project to collect and analyze the genetic sequence and variations of every gene expressed by 1,000 tumors.

Over the past year, working closely with physicians, the IGSB team collected complete sequence data for genes expressed by 100 tumors--primarily breast cancer, head and neck cancer, and leukemia. Correlating genetic data with patient outcomes, they have begun to identify genetic patterns within tumors that may help them predict how a cancer will behave. Many experts believe such information will increasingly guide treatment.

"The long-term goal," said IGSB Director Kevin White, James and Karen Frank Family Professor in human genetics and ecology and evolution, "is to translate genomic discoveries into useful diagnostic tools and therapeutic strategies. This should improve patient care."

Not to be confused with the "1,000 Genomes Project"--an international effort to sequence all of the DNA from 1,000 individuals selected from hundreds of distinct populations worldwide--the Chicago 1,000-cancer-genomes project is based entirely at the University of Chicago and tightly focused on the genetics of this common disease.

"The Chicago Cancer Genome Project is aimed at teaching us how to use the genetic state of the cells as a guidepost for which treatments should be offered to specific patients," White said.

Cancer is a genetic disease. Each tumor's genes provide clues about the severity of the disease. They can sometimes predict whether a cancer will respond to specific treatments, develop resistance to radiation or chemotherapy, relapse after therapy, or spread to a distant site.

Many established cancer treatments grew out of genetic information, beginning at the University of Chicago with Elwood Jensen's discovery of the estrogen receptor in 1958, which led to the development of estrogen blockers such as tamoxifen, and Janet Rowley's descriptions of the first chromosomal translocations in 1972, work that led to the targeted therapy known as Glevec.

But the Chicago Cancer Genome Project is among the first efforts to combine a focus on the genes expressed by multiple cancers with broad scale, systematic implementation. During the pilot phase--sequencing expressed genes from the first 100 tumors--the team established and refined a project framework utilizing the latest in gene-sequencing technology and computational analysis.

"We now know how to do this," said White. "We have the basic structure in place. In the process, we have identified novel genes associated with clinical outcome in selected cancers."

The next steps are to determine how these altered genes act and expand the project to include more tumor types, including cancers of the bladder, lung, pancreas, prostate, as well as several childhood cancers such as rhabdosarcomas and neuroblastomas.

Analyzing a wide variety of tumors may reveal previously unknown genetic similarities in cancers typically classified as different according to tissue of origin, White said.

The genetics of cancer can be extraordinarily complex, said Michelle LeBeau, PhD, director of the University of Chicago Cancer Research Center. "Kevin's team at the IGSB brings all the right tools," she said. "They have the ability to collect and manipulate large amounts of genetic data, the capacity to study not just single genes but entire genetic pathways and their interactions, and a close working relationship with multiple teams of cancer specialists."

The Chicago approach differs from several large-scale cancer-genome efforts in progress. A year ago a team from Washington University published the first cancer genome, from a patient with leukemia. Since then, genomes for breast cancer, melanoma and lung cancer have appeared, and the National Cancer Institute is compiling its Cancer Genome Atlas.

Unlike those projects, the Chicago researchers will study only the genes that are expressed by these tumors - one to two percent of an individual's genome--but will collect genetic data from many more tumors.

"If we eliminate 98 percent of the genome, that makes it 50 times cheaper and easier," said White. "That's still quite a lot of DNA," he emphasized, the equivalent of 20 entire genomes, or about 60 billion base pairs. Collecting genetic information from 1,000 tumors will take about three years, he said, but it will provide information that "can more rapidly be applied to answer clinical questions."

The project also will gather genetic data on how the genes expressed by tumors evolve over time. Whenever possible, the researchers will compare tumor samples taken from a patient before and after treatments, to learn how cancers accumulate additional genetic changes that enable them to resist radiation or chemotherapy or to spread to distant sites.

All patients must provide prior consent for their tissues to be catalogued and studied. Because the researchers are focused on how genetic clues can predict cancer behavior, the team follows each patient's progress through his or her clinical course.

Most patients have been eager to donate, said cancer specialist Kevin Roggin, MD, assistant professor of surgery, who offers each patient with a pancreatic cancer the opportunity to contribute to a project that could, over time, make a difference in treatment and outcome.

"It is already starting to help," he added. "We are accumulating data that we hope to develop into a molecular fingerprint, a DNA profile that may help us predict which pancreatic cystic tumors are likely to remain benign and which ones will develop into cancers."

Donating tumor tissue requires no extra effort or expense for the patient, said Roggin. "First we make sure we don't compromise the pathologists' ability to make a diagnosis. Second, if there is extra tissue, we flash freeze it to 80 below zero and log it into a database. Then we can store the tissue indefinitely and take what we need to generate DNA and RNA."

The project meshes well with the Medical Center's established program in cancer pharmacogenomics, which studies how certain gene variations influence patient responses to various anti-cancer drugs and develops genetic tests to predict side effects.

"By studying both the tumor and the patient we will, increasingly, be able to design optimal treatment strategies that offer the best hope for control of the cancer with the least toxicity for the patient," said Richard Schilsky, MD, professor of medicine and chief of hematology/oncology at the Medical Center and past president of the American Society for Clinical Oncology.

"It's a long road from having a piece of genome sequence to improving patient care," White cautioned. "But the path of discovery is clear. In many cases we know enough now to connect the dots."

We now know that the brain controls the formation of bone

The brain acts as a profound regulatory centre, controlling myriad processes throughout the body in ways we are only just beginning to understand. In new findings, Australian scientists have shown surprising connections between the brain and regulation of bone mass.

One of the key functions of our skeletons is to provide mechanical support. In order to fulfil this role, bone tissue is modified throughout our lives, in response to changing activity levels and body weight. Bone mass increases as we gain weight and decreases as we lose it.

The new findings show that bone formation, far from being a straightforward mechanical process dependent on body weight, is delicately orchestrated by the brain, which sends and receives signals through the body’s neural and hormone systems.

It is now clear that the neural network which controls appetite and energy also alters bone density. When we are starving, our brains don’t allow us to waste energy by reproducing, making fat or creating new bone. When we are eating too much, on the other hand, our brains make it easier to reproduce, store fat and create bone.

Dr Paul Baldock, a neuroscientist from Sydney's Garvan Institute of Medical Research, has demonstrated in mice that the neurotransmitter Neuropeptide Y (NPY) directly controls osteoblasts, the cells that make bone. His findings are published today in the international online journal Public Library of Science ONE (PLoS ONE).

"It has always been thought that changes in bone mass are purely mechanical - you get heavier and your bones get denser to support the increased load," said Baldock. "While that's true to some extent, our findings show a sophisticated central surveillance system at work. It's as if the brain, as boss, sends out a global memo saying 'make more bone'."

"Bone-making cells at local level appear to have the ability to fine-tune this directive, like office workers saying 'we're not going to waste time putting on bone here when it's needed more over there'. So what happens in practice is that places exposed to more load put on more bone, while those exposed to less load put on less bone."

All the intricate central processing takes place in the hypothalamus, a small yet complex region of the brain that links the nervous and hormone systems.

According to Baldock, the NPY system in the brain evolved to allow survival of humans during very lean times as well as plenty. "In evolutionary terms, people are kept alive so that they can reproduce, and body systems are all integrated to preserve that function. I have no doubt that osteoporosis treatments of the future will find a safe way to block NPY receptors on osteoblasts," said Baldock.

"Obviously, the development of such treatments would have to take account of all the processes affected by the NPY system – including appetite and mood. You'd need something that increased bone mass without also making people fat, skinny, sad or angry at the same time."

As a first step, Baldock is showing the orthopaedic relevance of his findings at the Children's hospital at Westmead, where he is collaborating with an orthopaedic surgeon, Associate Professor David Little.

ABOUT GARVAN

The Garvan Institute of Medical Research was founded in 1963. Initially a research department of St Vincent's Hospital in Sydney, it is now one of Australia's largest medical research institutions with nearly 500 scientists, students and support staff. Garvan's main research programs are: Cancer, Diabetes & Obesity, Immunology and Inflammation, Osteoporosis and Bone Biology, and Neuroscience. The Garvan's mission is to make significant contributions to medical science that will change the directions of science and medicine and have major impacts on human health. The outcome of Garvan's discoveries is the development of better methods of diagnosis, treatment, and ultimately, prevention of disease.

Earth on track for epic die-off, scientists say

Peter Fimrite, Chronicle Staff Writer

Artwork: Mauricio Anton / Courtesy of UCLA

If the course of human history is any model, then the wheels are already turning on Earth's sixth mass extinction, thanks to habitat destruction, pollution and now global warming, a scientific analysis of millions of years of data revealed Friday.

The study of the fossil and archaeological record over the past 30 million years by UC Berkeley and Penn State University researchers shows that between 15 and 42 percent of the mammals in North America disappeared after humans arrived.

That means North American mammals are well on the way - perhaps as much as half way - to a level of extinction comparable to other epic die-offs, like the one that wiped out the dinosaurs.

Anthony Barnosky, a UC Berkeley professor of integrative biology and co-author of the study, said the most dramatic human-caused impacts on the ecosystem have occurred in the last century.

"We are seeing a lot of geographic range reductions that are of a greater magnitude than we would expect, and we are seeing loss of subspecies and even a few species," Barnosky said. "So it looks like we are going into another one of these extinction events."

The analysis by Barnosky, research associate Marc Carrasco and Penn State's Russell Graham was published this week in the scientific journal PLoS ONE. It compares the extinctions of mammals in North America after humans arrived 13,000 years ago to the five mass extinctions on Earth over the past 450 million years.

The least severe of those extinctions wiped out the dinosaurs 68 million years ago and killed off 75 percent of the species on the planet.

Add human impact

Although humans clearly did not have anything to do with the previous extinctions, many scientists are afraid that global warming and other environmental problems caused by the ever-increasing human population could have similarly catastrophic consequences.

"Here we are again, astronomically increasing the number of humans on the face of the globe, plus unusual climate change," Barnosky said. "That seems to be a recipe for extinction that we saw in the past, and we are seeing again."

The work, which was supported by the National Science Foundation, looked at the number, distribution and range of every mammal from shrews to mammoths in the area of the continental United States between 500 years ago and 30 million years ago.

Previous research has shown that most mammal extinctions in North America, Australia, Europe and Northern Asia have occurred within a few thousand years after the arrival of humans. This study puts that data into historical perspective, providing the percentage of animals that went extinct during certain time periods compared with other epochs.

50 gone in 2,000 years

Humans reached North America about 13,000 years ago and more than 50 species disappeared over the next 2,000 years, including mammoths, saber-toothed cats, giant ground sloths and other large animals, according to the study.

The arrival of humans coincided with the end of the last ice age, but the study pointed out that 38 other ice ages had occurred in North America over the past 2 million years and there were no comparable die-offs during the others. "The only difference is that 13,000 years ago, humans appear on the scene," Carrasco said. "The bottom line is, mammals in general were able to deal with these changes in the past. Only when humans arrive do the numbers fall off a cliff."

There is, nevertheless, reason for optimism, Barnosky said. The number of extinctions has leveled off over the past 10,000 years, he said, and it is not too late to prevent a resurgence. "If we redouble our conservation efforts, we can stem the tide of extinctions and have those species around in the future," he said. "There is a bit of urgency here. By demonstrating that we have already lost 15 to 42 percent of mammalian diversity, the question is, do we really want to lose any more? I think the answer to that is pretty obvious."

Future studies are expected to analyze the extinctions that occurred 40,000 years ago, when modern humans emerged from Africa into Europe and Asia.

Killed off

At least 50 species went extinct in North America soon after humans arrived on the continent 13,000 years ago. Among the mammals that disappeared were California tapirs, peccaries, lions and cheetahs, llamas, ox, horses, mammoths and mastodons.

Some of the most notable extinctions were: shortfaced bear (Arctodus simus); dire wolf (Canis dirus); sabertooth cat (Smilodon fatalis); American Scimitar cat (Homotherium serum); giant beaver (Castoroides ohioensis); beautiful armadillo (Dasypus bellus); American camel (Camelops hesternus);and Columbian mammoth (Mammuthus columbi).

Personal Health

Risks, as Well as Hope, for Very Tiny Infants

By JANE E. BRODY

Marlo Prescott calls her daughter, Alexis, “our miracle baby.” Born after just 25 weeks in the womb weighing only 13.5 ounces, Alexis is described by her mother as “a very sweet, very kind, ambitious, artistically talented and academically gifted” 11-year-old who has already written and illustrated three books. She is slender and, unlike most children born so early and so small, she is tall for her age.

Alexis was born on Jan. 22, 1998, at Inova Fairfax Hospital for Children in Falls Church, Va., where she spent the first five months of her life, coming home at last on May 19 at four and a half pounds.

She is one of a growing number of extremely preterm, extremely tiny babies who now survive and even thrive at this and other hospitals, thanks to expert, highly coordinated prenatal and postnatal care.

The problem of prematurity has remained stubbornly resistant to change, even increasing in recent years as assisted reproductive techniques have resulted in pregnancies with two or more babies at a time. But there has been no significant increase in extreme prematurity, which can result from a variety of factors - in Alexis’s case, a leakage of amniotic fluid that threatened to rupture her mother’s liver.

A Host of Problems

Of course, not all babies as small as Alexis make it and do as well as she has. Her neonatologist, Dr. Robin Baker, explained in an interview that gestation can make a bigger difference than birth weight. At 25 weeks, Dr. Baker said, Alexis had a much better chance than those born on the cusp of viability, 23 or 24 weeks.

Unlike Alexis, who was spared the most common hazards of microprematurity, as neonatologists describe babies weighing less than 500 grams (1.1 pounds), many of these tiny survivors face a lifetime of cognitive, developmental and physical deficits. Some physicians question whether it is always wise to try to keep them alive.

In 2004, for example, the Vermont Oxford Network, a consortium of about 500 hospitals with neonatal intensive care units, reported the results of 4,172 births of infants who weighed 401 to 500 grams. Only 17 percent - 690 babies - survived to be discharged from the neonatal intensive care unit. Most had multiple problems common to extreme prematurity, among them a hole between heart chambers, retinopathy and chronic lung disease.

Most follow-up studies of such tiny survivors have found high rates of poor growth and development, multiple medical problems, including cerebral palsy, and cognitive deficits, including mental retardation.

Serious risks remain even for somewhat bigger babies born weighing 500 to 1,000 grams (2.2 pounds), the cutoff for extremely low birth weight. The likelihood that surviving babies will experience developmental lags is especially high among those born to poorly educated and financially challenged parents.

Even in these circumstances, however, babies of extremely low birth weight are now doing better than ever.

At the MacDonald Women's Hospital and the Rainbow Babies' and Children's Hospital in Cleveland, which serve primarily a poor population, researchers have been studying the survival and neurological development of extremely small babies for several decades. From the 1980s to the early 2000s, major increases occurred in the percentage of surviving babies (to 71 percent, from 49 percent) and babies who survived without neurological impairment (to 71 percent of survivors, from 65 percent) when re-examined at the corrected age of 20 months.

Survival at Inova Fairfax, which serves mostly well-educated and middle-class families, is now close to 90 percent. The hospital prides itself in the kind of care its tiny babies get from what Dr. Baker called "a very well-orchestrated, consistent, methodical approach, like a dance." Care starts prenatally, he said, with everything possible done to delay a baby's premature birth.

Once a tiny baby is born, Dr. Baker said, "senior people lead the show, each baby has its own board-certified neonatologist, and the nurses all know what to do.

"The focus is on the total infant," he continued. "Every day each baby is looked at system by system. Every morning and every night, we check with one another and discuss what each baby may need."

Especially close attention is paid the baby's blood pressure and coagulation, keeping both as normal as possible to reduce the risk of bleeding into the brain, which can cause lasting neurological damage.

'Million-Dollar Babies'

Four years ago, the hospital hired Ida Sue Baron, an independent clinical neuropsychologist, to evaluate the long-term results of their efforts at saving babies born weighing less than 2.2 pounds. Dr. Baron has so far extensively tested more than 100 of the 6-year-olds and compared them with a similar number of normal children born full-term.

This year, in the journal Early Human Development, Dr. Baron and colleagues reported finding "age-appropriate neurocognitive and behavioral function" in a group of school-age children whose birth weight had left them "at high risk for impairment." The team was surprised to find comparable test results among those born before or after 26 weeks' gestation and those born at less or more than 750 grams (1.65 pounds).

"The children are not perfect," Dr. Baron said in an interview. "They're more vulnerable to problems with attention, planning and working memory, even among those with average I.Q.'s. But they're doing much better than predicted. "We've begun to look at them again at age 9 and are finding no deterioration as they get into higher grades. Their academic skills have not declined and their behavioral functions have remained stable."

Dr. Michele Walsh, a neonatologist at the children's hospital in Cleveland, said in an interview that the Vermont network maintained "an active quality-improvement program."

Dr. Walsh listed four changes that could account for recent improvement: more selective use of medications, especially corticosteroids that are intended to protect the babies' lung function but that can damage the brain when overused; doing everything possible to avoid infection; using better methods of ventilation to reduce lung damage; and improved nutrition.

Though it was long feared that feeding these tiny newborns could result in a fatal intestinal infection, now the babies are getting mother's milk and much more protein intravenously to support their brain development.

Although Dr. Walsh acknowledged that it was expensive to maintain these "million-dollar babies" for many months in neonatal intensive care unit, "spread over a normal healthy lifespan, it's very cost-effective: there's a return on the investment when they get out into the work force and pay taxes."

Growing evidence suggests progesterone should be considered a treatment option for traumatic brain injuries

Researchers at Emory University in Atlanta, GA, recommend that progesterone (PROG), a naturally occurring hormone found in both males and females that can protect damaged cells in the central and peripheral nervous systems, be considered a viable treatment option for traumatic brain injuries, according to a clinical perspective published in the January issue of the American Journal of Roentgenology.

"Traumatic brain injury (TBI) is an important clinical problem in the United States and around the world," said Donald G. Stein, PhD, lead author of the paper. "TBI has received more attention recently because of its high incidence among combat casualties in Iraq and Afghanistan. Current Department of Defense statistics indicated that as many as 30 percent of wounded soldiers seen at Walter Reed Army Hospital have suffered a TBI, a finding that has stimulated government interest in developing a safe and effective treatment for this complex disorder," said Stein.

"Growing evidence indicates that post-injury administration of PROG in a variety of brain damage models can have beneficial effects, leading to substantial and sustained improvements in brain functionality. PROG given to both males and females can cross the blood-brain barrier and reduce edema (swelling) levels after TBI; in different models of cerebral ischemia (restriction of blood supply), significantly reduce the area of necrotic cell death and improve behavioral outcomes; and protect neurons distal to the injury that would normally die," said Stein.

PROG was recently tested in two phase 2 clinical trials for traumatic brain injury and will begin a phase 3 NIH sponsored trial soon. "Given its relatively high safety profile, its ease of administration, its low cost and ready availability, PROG should be considered a viable treatment option - especially because, in brain injury, so little else is currently available," said Stein.

This study appears in the January issue of the American Journal of Roentgenology. For a copy of the full study, please contact Heather Curry via email at hcurry@acr-arrs.org or at 703-390-9822.

Building a Search Engine of the Brain, Slice by Slice

By BENEDICT CAREY

SAN DIEGO- On a gray Wednesday afternoon here in early December, scientists huddled around what appeared to be a two-gallon carton of frozen yogurt, its exposed top swirling with dry-ice fumes.

As the square container, fixed to a moving platform, inched toward a steel blade mounted level with its surface, the group held its collective breath. The blade peeled off the top layer, rolling it up in slow motion like a slice of pale prosciutto. “Almost there,” someone said.

Off came another layer, another, and another. And then there it was: a pink spot at first, now a smudge, now growing with every slice like spilled rosé on a cream carpet - a human brain. Not just any brain, either, but the one that had belonged to Henry Molaison, known worldwide as H. M., an amnesic who collaborated on hundreds of studies of memory and died last year at age 82. (Mr. Molaison agreed to donate his brain years ago, in consultation with a relative.)

“You can see why everyone’s so nervous,” said Jacopo Annese, an assistant professor of radiology at the University of California, San Diego, as he delicately removed a slice with an artist’s paintbrush and placed it in a labeled tray of saline solution. “I feel like the world is watching over my shoulder.”

And so it was: thousands logged on to view the procedure via live Webcast. The dissection marked a culmination, for one thing, of H. M.’s remarkable life, which was documented by Suzanne Corkin, a memory researcher at the Massachusetts Institute of Technology who had worked with Mr. Molaison for the last five decades of his life.

But it was also a beginning of something much larger, Dr. Annese and many other scientists hope. “The advent of brain imaging opened up so much,” said Sandra Witelson, a neuroscientist with the Michael G. DeGroote School of Medicine at McMaster University in Canada, who manages a bank of 125 brains, including Albert Einstein’s. “But I think in all the excitement people have forgotten how important the anatomical study of brain tissue still is, and this is the sort of project that could really restart interest in this area.”

The Brain Observatory at U.C. San Diego, set up to accept many donated brains, is an effort to bridge past and future. Brain dissection is a craft that goes back centuries and has helped scientists to understand where functions like language processing and vision are clustered, to compare gray and white matter and cell concentrations across different populations and to understand the damage done in ailments like Alzheimer’s disease and stroke.

Yet there is no single standard for cutting up a brain. Some researchers slice from the crown of the head down, parallel to the plane that runs through the nose and ears; others cut the organ into several chunks, and

proceed to section areas of interest. No method is perfect, and any cutting can make it difficult, if not impossible, to reconstruct circuits that connect cells in disparate areas of the brain and somehow create a thinking, feeling mind.

To create as complete a picture as possible, Dr. Annese cuts very thin slices - 70 microns each, paper-thin - from the whole brain, roughly parallel with the plane of the forehead, moving from front to back. Perhaps the best-known pioneer of such whole-brain sectioning is Dr. Paul Ivan Yakovlev, who built a collection of slices from hundreds of brains now kept at a facility in Washington.

But Dr. Annese has something Dr. Yakovlev did not: advanced computer technology that tracks and digitally reproduces each slice. An entire brain produces some 2,500 slices, and the amount of information in each one, once microscopic detail is added, will fill about a terabyte of computer storage. Computers at U.C.S.D. are now fitting all those pieces together for Mr. Molaison's brain, to create what Dr. Annese calls a "Google Earthlike search engine," the first entirely reconstructed, whole-brain atlas available to anyone who wants to log on.

"We're going to get the kind of resolution, all the way down to the level of single cells, that we have not had widely available before," said Donna Simmons, a visiting scholar at the Brain Architecture Center at the University of Southern California. The thin whole-brain slicing "will allow much better opportunities to study the connection between cells, the circuits themselves, which we have so much more to learn about."

Experts estimate that there are about 50 brain banks in the world, many with organs from medical patients with neurological or psychiatric problems, and some with a stock donated by people without disorders. "Ideally, anyone with the technology could do the same with their own specimens," Dr. Corkin said.

The technical challenges, however, are not trivial. To prepare a brain for dissection, Dr. Annese first freezes it in a formaldehyde and sucrose solution, to about minus 40 degrees Celsius. The freezing in the case of H. M. was done over four hours, a few degrees at a time: the brain, like most things, becomes more brittle when frozen. It can crack.

Mr. Molaison lost his ability to form new memories after an operation that removed a slug-size chunk of tissue from deep in each hemisphere of his brain, making it more delicate than most.

"A crack would have been a disaster," Dr. Annese said. It did not happen.

With the help of David Malmberg, a mechanical engineer at U.C.S.D. who had designed equipment for use in the Antarctic, the laboratory fashioned a metal collar to keep the suspended brain at just the right temperature. A few degrees too cold and the blade would chatter instead of cutting cleanly; too warm, and the blade wants to dip into the tissue. Mr. Malmberg held the temperature steady by pumping ethanol through the collars continually, at minus 40 degrees. He suspended the hoses using surfboard leashes picked up days before the dissection.

After the slicing and storing, a process that took some 53 hours, Dr. Annese's laboratory will soon begin the equally painstaking process of mounting each slice in a glass slide. The lab will stain slides at regular intervals, to illustrate the features of the reconstructed organ. And it plans to provide slides for study. Outside researchers can request samples and use their own methods to stain and analyze the composition of specific high-interest areas. "For the work I do, looking at which genes are preferentially expressed in different areas of the brain, this will be an enormous resource," Dr. Simmons said.

If all goes as planned, and the Brain Observatory catalogs a diverse collection of normal and abnormal brains - and if, crucially, other laboratories apply similar techniques to their own collections - brain scientists will have data that will keep them busy for generations. In her own work, Dr. Witelson has found interesting anatomical differences between male and female brains; and, in Einstein's brain, a parietal lobe, where spatial perception is centered, that was 15 percent larger than average.

"With more of this kind of data," Dr. Witelson said, "we'll be able to look at all sorts of comparisons, for example, comparing the brain of people who are superb at math with those who are not so good."

"You could take someone like Wayne Gretzky, for example," she added, "who could know not only where the puck was but where it was going to be - who was apparently seeing a fourth dimension, time - and see whether he had any special anatomical features." (For the time being, Mr. Gretzky is still using his brain.)

So it is that Mr. Molaison, who kicked off the modern study of memory by cooperating in studies in the middle of the 20th century, may help inaugurate a new era in the 21st century. That is, as soon as Dr. Annese and his lab team finish sorting the slices they have collected.

"It's very exciting work to talk about," Dr. Annese said. "But to see it being done, it's like watching the grass grow."

Study redefines placebo effect as part of effective treatment

It's not drug or placebo, it's drug and placebo

Researchers used the placebo effect to successfully treat psoriasis patients with one quarter to one half of their usual dose of a widely used steroid medication, according to an early study published online today in the journal Psychosomatic Medicine. Early results in human patients suggest that the new technique could improve treatment for several chronic diseases that involve mental state or the immune system, including asthma, multiple sclerosis and chronic pain.

By designing treatment regimens that mix active drug and placebo, researchers at the University of Rochester Medical Center hope to maximize drug benefits, reduce side effects, increase the number of patients who take their medicine and extend the use of drugs otherwise limited by addiction risk or toxicity. Using a fraction of the usual drug dose to get the same effect could also make possible a dramatic and timely reduction in healthcare costs, according to the authors.

The publication is a product of decades of research in the emerging field of "psychoneuro-immunology," which holds that the ability of the human immune system to fight disease is closely linked with a person's mind. Thoughts and moods are captured in neurochemicals that cause the release of hormones which interact with disease-fighting cells.

The current research team chose psoriasis for their first human experiments because it is chronic, gets worse when patients feel stress and involves the immune system. The condition causes pain and disability in four million Americans as inherited traits and irritants cause the immune system to trigger the too fast production of skin cells, resulting in red, scaly patches of dead skin.

"Our study provides evidence that the placebo effect can make possible the treatment of psoriasis with an amount of drug that should be too small to work," said Robert Ader, Ph.D., M.D.(hc), distinguished university professor in the University of Rochester School of Medicine & Dentistry. "While these results are preliminary, we believe the medical establishment needs to recognize the mind's reaction to medication as a powerful part of many drug effects, and start taking advantage of it," said Ader, principal investigator of the study. The placebo effect, obviously, cannot help unconscious patients, or replace substances that the body itself is unable to produce, he added. In the absence of functioning islet cells, for example, placebos cannot stimulate the release of insulin in a Type l diabetic.

Study Details

A description of the current findings requires expanding the definition of placebo effects to include phenomena that are not fully understood by modern medicine, Ader said. Although placebos, "dummy pills" that have no therapeutic effect by themselves, are prescribed by many physicians today, their use still carries a stigma. It's as if the effect of a pill containing no medication is not "real," part magic and part deception.

To accurately define and study the placebo effect, Ader and colleagues chose to frame it as an example of a well established psychological phenomenon: the conditioned response. Nineteenth century Russian physiologist Ivan Pavlov was the first to study the phenomenon of conditioning. By ringing a bell (a conditioned stimulus) each day before giving his dogs food (an unconditioned stimulus), Pavlov found that the dogs would eventually salivate (a conditioned response) at the sound of the bell alone.

In the current study, Ader and colleagues sought to determine if a drug's therapeutic effect could be triggered by qualities associated with the drug, like its shape, color, smell and packaging, as well as by its administration by an authority figure in a white lab coat. These repeated associations, Ader argues, create conditioned responses, drug-like therapeutic effects of treatment caused, not by a drug's ingredients alone, but elicited by stimuli associated with the effects of active drug treatment. The results provide the first evidence that conditioned responses might be harnessed to influence the design of drug regimens in humans.

Research teams at the University of Rochester Medical Center and Stanford University conducted an 11 to 14-week, doubleblind, randomized clinical trial in 46 patients with mild-to-moderate psoriasis. Patients were on no other medications during the study, and had signed consent forms after being informed they might receive a reduced dose of topical steroid.

At the start of the study, researchers randomly selected two "target" psoriatic lesions or sores on each patient. Twice each day during a three-week baseline period, all patients spread a lotion containing a full dose of steroid medication (0.1% Aristocort A, triamcinolone acetonide) onto one of their two study lesions. The second lesion was coated with a moisturizing cream. Medicated and unmedicated creams were distributed in coded syringes to make them indistinguishable.

Nearly all past drug studies divided patients into two groups only. One would get the full dose of the drug all of the time (a 100 percent reinforcement schedule). The other would get zero drug all of the time (zero percent

reinforcement). The current study asks for the first time: what if we treat patients with something in between drug and placebo? After the three-week baseline period, patients were randomly assigned to one of three groups.

The first continued to receive 100 percent of the treatment drug at each administration for the rest of the study on his or her study lesion. A second, the partial reinforcement group, also continued to receive a full dose, but only 25 or 50 percent of the time, and a steroid-free emollient the rest of the time. The study was designed so that this second group could benefit from exposure to cues they had previously associated with active drug treatment (a conditioned therapeutic effect). A third group, the "dose control group," received active drug at every administration, but at 25 or 50 percent of the full dose used in the first and second groups. Thus, the partial reinforcement and "dose control" groups received the same total amount of active medication, but in different patterns.

Results were measured in two ways. First, a "blinded" dermatologist measured the severity of a patient's psoriasis lesions weekly using the Psoriasis Severity Scale (PSS), a standard tool used to track the redness, hardening and thickening of skin. The second measure was whether a patient experienced a "relapse" in lesion severity, defined arbitrarily as a return to a PSS score within two units of a patient's initial score.

In terms of the overall PSS severity scores, results were mixed. The Stanford study site found no group differences in PSS scores that could be attributed to the different treatment regimens. Ader believes that elevated baseline PSS scores in the randomly selected Dose Control subjects at Stanford might have obscured the differences between the dose control and partial reinforcement groups. For instance, results could have been influenced by differences in the amount of sun patients were exposed to in Upstate New York and California (ultraviolet light is an established treatment for psoriasis).

In Rochester, there were no differences between the PSS values of the Partial Reinforcement and Dose Control groups at the point in the study where experimental treatment began. In this case, partial reinforcement brought about a greater reduction in lesion severity during the experimental period than continuous reinforcement with the same cumulative amount of drug.

The relapse results were clearer. Four of 18 patients (22.2 percent) in the 100 percent reinforcement group (full dose all the time) relapsed within the eight-week experimental period. Among patients treated with a full dose of drug, but one half or one quarter of the time (50 or 25 percent reinforcement schedule), four of 15 patients (26.7 percent) relapsed. Thus, the incidence of relapse did not differ substantially between patients receiving a full dose of drug all the time and those treated under the partial reinforcement schedules, researchers said. In contrast, eight of the 13 patients (61.5 percent) in the dose control group who received active drug each time, but not the full does, relapsed in the same period of time.

Thus, the incidence of relapse in the partial reinforcement group (26.7 percent) was significantly less than in dose control patients (61.5 percent) that received the same cumulative amount of drug. Further studies are underway, and others are planned, to confirm the effect, answer the questions raised and explore the effect in other autoimmune diseases.

"The pharmaceutical industry may choose to ignore the conditioning component of drug treatment regimens," Ader said. "Alternatively, they may now consider exploring ways to exploit conditioning in the design of drug treatment protocols, especially in chronic conditions where patients acquire conditioned responses over time. I believe industry will eventually support this approach because it promises to increase safety and reduce production costs."

The study was conducted jointly by the Departments of Psychiatry and Dermatology within the School of Medicine & Dentistry at the University of Rochester and the Stanford University School of Medicine. Along with Ader, the study was authored in Rochester by Mary Gail Mercurio, James Walton and Deborra James. Leading the effort at Stanford were David Fiorentino, Alexa Kimball, Michael Davis and Valerie Ojha. The study was funded by a grant from the National Institute of Arthritis, Metabolic and Skin Disease (NIAMS), part of the National Institutes of Health (NIH).

Bacteria make the artificial blood vessels of the future

The cellulose produced by bacteria could be used for artificial blood vessels in the future as it carries a lower risk of blood clots than the synthetic materials currently used for bypass operations, reveals a thesis from the Sahlgrenska Academy at the University of Gothenburg, Sweden.

Produced by a bacterium known as Acetobacter xylinum, the cellulose is strong enough to cope with blood pressure and works well with the body's own tissue. The thesis shows that the material also carries a lower risk of blood clots than the synthetic materials currently in use.

"There are hardly any blood clots at all with the bacterial cellulose, and the blood coagulates much more slowly than with the materials I used as a comparison," says molecular biologist Helen Fink, who wrote the

thesis. "This means that the cellulose works very well in contact with the blood and is a very interesting alternative for artificial blood vessels."

Real blood vessels have an internal coating of cells that ensure that the blood does not clot. Helen Fink and her colleagues have modified the bacterial cellulose so that these cells adhere better.

"We've used a brand new method which allows us to increase the number of cells that grow in the bacterial cellulose without changing the material's structure," says Fink.

Bypass Operations

If the coronary vessels around the heart are blocked as a result of hardening of the arteries, it may be necessary to carry out a bypass operation. Every year around 6,000 of these operations are carried out in Sweden. The surgeon takes a section of a vein from, for example, the patient's leg, and uses it to divert the blood around the hardened artery. Where patients do not have any suitable vessels, a vessel made of synthetic material is used instead.

Thesis for the degree of Doctor of Medicine at the Department of Surgery, Institute of Clinical Sciences, Sahlgrenska Academy
Title of thesis: Artificial blood vessels - studies on endothelial cell and blood interactions with bacterial cellulose

Remarkable Creatures

Whatever Doesn't Kill Some Animals Can Make Them Deadly

By SEAN B. CARROLL

Have you ever tried to think up the worst meal you could imagine? How about blue-ringed octopus, floral egg crab, basket shell snails and puffer fish.

Sure, some people may think these are delicacies, and puffer fish is certainly treated as such in parts of Asia. But each dish has something more important in common: they are all deadly. Each of these animals is chock full of a powerful neurotoxin called tetrodotoxin.

First isolated from the puffer fish, tetrodotoxin is among the most potent toxins known. It is 100 times as toxic by weight as potassium cyanide - two milligrams can kill an adult human - and it is not destroyed by cooking. Just half an ounce of the fish liver, known as fugu kimo in Japan and eaten by daring connoisseurs, can be lethal. When ingested, the toxin paralyzes nerves and muscles, which leads to respiratory failure and, in some cases each year, death.

In 1975, the Kabuki actor Bando Mitsugoro VIII ordered four fugu kimo in a restaurant in Kyoto, claiming he could resist the poison. He was wrong.

Tetrodotoxin is found in more than just marine creatures. It is present in high concentrations in the skin of certain newts in North America and Japan, and in several kinds of frogs in Central and South America and Bangladesh. The widespread occurrence of tetrodotoxin poses some intriguing riddles. First, how is it that such different animals, belonging to separate branches of the animal kingdom, have all come to possess the same deadly poison? And how is it that they are able to tolerate high levels of tetrodotoxin while others cannot?

The questions are particularly interesting because, in general, animal toxins are distinct and specific to each group. For instance, the venoms produced by snakes and scorpions are made of different kinds of toxins. But the tetrodotoxin found in each dish of that deadly buffet is identical.

One explanation could be that each of these animals has independently found a way to synthesize tetrodotoxin. But the toxin is a rather complex molecule that requires several chemical steps to assemble. It seems very unlikely that the molecule would be invented many times over in different animals. Rather, the evidence suggests that animals do not make the toxin themselves.

For instance, when puffer fish are raised in aquariums with filtered, bacteria-free water, they are nontoxic. Similarly, when Japanese newts or Panamanian frogs are raised on special diets, they lose their toxicity. These experiments indicate that tetrodotoxin-bearing animals obtain the toxin from the food chain. Indeed, several species of tetrodotoxin-producing bacteria have now been isolated from puffer fish, the blue-ringed octopus, certain snails and other animals. It appears that the animals become toxic by sequestering the bacterially produced toxin in their tissues.

While those discoveries solve the mystery of the source of tetrodotoxin, they do not quite explain how so many kinds of animals exploit it. Tetrodotoxin attacks an ancient feature of the animal kingdom, blocking channels that normally control the movement of sodium ions across nerve and muscle cell membranes and halting their electrical activity. All animals have these sodium ion channels, and the part of the channel that tetrodotoxin fits into and blocks is generally very similar among them.

This fact raises a simple question: Why aren't puffer fish dead? How are tetrodotoxin-bearing animals able to withstand high levels of a substance that attacks their nervous systems?

One clue is that not all 120 or so species of puffer fish are toxic or resistant to tetrodotoxin. Toxic species can withstand about 500 to 1,000 times the concentration of tetrodotoxin compared with nontoxic puffers or other fish. The flower egg crab is similarly resistant, and the Japanese newt can withstand an even greater relative concentration of toxin. Most other crabs and newts are sensitive to tetrodotoxin. There must be something different then about toxic, tetrodotoxin-resistant species.

That difference becomes clear from examining their sodium channels in detail. Puffer fish have eight versions of these channels encoded by eight separate genes. Manda Clair Jost and her colleagues at the University of Texas at Austin and the University of Chicago have discovered that in toxic puffer fish, most or all of these channels have evolved resistance to tetrodotoxin and different groups of puffer fish appear to have independently acquired resistance. Toxin-resistant channels have also been identified in a Japanese newt.

So the most plausible chain of events for the evolution of high-level toxin resistance is that mutations initially occur that afford some protection and that the continuing presence of tetrodotoxin in the environment selects for animals bearing additional mutations until, over time, many or all channels are highly resistant. In this sense, what does not kill the evolving animals makes them stronger, and deadly.

In most cases, tetrodotoxin is an effective defensive weapon. But in the game of natural selection, victory is rarely total or permanent. Predators could evolve resistance via the same path that made prey toxic, and this is exactly what has happened in some snakes in the western United States that now feast on highly toxic newts.

Unlike most snakes that are immobilized, sickened or killed when they try to ingest these newts, members of three species of garter snakes are able to dine on the toxic amphibians. A team of researchers led by Edmund Brodie Jr. of Utah State University and his son Edmund Brodie III of the University of Virginia found that the species have independently evolved tetrodotoxin-resistant sodium channels. Indeed, some snakes from California are so resistant that the dose of toxin needed to immobilize them is sufficient to kill 900 people.

Remarkably, some of the same channel gene mutations responsible for conferring partial resistance to tetrodotoxin have occurred in different snake species. Moreover, some of these and other mutations have also occurred repeatedly in puffer fish channels.

These precise parallels in channel evolution among species reveal a surprising facet of evolution that biologists had no inkling of before the ability to pinpoint adaptive changes in DNA - namely, that evolution is more reproducible than previously thought. The simple explanation for that profound insight is that given similar agents of natural selection (tetrodotoxin in this case), very different species living in different places on the planet will evolve similar or identical adaptations.

It follows then that evolution is somewhat predictable. Given the prevalence of tetrodotoxin-producing bacteria and the many known uses of the toxin as a defensive weapon strategy, we should expect to find more toxic animal species. With luck, the discoveries will not be made at dinner.

Sean B. Carroll, a molecular biologist and geneticist, is the author of “Remarkable Creatures: Epic Adventures in the Search for the Origin of Species.”

Got smell?

New Brandeis research shows that accurate taste perception relies on a functioning olfactory system

Waltham, MA - As anyone suffering through a head cold knows, food tastes wrong when the nose is clogged, an experience that leads many to conclude that the sense of taste operates normally only when the olfactory system is also in good working order. Evidence that the taste system influences olfactory perception, however, has been vanishingly rare - until now. In a novel study this week in Nature Neuroscience, Brandeis researchers report just such an influence.

Neuroscientist Don Katz and colleagues discovered that if the taste cortex in rats is inactivated when a rat first smells an odor, at least a food odor, then the rat subsequently will only recognize the food associated with that odor if the taste cortex is again inactivated.

"We discovered that rats use their taste system to smell with, so when you knock out the taste cortex, even for an hour, as we did, you alter their sense of smell," explained Katz. The researchers wrote that "this is the only example of state dependency in neural circuit function of which we are aware."

Katz and his colleagues used a multi-step training process to test the interdependence of the taste and olfactory systems. In the first step, a demonstrator rat that had just eaten chow flavored with one of four spices was introduced to a subject rat, which then smelled the demonstrator rat's breath.

In the second step, the subject rat was offered two choices of chow: one dish with the same flavor previously consumed by the demonstrator rat and another with a different flavor. The subject rat reliably preferred the food

that it had previously smelled on the demonstrator rat's breath the day before. The researchers concluded that the social "smell test" of rat's breath is a good enough cue for rats to prefer one food over another.

At the outset they predicted that the rat's sense of smell would not be affected by changes in its taste system. "But we were wrong," said Katz. "Most surprisingly, the rats whose taste cortex was knocked out again the next day preferred the chow that they had experienced in an altered state, with no taste cortex.

"We discovered in this experiment that the sensory systems don't work in isolation from each other, said Katz. "One part of the cortex takes direct input from the nose, and one part from the tongue, and while it's convenient to think that the nose and taste receptors operate independently, they don't."

Katz actually tested two possible explanations for the basic result: First, taste cortex might be an integral component of how the animal processes smells. Alternatively, it might be that taste cortex changes, or modulates, olfactory circuits rather than coding them, fundamentally changing perception of smell at that point in time. Such "incorrect" memories of smell apparently last across at least a week of the rats' lives, and perhaps forever.

The Katz lab is now using brain recordings to pinpoint which parts of the olfactory system are affected when taste cortex is silenced, and to characterize the nature of the interaction between the taste and smell systems during feeding.

"I am hoping that ultimately this discovery will help drive us to an entirely different approach to brain function," said Katz. "It doesn't make sense to probe one system separately from the other. Just like in a chorus, you can't appreciate the fullness of the music if you hear only the bass or the tenor in isolation."

Yaihara Fortis-Santiago was the first author of the study. Benjamin A. Rodwin, Selin Neseliler, and Caitlin E. Piette also contributed to the study.

Innovation: The sinister powers of crowdsourcing

*** 12:42 22 December 2009 by MacGregor Campbell**

Innovation is our regular column that highlights emerging technological ideas and where they may lead

When an ad hoc team of 5000 people who assembled in just two hours found 10 weather balloons hidden across the US by the Pentagon's research agency earlier this month, it was just another demonstration of the power of crowdsourcing – solving a task by appealing to a large undefined group of web users to each do a small chunk of it.

So far crowdsourcing has been associated with well-meaning altruism, such as the creation and maintenance of Wikipedia or searching for lost aviators. But crowdsourcing of a different flavour has started to emerge.

Law enforcement officials in Texas have installed a network of CCTV cameras to monitor key areas along that state's 1900-kilometre-long border with Mexico. To help screen the footage, a website lets anyone log in to watch a live feed from a border camera and report suspicious activity. A similar system called Internet Eyes, which pays online viewers to spot shoplifters from in-store camera feeds, is set to launch in the UK in 2010. An Iranian website is offering rewards for identifying people in photos taken during protests over June's elections.

Crowd chilling

Some people have declared those examples chilling. Now Jonathan Zittrain, a Harvard University law professor and co-founder of the Berkman Center for Internet and Society, says the next step may be for such efforts to get web users to help out covertly.

In a recent talk, "Minds for Sale", at the Computer History Museum in Mountain View, California, he pointed out that this could be done right away, using Amazon's Mechanical Turk, a service that provides a platform for anyone to farm out simple tasks.

In a speculative example, Zittrain has calculated that, assuming a population in Iran of around 72 million people, it would cost around $17,000 for the government to use Mechanical Turk to identify any arbitrary person's picture, without the users that are doing it realising the cause they have enlisted in. The scheme would show "Turkers" a photo of a protest, or just faces extracted from one, along with five randomly chosen photos from the country's ID card database, and asked to say whether or not there is any match.

Users would receive a few cents each time they contribute. Furthermore, Zittrain says that such a task might be made into an addictive game, similar to Google's image labeller.

"The people making the identifications in India or the US, idly doing this on their lunch hour instead of Minesweeper, would have no idea of the implications of what they are doing," Zittrain said in the talk. "I think people ought to know how their work is being used," he told New Scientist.

Crowdsourcing's power to compartmentalise and abstract away the true meaning of tasks turns human intelligence into a commodity. Zittrain's thought experiment shows how it could potentially entice people into participating in a project that they otherwise wouldn't support.

Basics

Sorry, Vegans: Brussels Sprouts Like to Live, Too

By NATALIE ANGIER

I stopped eating pork about eight years ago, after a scientist happened to mention that the animal whose teeth most closely resemble our own is the pig. Unable to shake the image of a perky little pig flashing me a brilliant George Clooney smile, I decided it was easier to forgo the Christmas ham. A couple of years later, I gave up on all mammalian meat, period. I still eat fish and poultry, however and pour eggnog in my coffee. My dietary decisions are arbitrary and inconsistent, and when friends ask why I' m willing to try the duck but not the lamb, I don't have a good answer. Food choices are often like that: difficult to articulate yet strongly held. And lately, debates over food choices have flared with particular vehemence.

In his new book, "Eating Animals," the novelist Jonathan Safran Foer describes his gradual transformation from omnivorous, oblivious slacker who "waffled among any number of diets" to "committed vegetarian." Last month, Gary Steiner, a philosopher at Bucknell University, argued on the Op-Ed page of The New York Times that people should strive to be "strict ethical vegans" like himself, avoiding all products derived from animals, including wool and silk. Killing animals for human food and finery is nothing less than "outright murder," he said, Isaac Bashevis Singer's "eternal Treblinka."

But before we cede the entire moral penthouse to "committed vegetarians" and "strong ethical vegans," we might consider that plants no more aspire to being stir-fried in a wok than a hog aspires to being peppercorn-studded in my Christmas clay pot. This is not meant as a trite argument or a chuckled aside. Plants are lively and seek to keep it that way. The more that scientists learn about the complexity of plants - their keen sensitivity to the environment, the speed with which they react to changes in the environment, and the extraordinary number of tricks that plants will rally to fight off attackers and solicit help from afar - the more impressed researchers become, and the less easily we can dismiss plants as so much fiberfill backdrop, passive sunlight collectors on which deer, antelope and vegans can conveniently graze. It's time for a green revolution, a reseeding of our stubborn animal minds.

When plant biologists speak of their subjects, they use active verbs and vivid images. Plants "forage" for resources like light and soil nutrients and "anticipate" rough spots and opportunities. By analyzing the ratio of red light and far red light falling on their leaves, for example, they can sense the presence of other chlorophyllated competitors nearby and try to grow the other way. Their roots ride the underground "rhizosphere" and engage in cross-cultural and microbial trade.

"Plants are not static or silly," said Monika Hilker of the Institute of Biology at the Free University of Berlin. "They respond to tactile cues, they recognize different wavelengths of light, they listen to chemical signals, they can even talk" through chemical signals. Touch, sight, hearing, speech. "These are sensory modalities and abilities we normally think of as only being in animals," Dr. Hilker said.

Plants can't run away from a threat but they can stand their ground. "They are very good at avoiding getting eaten," said Linda Walling of the University of California, Riverside. "It's an unusual situation where insects can overcome those defenses." At the smallest nip to its leaves, specialized cells on the plant's surface release chemicals to irritate the predator or sticky goo to entrap it. Genes in the plant's DNA are activated to wage systemwide chemical warfare, the plant's version of an immune response. We need terpenes, alkaloids, phenolics - let's move.

"I'm amazed at how fast some of these things happen," said Consuelo M. De Moraes of Pennsylvania State University. Dr. De Moraes and her colleagues did labeling experiments to clock a plant's systemic response time and found that, in less than 20 minutes from the moment the caterpillar had begun feeding on its leaves, the plant had plucked carbon from the air and forged defensive compounds from scratch.

Just because we humans can't hear them doesn't mean plants don't howl. Some of the compounds that plants generate in response to insect mastication - their feedback, you might say - are volatile chemicals that serve as cries for help. Such airborne alarm calls have been shown to attract both large predatory insects like dragon flies, which delight in caterpillar meat, and tiny parasitic insects, which can infect a caterpillar and destroy it from within.

Enemies of the plant's enemies are not the only ones to tune into the emergency broadcast. "Some of these cues, some of these volatiles that are released when a focal plant is damaged," said Richard Karban of the University of California, Davis, "cause other plants of the same species, or even of another species, to likewise become more resistant to herbivores." Yes, it's best to nip trouble in the bud.

Dr. Hilker and her colleagues, as well as other research teams, have found that certain plants can sense when insect eggs have been deposited on their leaves and will act immediately to rid themselves of the incubating

menace. They may sprout carpets of tumorlike neoplasms to knock the eggs off, or secrete ovicides to kill them, or sound the S O S. Reporting in The Proceedings of the National Academy of Sciences, Dr. Hilker and her coworkers determined that when a female cabbage butterfly lays her eggs on a brussels sprout plant and attaches her treasures to the leaves with tiny dabs of glue, the vigilant vegetable detects the presence of a simple additive in the glue, benzyl cyanide. Cued by the additive, the plant swiftly alters the chemistry of its leaf surface to beckon female parasitic wasps. Spying the anchored bounty, the female wasps in turn inject their eggs inside, the gestating wasps feed on the gestating butterflies, and the plant's problem is solved.

Here's the lurid Edgar Allan Poetry of it: that benzyl cyanide tip-off had been donated to the female butterfly by the male during mating. "It's an anti-aphrodisiac pheromone, so that the female wouldn't mate anymore," Dr. Hilker said. "The male is trying to ensure his paternity, but he ends up endangering his own offspring."

Plants eavesdrop on one another benignly and malignly. As they described in Science and other journals, Dr. De Moraes and her colleagues have discovered that seedlings of the dodder plant, a parasitic weed related to morning glory, can detect volatile chemicals released by potential host plants like the tomato. The young dodder then grows inexorably toward the host, until it can encircle the victim's stem and begin sucking the life phloem right out of it. The parasite can even distinguish between the scents of healthier and weaker tomato plants and then head for the hale one.

"Even if you have quite a bit of knowledge about plants," Dr. De Moraes said, "it's still surprising to see how sophisticated they can be."

It's a small daily tragedy that we animals must kill to stay alive. Plants are the ethical autotrophs here, the ones that wrest their meals from the sun. Don't expect them to boast: they're too busy fighting to survive.

New strain of MRSA poses antibiotic resistance concerns

PORTLAND, Ore. – The often feared and sometimes deadly infections caused by MRSA – methicillin-resistant Staphylococcus aureus – are now moving out of hospitals and emerging as an even more virulent strain in community settings and on athletic teams, and raising new concerns about antibiotic resistance.

Right now, the new community-associated strain of MRSA is responsive to more, but sometimes different antibiotics than its hospital relative, experts say. But those antibiotics will almost certainly lose their effectiveness as they are used more widely, and efforts are under way to combat that issue.

A new study by pharmacy researchers at Oregon State University has identified two antibiotics that appear less likely to cause future antibiotic resistance, and others that if used would allow resistance to emerge more quickly. This analysis, just published in the International Journal of Antimicrobial Agents, offers physicians some direction to help deal with this problem until more research can be done, they said.

"The problem with invasive MRSA infections is very real and is now moving from the hospital setting to the community," said George Allen, an assistant professor in the OSU College of Pharmacy. "The community-based strain in some ways is even more apt to cause serious problems than those most often acquired in hospitals, and increasing quite dramatically in prevalence.

"The good news is that so far the community strain is more treatable, if we can keep it that way," he said.

Staphylococcus aureus, a common bacterium that's often associated with skin infections, was once treated easily by penicillin. But over many years it acquired resistance to that, as well as the penicillin-derivative methicillin and other antibiotics, leaving limited options to address it. Although infections are usually minor, some can spread rapidly, cause pneumonia, tissue necrosis, blood infections, shock and death.

In the new research based on laboratory analysis, scientists identified linezolid and moxifloxacin as two antibiotics that would be effective against, and less apt to induce antibiotic resistance in the new strain of community-associated MRSA. That's of some interest because moxifloxacin, like other antibiotics in its class, has not been traditionally thought of as an appropriate agent for MRSA because resistance to it often develops rapidly. Antibiotics that are most apt to cause rapid development of resistance against the community-associated strain of MRSA include clindamycin and doxycycline, the research found. The study was supported by the Society of Infectious Diseases Pharmacists.

"We didn't find one perfect choice of a drug that everyone could use and it won't ever develop resistance," Allen said. "That's not surprising, since with constant use every antibiotic breeds resistance to it in various bacteria. Part of the goal here is just to slow down the increase in resistance while we continue to develop new approaches."

More research, animal and clinical trials would still be of value to further explore this issue, Allen said. The issue of antibiotic resistance in general and MRSA resistance in particular is huge and getting worse.

Meanwhile, the general public should be aware that MRSA infections are no longer confined to the hospital, and can be acquired in ordinary community settings, he said. They are often associated with close personal

contact, and have been a particular problem with some athletic sports such as wrestling or football when multiple members of a team have been infected.

MRSA usually, but not always shows first as a skin infection, with such symptoms as swelling, pain, pus or fever. Any significant symptoms or evidence of spread of the infection should be seen by a physician, Allen said. Basic first aid – soap, water and a bandage – on cuts and scrapes is a good first line of defense, he said, and some antibacterial ointments are available that have been proven to have enhanced effectiveness against MRSA infections.

Complicating the issue, experts say, is that the new community-associated strain of MRSA is now showing up in hospitals, as well, and optimal treatment regimens for the two strains may differ.

“Our data suggest that resistance to all of the tested antimicrobials will develop with their continued use,” the researchers wrote in their report.

Could acetaminophen ease psychological pain?

Headaches and heartaches. Broken bones and broken spirits. Hurting bodies and hurt feelings. We often use the same words to describe physical and mental pain. Over-the-counter pain relieving drugs have long been used to alleviate physical pain, while a host of other medications have been employed in the treatment of depression and anxiety. But is it possible that a common painkiller could serve double duty, easing not just the physical pains of sore joints and headaches, but also the pain of social rejection? A research team led by psychologist C. Nathan DeWall of the University of Kentucky College of Arts and Sciences Department of Psychology has uncovered evidence indicating that acetaminophen (the active ingredient in Tylenol) may blunt social pain.

"The idea - that a drug designed to alleviate physical pain should reduce the pain of social rejection - seemed simple and straightforward based on what we know about neural overlap between social and physical pain systems. To my surprise, I couldn't find anyone who had ever tested this idea," DeWall said.

According to a study due to be published in the journal Psychological Science, DeWall and colleagues were correct. Physical and social pain appear to overlap in the brain, relying on some of the same behavioral and neural mechanisms.

DeWall and colleagues investigated this connection through two experiments. In the first experiment, 62 healthy volunteers took 1,000 milligrams daily of either acetaminophen or a placebo. Each evening, participants reported how much they experienced social pain using a version of the "Hurt Feelings Scale" - a measurement tool widely accepted by psychologists as a valid measure of social pain. Hurt feelings and social pain decreased over time in those taking acetaminophen, while no change was observed in subjects taking the placebo. Levels of positive emotions remained stable, with no significant changes observed in either group. These results indicate that acetaminophen use may decrease self-reported social pain over time, by impacting emotions linked to hurt feelings.

"We were very excited about these initial findings," DeWall said. "The next step was to identify the neural mechanisms underlying the findings."

In the second experiment, 25 healthy volunteers took 2,000 milligrams daily of either acetaminophen or a placebo. After three weeks of taking the pills, subjects participated in a computer game rigged to create feelings of social rejection. Functional magnetic resonance imaging (fMRI) employed during the game revealed that acetaminophen reduced neural responses to social rejection in brain regions associated with the distress of social pain and the affective component of physical pain (the dorsal anterior cingulate cortex and anterior insula). In other words, the parts of the brain associated with physical lit up in the placebo subjects when they were rejected, while the acetaminophen group displayed significantly less activity in these brain areas in response to rejection.

According to the academic paper detailing the experiments: "...findings suggest that at least temporary mitigation of social pain-related distress may be achieved by means of an over-the-counter painkiller that is normally used for physical aches and pains. Furthermore, many studies have shown that being rejected can trigger aggressive and antisocial behavior, which could lead to further complications in social life... .If acetaminophen reduces the distress of rejection, the antisocial behavioral consequences of rejection may be reduced as well."

Researchers caution that readers should not immediately stock up on acetaminophen to ease social pain and anxiety, noting "[t]o be sure, our findings do not constitute a call for widespread use of acetaminophen to cope with all types of personal problems. Future research is needed to verify the potential benefits of acetaminophen on reducing emotional and antisocial responses to social rejection." Long-term use of acetaminophen has also been linked to serious liver damage, so it is important for patients to follow all package directions and consult their physicians if they are contemplating taking any medication for an off-label use.

"This research has the potential to change how scientists and laypersons understand physical and social pain. Social pain, such as chronic loneliness, damages health as much as smoking and obesity. We hope our findings can pave the way for interventions designed to reduce the pain of social rejection," DeWall said.

For a copy of this report please contact Catherine Allen-West at 202-293-9300 or cwest@psychologicalscience.org or Allison Elliott, University of Kentucky Public Relations, at (859) 257-1754 ext. 249 or via e-mail at allison.elliott@uky.edu.

Are we looking in the wrong places for water on the moon?

* 22:48 22 December 2009 **by Dana Mackenzie**, San Francisco

Water is turning up in unexpected places on the moon, controversial new observations suggest.

According to theory, water is not stable on the moon's surface above -167 °C. As a result, ice should be concentrated in "cold traps" near the lunar poles, in craters that never get any sunlight. NASA's LCROSS spacecraft found water when it crashed into one such crater, called Cabeus in October.

But new observations from the Lunar Reconnaissance Orbiter (LRO) suggest that many of the permanently shadowed regions near the south pole are dry and several potentially wet regions are sunlit.

Conventional theory says water ice should be concentrated in permanently shadowed craters near the poles, but that's not where it seems to be turning up (Image: NASA/GSFC/Arizona State University)

The observations come from the Lunar Exploration Neutron Detector (LEND) experiment, which looks for possible water deposits by measuring neutrons emitted from the moon. Water or other hydrogen-bearing compounds reduce the number of fast neutrons.

LEND examined 37 permanently shadowed craters near the south pole and found that only three of them – Cabeus, Faustini, and Shoemaker – showed significant amounts of hydrogen. Several illuminated regions also appear to be hydrogen rich.

"I think we have a paradigm-busting set of observations here," says Jim Garvin, the chief scientist at NASA's Goddard Space Flight Center.

Targeted search

LEND's principal scientist, Igor Mitrofanov of the Russian Space Research Institute, reported these "neutron suppressed regions" last week at the American Geophysical Union meeting in San Francisco.

He believes that a half-metre-thick layer of dry soil may cover a layer of dirty ice, preventing the ice from evaporating into space. He and his colleagues calculate that the icy layer, which may have been delivered to the moon by asteroids or comets, could contain concentrations of water as high as 3 to 5 per cent.

However, the new results remain controversial. The LEND instrument contains a new feature that is designed to improve its focus, so that it only picks up neutrons from a small patch of ground below it. But it has not been tested on a planetary mission before, and some researchers suspect it may be detecting neutrons from surrounding regions as well.

"There are a lot of questions about the instrument response that need to be answered," says Rick Elphic of NASA Ames Research Center. "The jury's still out on the validity of what they are claiming to see."

Fortunately, LRO is expected to continue gathering data for two more years, and LEND's results will grow more accurate over time. "I think our story will be a lot sharper by next summer," Garvin says.

Genomic toggle switches divide autoimmune diseases into distinct clusters, Stanford study shows

STANFORD, Calif. - Genomic switches can predispose an individual to one set of autoimmune disorders but protect the same person against another set of them, scientists at Stanford University School of Medicine have found.

"Maybe we should stop considering all autoimmune diseases in one lumped category," said Atul Butte, MD, PhD, assistant professor of pediatrics and of biomedical informatics and director of the Center for Pediatric Bioinformatics at Lucile Packard Children's Hospital. "It looks as if there may be at least two different kinds."

Pairs of autoimmune diseases have been linked in clinical practice, Butte said. People with type-1 diabetes are routinely screened for autoimmune thyroid disease, for which they are known to be at heightened risk. But no one has ever known why.

A study to be published online Dec. 24 in PLoS-Genetics provides a genetic basis for this clustering effect, while extending it to show how two such clusters tend to be mutually exclusive. Butte, who is the study's senior author, and his colleagues looked at data from several large genome-wide association studies of single-nucleotide polymorphisms, or SNPs: tiny genomic variations that constitute the genetic underpinning for inter-individual human differences from eye color to nose shape to personality quirks.

The human genome can be thought of as a 3-billion-unit-long sequence, with each unit consisting of one of four different chemical residues. At almost every specific location along two different people's genomes, the resident chemical unit is the same. But at about one or two out of every 1,000 positions, the first person's genome may boast one variety of chemical unit, while the second's hosts another type. This single-unit difference is a SNP (pronounced "snip").

There are several million SNPs in the human genome, making for a gigantic number of possible different versions of a human being, said the study's lead author, Marina Sirota, a fourth-year PhD student under Butte's supervision in Stanford's Biomedical Informatics Program. In so-called genome-wide association studies, SNPs linked to disease susceptibility are found by assessing genomes from two large groups of people, one composed of patients with, say, rheumatoid arthritis or heart disease and another of people without the condition. If, at a given SNP location, the frequency of one particular chemical unit is significantly greater or smaller among the diseased people than in the healthy ones, that SNP is presumed to lie close to or within a biologically important genomic region that increases or diminishes genetic susceptibility to the disease, Sirota said.

In the past few years the industrial-scale characterization of SNPs has been hugely enhanced by sophisticated electronic devices called gene chips, pioneered at Stanford about a decade ago. Gene chips can quickly scan an individual's genome to identify the chemical unit occupying each of more than a million SNP locations.

"More than 400 genome-wide association studies have been published since gene-chip technology took off a few years ago," said Butte. From these published studies, Sirota, Butte and their colleagues culled about a half-dozen that had been conducted on patients with or without autoimmune diseases including type-1 diabetes, rheumatoid arthritis, multiple sclerosis, autoimmune thyroid disease and a spinal condition called ankylosing spondylitis. The investigators restricted their attention to SNPs that were examined in all the studies they were focusing on. That worked out to 573 SNPs. Of those, the researchers found 15 SNPs for which having a particular chemical unit at that site predisposed an individual to several autoimmune diseases.

That wasn't surprising, said Sirota. "We had started out looking for just such similarities. What was surprising was our finding that at nine locations generally associated with autoimmunity risk, where a particular chemical unit conferred a heightened risk of certain autoimmune diseases, but reduced risk of getting certain others."

For instance, a particular chemical unit at a SNP site shown to predispose people to multiple sclerosis also rendered them, as a group, more likely to have autoimmune thyroid disease, while the alternative chemical unit at the same site predisposed them to rheumatoid arthritis and ankylosing spondylitis. Most intriguing of all, people predisposed to one pair of diseases were protected against the other.

The scenario is akin to switches controlling banks of Christmas-tree lights. In addition to a master on/off switch that determines whether electricity (a general predisposition to autoimmune disease) will flow through the circuit, a second set of toggle switches determines whether, say, red or blue lights (one versus another autoimmune-disease cluster) will be on.

"As more genomic information becomes available on increasingly advanced platforms, this sort of analysis can be done on more diseases, possibly hundreds of them. Plus, the original set of 573 common SNPs we were able to inspect will grow much larger. So we'll be able to find more relationships like these," Sirota said.

Butte said finding SNPs predisposing people to one or another cluster of autoimmune diseases may help catch the onset of a disease earlier. "And if a patient has a particular autoimmune disease, this might help us know what else to screen that patient for, or guess whether a drug that works well in a different autoimmune disorder could be useful in treating this patient."

It might also help guide drug development, he added. "Several of these nine interesting SNPs we've found are located in or near genes that code for molecules found on cell surfaces, which makes them potentially easier targets for the drugs pharmaceutical researchers are best at producing."

Other Stanford co-authors were PhD student Marc Schaub and associate professor Serafim Batzoglou, PhD, of the computer science department, and William Robinson, MD, PhD, assistant professor of immunology and rheumatology. The study was funded by the Lucile Packard Foundation for Children's Health, National Institute of General Medical Sciences, National Library of Medicine, Howard Hughes Medical Institute and Pharmaceutical Research and Manufacturers of America Foundation.

Yale researchers reveal secrets of duck sex: It's all screwed up

Female ducks have evolved an intriguing way to avoid becoming impregnated by undesirable but aggressive males endowed with large corkscrew-shaped penises: vaginas with clockwise spirals that thwart oppositely spiraled males. More details of this evolutionary battle of the sexes fought at the level of genitalia are described by Yale researchers in the December 23 issue of the journal Proceedings of the Royal Society B.

"In species where forced copulation is common, males have evolved longer penises, but females have coevolved convoluted vaginas with dead-end cul-de-sacs and spirals in the opposite direction of the male

penis," said Patricia L.R. Brennan, lead author of the paper and postdoctoral researcher in the Yale Department of Ecology and Evolutionary Biology. "This coevolution results from conflict between the sexes over who is going to control fertilization."

The research builds upon a 2007 Yale study that first described the strange morphology of a duck's sexual organs. While most birds have no phalluses, ducks turn out to have relatively large, flexible penises - up to 20 centimeters - tucked inside their bodies. During sex, male ducks extend, or evert, their phalluses inside the female. Brennan and her Yale colleagues used high-speed video to document the erection of the duck penis for the first time and found the whole process takes less than half a second - an act the Yale team described as "explosive."

Such large phalluses are supposed to give males a reproductive advantage when there is much forced mating. However, the Yale team hypothesized that females could make copulation difficult for the males with their complex genitalia. And, they wondered, do the convoluted vaginas of some waterfowl help those females exclude forced copulation?

To test the hypothesis, Brennan and colleagues examined duck penis eversion in a set of glass tubes with different shapes. A straight tube or a tube that spirals in the same counter-clockwise direction as the male penis doesn't slow down the eversion process. But glass tubes that mimic the female vaginal shapes with a clockwise spiral or a sharp bend can completely stop the penis from everting. These results suggest females have evolved anatomical mechanisms to impede forced copulation, and provide new insights into the evolutionary consequences of sexual conflict over reproduction, say the scientists.

The anatomical evolutionary race to control reproduction is one of the more dramatic examples of sexual conflict in nature. "Although we predict that sexual conflict should be ubiquitous, finding a system where the 'arms race' between the sexes is so dramatic is exceedingly rare. Ducks are providing us with an incredible opportunity to understand the evolutionary consequences of conflict," said Brennan.

Other authors on the paper are Christopher J. Clark and Richard O. Prum, both from Yale. The study was funded by Yale University.

Genetic study reveals the origins of cavity-causing bacteria

Researchers have uncovered the complete genetic make-up of the cavity-causing bacterium Bifidobacterium dentium Bd1, revealing the genetic adaptations that allow this microorganism to live and cause decay in the human oral cavity. The study, led by Marco Ventura's Probiogenomics laboratory at the University of Parma, and Prof. Douwe van Sinderen and Dr Paul O'Toole of the Alimentary Pharmabiotic Centre at University College Cork, is published December 24 in the open-access journal PLoS Genetics.

Bifidobacteria, largely known as long-term beneficial gut bacteria, are often included as probiotic components of food to aid digestion and boost the immune system. However, not all species within the genus Bifidobacterium provide beneficial effects to the host's health. In fact, the Bifidobacterium dentium species is an opportunistic pathogen since it has been linked to the development of tooth decay. The genome sequence of B. dentium Bd1 reveals how this microorganism has adapted to the oral environment through specialized nutrient acquisition features, acid tolerance, defences against antimicrobial substances and other gene products that increase fitness and competitiveness within the oral niche.

This report identifies, through various genomic approaches, specific adaptations of a Bifidobacterium taxon to a lifestyle as a tooth decay-causing bacterium. The data in this study indicate that the genome of this opportunistic pathogen has evolved through only a small number of horizontal gene acquisition events, highlighting the narrow boundary that separates bacteria that are long-term residents on or in the human body from opportunistic pathogens.

CITATION: *Ventura M, Turroni F, Zomer A, Foroni E, Giubellini V, et al. (2009) The Bifidobacterium dentium Bd1 Genome Sequence Reflects Its Genetic Adaptation to the Human Oral Cavity. PLoS Genet 5(12): e1000785. doi:10.1371/journal.pgen.1000785 http://www.plosgenetics.org/article/info:doi/10.1371/journal.pgen.1000785*

Scientists Chart Velocity Of Climate Change

New study finds that the average ecosystem will need to shift about a quarter mile per year to keep pace with global climate change

SAN FRANCISCO - From beetles to barnacles, pikas to pine warblers, many species are already on the move in response to shifting climate regimes. But how fast will they - and their habitats - have to move to keep pace with global climate change over the next century? In a new study, a team of scientists including Dr. Healy Hamilton from the California Academy of Sciences have calculated that on average, ecosystems will need to shift about 0.42 kilometers per year (about a quarter mile per year) to keep pace with changing temperatures across the globe. Mountainous habitats will be able to move more slowly, since a modest move up or down slope can result in a large change in temperature. However, flatter ecosystems, such as flooded grasslands,

mangroves, and deserts, will need to move much more rapidly to stay in their comfort zone - sometimes more than a kilometer per year. The team, which also included scientists from the Carnegie Institute of Science, Climate Central, and U.C. Berkeley, will publish their results in the December 24 issue of Nature.

"One of the most powerful aspects of this data is that it allows us to evaluate how our current protected area network will perform as we attempt to conserve biodiversity in the face of global climate change," says Healy Hamilton, Director of the Center for Applied Biodiversity Informatics at the California Academy of Sciences. "When we look at residence times for protected areas, which we define as the amount of time it will take current climate conditions to move across and out of a given protected area, only 8% of our current protected areas have residence times of more than 100 years. If we want to improve these numbers, we need to both reduce our carbon emissions and work quickly toward expanding and connecting our global network of protected areas."

The team calculated the velocity of global climate change by combining data on current climate and temperature regimes worldwide with a large suite of climate model projections for the next century. Their calculations are based on an "intermediate" level of projected greenhouse gas emissions over the next century (the A1B emissions scenario from The Intergovernmental Panel on Climate Change). Under these emissions levels, the velocity of climate change is projected to be the slowest in tropical and subtropical coniferous forests (0.08 kilometers per year), temperate coniferous forests (0.11 kilometers per year), and montane grasslands and shrublands (0.11 kilometers per year). The velocity of climate change is expected to be the fastest in flatter areas, including deserts and xeric shrublands (0.71 kilometers per year), mangroves (0.95 kilometers per year), and flooded grasslands and savannas (1.26 kilometers per year).

The vulnerability of these respective biomes depends not only on the average velocity of climate change they will experience, but also on the sizes of the protected areas in which they are found. For instance, while the velocity of climate change is expected to be high in deserts, this threat is mediated by the fact that protected areas for deserts tend to be larger. On the other hand, the small size and fragmented nature of most protected areas in Mediterranean temperate broadleaf and boreal forest biomes make these habitats particularly vulnerable.

What does this mean for beetles, barnacles, and other groups of species? The researchers note that their index estimates the velocities and residence times of climates, not species. Individual species that have a wide tolerance for a range of temperatures may be able to adapt in place as the climate around them shifts. However, for species that can only tolerate a narrow band of temperatures, the velocity estimates in the study are a close approximation for the migration speeds needed to potentially avoid extinction. Nearly a third of the habitats in the study have velocities higher than even the most optimistic plant migration estimates, suggesting that plants in many areas will not be able to keep up with the shifting climate. Even more problematic is the fact that natural habitats have been extensively fragmented by human development, which will leave many species with "nowhere to go," regardless of their migration rates.

The team's results not only underscore the importance of lowering greenhouse gas emissions - they also provide data for conservation managers who must now plan for the impact of global climate change.

The research was funded by the Gordon and Betty Moore Foundation and the Stanford University Global Climate and Energy Project.

Sun and moon trigger deep tremors on San Andreas Fault

Link to earthquakes unclear, but tremors seem to increase stress on shallower fracture zone

The faint tug of the sun and moon on the San Andreas Fault stimulates tremors deep underground, suggesting that the rock 15 miles below is lubricated with highly pressurized water that allows the rock to slip with little effort, according to a new study by University of California, Berkeley, seismologists.

"Tremors seem to be extremely sensitive to minute stress changes," said Roland Bürgmann, UC Berkeley professor of earth and planetary science. "Seismic waves from the other side of the planet triggered tremors on the Cascadia subduction zone off the coast of Washington state after the Sumatra earthquake last year, while the Denali earthquake in 2002 triggered tremors on a number of faults in California. Now we also see that tides – the daily lunar and solar tides – very strongly modulate tremors."

In a paper appearing in the Dec. 24 issue of the journal Nature, UC Berkeley graduate student Amanda M. Thomas, seismologist Robert Nadeau of the Berkeley Seismological Laboratory and Bürgmann argue that this extreme sensitivity to stress – and specifically to shearing stress along the fault – means that the water deep underground is under extreme pressure. "The big finding is that there is very high fluid pressure down there, that is, lithostatic pressure, which means pressure equivalent to the load of all rock above it, 15 to 30 kilometers (10 to 20 miles) of rock," Nadeau said. "Water under very high pressure essentially lubricates the rock, making the fault very weak."

Though tides raised in the Earth by the sun and moon are not known to trigger earthquakes directly, they can trigger swarms of deep tremors, which could increase the likelihood of quakes on the fault above the tremor zone, the researchers say. At other fault zones, such as at Cascadia, swarms of tremors in the ductile zone deep underground correlate with slip at depth as well as increased stress on the shallower "seismogenic zone," where earthquakes are generated. The situation on the San Andreas Fault is not so clear, however.

"These tremors represent slip along the fault 25 kilometers (15 miles) underground, and this slip should push the fault zone above in a similar pattern," Bürgmann said. "But it seems like it must be very subtle, because we actually don't see a tidal signal in regular earthquakes. Even though the earthquake zone also sees the tidal stress and also feels the added periodic behavior of the tremor below, they don't seem to be very bothered."

Nevertheless, said Nadeau, "It is certainly in the realm of reasonable conjecture that tremors are stressing the fault zone above it. The deep San Andreas Fault is moving faster when tremors are more active, presumably stressing the seismogenic zone, loading the fault a little bit faster. And that may have a relationship to stimulating earthquake activity."

Seismologists were surprised when tremors were first discovered more than seven years ago, since the rock at that depth – for the San Andreas Fault, between 15 and 30 kilometers (10 to 20 miles) underground – is not brittle and subject to fracture, but deformable, like peanut butter. They called them non-volcanic tremors to distinguish them from tremors caused by fluid – water or magma – fracturing and flowing through rock under volcanoes. It was not clear, however, what caused the non-volcanic tremors, which are on the order of a magnitude 1 earthquake.

To learn more about the source of these tremors, UC Berkeley seismologists began looking for tremors five years ago in seismic recordings from the Parkfield segment of the San Andreas Fault obtained from sensitive bore-hole seismometers placed underground as part of the UC Berkeley's High-Resolution Seismic Network. Using eight years of tremor data, Thomas, Bürgmann and Nadeau correlated tremor activity with the effects of the sun and moon on the crust and with the effects of ocean tides, which are driven by the moon.

They found the strongest effect when the pull on the Earth from the sun and moon sheared the fault in the direction it normally breaks. Because the San Andreas Fault is a right-lateral strike-slip fault, the west side of the fault tends to break north-northwestward, dragging Los Angeles closer to San Francisco.

"When shear stress on a plane parallel to the San Andreas Fault most encourages slipping in its normal slip direction is when we see the maximum tremor rate," Bürgmann said. "The stress is many, many orders of magnitude less than the pressure down there, which was really, really surprising. You essentially could push it with your hand and it would move."

In fact, the shear stress from the sun, moon and ocean tides amount to around 100 Pascals, or one-thousandth atmospheric pressure, whereas the pressure 25 kilometers underground is on the order of 600 megaPascals, or 6 million times greater.

Nadeau and colleagues reported earlier this year that earthquakes in 2003 and 2004 near the Parkfield segment of the San Andreas Fault increased both tremor activity and stress on the fault itself.

In addition, Nadeau noted, other scientists have shown small tidal effects on tremors in the Cascadia subduction zone, with increased amplitude during certain periods, though they were unable to distinguish between tugs along the fault and tugs across, or normal to, the fault.

"We were really able to tighten the nuts down on whether it is a normal-fault stress change or an along-fault stress change that is stimulating the tremor," he said. The fact that tremors are triggered by along-fault shear stress "means that fluids are probably the explanation."

It may be that tremors only occur on faults where fluid is trapped deep underground with no cracks or fractures allowing it to squirt away, Nadeau added. That may explain why tremors are not observed on other faults, despite intense searching.

"There is still all lot to learn about tremor and earthquakes in fault zones," he said. "The fact that we find tremors adjacent to a locked fault, like the one at Parkfield, makes you think there are some more important relationships going on here, and we need to study it more."

The work was supported by the National Science Foundation and the U.S. Geological Survey.

New insights into mushroom-derived drug promising for cancer treatment

A promising cancer drug, first discovered in a mushroom commonly used in Chinese medicine, could be made more effective thanks to researchers who have discovered how the drug works. The research is funded by the Biotechnology and Biological Sciences Research Council and was carried out at The University of Nottingham.

In research to be published in the Journal of Biological Chemistry, Dr Cornelia de Moor of The University of Nottingham and her team have investigated a drug called cordycepin, which was originally extracted from a rare kind of wild mushroom called cordyceps and is now prepared from a cultivated form.

Dr de Moor said: “Our discovery will open up the possibility of investigating the range of different cancers that could be treated with cordycepin. We have also developed a very effective method that can be used to test new, more efficient or more stable versions of the drug in the Petri dish. This is a great advantage as it will allow us to rule out any non-runners before anyone considers testing them in animals.”

Cordyceps is a strange parasitic mushroom that grows on caterpillars (see image). Properties attributed to cordyceps mushroom in Chinese medicine made it interesting to investigate and it has been studied for some time. In fact, the first scientific publication on cordycepin was in 1950. The problem was that although cordycepin was a promising drug, it was quickly degraded in the body. It can now be given with another drug to help combat this, but the side effects of the second drug are a limit to its potential use.

Dr de Moor continued: “Because of technical obstacles and people moving on to other subjects, it’s taken a long time to figure out exactly how cordycepin works on cells. With this knowledge, it will be possible to predict what types of cancers might be sensitive and what other cancer drugs it may effectively combine with. It could also lay the groundwork for the design of new cancer drugs that work on the same principle.”

The team has observed two effects on the cells: at a low dose cordycepin inhibits the uncontrolled growth and division of the cells and at high doses it stops cells from sticking together, which also inhibits growth. Both of these effects probably have the same underlying mechanism, which is that cordycepin interferes with how cells make proteins. At low doses cordycepin interferes with the production of mRNA, the molecule that gives instructions on how to assemble a protein. And at higher doses it has a direct impact on the making of proteins.

Professor Janet Allen, BBSRC Director of Research said: “Research to understand the underlying bioscience of a problem is always important. This project shows that we can always return to asking questions about the fundamental biology of something in order to refine the solution or resolve unanswered questions. The knowledge generated by this research demonstrates the mechanisms of drug action and could have an impact on one of the most important challenges to health.”

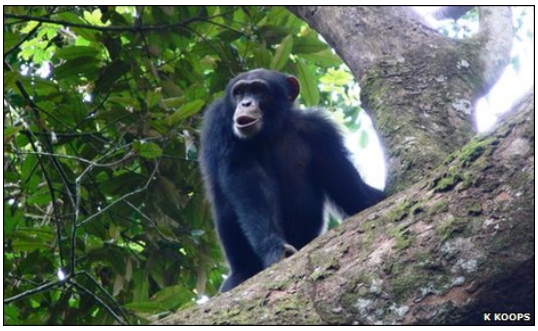
Chimps use cleavers to chop food

By Matt Walker Editor, Earth News

For the first time, chimpanzees have been seen using tools to chop up and reduce food into smaller bite-sized portions.

Chimps in the Nimba Mountains of Guinea, Africa, use both stone and wooden cleavers, as well as stone anvils, to process Treculia fruits. The apes are not simply cracking into the Treculia to get to otherwise unobtainable food, say researchers. Instead, they are actively chopping up the food into more manageable portions. Observations of the behaviour are published in the journal Primates. It's the first time wild chimpanzees have been found to use two distinct types of percussive technology to achieve the same goal

PhD student Kathelijne Koops and Professor William McGrew of the Leverhulme Centre for Human Evolutionary Studies, University of Cambridge, UK, studied a group of chimps living wild in the Nimba Mountains. Ms Koops research is focused on the use by the chimps of elementary technology, such as the use of tools while foraging.



Poni, a chimp who likes to chop his food

"Chimpanzees across Africa vary greatly in the types of tools they use to obtain food. Some groups use stones as hammers and anvils to crack open nuts, whereas others use twigs to fish for termites," she says.

The apes' use of such tools can be surprisingly sophisticated.

"For example, nut-cracking in the Bossou chimpanzee community in Guinea involves the use of a movable hammer and anvil, and sometimes the additional use of stabilising wedges to make the anvil more level and so more efficient," explains Ms Koops. "Termite fishing in some chimpanzee communities in the Republic of Congo involves the use of a tool set, i.e. different tool components used sequentially to achieve the same goal.

"These chimpanzees were found to deliberately modify termite fishing probes by creating a brush-end, before using them to fish for termites."

Volleyball-sized fruit

But together with Prof McGrew and Prof Tetsuro Matsuzawa of the Primate Research Institute at Kyoto University in Japan, Ms Koops has discovered another startling use of tools not previously recorded.

During a monthly survey of chimps (Pan troglodytes) living in the mountain forests, she came across stone and rocks that had clearly be used by the apes to process Treculia fruits. These fruits, which can be the size of a volleyball and weigh up to 8.5kg, are hard and fibrous. But despite lacking a hard outer shell, they are too big

for a chimpanzee to get its jaws around and bite into. So, instead, the chimps use a range of tools to chop them into smaller pieces.

Ms Koops found stone and wooden cleavers, as well as stone anvils used to fracture the large fruits. All were covered by the remains of smashed fruit and seeds. The cleavers were clearly used to pound the fruit, rather than the fruit pounded upon the stones. And the anvils were made from immoveable rocky outcrops.

This is the first account of chimpanzees using a pounding tool technology to break down large food items into bite-sized chunks rather than just extract it from other unobtainable sources such as baobab nuts, Ms Koops told the BBC. "And it's the first time wild chimpanzees have been found to use two distinct types of percussive technology, i.e. movable cleavers versus a non-movable anvil, to achieve the same goal."

Surprisingly, neighbouring chimps living in the nearby region of Seringbara do not process their food in this way, reinforcing how tool use among apes is culturally learnt.

Ancient Tree (Almost) Older Than Dirt

An unassuming tree in southern California has overcome the test of time by surviving for more than 13,000 years.

By Michael Reilly Wed Dec 23, 2009 08:40 AM ET

At the top of a small hill in suburban southern California, there is what appears to be a thicket of stunted, gnarled oak trees wedged between a pile of boulders. A passerby would likely miss this ancient, biological wonder. The entire grove of trunks is in fact one plant, a newly discovered Palmer's oak (Quercus palmeri) that researchers estimate is over 13,000 years old, making it one of the oldest plants on Earth.

Researchers, led by Michael May of the University of California, Davis, found the tree a decade ago during a routine survey of local plant life. It's easy to miss; none of its 70 stems get more than a few feet tall, and it grows in a boulder pile that doubles as shelter from the area's buffeting winds.

At first glance, the scientists thought it was an isolated grove of trees, but something didn't add up: None of them produced fertile acorns, so the plants couldn't reproduce. The trees were a little too similar in appearance, too - almost like identical twins. And Palmer's oaks typically don't grow in the hot, parched environs of Riverside County. The team began to suspect they were looking at a clone.

Genetic analysis confirmed their suspicion. Each of the 70 stems are genetically identical; they are the same plant, currently growing in an oval 25 yards long and 8 yards wide. Plants can clone themselves in a number of ways. Aspen, for example, sprout roots that grow into new stems, allowing these plants to spread several feet each year.

Scientists estimate an Aspen stand in Utah, called Pando, may be tens of thousands of years old, though estimates vary widely. And a creosote bush growing in the Mojave Desert -- dubbed King Clone -- has been reliably dated at nearly 12,000 years old using carbon isotopes.

"Getting a handle on how old these organisms are is hard; most estimates are based on growth rates," which can have large errors, team member Jeffrey Ross-Ibarra also of the University of California, Davis said.

The team estimated that the newly discovered oak, which they named the Jurupa Oak after the mountains in which it grows, started from a central trunk and grew outward at a rate of one-twentieth of an inch each year, relying on fire to burn down stems and trigger the plant to send out new sprouts. The team's findings are reported in the online journal PLoS One.

But any trace of ancient wood has been lost to termites, so they team is left with a guess. It could be anywhere from 5,000 to 30,000 years old, Ross-Ibarra said, dating to a time when the Jurupa Mountains were cooler and wetter, and Palmer's oaks were prevalent.

"If they're right about how the oak regenerates, then their age estimate seems valid and true," Jennifer DeWoody of the University of Southampton in the United Kingdom said. "This could be a very old tree."

Today the tree's closest neighbors are a housing development, invasive grasses and a nearby limestone quarry. And while it has proven its ability to weather natural climate change, Ross-Ibarra fears the Jurupa Oak's future is in jeopardy at the hands of the developer's bulldozer.

"I'm cynical about its chances over the next hundred years," he said.

Citrus surprise: Vitamin C boosts the reprogramming of adult cells into stem cells

Famous for its antioxidant properties and role in tissue repair, vitamin C is touted as beneficial for illnesses ranging from the common cold to cancer and perhaps even for slowing the aging process. Now, a study published online on December 24th by Cell Press in the journal Cell Stem Cell uncovers an unexpected new role for this natural compound: facilitating the generation of embryonic-like stem cells from adult cells.

Over the past few years, we have learned that adult cells can be reprogrammed into cells with characteristics similar to embryonic stem cells by turning on a select set of genes. Although the reprogrammed cells, called

induced pluripotent stem cells (iPSCs), have tremendous potential for regenerative medicine, the conversion is extremely inefficient.

"The low efficiency of the reprogramming process has hampered progress with this technology and is indicative of how little we understand it. Further, this process is most challenging in human cells, raising a significant barrier for producing iPSCs and serious concerns about the quality of the cells that are generated," explains senior study author Dr. Duanqing Pei from the South China Institute for Stem Cell Biology and Regenerative Medicine at the Guangzhou Institutes of Biomedicine and Health, Chinese Academy of Sciences.

Dr. Pei and colleagues measured the production of reactive oxygen species or ROS during reprogramming and discovered a potential link between high ROS and low reprogramming efficiency. They became particularly interested in antioxidants, hypothesizing that they might suppress ROS and cell senescence, which seems to be a major roadblock for the generation of iPSCs.

The researchers found that adding vitamin C, an essential nutrient that is abundant in citrus fruits, enhanced iPSC generation from both mouse and human cells. Vitamin C accelerated gene expression changes and promoted a more efficient transition to the fully reprogrammed state. Somewhat to their surprise, they found that other antioxidants do not have the same effect, but vitamin C does seem to act at least in part through slowing cell senescence.

"Our results highlight a simple way to improve iPSC generation and provide additional insight into the mechanistic basis of reprogramming," concludes Dr. Pei. "It is also of interest that a vitamin with long-suspected anti-aging effects has such a potent influence on reprogramming, which can be considered a reversal of the aging process at the cellular level. It is likely that our work may stimulate further research in this area as well."

The researchers include Miguel Angel Esteban, South China Institute for Stem Cell Biology and Regenerative Medicine, Guangzhou Institutes of Biomedicine and Health, Chinese Academy of Sciences, Guangzhou, China; Tao Wang, South China Institute for Stem Cell Biology and Regenerative Medicine, Guangzhou Institutes of Biomedicine and Health, Chinese Academy of Sciences, Guangzhou, China; Baoming Qin, South China Institute for Stem Cell Biology and Regenerative Medicine, Guangzhou Institutes of Biomedicine and Health, Chinese Academy of Sciences, Guangzhou, China; Jiayin Yang, South China Institute for Stem Cell Biology and Regenerative Medicine, Guangzhou Institutes of Biomedicine and Health, Chinese Academy of Sciences, Guangzhou, China; Dajiang Qin, South China Institute for Stem Cell Biology and Regenerative Medicine, Guangzhou Institutes of Biomedicine and Health, Chinese Academy of Sciences, Guangzhou, China; Jinglei Cai, South China Institute for Stem Cell Biology and Regenerative Medicine, Guangzhou Institutes of Biomedicine and Health, Chinese Academy of Sciences, Guangzhou, China; Wen Li1, Zhihui Weng, South China Institute for Stem Cell Biology and Regenerative Medicine, Guangzhou Institutes of Biomedicine and Health, Chinese Academy of Sciences, Guangzhou, China; Su Ni, South China Institute for Stem Cell Biology and Regenerative Medicine, Guangzhou Institutes of Biomedicine and Health, Chinese Academy of Sciences, Guangzhou, China; Keshi Chen, South China Institute for Stem Cell Biology and Regenerative Medicine, Guangzhou Institutes of Biomedicine and Health, Chinese Academy of Sciences, Guangzhou, China; Yuan Li, South China Institute for Stem Cell Biology and Regenerative Medicine, Guangzhou Institutes of Biomedicine and Health, Chinese Academy of Sciences, Guangzhou, China; Xiaopeng Liu, South China Institute for Stem Cell Biology and Regenerative Medicine, Guangzhou Institutes of Biomedicine and Health, Chinese Academy of Sciences, Guangzhou, China; Jianyong Xu, South China Institute for Stem Cell Biology and Regenerative Medicine, Guangzhou Institutes of Biomedicine and Health, Chinese Academy of Sciences, Guangzhou, China; Shiqiang Zhang, South China Institute for Stem Cell Biology and Regenerative Medicine, Guangzhou Institutes of Biomedicine and Health, Chinese Academy of Sciences, Guangzhou, China; Feng Li, South China Institute for Stem Cell Biology and Regenerative Medicine, Guangzhou Institutes of Biomedicine and Health, Chinese Academy of Sciences, Guangzhou, China; Wenzhi He1, Krystyna Labuda, Ludwig Boltzmann Institute for Clinical and Experimental Traumatology, Vienna, Austria, Austrian Cluster for Tissue Regeneration, Vienna, Austria, Yancheng Song, Austrian Cluster for Tissue Regeneration, Vienna, Austria; Anja Peterbauer, Austrian Cluster for Tissue Regeneration, Vienna, Austria, Red Cross Blood Transfusion Service of Upper Austria, Linz, Austria; Susanne Wolbank, Ludwig Boltzmann Institute for Clinical and Experimental Traumatology, Vienna, Austria, Austrian Cluster for Tissue Regeneration, Vienna, Austria, Heinz Redl, Ludwig Boltzmann Institute for Clinical and Experimental Traumatology, Vienna, Austria, Austrian Cluster for Tissue Regeneration, Vienna, Austria, Daozhang Cai, Austrian Cluster for Tissue Regeneration, Vienna, Austria; Lingwen Zeng, South China Institute for Stem Cell Biology and Regenerative Medicine, Guangzhou Institutes of Biomedicine and Health, Chinese Academy of Sciences, Guangzhou, China; and Duanqing Pei, South China Institute for Stem Cell Biology and Regenerative Medicine, Guangzhou Institutes of Biomedicine and Health, Chinese Academy of Sciences, Guangzhou, China.

Alcohol's Neolithic Origins

Brewing Up a Civilization

By Frank Thadeusz

Did our Neolithic ancestors turn to agriculture so that they could be sure of a tipple? US Archaeologist Patrick McGovern thinks so. The expert on identifying traces of alcohol in prehistoric sites reckons the thirst for a brew was enough of an incentive to start growing crops.

It turns out the fall of man probably didn't begin with an apple. More likely, it was a handful of mushy figs that first led humankind astray.

Here is how the story likely began -- a prehistoric human picked up some dropped fruit from the ground and popped it unsuspectingly into his or her mouth. The first effect was nothing more than an agreeably bittersweet flavor spreading across the palate. But as alcohol entered the bloodstream, the brain started sending out a new message -- whatever that was, I want more of it!

Humankind's first encounters with alcohol in the form of fermented fruit probably occurred in just such an accidental fashion. But once they were familiar with the effect, archaeologist Patrick McGovern believes, humans stopped at nothing in their pursuit of frequent intoxication.

A secure supply of alcohol appears to have been part of the human community's basic requirements much earlier than was long believed. As early as around 9,000 years ago, long before the invention of the wheel, inhabitants of the Neolithic village Jiahu in China were brewing a type of mead with an alcohol content of 10 percent, McGovern discovered recently.

McGovern analyzed clay shards found during excavations in China's Yellow River Valley at his Biomolecular Archaeology Laboratory for Cuisine, Fermented Beverages, and Health at the University of Pennsylvania Museum.

The bearded archaeologist is recognized around the world as an expert when it comes to identifying traces of alcoholic drinks on prehistoric finds. He ran so-called liquid chromatography coupled with mass spectrometry on the clay remnants from Asia and found traces of tartaric acid -- one of the main acids present in wine -- and beeswax in the shards' pores. It appears that prehistoric humans in China combined fruit and honey into an intoxicating brew.

Clever Survival Strategy

Additionally, plant sterols point to wild rice as an ingredient. Lacking any knowledge of chemistry, prehistoric humans eager for the intoxicating effects of alcohol apparently mixed clumps of rice with saliva in their mouths to break down the starches in the grain and convert them into malt sugar. These pioneering brewers would then spit the chewed up rice into their brew. Husks and yeasty foam floated on top of the liquid, so they used long straws to drink from narrow necked jugs. Alcohol is still consumed this way in some regions of China. McGovern sees this early fermentation process as a clever survival strategy. "Consuming high energy sugar and alcohol was a fabulous solution for surviving in a hostile environment with few natural resources," he explains.

The most recent finds from China are consistent with McGovern's chain of evidence, which suggests that the craft of making alcohol spread rapidly to various locations around the world during the Neolithic period. Shamans and village alchemists mixed fruit, herbs, spices, and grains together in pots until they formed a drinkable concoction.

But that wasn't enough for McGovern. He carried the theory much further, aiming at a complete reinterpretation of humanity's history. His bold thesis, which he lays out in his book "Uncorking the Past. The Quest for Wine, Beer and Other Alcoholic Beverage," states that agriculture -- and with it the entire Neolithic Revolution, which began about 11,000 years ago -- are ultimately results of the irrepressible impulse toward drinking and intoxication.

"Available evidence suggests that our ancestors in Asia, Mexico, and Africa cultivated wheat, rice, corn, barley, and millet primarily for the purpose of producing alcoholic beverages," McGovern explains. While they were at it, he believes, drink-loving early civilizations managed to ensure their basic survival.

A Hybrid Swill

Archaeologists have long pondered the question of which came first, bread or beer. McGovern surmises that these prehistoric humans didn't initially have the ability to master the very complicated process of brewing beer. However, they were even more incapable of baking bread, for which wild grains are extremely unsuitable. They would have had first to separate the tiny grains from the chaff, with a yield hardly worth the great effort. If anything, the earliest bakers probably made nothing more than a barely palatable type of rough bread, containing the unwanted addition of the grain's many husks.

It's likely, therefore, that early farmers first enriched their diet with a hybrid swill -- half fruit wine and half mead -- that was actually quite nutritious. Neolithic drinkers were devoted to this precious liquid. At the excavation site of Hajji Firuz Tepe in the Zagros Mountains of northwestern Iran, McGovern discovered prehistoric wine racks used to store airtight carafes. Inhabitants of the village seasoned their alcohol with resin from Atlantic Pistachio trees. This ingredient was said to have healing properties, for example for infections, and was used as an early antibiotic.

The village's Neolithic residents lived comfortably in spacious mud brick huts, and the archaeologist and his team found remnants of wine vessels in the kitchens of nearly all the dwellings. "Drinking wasn't just a privilege of the wealthy in the village," McGovern posits, and he adds that women drank their fair share as well.

A Mysterious Inscription?

In Iran of all countries, where alcohol consumption is now punishable by whipping, the American scientist found vessels containing the first evidence of prehistoric beer. At first he puzzled over the purpose of the bulbous vessels with wide openings found in the prehistoric settlement Godin Tepe. Previously known wine vessels all had smaller spouts. McGovern was also perplexed by crisscrossed grooves scratched into the bottoms of the containers. Could it be some kind of mysterious inscription?

But back in the laboratory, he isolated calcium oxalate, known to brewers as an unwanted byproduct of beer production. Nowadays, breweries can filter the crystals out of their brew without any difficulty. Their resourceful predecessors, working 3,500 years B.C., scratched grooves into their 50-liter (13-gallon) jugs so that the tiny stones would settle out there. McGovern had discovered humankind's first beer bottles.

The ancient farmers in Godin Tepe harvested barley from fields near the village and mashed the crop using basalt stone. Then they brewed the ground grain into a considerable range of varieties, enjoying a sweet, caramel-flavored dark beer, an amber-hued lager-like concoction, and other pleasant-tasting beverages.

Around the same time, the Sumerians were paying homage to their fertility goddess Nin-Harra, whom they considered to be the inventor of beer. The creators of Mesopotamian civilization scratched instructions for brewing beer onto small clay tablets in Nin-Harra's honor. The main ingredient in their variety of beer was emmer, a variety of wheat that has since nearly disappeared.

Thus the human project that started with the first hominids to stumble around under fruit trees reached completion with these prehistoric beer drinkers. "Moderate alcohol consumption was advantageous for our early ancestors," McGovern speculates, "and they adapted to it biologically."

It is a legacy that still burdens humankind today. The archaeologist, however, sees himself as reasonably balanced in this respect. Ancestors on one side of his family, the McGoverns, opened the very first bar in their hometown of Mitchell, South Dakota. On the other side, however, an especially puritanical branch of the family originated from Norway and strictly avoided alcohol consumption.

UCLA scientists find molecular switch to prevent Huntington's disease in mice

Finding suggests new approach for treating devastating genetic disorder

UCLA scientists have identified a molecular switch that prevents Huntington's disease from developing in mice. Published in the Dec. 24 edition of the journal Neuron, the discovery suggests a new approach to treating the genetic disorder, which ultimately leads to death in as little as 10 years.

Affecting one out of every 10,000 Americans, Huntington's progressively deprives patients of their ability to walk, speak, think clearly and swallow. People who inherit the disorder don't show symptoms until mid-life, after many have had children and unknowingly passed on the disease. Currently, there is no effective treatment to prevent the onset or slow the progression of the disease.

Huntington's is caused by a mutation in the polyglutamine (polyQ) region of a very large protein called huntingtin. Because huntingtin is found everywhere in the body, it is a challenge to study, and the function and mechanism behind the mutant protein still remain elusive.

"It's unclear how the mutant protein causes age-related and progressive loss of brain cells in patients with Huntington's disease," said senior study author X. William Yang, associate professor of psychiatry and biobehavioral sciences at the Semel Institute of Neuroscience and Human Behavior at UCLA. "We explored whether regions of the protein besides the polyQ mutation play a role in the development of the disorder."

Collaborators Joan Steffan and Leslie Thompson, of the University of California, Irvine, showed that two amino acids near the beginning of the huntingtin protein can be modified by a chemical process called phosphorylation, which cells use to control protein function after the proteins have been made.

To test whether phosphorylation could influence Huntington's disease in a living animal, Yang's laboratory generated two mouse models to carry the polyQ HD mutation and modified the two amino acids in two different ways — one to mimic phosphorylation, the other to prevent it.

The researchers found that preventing phosphorylation caused the mice to develop symptoms suggestive of Huntington's disease in humans. Mimicking phosphorylation, however, did not cause the disorder.

These results in mice have striking parallels to experiments performed by collaborator Ron Wetzel, of the University of Pittsburgh, who found that mimicking phosphorylation of a toxic fragment of mutant huntingtin reduces the protein's tendency to form clumps.

A separate UC Irvine study by Steffan and Thompson also suggests that phosphorylation of mutant huntingtin may help cells dispose of the toxic form of mutant huntingtin. Combined, these studies suggest new directions of research to understand the roles of huntingtin misfolding, clumping and clearance in the disease mechanism.

"Our study identified a critical molecular switch which lies next to the polyQ mutation in the huntingtin protein," Yang said. "We were surprised to find that subtle modification of only two amino acids in this very large protein can prevent the onset of disease. This finding suggests an exciting new avenue to develop therapeutics for Huntington's disease."

This study was funded by the Hereditary Disease Foundation and National Institute of Neurological Disorders and Stroke. Yang's UCLA co-authors included Xiaofeng Gu and Erin Greiner, from the Center for Neurobehavioral Genetics at the Semel Institute and the department of psychiatry and biobehavioral sciences at the David Geffen School of Medicine at UCLA. Other collaborators included Rakesh Mishra, Ravindra Kodali and Wetzel, from the University of Pittsburgh; Thompson and Steffan, from UC Irvine; Alex Osmand, from the University of Tennessee; and Steven Finkbeiner, from the University of California, San Francisco.

'Self-seeding' of cancer cells may play a critical role in tumor progression

Cancer progression is commonly thought of as a process involving the growth of a primary tumor followed by metastasis, in which cancer cells leave the primary tumor and spread to distant organs. A new study by researchers at Memorial Sloan-Kettering Cancer Center shows that circulating tumor cells – cancer cells that break away from a primary tumor and disseminate to other areas of the body – can also return to and grow in their tumor of origin, a newly discovered process called "self-seeding."

The findings of the study, published in the December 25 issue of the journal Cell, suggest that self-seeding can enhance tumor growth through the release of signals that promote angiogenesis, invasion, and metastasis.

"Our work not only provides evidence for the self-seeding phenomenon and reveals the mechanism of this process, but it also shows the possible role of self-seeding in tumor progression," said the study's first author Mi-Young Kim, PhD, Research Fellow in the Cancer Biology and Genetics Program at Memorial Sloan-Kettering.

According to the research, which was conducted in mice, self-seeding involves two distinct functions: the ability of a tumor to attract its own circulating progeny and the ability of circulating tumor cells to re-infiltrate the tumor in response to this attraction. The investigators identified four genes that are responsible for executing these functions: IL-6 and IL-8, which attract the most aggressive segment of the circulating tumor cells population, and FSCN1 and MMP1, which mediate the infiltration of circulating tumor cells into a tumor.

The findings also show that circulating breast cancer cells that are capable of self-seeding a breast tumor have a similar gene expression pattern to breast cancer cells that are capable of spreading to the lungs, bones, and brain, and therefore have an increased potential to metastasize to these organs. Additional experiments revealed that self-seeding can occur in cancer cells of various tumor types in addition to breast cancer, including colon cancer and melanoma.

"These results provide us with opportunities to explore new targeted therapies that may interfere with the self-seeding process and perhaps slow or even prevent tumor progression," said the study's senior author, Joan Massagué, PhD, Chair of the Cancer Biology and Genetics Program at Memorial Sloan-Kettering and a Howard Hughes Medical Institute investigator.

The concept of self-seeding sheds light on clinical observations such as the relationship between the tumor size, prognosis, and local relapse following seemingly complete removal of a primary breast tumor. "We know there is an association between large tumor size and poor prognosis. This was always thought to reflect the ability of larger cancers to release more cells with metastatic potential. But this association may actually be caused by the ability of aggressive cancer cells to self-seed, promoting both local tumor growth and distant metastases by similar mechanisms," said study co-author Larry Norton, MD, Deputy Physician-in-Chief for Breast Cancer Programs at Memorial Sloan-Kettering.

This work was funded by grants from the National Institutes of Health, the Hearst Foundation, the Alan and Sandra Gerry Metastasis Research Initiative, and the Department of Defense.

Mammalodon probably lived by sucking small animals up from the seafloor
Ancient whale sucked mud for food
Artist's impression of Mammalodon (Carl Buell)
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Mammalodon probably lived by sucking small animals up from the seafloor

An ancient "dwarf" whale appears to have fed by sucking small animals out of the seafloor mud with its short snout and tongue, experts say.

Researchers say the 25 million-year-old fossil is related to today's blue whales - the largest animals on Earth.

The ancient animal's mud slurping may have been a precursor to the filter feeding seen in modern baleen whales. These whales strain huge quantities of tiny marine animals through specialised "combs" which take the place of teeth. The research is published in the Zoological Journal of the Linnean Society.

The fossilised remains of the primitive baleen whale Mammalodon colliveri were discovered near Torquay, in Victoria, Australia.

This animal still had teeth; it had not yet evolved the baleen plates - used for filter-feeding - which characterise present-day baleen whales.

Although Mammalodon was discovered in 1932 and named in 1939, it has not been widely studied, according to Museum Victoria, which holds specimens of this group.

The study's author, Dr Erich Fitzgerald from Museum Victoria, said that his study of the fossil led him to the conclusion that Mammalodon was a bottom-feeding mud-sucker.

Splinter group

The idea would support Charles Darwin's observation about whale evolution in his seminal book On the Origin of Species. In it, Darwin speculated that some of the earliest baleen whales may have been suction feeders - and that this served as a precursor to the filter feeding of today's giants of the deep.

Mammalodon had a total body length of about 3m. But it appears to have been a bizarre evolutionary "splinter group" from the evolutionary lineage which later led to the 30m-long blue whale. It was effectively a dwarf whale; the research suggests that Mammalodon may have evolved into a relatively tiny form from larger ancestors.

Mammalodon belongs to the same family as Janjucetus hunderi, fossils of which were also found in 25 million-year-old Oligocene rocks near Torquay in Victoria. This family appears to be unique to south-east Australia. "Clearly the seas off southern Australia were a cradle for the evolution of a variety of tiny, weird whales that seem to have lived nowhere else," said Dr Fitzgerald.

The baleen plates which allow today's baleen whales to filter their food from water, distinguish this group from the toothed whales - a group which includes beaked whales and dolphins.

Baleen whales are a taxonomical group which includes not only the majestic blue whale, but also the right whales, fin whales and humpbacks, to name but a few.

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Mammalodon probably evolved from much bigger ancestors

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