Viral mimic induces melanoma cells to digest themselves

Recent research has uncovered an unexpected vulnerability in deadly melanoma cells that, when exploited, can cause the cancer cells to turn against themselves. The study, published by Cell Press in the August issue of the journal Cancer Cell, identifies a new target for development of future therapeutics aimed at selectively eliminating this aggressive skin cancer which is characterized by a notoriously high rate of metastasis and treatment-resistance.

"Although considerable effort has been devoted to the search for molecular mechanisms that contribute to the chemo- and immunoresistance of melanoma, the average survival of patients with inoperable metastases remains less than 10 months," explains senior study author Dr. Maria S. Soengas from the Melanoma Laboratory at the Spanish National Cancer Research Centre in Madrid, Spain. Melanoma has multiple complex genetic aberrations that make the cells difficult to destroy with current treatments.

One process that has not been studied in great detail with regards to melanoma is a type of autophagy (literally, self-eating) that involves sequestration of components within the cell for eventual degradation. Previous work has linked autophagy with both cancer cell death and survival and it is not clear whether this process might be a viable target for future drug development. Dr. Soengas and colleagues designed a series of studies to examine the interplay between autophagy and cell death in the context of tumor cell-selective elimination of melanoma cells.

The researchers discovered that melanoma cells retain the ability to recognize and respond to double-stranded RNA (dsRNA) located inside the cell cytoplasm. Most animal cells contain single-stranded RNA and see dsRNA, which is associated with viruses, as a threat. The melanoma cells responded to administration of the dsRNA mimic polyinosine-polycytidylic acid (pIC) by inducing an immune response that led to autophagy. However, the method of delivering the pIC to the melanoma cells was critical and required a carrier called polyethyleneimine (PEI) to ensure delivery of pIC to the cell cytoplasm.

The researchers went on to show that pIC links autophagy to apoptosis, a well studied cell death pathway. Significantly, the cell autonomous anti-tumor activity of pIC was observed even in animals with a suppressed immune system, a condition common to melanoma patients. "Altogether, our results provide the proof of principle for dsRNA sensors as therapeutic targets to overcome the inherent resistance of melanoma cells to current anticancer treatments," says Dr. Soengas.

Importantly, the pIC-PEI complex has two exciting advantages over other anticancer agents. "First, pIC-PEI can induce both autophagy and apoptosis in an efficient manner while other compounds are just partial inducers of one of the two processes. Second, pIC-PEI has a significant anti-melanoma activity in experimental mouse models without noticeable side effects." The researchers caution that further research is required before these results can be translated to the clinic.

The researchers include Damia` Tormo, Spanish National Cancer Research Centre (CNIO), Madrid, Spain; Agnieszka Checinska, Spanish National Cancer Research Centre (CNIO), Madrid, Spain; Direna Alonso-Curbelo, Spanish National Cancer Research Centre (CNIO), Madrid, Spain; Eva Perez-Guijarro, Spanish National Cancer Research Centre (CNIO), Madrid, Spain; Estela Canon, Spanish National Cancer Research Centre (CNIO), Madrid, Spain; Erica Riveiro-Falkenbach, Spanish National Cancer Research Centre (CNIO), Madrid, Spain; Tonantzin G. Calvo, Spanish National Cancer Research Centre (CNIO), Madrid, Spain; Lionel Larribere, Spanish National Cancer Research Centre (CNIO), Madrid, Spain' Diego Megias, Spanish National Cancer Research Centre (CNIO), Madrid, Spain; Francisca Mulero, Spanish National Cancer Research Centre (CNIO), Madrid, Spain; Miguel A. Piris, Spanish National Cancer Research Centre (CNIO), Madrid, Spain; Rupesh Dash, Virginia Commonwealth University, School of Medicine, Richmond, VA; Paola M. Barral, Virginia Commonwealth University, School of Medicine, Richmond, VA; Jose´ L. Rodriguez-Peralto, Hospital Universitario, Madrid, Spain; Pablo Ortiz-Romero, Hospital Universitario, Madrid, Spain; Thomas Tuting, University of Bonn, Bonn, Germany; Paul B. Fisher, Virginia Commonwealth University, School of Medicine, Richmond, VA; and Maria S. Soengas, Spanish National Cancer Research Centre (CNIO), Madrid, Spain.

Groundbreaking study shows exercise benefits leukemia patients

CHAPEL HILL, N.C. – One of the most bothersome symptoms of leukemia is extreme fatigue, and asking these patients to exercise doesn't sound like a way to help them feel better.

A new study from the University of North Carolina at Chapel Hill indicates that exercise may be a great way to do just that, combating the debilitating fatigue that these patients experience.

In a first-of-its-kind clinical trial, a team of researchers from the Department of Exercise and Sport Science and UNC Lineberger Comprehensive Cancer Center have shown that physical activity can significantly improve symptoms of fatigue and depression, increase cardiovascular endurance and maintain quality of life for adult patients undergoing treatment for leukemia.

A total of 10 patients undergoing treatment participated in the EQUAL (Exercise and Quality of Life in Leukemia/ Lymphoma Patients) study. Each patient was provided with specially-treated exercise equipment to

minimize the risk of infection. They participated in an individualized exercise session while in the hospital for the 3-5 weeks of the induction phase of leukemia treatment. The exercise prescription comprised of aerobic and resistance exercises, core exercises, and light stretches tailored to the patient's level of fitness and leukemia symptoms. Upon their discharge from the hospital, each patient received an aerobic- based exercise prescription to use during their 2-week home recovery period.

Before and after the exercise program, the researchers tested key physiological measurements including resting heart rate, blood pressure and hemoglobin, body weight and height, body composition, cardiorespiratory fitness and muscular endurance. Psychological measures were tested using standard scales for assessing fatigue, depression and quality of life in cancer patients. Blood samples were also taken at baseline, mid, and at the conclusion of the study, and analyzed for cytokines, biomarkers of inflammation. The results of the study were recently published in the journal Integrative Cancer Therapies.

"We found that the patients experienced significant reduction in total fatigue and depression scores, as well as improved cardiorespiratory endurance and maintenance of muscular endurance," said Claudio Battaglini, Ph.D., assistant professor of exercise and sport science and UNC Lineberger member.

"This is important because of the numerous side-effects related to cancer treatment, and particularly leukemia treatment, which requires confinement to a hospital room for 4-6 weeks to avoid the risk of infection. We have demonstrated that these patients not only can complete an exercise program in the hospital but that they may receive both physiological and psychological benefits that could assist in their recovery," he added.

EQUAL phase II is in development. The follow-up study will consisted of a randomized clinical-controlled trial to assess the effects on an individualized exercise prescription in acute leukemia patients vs. a group of leukemia patients receiving the usual treatment. If the results prove to be beneficial to patients, the goal of the research team will be to expand the trial by developing a multi-site research program involving other cancer centers throughout North Carolina and around the United States.

Along with Battaglini, study co-authors include professor Anthony Hackney, Ph.D., associate professor Diane Groff, Ed.D., and graduate student Elizabeth Evans from the Department of Exercise and Sport Science. Hackney and Groff are also members of UNC Lineberger Comprehensive Cancer Center, along with nurse consultant Rey Garcia and Thomas Shea, M.D., professor of hematology/oncology and director of the UNC bone marrow transplant program.

This research was supported by a UNC Lineberger Internal Grants Award, a UNC Junior Faculty Development Award, and a UNC Institute of Aging, Stimulus Grant in Aging and made possible due to cooperation by UNC Hospitals.

Stanford scientists discover bladder cancer stem cell

STANFORD, Calif. — Researchers at Stanford's School of Medicine have identified the first human bladder cancer stem cell and revealed how it works to escape the body's natural defenses.

"This is first time we've found this 'don't eat me signal' in a stem cell of a solid cancer," said Irving Weissman, MD, the Virginia & D.K. Ludwig Professor for Clinical Investigation in Cancer Research at the medical school. "We're now moving as fast as we can to look at other tumors to see if this is a universal strategy of all or most cancer stem cells." If so, the signal may be a valuable therapeutic target for many types of cancers.

Weissman, who directs Stanford's Stem Cell Biology and Regenerative Medicine Institute, is also a member of Stanford's Cancer Center. He is the senior author of the work, which will be published in the Proceedings of the National Academy of Sciences on Aug. 3. His laboratory recently published two studies in the journal Cell showing that human leukemia stem cells use the same protective molecular signature on their surface to evade cells called macrophages that engulf and destroy sick or cancerous cells.

Like queen bees, cancer stem cells are constantly replenishing their "hive" of tumor cells. Therapies that kill off the workers might reduce the size of the tumor and the symptoms of the disease, but will ultimately be unsuccessful unless they also eliminate the stem cells working behind the scenes.

Support for the current research came from a gift from Jim and Carolyn Pride. In 2002, the couple attended a talk by Weissman in which he discussed the then-emerging idea of cancer stem cells. Jim Pride, who had been diagnosed with bladder cancer, approached Weissman after the talk and offered to sponsor a post-doctoral fellow — Keith Syson Chan, PhD — to investigate whether there was a bladder cancer stem cell.

"The whole concept of cancer stem cells is that they are often resistant to current therapies," said Chan, who is the first author of the work, "and, at least in the case of bladder cancer, they drive the progression of the disease." Identifying and following these cells may be one way to monitor tumor status, the researchers feel, and targeting the cells for destruction may be a good way to eradicate the cancer. Although Pride lost his life to the disease in 2004, his gift launched the experiments necessary to obtain NIH funding for the project.

There are two main types of bladder cancer: one that invades the muscle around the bladder and metastasizes to other organs, and another that remains confined to the bladder lining. Unlike the more-treatable non-invasive

cancer — which comprises about 70 percent of bladder cancers — the invasive form is largely incurable. Although about 15 percent of non-invasive cancers eventually become invasive, there is no current diagnostic method that can predict which will progress.

Chan used breast cancer stem cell markers to identify a subpopulation of human bladder cancer cells with stem cell qualities: The cells formed tumors when transplanted into mice with compromised immune systems. He then looked to see which genes were more highly expressed in these cells than in other bladder cancer cells from the same tumor. He found that most, but not all, non-invasive bladder cancers expressed lower levels of these genes than did invasive cancers. Further research showed that the anomalous non-invasive cancers with higher levels of gene expression behaved more aggressively: About 80 percent recurred within 25 months of initial diagnosis, whereas only about 20 percent of the low-expressing tumors did so.

"The fact that we were able to pull out the subpopulation of these cancers that will become invasive is an important step in identifying those that will be more dangerous," said Chan. "It may be possible to follow the progress of the tumor by analyzing the expression levels of these genes."

Chan found particularly interesting one gene, which encodes a cell-surface molecule called CD47. He knew from previous research in Weissman's lab that CD47 works to prevent leukemia cells from being engulfed by macrophages by binding to a molecule on the surface of the macrophage. Blocking this interaction with an antibody specific for CD47 allows the macrophages to swallow the leukemia cells. When he tried a similar experiment with the bladder cancer stem cells in a test tube, the same thing happened - human macrophages began to destroy the cancer cells.

"Leukemia is totally different from the kind of epithelial cancer we see in the bladder," said Chan, "so it was very exciting to see that these two kinds of cancer stem cells use a similar mechanism to escape the macrophages. It's also very interesting to find that macrophages seem to be playing such a major role in cancer progression."

The researchers are now investigating whether CD47 is expressed at high levels on other cancer stem cells and pondering ways to help circulating macrophages better infiltrate solid tumors - always with an eye towards therapy. "Jim knew our research results would be too late for him," said Weissman, who visited Pride in the hospital before he died, "but he hoped that they would help others."

In addition to Weissman and Chan, other Stanford collaborators on the paper include post-doctoral fellow Inigo Espinosa, MD; graduate student Mark Chao; post-doctoral fellow David Wong, PhD; senior research associate Laurie Ailles, PhD; post-doctoral fellow Max Diehn, MD, PhD; professor of urology Joseph Presti, MD; associate professor of dermatology Howard Chang, MD, PhD; professor of pathology Matt van de Rijn, MD, PhD; and professor of urology Linda Shortliffe, MD.
The research was supported by the Pride Family Fund, the Smith Family Fund, the National Institutes of Health and the National Cancer Institute.

Project Zero Delay accelerates drug's path to clinical trial

M. D. Anderson and AstraZeneca cut 3-6 months off phase I clinical trial start-up time

HOUSTON - A phase I clinical trial enrolled its first patient only two days after U.S. Food and Drug Administration clearance of the experimental drug for a first-in-human cancer trial, a milestone that normally takes three to six months. Investigators from The University of Texas M. D. Anderson Cancer Center and pharmaceutical company AstraZeneca have reported their work in the Journal of Clinical Oncology published online on August 3rd.

The joint effort, dubbed Project Zero Delay, is part of a strategic collaboration between the two organizations designed to safely accelerate development of new cancer drugs. In many cases that process takes about 12 years and the cost of bringing a new drug to patients has been estimated at around $1.3 billion. [Ref: J. A. DiMasi and H. G. Grabowski, "The Cost of Biopharmaceutical R&D: Is Biotech Different?" Managerial and Decision Economics 28 (2007): 469-479.]

"Project Zero Delay demonstrates how we can shrink the time it takes to bring new drugs to cancer patients," said Robert C. Bast Jr., M.D., vice president for translational research at M. D. Anderson and the paper's senior author. "We need to find out as promptly as possible whether new therapies will help. Zero Delay is a significant step in that direction. Close cooperation allowed us to eliminate unnecessary delays while fully meeting regulatory requirements for scientific and human safety review."

The key to Zero Delay was performing most tasks in parallel instead of sequentially, said lead author Razelle Kurzrock, M.D., professor and chair of M. D. Anderson's Department of Investigational Therapeutics. In addition, tasks usually done after FDA clearance of an Investigational New Drug (IND) application were instead done in advance. No administrative steps were skipped.

This approach can be applied in other areas of drug development and by other institutions willing to cooperate closely, the authors note. "Zero Delay addressed one aspect of drug development - clinical trial start-up time," Kurzrock said. "Substantial time could be cut from other steps by applying the same principles."

The time between having a complete written protocol and enrollment of the first patient is typically 135 days in M. D. Anderson's Phase I Clinical Trial Program when processing of the protocol starts after IND approval. Zero Delay went from having a complete written protocol to first patient in 46 days, with FDA clearance of the IND on day 44. Research elsewhere cited in the Zero Delay paper indicates enrollment of the first patient after having a final protocol typically takes 3-6 months.

Administrative tasks accomplished before the FDA's ruling included budget and contract negotiations, site visits and preparation, training and a series of mandatory institutional reviews at M. D. Anderson.

"M.D. Anderson and AstraZeneca share a common goal of using leading edge science to deliver medicines that will benefit patients now and in the future, while speeding up the process and making it more cost efficient," said Alan Barge, vice president and Head of Oncology at AstraZeneca. "AZ is always looking to improve our processes and to optimize value along our pipeline. This achievement is a great example of what can be accomplished when we pair our first class internal capabilities with the strengths of one of our key alliance partners in the U.S."

In 2005, M. D. Anderson and AstraZeneca established a strategic alliance that includes a master agreement for clinical and translational/preclinical research specifying terms for standard items that can cause lengthy negotiations. The master agreement ensures that new research projects and clinical trials are initiated without delays caused by contracting issues. New clinical trials can simply be appended to an existing master agreement, often as quickly as in a day.

"Zero Delay demonstrates what can be accomplished in an atmosphere of trust and collaboration that we've cultivated through our strategic alliance," Bast said. The alliance agreement also includes a commitment to regular meetings, a point of contact to remove obstacles, support of collaborative projects and a commitment to accelerate drug development.

"The next challenge, said Barge, will be to do this consistently in order to develop truly innovative therapies that will someday offer new benefits to cancer patients."

Co-authors with Kurzrock and Bast are: Susan Pilat, Marcel Bartolazzi, and Dwana Sanders, all of M. D. Anderson's Department of Investigational Therapeutics; Stanley Tucker, Ph.D., Office of Translational Research. From AstraZeneca: Jill Hood, Ph.D., Kevin Webster, Michael Mallamaci, Steven Strand and Eileen Babcock.

Cannibalistic cells may help prevent infections, researchers report

DALLAS — Aug. 3, 2009 — Infectious-disease specialists at UT Southwestern Medical Center have demonstrated that a cannibalistic process in cells plays a key role in limiting Salmonella infection.

Salmonella, the causative agent of salmonellosis, causes many of the intestinal infections and food-related illnesses reported in the U.S. About 600 people die each year as a result of these infections, accounting for roughly 30 percent of all reported food-related deaths. It is particularly dangerous among the elderly.

The new findings, available online and in an upcoming issue of the Proceedings of the National Academy of Sciences, are among the first to demonstrate that a process called autophagy (pronounced “aw-TAH-fah-gee”) prevents harmful bacteria such as Salmonella from becoming successful pathogens. The findings also suggest that decreases in autophagy — such as those that occur in the elderly and in certain patients with Crohn’s disease, an inflammatory bowel disorder — may lead to abnormalities in the way the intestinal tract deals with bacterial infections.

“It’s known that as you get older you become more susceptible to infectious diseases and also that autophagy decreases,” said Dr. Beth Levine, chief of the division of infectious diseases at UT Southwestern and senior author of the new study in PNAS. “In this paper, we’ve shown that signaling pathways that extend life and protect against bacterial invaders do so by triggering autophagy. This suggests that therapeutic strategies to increase autophagy may be effective in defeating harmful bacteria that can enter inside cells.”

Autophagy is the way cells devour their own unwanted or damaged parts. It is a highly regulated and completely normal process by which cells remain healthy by performing “routine housekeeping” and “garbage disposal.” Prior research has shown that the process appears to be an adaptive response that our bodies employ during times of stress or starvation, and which also helps protect our bodies against cancer and neurodegenerative diseases.

It’s unclear why older people become more susceptible to infections, but research has shown that autophagy does decrease with age. Dr. Levine, a professor of internal medicine and microbiology, said it is possible that by reversing or regulating this process, researchers could prevent the elderly and others with weakened immune systems from becoming more susceptible to infections.

For this study, the researchers studied the effects of Salmonella infections in two organisms they had genetically engineered to lack active autophagy genes. The organisms included Caenorhabditis elegans, a common research worm also known as a nematode, and Dictyostelium discoideum, a soil amoeba that functions much like certain cells in the human immune system.

In both cases, the animals with inactive autophagy genes fared far worse than those with active ones. Rather than being targeted for elimination, the Salmonella bacterium was able to invade the host cells, where it started replicating, Dr. Levine said.

She said the findings indicate that the autophagy process plays an important role in resistance to certain types of pathogens, specifically those that can enter inside our cells.

The next step, Dr. Levine said, is to begin studying the efficacy of a new autophagy-inducing molecule in treating a number of intracellular bacterial infections including salmonellosis, tuberculosis, tularemia and listeriosis.

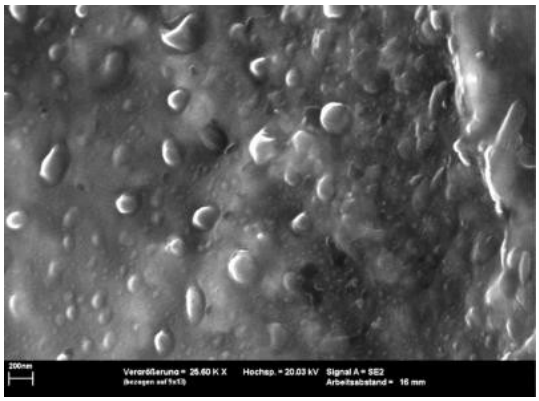
Other UT Southwestern researchers involved in the study were Dr. Kailiang Jia, lead author and instructor in internal medicine; Dr. Muhammad Akbar, clinical instructor in internal medicine; Dr. Qihua Sun, research scientist in internal medicine; Beverley Adams-Huet, assistant professor of clinical sciences; Dr. Christopher Gilpin, assistant professor of cell biology; and Dr. Collin Thomas, a former research associate in internal medicine.

This study was supported by the National Institutes of Health and The Ellison Medical Foundation.

Self-healing surfaces

This release is available in German.

Human skin is a phenomenon – small scratches and cuts heal quickly, leaving no trace of a scar after just a few days. It's a different matter with materials, such as metals – if the electroplated layer protecting the metals from corrosion is scratched, rust protection is lost. Engineers are working on transferring the self-healing effect of skin to materials. The idea behind this is to introduce evenly distributed fluid-filled capsules into the electroplated layer – rather like raisins in a cake. If the layer is damaged, the pellets at the point of damage burst, the fluid runs out and 'repairs' the scratch. Until now, these plans have failed due to the size of the capsules – at 10 to 15 micrometers they were too large for the electroplated layer, which is around 20 micrometers thick. The capsules altered the mechanical properties of the layer.



The nano-capsules in the electroplated layer contain a fluid. If the layer is scratched, the layers burst, the fluid escapes and repairs the scratch. **Fraunhofer IPA**

Researchers from the Fraunhofer Institute for Manufacturing Engineering and Automation IPA in Stuttgart, together with colleagues from Duisburg-Essen University, have developed a process for producing electroplated layers with nano-capsules, in a project being financed by the Volkswagen Foundation. At only a few hundred nanometers in diameter, the capsules are measured on another scale entirely, compared with previous results. "The challenge lies in not damaging the capsules when producing the electroplated layer", says Dr. Martin Metzner, Head of Department at IPA. "The smaller the capsules, the thinner and more sensitive their casing. The electrolytes used for these electroplated-technical processes are extremely aggressive chemically and can easily destroy the capsules". The researchers therefore had to find a compatible material for the capsule casing depending on the electrolytes used.

Mechanical bearings are one example of possible applications – the materials of the bearings usually have a electroplated coating, in which the capsules can be embedded. If there is a temporary shortage of lubricant, part of the bearing's coating is lost, the capsules at the top of the layer burst and release lubricant. The bearing is not therefore damaged if it temporarily runs dry. The researchers have produced the first copper, nickel and zinc coatings with the new capsules, although surface coverage does not extend beyond the centimeter scale. Experts estimate that it will be another one and a half to two years before whole components can be coated. In a further step the team worked on more complex systems – involving differently filled capsules, for example, whose fluids react with one another like a two component adhesive.

Heavy drinkers face significantly increased cancer risk

Montreal study links heavy consumption of beer and spirits to 6 different cancers

This release is available in French.

Heavy drinkers of beer and spirits face a much higher risk of developing cancer than the population at large, says a group of Montreal epidemiologists and cancer researchers. Their findings show that people in the highest

consumption category increased their risk of developing oesophageal cancer sevenfold, colon cancer by 80% and even lung cancer by 50%.

In all, the researchers found statistically significant relationships between heavy consumption of beer and spririts and six different cancers. Moderate drinking (i.e. less than daily) and wine consumption did not show the same effects, however.

The research was conducted by Dr. Andrea Benedetti of McGill University, Dr. Marie-Elise Parent of INRS-Institut Armand Frappier and Dr. Jack Siemiatycki of the Université de Montréal.

"We looked at the data in two ways," said Benedetti, an assistant professor at McGill's Departments of Medicine and of Epidemiology, Biostatistics and Occupational Health. "We compared people who drank heavily to our reference group, who abstained or drank only very occasionally. We also looked for trends across our categories: non-drinkers, weekly drinkers and daily drinkers.

The results were astounding. "We saw increased risk for esophageal cancer, stomach cancer, colon cancer, liver cancer, pancreatic cancer, lung cancer and prostate cancer," Benedetti added. "The strongest risk was for esophageal and liver cancer."

"This study crystalizes many strands of evidence from different studies on different types of cancer and alcohol consumption," said Dr. Jack Siemiatycki, professor, Canada Research Chair and Guzzo Chair in Environment and Cancer, at the Université de Montréal.

The researchers used data originally collected for a large occupational cancer study conducted in Montreal in the 1980s. The information was a treasure-trove, said Benedetti.

"Lifetime interviews were conducted with people about their job histories, and detailed information about all the things they could have been exposed to was collected," she explained. "As it turns out, the data also included information about non-occupational factors such as drinking alcohol, smoking cigarettes, diet and socio-economic status, among others."

Benedetti, the study's lead author, conducted this research while still a postdoctorial fellow under the supervision of her co-authors, Dr. Siemiatycki and Dr. Parent. Their results were published in the current issue of the journal Cancer Detection and Prevention.

"For the most part we showed that light drinkers were less affected or not affected at all," said Benedetti. "It is people who drink every day or multiple times a day who are at risk. This adds to the growing body of evidence that heavy drinking is extremely unhealthy in so many ways. Cancer very much included."

New microchip technology performs 1,000 chemical reactions at once

Technique may accelerate drug discovery for cancer, other diseases

Flasks, beakers and hot plates may soon be a thing of the past in chemistry labs. Instead of handling a few experiments on a bench top, scientists may simply pop a microchip into a computer and instantly run thousands of chemical reactions, with results — literally shrinking the lab down to the size of a thumbnail.

Toward that end, UCLA researchers have developed technology to perform more than a thousand chemical reactions at once on a stamp-size, PC-controlled microchip, which could accelerate the identification of potential drug candidates for treating diseases like cancer.

This is a microfluidic device held in the palm of the hand. **UCLA**

Their study appears in the Aug. 21 edition of the journal Lab on a Chip and is currently available online.

A team of UCLA chemists, biologists and engineers collaborated on the technology, which is based on microfluidics — the utilization of miniaturized devices to automatically handle and channel tiny amounts of liquids and chemicals invisible to the eye. The chemical reactions were performed using in situ click chemistry, a technique often used to identify potential drug molecules that bind tightly to protein enzymes to either activate or inhibit an effect in a cell, and were analyzed using mass spectrometry.

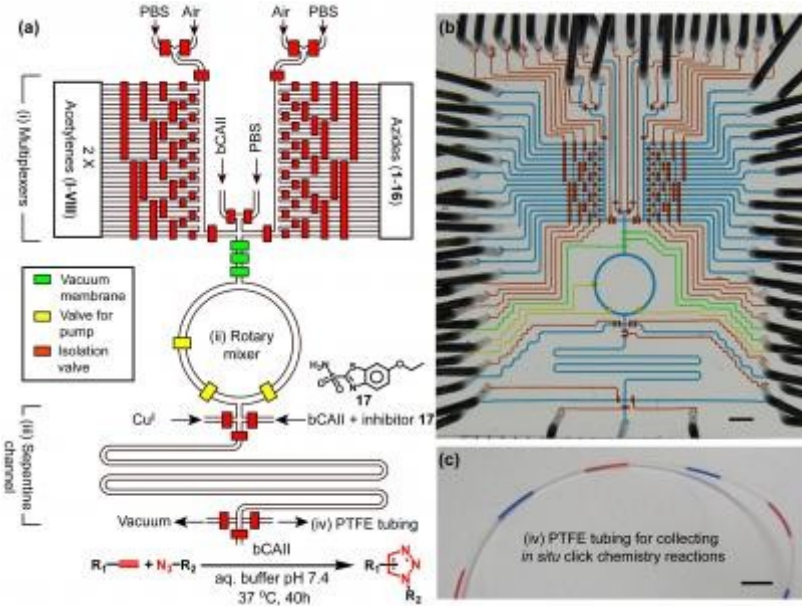
While traditionally only a few chemical reactions could be produced on a chip, the research team pioneered a way to instigate multiple reactions, thus offering a new method to quickly screen which drug molecules may work most effectively with a targeted protein enzyme. In this study, scientists produced a chip capable of conducting 1,024 reactions simultaneously, which, in a test system, ably identified potent inhibitors to the enzyme bovine carbonic anhydrase.

A thousand cycles of complex processes, including controlled sampling and mixing of a library of reagents and sequential microchannel rinsing, all took place on the microchip device and were completed in just a few hours. At the moment, the UCLA team is restricted to analyzing the reaction results off-line, but in the future,

they intend to automate this aspect of the work as well.

"The precious enzyme molecules required for a single in situ click reaction in a traditional lab now can be split into hundreds of duplicates for performing hundreds of reactions in parallel, thus revolutionizing the laboratory process, reducing reagent consumption and accelerating the process for identifying potential drug candidates," said study author Hsian-Rong Tseng, a researcher at UCLA's Crump Institute for Molecular Imaging, an associate professor molecular and medical pharmacology at the David Geffen School of Medicine at UCLA, and a member of the California NanoSystems Institute at UCLA.

Kym F. Faull, director of the Pasarow Mass Spectrometry Lab at UCLA, helped the team with several challenges, including reducing the amount of chemicals needed for reactions on the chip, enhancing test sensitivity and speeding up reaction analysis.



This is the design of the second generation integrated microfluidic device. **Credit: UCLA**

"The system allows researchers to not only test compounds quicker but uses only tiny amounts of materials, which greatly reduces lab time and costs," said Faull, a professor of psychiatry and biobehavioral sciences at the Geffen School of Medicine.

Next steps for the team include exploring the use of this microchip technology for other screening reactions in which chemicals and material samples are in limited supply — for example, with a class of protein enzymes called kinases, which play critical roles in the malignant transformation of cancer.

According to the researchers, the technology may open up many areas for biological and medicinal study.

The study team relied on work in the UCLA labs of Michael E. Phelps, Norton Simon Professor and chair of molecular and medical pharmacology, and Clifton K.F. Shen, assistant professor of molecular and medical pharmacology. Key research contributors included Yanju Wang, Wei-Yu Lin and Kan Liu, who work in Tseng's lab and intend to continue this line of research in independent careers after completing their training with Tseng.

The study was funded by the U.S. Department of Energy and the National Institutes of Health.

Other authors include: Rachel J. Lin of UCLA's Crump Institute for Molecular Imaging; Matthias Selke of the department of chemistry and biochemistry at California State University, Los Angeles; Hartmuth C. Kolb of Siemens Medical Solutions; Nangang Zhang of UCLA's Crump Institute for Molecular Imaging and the department of physics and Center of Nanoscience and Nanotechnology at China's Wuhan University; and Xing-Zhong Zhao of the department of physics and Center of Nanoscience and Nanotechnology at China's Wuhan University.

Scientists report original source of malaria

Deadly parasite jumped to humans from chimpanzees, perhaps through 1 mosquito

Irvine, Calif. – Researchers have identified what they believe is the original source of malignant malaria: a parasite found in chimpanzees in equatorial Africa.

UC Irvine biologist Francisco Ayala and colleagues think the deadly parasite was transmitted to humans from chimpanzees perhaps as recently as 5,000 years ago – and possibly through a single mosquito, genetic analyses indicate. Previously, malaria's origin had been unclear.

This discovery could aid the development of a vaccine for malaria, which sickens about 500 million people and kills about 1.5 million each year. It also furthers understanding of how infectious diseases such as HIV, SARS, and avian and swine flu can be transmitted to humans from animals.

"When malaria transferred to humans, it became very severe very quickly," said Ayala, co-author of the study that reports these findings. "The disease in humans has become resistant to many drugs. It's my hope that our discovery will bring us closer to making a vaccine."

The study appears online the week of Aug. 3 in the Proceedings of the National Academy of Sciences.

Human malignant malaria is caused by a parasite called Plasmodium falciparum, which is responsible for 85 percent of all infections and nearly all malaria deaths. Chimpanzees were known to carry a closely related parasite called Plasmodium reichenowi, but most scientists assumed the two had existed separately in humans and chimpanzees for the last 5 million years.

Scientists in the current study examined several new strains of the parasite found in blood taken from wild and wild-born chimpanzees in Cameroon and Ivory Coast sanctuaries during routine health exams.

A gene analysis linked one chimpanzee strain to all worldwide strains of the human malaria parasite. This connection suggests that one mosquito may have transferred malaria to humans. Because there is little genetic variance among strains of the human parasite, scientists believe the transmission occurred in the recent past – maybe 5,000 to 2 million years ago – though an exact time could not be determined.

The results support an earlier hypothesis by Dr. Ajit Varki of UC San Diego and colleagues that genetic mutations made humans first resistant to sickness from the chimpanzee parasite, then extremely susceptible to illness from the human form.

They also corroborate an earlier finding by Ayala and former UCI graduate student Stephen Rich that malignant malaria started spreading throughout the tropics and world about 5,000 years ago, when agriculture began in Africa. Rich, now a professor at the University of Massachusetts Amherst, also is the lead author of the current PNAS study.

In addition to Ayala and Rich, Nathan Wolfe of Stanford University worked on the study, along with collaborators from the Robert Koch Institute and the Max Planck Institute for Evolutionary Anthropology in Germany; the Global Viral Forecasting Initiative in San Francisco; the Biotechnology Centre in Cameroon; the U.S. Department of Agriculture; and the Ebola Tai Forest Project in the Ivory Coast.

The study was funded by the National Institutes of Health, with additional support from the Cummings School of Veterinary Medicine at Tufts University and the National Geographic Society Committee for Research & Exploration.

Is there long-term brain damage after bypass surgery? More evidence puts the blame on heart disease

Brain scientists and cardiac surgeons at Johns Hopkins have evidence from 227 heart bypass surgery patients that long-term memory losses and cognitive problems they experience are due to the underlying coronary artery disease itself and not ill after-effects from having used a heart-lung machine.

Researchers say their latest findings explain study results presented last year, which showed that the heart-lung machines – used to pump blood and supply the body with oxygen while the heart is stopped during surgery – did not cause postoperative long-term brain deficits.

"Our results hammer home the message that heart-lung machines are not to be blamed for cognitive declines observed years later in people who have had bypass surgery," says lead study investigator Ola A. Selnes, Ph.D., a professor in the Division of Cognitive Neuroscience in the neurology department at the Johns Hopkins University School of Medicine.

The new results stand in contrast to the impact of heart-lung machines on so-called "pumphead" syndrome, the temporary memory loss, vision and slurred speech observed right after surgery in many heart bypass patients.

According to another of the study's investigators, William A. Baumgartner, M.D., former cardiac surgeon in charge at The Johns Hopkins Hospital, the short-term syndrome led many surgeons and patients alike to assume that long-term losses must also be due to use of heart-lung machines, an assumption proven wrong by the latest evidence.

"Now we can assure these people that the disease, not the machine itself, is the cause of the problem," says Baumgartner, vice dean for clinical affairs and the Vincent L. Gott Professor in Cardiac Surgery at the Johns Hopkins University School of Medicine and its Heart and Vascular Institute.

Neurologists on the study team say the results highlight the need for further research into the long-term consequences of cardiovascular disease on the brain, and the brain's complex network of tiny blood vessels.

"Neuroscientists do not yet have good measures on heart disease and how the burden of this disease impacts brain function," says study senior investigator and neurologist Guy McKhann, M.D., a professor at Johns Hopkins, who next plans brain imaging studies to look at changes before and after heart bypass surgery to determine if there are any early, even predictive signs of cognitive problems, and if surgery could fix them.

McKhann notes that previous studies have found some 50 percent of patients awaiting heart bypass surgery already have some early indication of brain damage.

"If we can eventually figure out how heart disease and declines in brain function are linked over the long term, then it is feasible to think that we can diagnose problems earlier and, ultimately, intervene and prevent, or even lessen, these cognitive problems," says McKhann.

During heart bypass surgery, more formally known as coronary artery bypass grafting, or CABG, blood vessels from other parts of the body are removed and re-attached to the heart to restore open blood flow when the natural blood supply becomes constrained from coronary arteries that are diseased and blocked. Patients often spend an hour or more connected to a heart-lung machine during the surgery.

Results of the new study, published in the August 2009 issue of Annals of Thoracic Surgery, showed no differences in brain impairment in those who had heart bypass surgery, including a group of 75 heart patients

who had so-called off-pump bypass surgery, and another group of 99 heart patients who opted for drugs and arterial stents to keep their blood vessels open instead of bypass, with none requiring use of a heart-lung device.

But all 326 patients in the three groups were found to have experienced significant cognitive decline over the six-year study period on 16 different scores of verbal and visual memory when compared to 69 heart-healthy people who had no known risk factors for coronary artery disease.

The study, on heart patients from the Baltimore-Washington, D.C., region, is believed to be the first controlled study of its kind directly looking at the underlying causes of brain impairment, a phenomenon seen since the 1960s, when the CABG procedure was first introduced.

Adding to patients' fears was a 2001 report by researchers elsewhere, which found that 42 percent of heart bypass patients experienced some long-term cognitive impairment.

McKhann says CABG has "really evolved" along with heart disease treatment since the heart bypass machines and restorative procedure were first introduced, with procedure volumes peaking in the 1990s, but dropping afterwards, as physicians and patients began opting for less-invasive procedures. According to the latest estimates from the American Heart Association, roughly 469,000 CABG procedures were performed in the United States in 2005 on some 261,000 patients.

He points out that the procedure remains in widespread practice as patients considered safe to have the CABG procedure are getting older and sicker. People as old as 80, he says, are now candidates for CABG.

"With these new data, patients can now more accurately and confidently weigh the risks and benefits of bypass surgery against off-pump surgery or even more conservative options," says McKhann.

All study participants underwent an hour-long series of cognitive tests five times and during regularly scheduled annual study visits. In one test of verbal memory, patients had to memorize 15 words in a specific order and within 30 minutes. In another test of visual memory, patients had to trace on paper a complex diagram, which was then taken away, and then redraw the diagram from scratch.

Funding support for this study was provided by the U.S. National Institute of Neurological Disorders and Stroke, a member of the U.S. National Institutes of Health, and the Dana Foundation.

Besides McKhann, Baumgartner, and Selnes, other researchers involved in this study, conducted from 1997 through 2008, were Maura Grega, M.S.N.; Maryanne Bailey, M.P.H.; Luu D. Pham, M.Sc.; and Scott Zeger, Ph.D.

University of Minnesota researchers discover breakthrough method for chemical separations

New process could greatly reduce energy used in the production of biofuels

A team of researchers, led by chemical engineering and materials science professor Michael Tsapatsis in the University of Minnesota's Institute of Technology, have developed a more energy-efficient method of chemical separations that could revolutionize processes in the petrochemical and biofuels industries. The new discovery is published in the July 31 issue of Science, a leading journal of scientific research published by the American Association for the Advancement of Science.

The ability to separate and purify specific molecules in a chemical mixture is essential to chemical manufacturing. Many industrial separations rely on distillation, a process that is easy to design and implement but consumes a lot of energy.

With a grant from the National Science Foundation (NSF), Tsapatsis and his team have developed a new method for creating high-performance membranes from crystal sieves, called zeolites. The method could significantly increase the energy efficiency of chemical separations over conventional methods and enable higher production rates. The researchers developed a rapid heating treatment to remove structural defects in zeolite membranes that limit their performance, a problem that has plagued the technology for decades.

"Using membranes rather than energy-intensive processes such as distillation and crystallization could have a major impact on industry," said NSF program officer Rosemarie Wesson. This discovery could increase the energy efficiency of producing important chemical solvents such as xylene and renewable biofuels, such as ethanol and butanol, she said.

Tsapatsis explained that a universal challenge for biofuel production is the significant energy input required to separate and purify the desired products. Distillation is a commonly-used but energy-intensive separation method. Some experts project that the production of biofuels, such as ethanol, will reach 20 million barrels per day worldwide by 2030, Tsapatsis said. Assuming that technologically mature processes such as distillation continue to be used, the equivalent of 3 percent of the world's current total energy consumption would be needed for biofuel separations, he said.

Other biofuels, such as butanol, are also growing in popularity because of their compatibility with existing pipeline infrastructure, mixing capability with existing hydrocarbon fuels, and higher energy content. However, these heavier biofuels, with higher boiling points than water, are even more challenging to purify, Tsapatsis

said. Membrane-based separation processes, like those developed by University of Minnesota researchers, can eliminate all but a small fraction of the energy usage associated with this type of biofuel production. “We are very excited about our breakthrough research and the possibilities for the future," Tsapatsis said. "Great things can happen if these zeolite membranes work in industry the way we've seen them work in the lab."

Tsapatsis involved several University of Minnesota graduate students and post-doctoral fellows in this project. They include: Jungkyu Choi, now a postdoctoral fellow at the University of California, Berkeley, who performed most of the experiments; Mark Snyder, now an assistant professor at Lehigh University, who performed confocal microscopy experiments while a postdoctoral fellow in Tsapatsis's group, and Jared Stoeger, currently a Ph.D. candidate at the University of Minnesota, who performed permeation measurements using stainless steel tube supported membranes. Hae-Kwon Jeong, now an assistant professor at Texas A&M University, also performed some early rapid heating treatments while a postdoctoral fellow at the University of Illinois at Urbana–Champaign with engineering professor Richard Masel.

Tsapatsis and collaborators are now working on making zeolite membranes 10 to 100 times thinner to allow molecules to pass through more quickly. They hope to eventually implement their treatment process with its beneficial effects to these membranes as well.

NYU physicists make room for oddballs

New research on random packing could mean big advance for industry

Here's a question. How many gumballs of different sizes can fit in one of those containers at the mall so as to reward a well-spent quarter? It's hard to believe that most people never consider it even when guessing the number of candies in a bowl at Halloween.

But physicists at the Materials Research Science and Engineering Center at New York University recently developed a new way to help answer the question. They say the solution is found in how the particles pack in terms of many neighboring gumballs a single gumball can randomly touch within a given container.

Though it may seem intuitive, confirming the answer has long proven elusive because of super complex geometry when dealing with three-dimensional objects of mixed sizes and shapes. But in a recent breakthrough, researchers Maxime Clusel, Eric Corwin and Alex Siemens led by NYU physics professor Jasna Brujic, derived and tested a statistical model that potentially could help industry sort through a variety of packing problems from gumballs in vending machines to grain storage in silos or dry clothes detergent in retail boxes.

"We have discovered a simple organizing principle for particulate packing that predicts our experimental findings," said Brujic. The latest issue of the journal Nature reports the findings. The National Science Foundation funds the research.

The new model predicts the geometry of randomly packing spheres of different sizes in terms of how many nearest neighbors a particle can have, how far apart those neighbors can be and how free space is distributed throughout the packing. It does all this by determining geometric possibilities from the viewpoint of a single particle, which the authors term the "granocentric" view.

"Bigger particles pack with more neighbors, while smaller particles have on average fewer neighbors," said Corwin, a postdoctoral research fellow. "By combining this simple insight with probabilistic mathematics we created an accurate model demonstrating how this organizing rule gives rise to packings where particles have a wide range or distribution of contacts, neighbors and local densities."

The research team used a two step process to verify the model. First they used a 3-D microscope to spy how oil droplets packed together in water. The research enabled the team to determine the number of nearest neighbors the oil droplets could have and other parameters. Then they compared what they found to what was predicted by the statistical model. "We were surprised to find that such a simple model, based on physical intuition alone, could capture the properties of a complex packing of droplets in an emulsion," Brujic said.

The model predicted the percentage of space occupied by the particles in a container, such that researchers could statistically estimate the number of particles without knowing all the positions of the particles.

The structure of a packing of spheres of equal size is an old problem, whose complexity has challenged mathematicians and physicists for centuries. At first one would think that the structure of packings of spheres of random sizes is even more complex, but surprisingly, the researchers discovered that this is not the case.

The results could be used in a variety of industrial packing processes. For example, the model could be used to determine how finely to mill medicines that pharmaceutical companies pack into drug capsules, producing more effective pills that are smaller and easier to swallow.

"Packing problems are ubiquitous in industry," said Corwin. "An unexpected area of application might be to the world of paint creation. Paint is composed of small particles of pigment suspended in a fluid. As the fluid evaporates the particles are packed tighter and tighter, slowing down the evaporation of the fluid. Thus, one could tune the distribution of particle sizes to achieve paint with particular drying characteristics."

Domestic dog origins challenged

By Judith Burns Science reporter, BBC News

The suggestion that the domestic dog originated in East Asia has been challenged. The huge genetic diversity of dogs found in East Asia had led many scientists to conclude that domestication began there. But new research published in the journal PNAS shows the DNA of dogs in African villages is just as varied.

An international group of researchers analysed blood samples from dogs in Egypt, Uganda and Namibia.

Today's dogs are descended from Eurasian grey wolves, domesticated between 15,000 and 40,000 years ago.

The authors say the process by which humans domesticated the dog is poorly understood.

Lead scientist, Dr Adam Boyko of the Department of Biological Statistics and Computational Biology at Cornell University, says he decided to look at village dogs because they are so much more genetically diverse than bred dogs that they may hold the key to the origins of dog domestication.

The team analysed DNA from 318 dogs from villages in Egypt, Uganda and Namibia and measured their genetic diversity.

They also analysed the genetic make up of dog breeds thought to be of African origin, for example the Saluki, the Rhodesian Ridgeback, and the Pharaoh Hound and compared all the resulting data with results for non African dogs such as Puerto Rican street dogs and non-pedigree dogs in the US.

African village dogs possess plenty of genetic diversity

The emphasis on African village dogs came about because Adam Boyko's co-authors, his brother and sister-in-law, were travelling in Africa on honeymoon. They collected all the blood samples from the African dogs.

Genetically diverse

The team found genetic diversity among African village dogs is just as diverse as that of East Asian dogs, leading them to question the hypothesis of an East Asian origin for dog domestication.

Dr Boyko told BBC News: "I think it means that the conclusion that was drawn before might have been premature. It's a consequence of having a lot of street dogs from East Asia that were sampled, compared to elsewhere. "The reason that East Asia looked more diverse than elsewhere was not because East Asia as a continent had more diverse dogs than elsewhere but because non breed street and village dogs are more diverse than breed dogs."

He said he was not ruling out East Asia as a possible location for the origin of the domestic dog - but it could equally have been anywhere else on the Eurasian landmass where there were both grey wolves and humans. Co-author Paul Jones of The Waltham Centre for Pet Nutrition, UK, said: "It's interesting to know the answer to the question of where dogs were first domesticated and this paper goes some way to giving us an answer."

The team are now in the process of sampling street and village dogs across Europe and Asia from Portugal to Papua New Guinea to pinpoint the areas of greatest genetic diversity.

Dr Boyko said that all the dogs sampled in the study have grey wolf DNA so he is not questioning the hypothesis that dogs descended from Eurasian wolves.

The results led the team to conclude that today's African village dogs are a mosaic of indigenous dogs descended from early migrants to Africa.

They also went some way to proving the origins of some pedigree dogs purported to be of African origin. For example the Saluki breed shares DNA with modern day village dogs from Egypt - as does the Afghan Hound, despite its name.

Likewise, the Basenji breed is genetically very similar to some Namibian and Ugandan village dogs.

However the Pharaoh Hound and Rhodesian Ridgeback have little in common with any African indigenous dogs which suggests that these two breeds have non African origins.

Looking at language

Eye movements of Parkinson's disease patients during sentence comprehension support subcortical role in processing syntax

Milan, Italy - The study of the neural basis of language has largely focused on regions in the cortex – the outer brain layers thought by many researchers to have expanded during human evolution. Research at Brown University's Department of Cognitive and Linguistic Sciences, reported in the September Issue of Cortex (http://www.elsevier.com/locate/cortex), published by Elsevier, adds to evidence that deeper, subcortical

regions are also critical by pinpointing when Parkinson's disease patients have difficulty while processing grammatically complex sentences. In Parkinson's disease, degeneration of subcortical dopamine-secreting neurons leads not only to motor symptoms but often also to cognitive deficits.

Jesse Hochstadt recorded eye movements of Parkinson's patients as they listened to sentences containing restrictive relative clauses ("The queen who was kicking the cook was fat") and tried to choose matching pictures. Patients who made more errors were slower to stop looking at pictures ruled out by the relative clause (a cook kicking a queen) when they had heard only as far as that clause's verb ("The queen who was kicking"). But at the ends of sentences, they were not slower to rule out pictures (such as a thin queen kicking a fat cook) that disagreed with the main clause ("The queen … was fat"), despite the memory demands imposed by the intervening relative clause. These patients again showed poor relative-clause and good main-clause processing when relative clauses were at the ends of sentences ("The queen was kicking the cook who was thin").

Patients with such syntax processing difficulty also had difficulty switching between making choices based on size or shape in a non-linguistic task. This association, Hochstadt proposes, may indicate that processing relative clauses requires structural "switching away" from main clauses; alternatively, because restrictive relative clauses generally refer to facts already mentioned, processing them may involve shifting attention to this "background" information from main-clause "foreground" information.

These joint effects of subcortical neurodegeneration on syntax and "set-switching" are consistent with widely publicized research indicating that mutations in the human FOXP2 gene cause deficits in language and cognition by affecting development of subcortical structures, and that evolution of modern Homo sapiens involved modification of this gene.

Notes to Editors: *The article is "Set-shifting and the on-line processing of relative clauses in Parkinson's Disease: Results from a novel eye-tracking method" by Jesse Hochstadt and appears in Cortex, Volume 45, Issue 8 (September 2009), published by Elsevier in Italy. Full text of the article featured above is available to members of the media upon request. Please contact the Elsevier press office, newsroom@elsevier.com. To schedule an interview, contact Dr. Jesse Hochstadt, jesseh@alumni.brown.edu*

Nerve-block anesthesia can improve surgical recovery, even outcomes

NewYork-Presbyterian Hospital offers nerve-block anesthesia, with advantages including improved pain relief

NEW YORK (August 4, 2009) -- When planning for surgery, patients too often don't consider the kind of anesthesia they will receive. In fact, the choice of anesthesia can improve recovery, even outcomes.

Regional nerve blocks, an anesthesia technique available at NewYork-Presbyterian Hospital, are known to improve pain relief, reduce side effects and allow patients to go home sooner when compared with general anesthesia. With the introduction of ultrasound guidance, nerve blocks have become more accurate, making the technique available in the treatment of an increasing variety of conditions, including breast cancer surgery.

Dr. Anthony Robin Brown is director of the Division of Regional Anesthesia at NewYork-Presbyterian Hospital/Columbia University Medical Center.

"Nerve blocks target a specific area of the body, such as an arm or chest. With this approach, patients can avoid the downsides of general anesthesia during surgery and opioid-based medications used to control pain during recovery. The upshot is fewer instances of nausea, confusion, sedation (sleepiness) and pain, and a quicker recovery," says Dr. Brown, who is clinical professor of anesthesiology at Columbia University College of Physicians and Surgeons. "If patients prefer, they can remain awake during surgery and watch the procedure as it happens on video monitors. They also have the option of sedation that puts them to sleep."

Another potentially major advantage: Preliminary published research indicates that nerve blocks could help prevent the recurrence of cancer[1]. The theory is that the stress of surgery can weaken the immune system, making recurrence more likely. General anesthesia and opioid-based medications only mask surgical stress. In contrast, nerve blocks work directly on the area of the body where the surgery is taking place. This prevents the initiation of the surgical stress response, with the result that the immune system function is not compromised.

Dr. Tiffany Tedore is director of the Division of Regional Anesthesia at NewYork-Presbyterian Hospital/Weill Cornell Medical Center. She is leading a clinical research study comparing nerve blocks with general anesthesia for breast cancer surgery to see which approach results in better pain control, fewer side effects and quicker recovery.

"Traditionally, breast cancer surgery has involved two kinds of anesthesia -- local anesthetic and sedation for biopsy, followed by general anesthesia for larger procedures such as mastectomy. Our study is looking at the benefits of replacing general anesthesia with a nerve block," says Dr. Tedore, who is also assistant professor of anesthesiology at Weill Cornell Medical College. "I anticipate our future studies will also look at cancer control."

NewYork-Presbyterian currently offers nerve blocks for most orthopedic procedures, as well as selected breast cancer and vascular surgeries. Additional surgical procedures are being explored in the coming months.
Regional nerve blocks involve injecting a local anesthetic like ropivacaine alongside a specific nerve or nerve bundle, such as the brachial plexus in the neck. The local anesthetic is absorbed into the nerve, where it blocks sodium channels, disabling its electrical-like action potential. This inhibits pain and causes a lack of sensation.

After the boom, is Wikipedia heading for bust?

* 12:12 04 August 2009 **by Jim Giles**

Wikipedia has rapidly become one of the most used reference sources in the world, but a new study shows that the website's explosive growth is tailing off and also suggests the community-created encyclopaedia has become less welcoming to new contributors.

Ed Chi and colleagues at the Palo Alto Research Center in California warn that the changes could compromise the encyclopaedia's quality in the long term. "It's easy to say that Wikipedia will always be here," says Chi, a computer scientist. "This research shows that is not a given."

Launched in 2001, the English language Wikipedia grew rapidly to its current size of almost 3 million articles. However, when the Palo Alto team analysed a downloaded version of the encyclopaedia they found its growth has peaked.

The number of articles added per month flattened out at 60,000 in 2006 and has since declined by around a third. They also found that the number of edits made every month and the number of active editors both stopped growing the following year, flattening out at around 5.5 million and 750,000 respectively.

Editor wars

The balance of power within the people who contribute to Wikipedia also appears to have shifted – away from casual contributors who make infrequent changes, toward more active and established contributors. Chi says the trend could shut out new users.

"Occasional" editors, those who make just a single edit a month, have 25 per cent of their changes erased, or reverted, by other editors, a proportion that in 2003 was 10 per cent. The revert rate for editors who make between two and nine changes a month grew from 5 to 15 per cent over the same period.

"This is evidence of growing resistance from the Wikipedia community to new content," say the Palo Alto team. Chi told New Scientist that the changes could harm Wikipedia in the longer term by deterring new editors from taking part and so reducing the number of people available to spot and correct the vandalism that constantly threatens the encyclopaedia. "Over time the quality may degrade," he warns.

Chi thinks that Wikipedia now includes so much information that some editors have turned from creating new articles to improving existing ones, resulting in more disputes about edits. Such disputes are not a level playing field because established editors sometimes draw on extensive knowledge of Wikipedia's guidelines to overwhelm opposition in a practice dubbed "wikilawyering".

Spam to blame?

The Wikimedia Foundation, the non-profit company that operates Wikipedia, has noted these changes and last month launched a strategic review of Wikipedia in an effort to understand them.

But one of the experts leading that review, Eugene Eric Kim of Blue Oxen Associates in San Francisco says that Chi's arguments are only one of several possible explanations for the changes seen in Wikipedia. The high number of reverts, for example, may be due to the increasing use of spam software that inserts promotional text, such as links to company websites, into articles.

Kim says the review will report this time next year and that any Wikipedia editor can contribute to the process.

The Palo Alto team will present their analysis at the International Symposium on Wikis and Open Collaboration in Orlando, Florida this October. A blog post by Chi summarises the study.

Fertile mice created from skin cells

THE birth of the first live mice created from mouse skin cells has confirmed the potential of converting pluripotent stem cells (iPS) into all tissues of the body, a property that could prove valuable for people undergoing reconstructive surgery.

Qi Zhou of the Chinese Academy of Sciences in Beijing and his colleagues started by making iPS cells from mouse skin cells. They then injected the cells into mouse embryos to create "chimeric" embryos, each containing four sets of chromosomes. The embryos were implanted into female mice, resulting in 27 live chimeric pups being born. Many of them were fertile (Nature, DOI: 10.1038/nature08267).

Injecting pluripotent stem cells into mouse embryos led to the creation of chimeric embryos

While creating a baby from iPS cells would be unethical, the breakthrough proves iPS cells made from an individual's own cells have the capability to turn into any tissue in the body.

Really?

The Claim: Cold Temperatures Improve Sleep

By ANAHAD O'CONNOR

THE FACTS Avoiding caffeine, sticking to a schedule and drinking a glass of warm milk are the usual tips for a good night's rest. But the right room temperature can also play a crucial role.

Leif Parsons

Studies have found that in general, the optimal temperature for sleep is quite cool, around 60 to 68 degrees Fahrenheit. For some, temperatures that fall too far below or above this range can lead to restlessness.

Temperatures in this range, it seems, help facilitate the decrease in core body temperature that in turn initiates sleepiness. A growing number of studies are finding that temperature regulation plays a role in many cases of chronic insomnia. Researchers have shown, for example, that insomniacs tend to have a warmer core body temperature than normal sleepers just before bed, which leads to heightened arousal and a struggle to fall asleep as the body tries to reset its internal thermostat.

For normal sleepers, the drop in core temperature is marked by an increase in temperature in the hands and feet, as the blood vessels dilate and the body radiates heat. Studies show that for troubled sleepers, a cool room and a hot-water bottle placed at the feet, which rapidly dilates blood vessels, can push the internal thermostat to a better setting.

THE BOTTOM LINE A slightly cool room and a lower core temperature are optimal for sleep.

Synthetic Life

By John Markoff

There is a growing consensus (at least in Silicon Valley) that the information age is about to give way to the era of synthetic genetics. That was underscored recently when Harvard geneticist George Church and J. Craig Venter - of the race to decode the human genome fame - gave lectures before a small group of scientists, technologists, entrepreneurs, and writers in West Hollywood.

The event, billed as "A Short Course on Synthetic Genomics," was organized by John Brockman, the literary impresario (and book agent for several New York Times reporters, including this one) who publishes the cybersalon-style website www.edge.org, a forum dedicated to scientists (many of whom are his clients) and their ideas.

In roughly six hours of lectures, both scientists tried to convey how the world will be changed by the ability to routinely read genetic sequences into computing systems and then store, replicate, alter and insert them back into living cells.

The rate at which this technology is now improving puts silicon to shame. Dr. Church noted that between 1970 and 2005 gene sequencing had taken place on a Moore's Law pace, improving at about 1.5 times per year. Since then it has improved at the rate of an order of magnitude, or ten times annually.

In the process the cost of sequencing the human genome has plunged from $3 billion to $5 thousand and continues to fall. Dr. Church identified 17 companies and one "open source" project all pursuing different technologies to further push down cost and speed up the pace of sequencing.

As a consequence, the structure of the emerging synthetic genetics industry is beginning to mirror that of the semiconductor and computer industries, which are based on modular components and design tools.

The key to the vast growth of the computer industry took place during the 1970s when physicist Carver Mead helped give the industry a standard design approach based on modular components. Now that appears to be happening in the synthetic biology world as well.

For someone who has spent the past three decades writing about computing, Dr. Venter's talk was eye-opening. "I view DNA as an analog information system," he said. " and I hope to convince you in fact that it is absolutely the software of life."

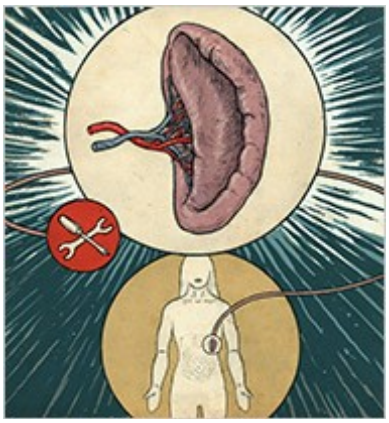
Basics

Finally, the Spleen Gets Some Respect

By NATALIE ANGIER

As a confirmed crab apple who has often been compared to the splenetic Lucy Van Pelt character from Peanuts, I am gratified to learn that should my real spleen ever decide to vent in earnest, the outburst may just help save my life. Scientists have discovered that the spleen, long consigned to the B-list of abdominal organs and known as much for its metaphoric as its physiological value, plays a more important role in the body's defense system than anyone suspected.

Reporting in the current issue of the journal Science, researchers from Massachusetts General Hospital and Harvard Medical School describe studies showing that the spleen is a reservoir for huge numbers of immune cells called monocytes, and that in the event of a serious trauma to the body like a heart attack, gashing wound or microbial invasion, the spleen will disgorge those monocyte multitudes into the bloodstream to tackle the crisis.



Jonathon Rosen

"The parallel in military terms is a standing army," said Matthias Nahrendorf, an author of the report. "You don't want to have to recruit an entire fighting force from the ground up every time you need it."

That researchers are only now discovering a major feature of a rather large organ they have been studying for at least 2,000 years demonstrates yet again that there is nothing so foreign as the place we call home.

"Often, if you come across something in the body that seems like a big deal, you think, 'Why didn't anybody check this before?' " Dr. Nahrendorf said. "But the more you learn, the more you realize that we're just scratching on the surface of life. We don't know the whole story about anything."

Dr. Nahrendorf, with Filip K. Swirski, Mikael J. Pittet and a dozen other colleagues, performed the initial studies using mice, but the scientists suspect the results will apply to humans as well.

Ulrich H. von Andrian, an immunologist at Harvard Medical School who was not involved with the research, agreed that the findings were a surprise. "If one had to guess the source of these cells, one would have thought it likely that they were mobilized from the bone marrow rather than from the spleen," he said. "The discovery adds another layer of complexity not previously associated with that organ."

The latest work also sounds a cautionary note against underestimating a body part or dismissing it as vestigial, expendable or past its prime. In an accompanying essay, Ting Jia and Eric G. Pamer of Memorial Sloan-Kettering Cancer Center admit that "the spleen lacks the gravitas of neighboring organs" like the liver or the stomach "because we can survive without it."

Spleens can rupture during contact sports, say, or in a motorcycle accident, at which point surgeons have no choice. "It's such a vascularized organ, and the risk of big-time hemorrhaging is so great, that if the spleen ruptures, it's a surgical emergency," said James N. George, a hematologist with the University of Oklahoma Health Sciences Center. "You have to remove it."

The new findings in no way counter the necessity of excising a ruptured spleen, the researchers said, but they do suggest that the loss of the organ is more than a mere "inconvenience," as it has often been depicted, and could help explain previous reports showing an enhanced risk of early death among people who have undergone splenectomies.

In one study that appeared in The Lancet in 1977, for example, researchers compared a group of 740 American veterans of World War II who had had their spleens removed as a result of battle injuries with a similar size sample of veterans who had suffered other war injuries but had kept their spleens. The splenectomized men, the researchers found, were twice as likely to die of cardiovascular disease as were the veterans in the control group. All of which means that despleening should be diligently guarded against, particularly among our little sports warriors, perhaps through the wearing of appropriate protective gear.

Researchers cite other cases in which organs were presumed to be so dispensable that they could be removed "prophylactically" — often with unfortunate outcomes. In recent years, for example, many older women undergoing hysterectomies have been advised to have their healthy ovaries removed at the same time, the rationale being: if you are past your childbearing years, why hang on to reproductive organs that might turn cancerous and kill you? Yet follow-up surveys have shown that women who underwent elective ovariectomy had a heightened risk of dying during a given study period, were more susceptible to heart disease and lung cancer and were twice as likely to develop Parkinson's disease compared with women who had kept their ovaries. "Evolution has an edge on us," Dr. Nahrendorf said. "I would be very careful about saying, 'You don't need this organ, get rid of it.' "

Another reason to esteem the spleen — a purplish, fist-size, five-ounce organ in the upper left quadrant of the abdominal cavity, just behind the stomach and under the diaphragm — is its illustrious medical and poetic history. Galen considered the spleen to be a source of one of the four bodily humors, specifically the black bile associated with irritable, melancholic cranks. In his poem, "Spleen," Charles Baudelaire describes a young narrator so weary and despondent, unresponsive even to beautiful women and jesting men, that it is as if the "green waters of Lethe" fills his veins.

More recently, researchers determined that the spleen is like an elaborate wetlands, a Mississippi bayou for filtering and freshening the blood. In other organs, blood flows through an interconnected mesh of increasingly narrow arteries, veins and capillaries. The spleen, by contrast, has a so-called noncapillary circulatory system: as the blood flows in, it is dumped into puddle-like sinusoids, and to get back out it must squeeze between cells. That dumping and squeezing help filter out blood-borne parasites, aging blood cells too brittle for compression and the little oxidized pellets, the BB's, with which red blood cells are often pocked. The spleen has often been called a graveyard for red blood cells, but it is more of a recycling center, for the iron and other components are plucked out of the cells and used to stock new hemoglobin cages.

Filtration, cannibalization, and now — serious monocyte cultivation. In the new study, the researchers began by looking at monocytes, the largest of the body's white blood cells. "It was recognized that these cells are the major repair workers after a heart attack," Dr. Nahrendorf said. "They remove dead muscle cells, they start rebuilding stable scar tissue, they stimulate the generation of new blood vessels."

The cells make haste to cut and paste. "Within 24 hours after a myocardial infarction," Dr. Nahrendorf said, "there are millions of monocytes" congregating around the broken heart. All of which would seem sensible, desirable, an excellent display of emergency preparedness, except that Dr. Nahrendorf and his principal colleagues were puzzled by one big unknown: Where did the rapid response team come from? The numbers circulating in the blood were simply too low. The researchers searched one organ after another, until they checked the spleen and found the monocytic mother lode. "The numbers there were huge, 10 times higher than what was in the bloodstream," Dr. Nahrendorf said.

By the researchers' reckoning, monocytes, like all blood cells, are born in the bone marrow and at some point migrate to the spleen, lured by cues yet to be identified. They sit and wait, a sessile bunch, but when aroused by such chemical signatures of damage as angiotensin, the cells surge forth without hesitation, a reaction the researchers hope someday to understand well enough to recapitulate at will. Hail to the chief, hail to the queen and hail to the monocytes residing in my spleen.

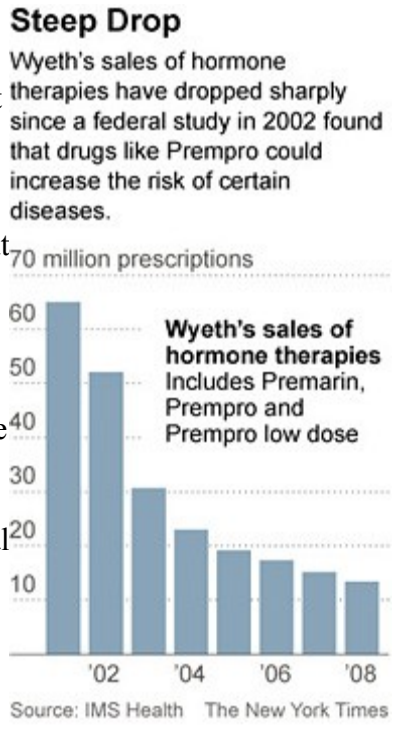
Medical Papers by Ghostwriters Pushed Therapy

By NATASHA SINGER

Newly unveiled court documents show that ghostwriters paid by a pharmaceutical company played a major role in producing 26 scientific papers backing the use of hormone replacement therapy in women, suggesting that the level of hidden industry influence on medical literature is broader than previously known.

The articles, published in medical journals between 1998 and 2005, emphasized the benefits and de-emphasized the risks of taking hormones to protect against maladies like aging skin, heart disease and dementia. That supposed medical consensus benefited Wyeth, the pharmaceutical company that paid a medical communications firm to draft the papers, as sales of its hormone drugs, called Premarin and Prempro, soared to nearly $2 billion in 2001.

But the seeming consensus fell apart in 2002 when a huge federal study on hormone therapy was stopped after researchers found that menopausal women who took certain hormones had an increased risk of invasive breast cancer, heart disease and stroke. A later study found that hormones increased the risk of dementia in older patients.



The ghostwritten papers were typically review articles, in which an author weighs a large body of medical research and offers a bottom-line judgment about how to treat a particular ailment. The articles appeared in 18 medical journals, including The American Journal of Obstetrics and Gynecology and The International Journal of Cardiology.

The articles did not disclose Wyeth's role in initiating and paying for the work. Elsevier, the publisher of some of the journals, said it was disturbed by the allegations of ghostwriting and would investigate.

The documents on ghostwriting were uncovered by lawyers suing Wyeth and were made public after a request in court from PLoS Medicine, a medical journal from the Public Library of Science, and The New York Times.

A spokesman for Wyeth said that the articles were scientifically accurate and that pharmaceutical companies routinely hired medical writing companies to assist authors in drafting manuscripts.

The court documents provide a detailed paper trail showing how Wyeth contracted with a medical communications company to outline articles, draft them and then solicit top physicians to sign their names, even though many of the doctors contributed little or

no writing. The documents suggest the practice went well beyond the case of Wyeth and hormone therapy, involving numerous drugs from other pharmaceutical companies.

"It's almost like steroids and baseball," said Dr. Joseph S. Ross, an assistant professor of geriatrics at Mount Sinai School of Medicine in New York, who has conducted research on ghostwriting. "You don't know who was using and who wasn't; you don't know which articles are tainted and which aren't."

Because physicians rely on medical literature, the concern about ghostwriting is that doctors might change their prescribing habits after reading certain articles, unaware they were commissioned by a drug company.

"The filter is missing when the reader does not know that the germ of an article came from the manufacturer," said James Szaller, a lawyer in Cleveland who has spent four years going through the ghostwriting documents on behalf of hormone therapy plaintiffs.

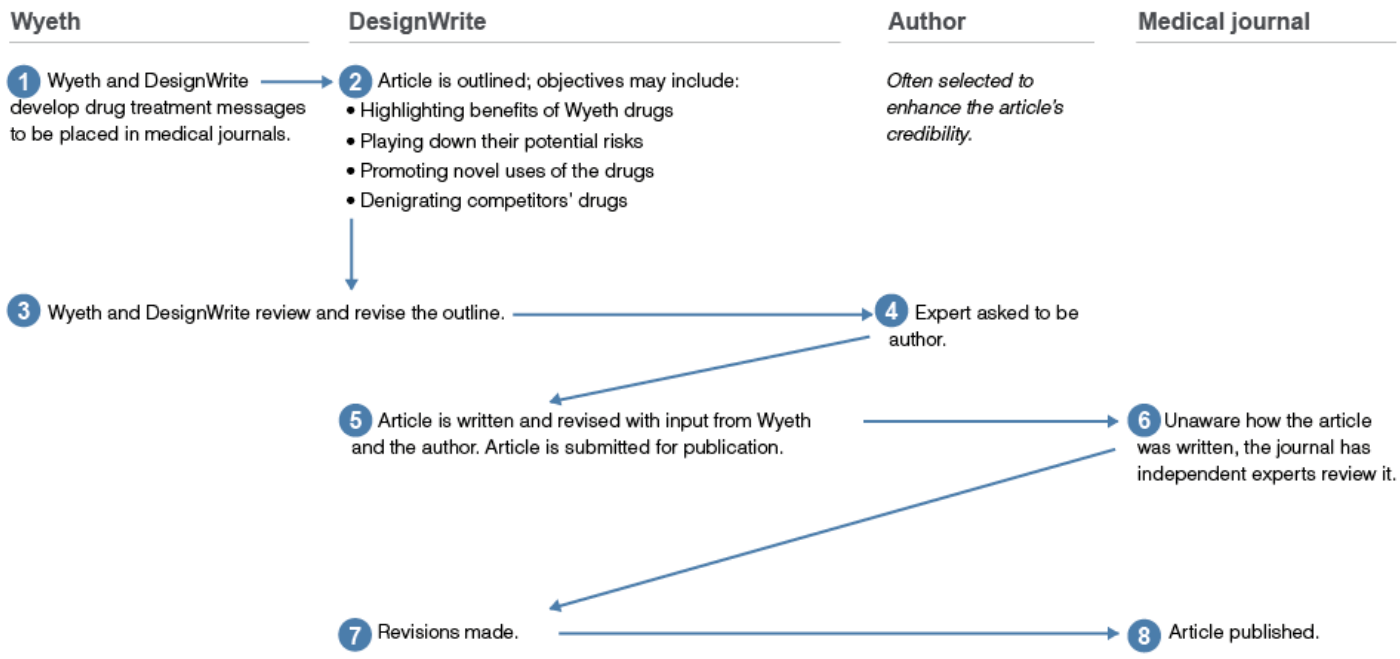
Wyeth faces about 8,400 lawsuits from women who claim that the company's hormone drugs caused them to develop illnesses. Twenty-three of the 31 cases that had been set for trial were resolved in Wyeth's favor; the company has also settled with five plaintiffs. Others cases are on appeal.

Doug Petkus, a spokesman for Wyeth, said the articles on hormone therapy were scientifically sound and subjected to rigorous review by outside experts on behalf of the medical journals that published them.

Although Wyeth continues to work with medical writing firms, the company adopted a policy in 2006 mandating that authors become involved early in the publication process and that any financial assistance by Wyeth or contributions by medical writers be acknowledged in the published text, said Stephen Urbanczyk, a lawyer representing Wyeth.

Doctors have long debated the merits and risks of hormone therapy to treat the symptoms of menopause. Although studies have shown that hormones have benefits like reducing the incidence of hip fractures, they have also shown that the drugs can increase the risk of various cancers.

At one time, the Premarin family of drugs, which dominated the market for hormone therapy, was among Wyeth's best-selling brands. And the company worked with several ghostwriting companies to maintain that dominance.



In 1997, for example, DesignWrite, a medical communications company in Princeton, N.J., proposed to Wyeth a two-year plan that would include the preparation of about 30 articles for publication in medical journals.

The development of an article on the treatment of menopausal hot flashes and night sweats illustrates DesignWrite's methodology. Sometime in 2003, a DesignWrite employee wrote a 14-page outline of the article; the author was listed as "TBD" - to be decided. In July 2003, DesignWrite sent the outline to Dr. Gloria Bachmann, a professor of obstetrics and gynecology at the Robert Wood Johnson Medical School in New Brunswick, N.J.

Dr. Bachmann responded in an e-mail message to DesignWrite: "Outline is excellent as written." In September 2003, DesignWrite e-mailed Dr. Bachmann the first draft of the article. She also pronounced that "excellent" and added, "I only had one correction which I highlighted in red."

The article, a nearly verbatim copy of the DesignWrite draft, appeared in 2005 in The Journal of Reproductive Medicine, with Dr. Bachmann listed as the primary author. It described hormone drugs as the "gold standard" for treating hot flashes and was less enthusiastic about other therapies.

The acknowledgments thanked several medical writers for their "editorial assistance," not disclosing that those writers worked for DesignWrite, which charged Wyeth $25,000 to generate the article.

Dr. Bachmann, who has 30 years of research and clinical experience in menopause, said she played a major role in the publication by lending her expertise. Her e-mail messages do not reflect contributions she may have made during phone calls and in-person meetings, she said.

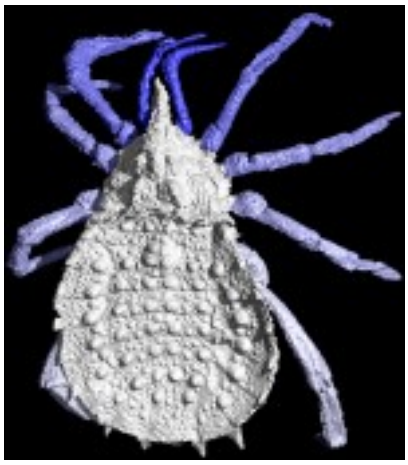
"There was a need for a review article and I said 'Yes, I will review the draft and make sure it is accurate,' " Dr. Bachmann said in an interview Tuesday. "This is my work, this is what I believe, this is reflective of my view."

In response to a query from a reporter, Michael Platt, the president of DesignWrite, wrote that the company "has not, and will not, participate in the publication of any material in which it does not have complete confidence in the scientific validity of the content, based upon the best available data."

As medical journals learn more about ghostwriting through documents released in lawsuits and in Congress, some editors have started asking authors harder questions. A few leading journals, like The Journal of the American Medical Association, have instituted authorship forms that require contributors to detail their role in an article and to disclose conflicts of interest. But many journals have yet to take such steps.

Scary ancient spiders revealed in 3-D models, thanks to new imaging technique

Early relatives of spiders that lived around 300 million years ago are revealed in new 3-D models, in research published today in the journal Biology Letters



Eophrynus prestivicii

Courtesy of the Natural History Museum and Imperial College London

Early relatives of spiders that lived around 300 million years ago are revealed in new three-dimensional models, in research published today in the journal Biology Letters.

Scientists at Imperial College London have created detailed 3D computer models of two fossilised specimens of ancient creatures called Cryptomartus hindi and Eophrynus prestvicii, closely related to modern-day spiders. The study reveals some of the physical traits that helped them to hunt for prey and evade predators.

The researchers created their images by using a CT scanning device, which enabled them to take 3,000 x-rays of each fossil. These x-rays were then compiled into precise 3D models, using custom-designed software.

Both Cryptomartus hindi and Eophrynus prestivicii were around the size of a 50 pence piece and they roamed the Earth during the Carboniferous period, 359 – 299 million years ago. This was a time before the dinosaurs, when life was emerging from the oceans to live on land. During this period, the world's continents were merging together near the equator to form one supercontinent and the first tropical rainforests were playing host to a diverse range of species.

Previous studies of the fossilised remains of Cryptomartus hindi allowed scientists to see some features of the creature, which had four pairs of legs and looked similar to a spider.

In the new study, the researchers' computer models reveal that Cryptomartus hindi's first two legs were angled towards the front of the body, which suggests that it used its legs to grab its prey before killing them. The researchers believe this find suggests the Cryptomartus hindi was an ambush predator, living in logs and fronds, waiting for prey such as insects to walk by before catching and killing them. This stance is seen in modern day crab spiders, which sit on the edge of flowers and wait for insects to land so that they can grab them.

The scientists also discovered that Cryptomartus hindi had ball-like growths at the base of its limbs, called coxal endites. The scientists believe the coxal endites could be an evolutionary hang-over from their last common ancestor, who probably used the growths at the base of their limbs to help them grind their food. These coxal endite-type growths can still be seen today in species such as horseshoe crabs, which use them to grind up their prey before pushing it into their backward-facing mouths.

The computer models also revealed that Cryptomartus hindi's mouth appendages, called pedipalps, had tiny 'tarsal' claws attached at the end to help the creature to manipulate its prey. These claws are seen in rare modern-day arachnids such as the Ricinulei. The researchers say that the existence of this common physical

feature, shared by the Cryptomartus hindi and the Ricinulei, lends further weight to the theory that they are closely related.

The models also reveal new information about Eophrynus prestivicii. Previous studies of fossilised remains of this creature suggested that it could have hunted on the open forest floor. It had long legs that enabled it to run through leaf litter to chase, catch and kill its prey.

The new models reveal, for the first time, that Eophrynus prestivicii had defensive spikes on its back. The researchers say that the spikes may have been a defensive adaption by Eophrynus prestivicii, to make them a less tempting meal for the amphibians that would have recently emerged from the oceans onto land.

The study's lead author, Mr Russell Garwood, PhD student from the Department of Earth Science and Engineering at Imperial College London, says: "Our models almost bring these ancient creatures back to life and it's really exciting to be able to look at them in such detail. Our study helps build a picture of what was happening during this period early in the history of life on land. We think one creature could have responded to increasing predation from the amphibians by growing spikes, while the other responded by becoming an ambush predator, hiding away and only exposing itself when it had to come out to eat."

At present, most palaeontologists analyse fossils by splitting open a rock and looking at the creatures encased inside. This means that scientists can often only see part of the fossil and cannot explore all of the fossil's physical features.

The researchers believe their new technique could be used to re-explore previously analysed fossils to provide a much clearer picture of how ancient extinct species survived on early Earth.

UNC researchers decode structure of an entire HIV genome

CHAPEL HILL – The structure of an entire HIV genome has been decoded for the first time by researchers at the University of North Carolina at Chapel Hill. The results have widespread implications for understanding the strategies that viruses, like the one that causes AIDS, use to infect humans.

The study, the cover story in the Aug. 6, 2009, issue of the journal Nature, also opens the door for further research which could accelerate the development of antiviral drugs.

HIV, like the viruses that cause influenza, hepatitis C and polio, carries its genetic information as single-stranded RNA rather than double-stranded DNA. The information encoded in DNA is almost entirely in the sequence of its building blocks, which are called nucleotides. But the information encoded in RNA is more complex; RNA is able to fold into intricate patterns and structures. These structures are created when the ribbon-like RNA genome folds back on itself to make three-dimensional objects.

Kevin Weeks, Ph.D., a professor of chemistry in UNC's College of Arts and Sciences who led the study, said prior to this new work researchers had modeled only small regions of the HIV RNA genome. The HIV RNA genome is very large, composed of two strands of nearly 10,000 nucleotides each.

Weeks, who is also a member of the UNC Lineberger Comprehensive Cancer Center, and Joseph M. Watts, a chemistry postdoctoral fellow supported by the Lineberger Center, used technology developed by Weeks' lab to analyze the architecture of HIV genomes isolated from infectious cultures containing trillions of viral particles that were grown by Robert Gorelick, Ph.D., and Julian Bess of the National Cancer Institute.

They then teamed up with UNC researchers in the College and the School of Medicine for further analysis: Christopher Leonard in the department of chemistry; Kristen Dang, Ph.D., from biomedical engineering; Ron Swanstrom, Ph.D., a professor of microbiology and immunology at UNC Lineberger; and Christina Burch, Ph.D., an associate professor of biology. They found that the RNA structures influence multiple steps in the HIV infectivity cycle.

"There is so much structure in the HIV RNA genome that it almost certainly plays a previously unappreciated role in the expression of the genetic code," Weeks said.

Swanstrom and Weeks note that the study is the key to unlocking additional roles of RNA genomes that are important to the lifecycle of these viruses in future investigations. "One approach is to change the RNA sequence and see if the virus notices," Swanstrom said. "If it doesn't grow as well when you disrupt the virus with mutations, then you know you've mutated or affected something that was important to the virus."

Weeks added: "We are also beginning to understand tricks the genome uses to help the virus escape detection by the human host."

Researchers from CIC bioGUNE have found a way to treat ischemic pathologies

A team of researchers from CIC bioGUNE from the Cellular Biology and Stem Cell Unit, alongside a team from Paris' Cardiovascular Research Centre (INSERM U970) have developed a new area of research which looks extremely promising as regards the development of new therapeutic responses to ischemic pathologies and cardiovascular diseases in general. The results of this research project, which was initiated in 2005 and is

supported by Bizkaia:Xede and the Basque Government's Etortek programme, were published in the prestigious scientific journal Circulation.

By activating a protein called HIF, the strategy is to stimulate revascularisation and the repair of the damaged organ following ischemia caused by the obstruction of a blood vessel preventing normal blood flow. These obstructions occur, for example, in the event of thrombosis in a limb, myocardial infarction or a stroke. In this sense, it is important to highlight the fact that cardiovascular diseases are the principal cause of death throughout the world (in the European Union, they account for 40% of all deaths, a figure equivalent to 2 million deaths per year).

In general, cells tend to respond to the lack of oxygen caused by poor blood flow by activating HIF. However, in the case of an ischemic pathology, HIF is not sufficiently activated.

Dr Berra, Cellular Biology and Stem Cell Unit's leader, stated that they decided to over-produce HIF following ischemia as an attractive therapeutic alternative. For their research purposes, they used an ischemic model provoked in a mouse leg through ligation of the femoral artery. In other words, they closed off the femoral artery and stopped the blood flow to the limb. When this happens, the leg develops necrosis and after a time, the mouse dies.

The aim was to artificially help stimulate the production of HIF after the femoral artery had been closed off. And they saw that when they did this, the mouse's leg revascularised and no longer entered into a degenerative process.

How is this high level of HIF production achieved? HIF is a protein which, when not required, degrades constitutively and this degradation is regulated by enzymes called PHDs.

These enzymes hydroxylate HIF and, as a result of this hydroxylation, the protein degrades. Therefore, when these enzymes are inhibited, HIF cannot degrade and so accumulates. To inhibit PHDs, they use siRNAs, explains Dr Berra.

Cooling treatment after cardiac arrest is cost-effective, Penn study shows

Researchers urge adoption of lifesaving treatment at more hospitals across the nation

(PHILADELPHIA) – A brain-preserving cooling treatment called therapeutic hypothermia is a cost-effective way to improve outcomes after out-of-hospital cardiac arrest, which claims the lives of more than 300,000 people each year in the United States and leaves thousands of others neurologically devastated. The treatment, which lowers body temperature to prevent damage to the brain and other major organs when blood flow is restored to the body following cardiac arrest, is considered a “good value” when compared to many other accepted and widely utilized medical treatments, including dialysis for kidney failure or complex heart surgeries, according to new University of Pennsylvania School of Medicine research published this week in Circulation: Cardiovascular Quality and Outcomes.

"Having already established that hypothermia improves neurological outcomes after cardiac arrest, we now know that the therapy is also a good use of health care resources," says lead author Raina M. Merchant, MD, MS, an emergency physician and Robert Wood Johnson Clinical Scholar at Penn Medicine. "We hope our findings will help more hospitals and insurers to adopt cooling protocols and help more survivors return to productive lives."

Despite national recommendations established in 2005 calling for out-of-hospital cardiac arrest patients to be treated with hypothermia when they remain comatose after resuscitation, many hospitals still don't offer the intervention. Among barriers to its use: Concerns about its cost, and difficulty coordinating the interdisciplinary resources and staff needed to employ the treatment. Merchant and her colleagues used a complex mathematical design to measure quality-adjusted survival after cardiac arrest, cost of hypothermia equipment and treatment, and cost of post-hospital discharge care. Factors affecting costs included additional nursing care required during cooling treatment, extra time spent in the intensive care unit and post-discharge care required. They found that hypothermia has a cost of less than $100,000 per quality-adjusted life year (QALY), a measurement designed to illustrate the gains in both extra years of life and quality of life from a particular treatment.

Previous research has shown that about six out-of-hospital cardiac arrest patients need to be treated with hypothermia in order for one additional patient to be discharged without the brain damage that characterizes many survivors. Even when the authors of the new study adjusted their model to increase the proportion of neurologically impaired survivors in the group who received hypothermia, results still showed favorable cost-effectiveness estimates for hypothermia.

The findings also revealed that hypothermia treatment is actually less expensive than other interventions that have been implemented to treat cardiac arrest across the United States, including widespread CPR and defibrillation training for the public. In addition, the new research is among few studies to examine the costs of

caring for patients who survive cardiac arrest with neurological deficits – a tremendous burden for the health care system and family caregivers.

"There are very few treatments for cardiac arrest victims, and hypothermia stands out as the only therapy which can improve neurologic survival," Merchant says. "Hospitals and physicians should promote rapid adoption of this treatment for patients, and cost should not be considered a barrier to use."

Other authors of the study include Peter W. Groeneveld, MD, MS, Lance B. Becker, MD, Benjamin S. Abella, MD, MPhil, and David A. Asch, MD, MBA. The study was funded by the Robert Wood Johnson Foundation Clinical Scholars Program (Merchant) and a Career Development Transition Award from the Veterans Affairs Health Services research and Development Service (Groeneveld).

Orang-utans fashion only known animal instrument

* 00:01 05 August 2009 **by Ewen Callaway**

As wind instruments go, folded vegetation seems a little on the primitive side. Orang-utans have been found to blow through leaves to modulate the sound of their alarm calls, making them the only animal apart from humans known to use tools to manipulate sound.

Orang-utans have been found to blow through leaves to modulate the sound of their alarm calls

The orang-utan's music, if you can call it that, is actually an alarm call known as a "kiss squeak".

"When you're walking the forest and you meet an orang-utan that not habituated to humans, they'll start giving kiss squeaks and breaking branches," says Madeleine Hardus, a primatologist at the University of Utrecht in the Netherlands, who documented the practice among wild apes in Indonesian Borneo.

She contends that orang-utans use leaves to make kiss squeaks to deceive predators, such as leopards, snakes and tigers, as to their actual size – a deeper call indicating a larger animal.

Baritone squeaks

Orang-utans also produce kiss squeaks with their lips alone or with their hands. To determine if the leaves make a difference, Hardus's team recorded a total of 813 calls produced by nine apes, and then measured the pitch of the different kinds of kiss squeaks made by each animal.

Across all nine orang-utans, the unaided kiss squeaks came out with the highest pitch, followed by calls produced when the apes put their hands over their mouths. But leaves lowered the high-pitched calls the most, Hardus' team found.

What's more, the orang-utans that were unaccustomed to Hardus' team produced leaf calls at far higher rates than apes that were used to humans. "It looks like orang-utans try to deceive the predator when using the kiss squeaks on leaves, because orang-utans only use it when they're highly distressed," she says.

Understanding others

That explanation implies that orang-utans can guess at what others know and don't know – a cognitive ability known as theory of mind.

"An orang-utan would have to understand how their calls are being perceived by other animals, a clear example of theory of mind," says Robert Shumaker, an orang-utan expert at the Great Ape Trust of Iowa, in Des Moines. "If, in fact, this is what they're doing, deception is a perfectly plausible possibility."

"It's a particularly interesting form of tool use, to me, because it gets away from a lot of the typical examples of foraging," Shumaker adds. "It's really, really nice to see an example that has absolutely nothing to do with food." ***Journal reference: Proceedings of the Royal Society B (DOI: 10.1098/rspb.2009.1027)***

Martian methane mystery deepens

By Judith Burns Science reporter, BBC News

Methane on Mars is produced and destroyed far faster than on Earth, according to analysis of recent data. Scientists in Paris used a computer climate model for the Red Planet to simulate observations made from Earth.

It shows the gas is unevenly distributed in the Martian atmosphere and changes with the seasons.

The presence of methane on Mars is intriguing because its origin could either be life or geological activity - including volcanism.

Writing in the journal Nature, Franck Lefevre and Francois Forget from the Universite Pierre et Marie Curie in Paris describe how they used a computer model of the Martian climate to reconstruct observations made by a US team.

Dr Lefevre says the chemistry of the Martian atmosphere is still a mystery. He told BBC News: "We put the dynamics and chemistry as we know it in the model and tried to match the measurements, to reproduce the uneven distribution they saw from Earth."

"The problem is if we just take into account the photochemistry as we know it on Earth and if we put it in the model, then we cannot reproduce the model and that was a surprise. The current chemistry as we know it is not consistent with the measurements of methane on Mars. There is something else going on, something that lowers the methane lifetime by a factor of 600. So if the measurements are correct, we must be missing something quite important."

Dr Lefevre says the work shows that if there is a much faster loss for methane on Mars there must also be a much stronger production of methane. But he urges caution: "It's a real challenge to measure methane on Mars from Earth and we've got only one example of this uneven distribution."

The results the French team used were published in January this year in the journal Science. They were gathered by an American team using a technique called infrared spectroscopy at three different ground-based telescopes to monitor about 90% of the planet's surface.

In 2003 "plumes" of methane were identified. At one point, the primary plume of methane contained an estimated 19,000 tonnes of the gas.

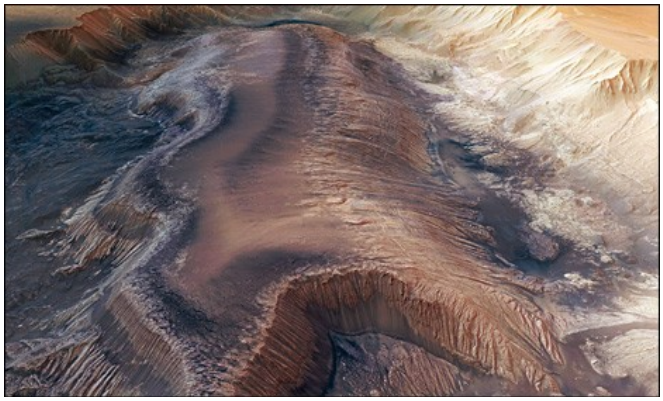
Dr Michael Mumma, director of Nasa's Goddard Center for Astrobiology and lead author on the previous paper, told BBC News it was vital to understand how methane was destroyed on Mars and to explain how so much of the gas is produced and destroyed so quickly on the Red Planet.

Dr Mumma does not rule out a biological explanation for the phenomenon but says it is possible that geology alone could be responsible. If the methane is produced by geological activity, it could either originate from active Martian volcanoes or from a process called serpentinisation.

The latter process occurs at low temperatures when rocks rich in the minerals olivine and pyroxene react chemically with water, releasing methane.

In December, Dr Mumma's team will begin another study of the Martian surface using the new technique of adaptive optics at the European Southern Observatory's Very Large Telescope (VLT) in Chile. They hope to replicate their earlier results.

Dr Lefevre says that if the variations are confirmed it would mean the Martian surface is very hostile for organics. But this would not necessarily exclude the possibility that life or the remnants of past life persist below ground, where conditions could be more benign.



The source of Martian methane might be biological or geological

Nasa is due to launch a $2.3bn nuclear-powered rover known as Mars Science Laboratory (also called "Curiosity") to the planet in 2011.

Under one possible scenario, the European and US space agencies would then send a European orbiter to the Red Planet in 2016 to track down the sources of methane.

A subsequent 2018 launch opportunity would be taken by the European ExoMars rover, launching on a US Atlas rocket. The proposal currently being discussed is that ExoMars should be joined by a slightly smaller rover in the class of the US Spirit and Opportunity vehicles that are on the surface today.

ExoMars and its smaller cousin could be targeted at the Methane sources identified by the 2016 orbiter.

Göbekli Tepe: Standing stones from humanity's oldest temple

August 3, 3:33 PM · **Gwynneth Anderson** - Archeological Travel Examiner

The massive limestone monoliths weigh between ten and twenty tons and are weirdly carved with fantastic scorpions, lions, spiders and snakes that testify to the difficult hunter's life. Unearthed after thousands of years of deliberate forgetfulness, these silent pillars stand in a circle located only a few miles south of the ancient town of Sanliurfa, Turkey, the legendary birthplace of the prophet Abraham.

Göbekli Tepe may have been accidentally rediscovered by a shepherd, but it's provenance is no mistake. Carbon dating has estimated the site to have been built in approximately 12,000 B.C., turning prior theories about our Neolithic hunter/gatherer past upside down.

Archeology Magazine reports that before the discovery of Göbekli Tepe, experts believed that societies in the early Neolithic were organized into small bands of hunter-gatherers and that the first complex religious practices were developed by groups that had already mastered agriculture. Scholars thought that the earliest

monumental architecture was possible only after agriculture provided Neolithic people with food surpluses, freeing them from a constant focus on day-to-day survival. A site of unbelievable artistry and intricate detail, Göbekli Tepe has turned this theory on its head.*

In other words, Göbekli Tepe was built before the invention of pottery, Sumerian writing tablets, the wheel, Stonehenge and the Pyramids at Giza.

Building such a site is an engineering challenge perhaps greater than the Egyptian pyramids. At least 500 people would be needed to shift these immense pillars from the limestone quarries to the temple site, all without the luxury of rollers. It's an administrative task requiring operational and organizational skills – not something readily believable of people still running around with clubs and communicating by grunts.

And why here?

Scanning the immediate valley area 1,000 feet below reveals an arid climate. Summer temperatures can easily soar to over 115 degrees Fahrenheit while winters enjoy rainy deluges. However, when speaking with Smithsonian magazine, Klaus Schmidt, an archeologist at the German Archeological Institute in Istanbul, observed:

"Imagine what the landscape would have looked like 11,000 years ago, before centuries of intensive farming and settlement turned it into the nearly featureless brown expanse it is today. Prehistoric people would have gazed upon herds of gazelle and other wild animals; gently flowing rivers, which attracted migrating geese and ducks; fruit and nut trees; and rippling fields of wild barley and wild wheat varieties such as emmer and einkorn. This area was like a paradise." **

A paradise indeed.

Göbekli Tepe is located at the far end of what was once known as the Fertile Crescent, the cradle of ancient agriculture. The world's first farmyard pigs were domesticated at Cayonu, just 60 miles away. Sheep, cattle and goats were also first domesticated in eastern Turkey. Worldwide wheat species descend from einkorn wheat - first cultivated on the hills near Göbekli. Other domestic cereals - such as rye and oats - also started here.***

And according to Schmidt, it was a paradise that was lost.

Farming changes the landscape. Trees are cut down, constant plowing leaches away valuable minerals and rivers are dammed, drying up the filtering swamps. Eventually, the soil became overstressed and crop returns were diminished.

The once lush climate became the dry, hilly plain now seen today.

And what of the temple silently standing watch over the plains?

Around 8,000 B.C., for some unknown reason, worshippers buried Göbekli Tepe under tons of earth, deliberately wiping out its existence until a Kurdish shepherd spotted a monolith's edge peeking out of the ground.

For a majestic visual of the breathtaking structure and other figurines found on site, check out ***this 6-minute YouTube video***. (Watch for the crocodile carving at the one minute, 30 second mark).

Abnormal Brain Circuits May Prevent Movement Disorder

MANHASSET, NY -- Most people who carry a genetic mutation for a movement disorder called dystonia will never develop symptoms, a phenomenon that has puzzled scientists since the first genetic mutation was identified in the 1990's. Now, scientists at The Feinstein Institute for Medical Research have figured out why these mutation carriers are protected from symptoms of the disorder – they have an additional lesion that evens the score.

Dystonia is marked by uncontrolled movements, particularly twisting and abnormal postures. Studies have shown that muscles contract abnormally and patients can't stop the involuntary movements. The identification of a specific abnormality in people with the genetic mutation who never develop symptoms could eventually pave the way towards new treatments for dystonia patients. There are half a million people in the United States alone. The brains of people with inherited dystonia are normal at autopsy and the exact cause of their movement abnormality is unknown.

David Eidelberg, MD, the senior author of the study published in the Journal of Neuroscience, said that they used diffusion tensor imaging – a type of magnetic resonance imaging (MRI) that measures changes in the integrity of white matter pathways in the brain – to study those with and without symptoms who carry the disease gene. There were 20 people in the study; 12 with symptoms and eight without. They also had a number of volunteers who agreed to brain scans who had no disease and no mutations in the gene for dystonia.

Dr. Eidelberg and his colleagues identified two discrete areas along the pathway that links the cerebellum to the motor cortex that together determine whether a mutation carrier will display clinical manifestations of the disease.

Their earlier work revealed that patients and non-patients with the disease gene have the same underlying functional brain abnormality, such as overactivity of motor circuits that make it hard to process sequential information. Nonetheless, mutation carriers have a characteristic circuit disorder involving a motor system that is revved up and idling at high speed, making it difficult to integrate the information needed to plan movements and to learn new motor skills. It was not suspected that these otherwise healthy individuals had such difficulties since doctors only saw those who presented with the uncontrollable movements.

While their brains show the same abnormal network, only approximately 30% of people who carry the mutated gene called DYT1 will develop the involuntary movements that can prevent them from living a normal life, according to Dr. Eidelberg. The puzzle was why.

In the latest study, the new advances in diffusion imaging allowed them to see something for the first time. They saw that there were two places along the motor pathway that seemed to stop the flow of neural signals from one part of the circuit to the other. Those with only one lesion in the circuit developed the debilitating movements and those with two lesions did not. “There is something about this second lesion that is protective,” the authors concluded. “We found a consistent cerebellar pathway problem in all DYT1 carriers. When we went back and looked at those without symptoms, we saw that they had an additional lesion downstream in the portion of the pathway connecting directly to the motor cortex.” This second area of pathway disruption abrogated the effects of the first lesion.

Normally, the cerebellum (a region that controls movement) puts the breaks on the motor cortex by potentiating inhibition at the cortical level. It is likely that mutation carriers have a developmental problem in the flow of neural signals along this circuit such that the brain can’t inhibit an unwanted movement. With the second pathway lesion, Dr. Eidelberg explained, “the flow is shut off and the abnormal activity stops.”

The research was supported by the National Institutes of Health, the Bachmann-Strauss Dystonia and Parkinson Foundation, and the General Clinical Research Center, located at the Feinstein Institute.

Blood transfusion study: Less is more

A new study suggests that blood transfusions for hospitalized cardiac patients should be a last resort because they double the risk of infection and increase by four times the risk of death.

The analysis of nearly 25,000 Medicare patients in Michigan also showed that transfusion practices after heart surgery varied substantially among hospitals, a red flag that plays into the health care reform debate.

A wide variation in care is a hot-button issue, as lawmakers and health reform experts discuss the best ways to address the variations. Some experts believe the country needs a system of medical guidelines, supported by scientific evidence, to aid doctors in decision-making. In fact, the Institute of Medicine has called for a national initiative of comparing the benefits and harms of certain methods to improve the delivery of care -- an effort referred to by health-care insiders as "comparative effectiveness" research.

Blood transfusion is an area that could be well served with stronger, research-based guidelines, since the current clinical practice is all over the map, said study co-author Neil Blumberg, M.D., professor of Pathology and Laboratory Medicine and director of Transfusion Medicine at the University of Rochester Medical Center.

"Doctors are simply doing what they were trained to do, but it turns out that their actions are more harmful than helpful in many cases," Blumberg said. "This is an instance in which clinical practice got way ahead of research. And changing the liberal use of transfusions is going to be difficult despite the evidence showing it is usually not essential."

The study was published July 31, 2009 in the journal, BMC Medicine. It was designed to assess patient outcomes as well as hospital variation in blood use.

Blumberg and lead author Mary Rogers, Ph.D., of the University of Michigan Health System, analyzed patient records in 40 hospitals, from admission to 30 days after discharge. All had received coronary artery bypass graft surgery from 2003 to 2006. They found that 30 percent of variation in transfusion practices seemed to be due to widely varied practices among hospital sites.

Also, blood use among women patients ranged from 72.5 percent to 100 percent, and blood use among men varied from about 50 percent to 100 percent. Transfusions with donor blood were associated with infections of the genitourinary system, respiratory tract, bloodstream, digestive tract and skin, the study said.

The risk of death in the hospital was nearly 5 times greater among patients who received a blood transfusion, and the risk of death in the next 30 days was nearly three times greater. Some of the risk may've been due to the underlying condition that led to transfusion but an increasingly convincing body of evidence demonstrates that some of the effect is almost certainly due to the transfusion itself, Blumberg said.

Blood transfusions are extremely common in the United States. Some of the typical reasons for transfusions include prevention of anemia and improving oxygen delivery in heart failure.

Blumberg has been a long-time advocate for fewer transfusions and, when they are necessary, for using blood from which the donor's white cells have been removed. This process, called leukoreduction, is believed to diminish the chances of infection and inflammation, research has shown.

"Blood transfusions are certainly necessary in life-threatening situations," Blumberg said. "But this study and other studies confirm they should be a last resort, not a first resort, as they often are."

For decades the URMC has been a leader in the study of blood transfusions, and Strong Memorial Hospital at URMC was among the first in the country to begin using leukoreduced blood for all its patients.

More recently, a team at Strong began to further refine the guidelines for blood transfusion. As a result the hospital has already seen a 10 to 15 percent drop in transfusions during the past six months. The improvement program is still in its early stages, and Blumberg said they will closely monitor the use of transfusions at Strong in the coming months.

Ancient bones show earliest 'human' infection

* 12:15 05 August 2009 **by Ewen Callaway**

Meat-eating – and diseases that come with it – have a long history among our ancestors, suggests a new study of an ancient hominin skeleton.

The analysis of 1.5 to 2.8 million-year-old vertebrae of Australopithecus africanus recovered in South Africa reveals signs of a bacterial infection that is normally contracted from eating meat or dairy foods.

"This is the most ancient case of an infectious disease in a hominin," says Ruggero D'Anastasio, a palaeoanthropologist at State University "Gabriele d'Annunzio" in Chieti, Italy, who diagnosed the skeleton with a disease called brucellosis.

First uncovered in the 1970s in the Sterkfontein caves, not far from Johannesburg, two of the vertebrae belonging to an older male are dotted with visible lesions. One study concluded that this damage was caused by ageing. However, after collecting X-rays and scanning electron micrographs of the bones, D'Anastasio now contends that brucellosis better explains the lesions.

Spine clues

Brucellosis causes a flu-like illness in humans, but if the bacteria reach muscles and bones, they tend to infect the same spinal vertebrae that are damaged in the Australopithecus bones. Other infections, like tuberculosis, also infect spinal bones, but they tend to be less discriminate and go after other vertebrae. D'Anastasio's team think ageing is an unlikely explanation for the damage for similar reasons.

"I think it's more probable that these lesions could be due to an infectious disease, and I think brucellosis is the most probable infection," D'Anastasio says.

It's impossible to determine how this individual contracted the disease, but contemporary patterns of infection suggest the bacteria probably came from an ungulate. Humans usually contract the Brucella bacteria from unpasteurised milk and cheese, however zebras, antelope and other South African fauna can carry a species that causes spontaneous abortions, Brucella abortus.

This australopithecine may have acquired brucellosis by eating fetal tissue from a similar animal, D'Anastasio says. "I think the consumption of meat was occasional in Australopithecus."

Mystery remains

A chemical analysis of Australopithecus teeth also supports that conclusion. A team led by Matt Sponheimer, at the University of Colorado in Boulder, analysed carbon isotopes in 3-million-year-old teeth, and found a chemical signature indicative of fruits, leaves and grasses. The team suggest that the grass signature was probably acquired through eating a herbivore.

Meanwhile, other research has suggested that Australopithecus had teeth adapted for meat eating.

However, none of these studies – the latest work included – can definitively determine the importance of meat in the australopithecine diet, says Sponheimer. Many anthropologists contend that meat eating didn't make up the bulk of our ancestor's calories until after the emergence of Homo erectus, roughly 2 million years ago.

Given the opportunity, chimpanzees eat monkeys, bugs, and small forest antelopes. "It would be strange if any of our more recent ancestors were not eating meat to some degree," Sponheimer says.

Journal reference: PLoS ONE (DOI: 10.1098/rspb.2009.1027)

Found: A pocket guide to prehistoric Spain

* 05 August 2009 **by Charles Choi and Catherine Brahic**

MODERN humans have got it easy. Anyone with a computer can look up just about any location and within seconds bring up a map complete with step-by-step directions from A to B.

The internet and centuries of map-making mean getting to, say, the prehistoric painted caves of France and Spain is child's play. "But imagine a group of hunter-gatherers, returning to an area they had not been to for a long time. How do you find a particular cave, especially if the vegetation has changed and its entrance may be masked?" asks independent archaeologist Paul Bahn.

The answer may be that hunter-gatherers had their own maps. A team of archaeologists have matched etchings made 14,000 years ago on a polished chunk of sandstone in northern Spain to the landscape in which it was found. They claim to have the earliest known map of a region in western Europe - a prehistoric hunting map.

The rock, roughly hand-sized and 14,000 years old, bears a mess of overlapping etchings. It was found in a cave in Navarre on the southern side of the Pyrenees and it took Pilar Utrilla of the University of Zaragoza, Spain, and colleagues the better part of 10 years to disentangle the lines and make sense of them (Journal of Human Evolution, DOI: 10.1016/j.jhevol.2009.05.005).

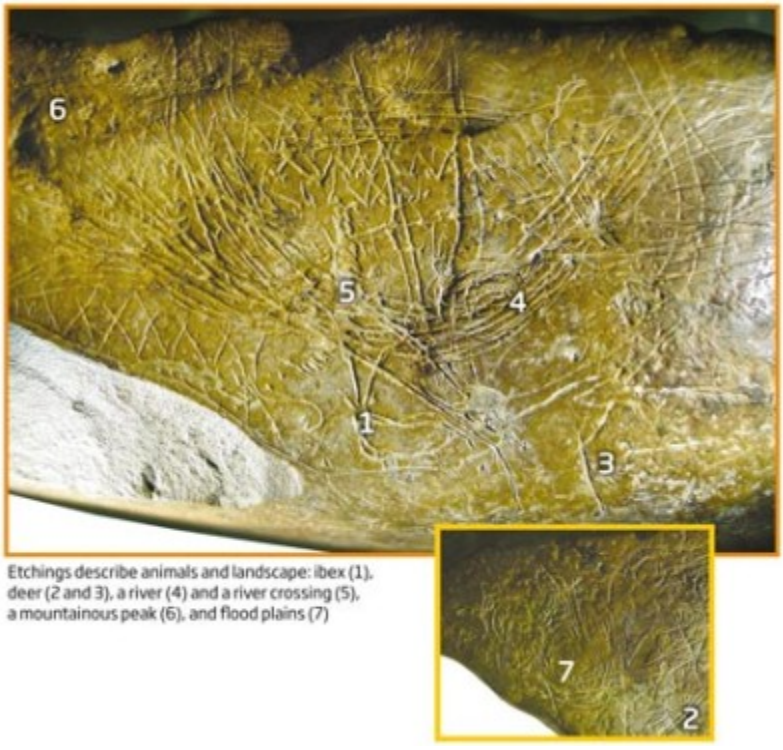
Above recognisable depictions of reindeer, a stag and some ibex are what Utrilla's team believe is a representation of the landscape surrounding the cave. Several etched lines resemble the shapes of mountains that are visible from the cave. Long, meandering etches match the course of a river that runs at the foot of one of the mountains and splits into two tributaries. A series of strokes that cut across the river near the mountain could represent places where it was easily crossed, or even bridges, the researchers say.

"This is a pretty spectacular find," says prehistoric archaeologist Lawrence Straus of the University of New Mexico in Albuquerque. "It may give us a glimpse into the ways in which people navigated and explained their territories." He says the slab was etched during a period of enormous cultural activity in northern Spain. "The human range was expanding northward and population density was increasing after people nearly died off in the last glacial maximum about 20,000 to 17,000 years ago. People were perhaps having to cooperate, carving up territories among different bands. They had to live by their wits and what the landscape provided." Strauss says engravings and paintings would have helped with territorial definition, hunting, human aggregation and mobility, and generally making sense of the world.

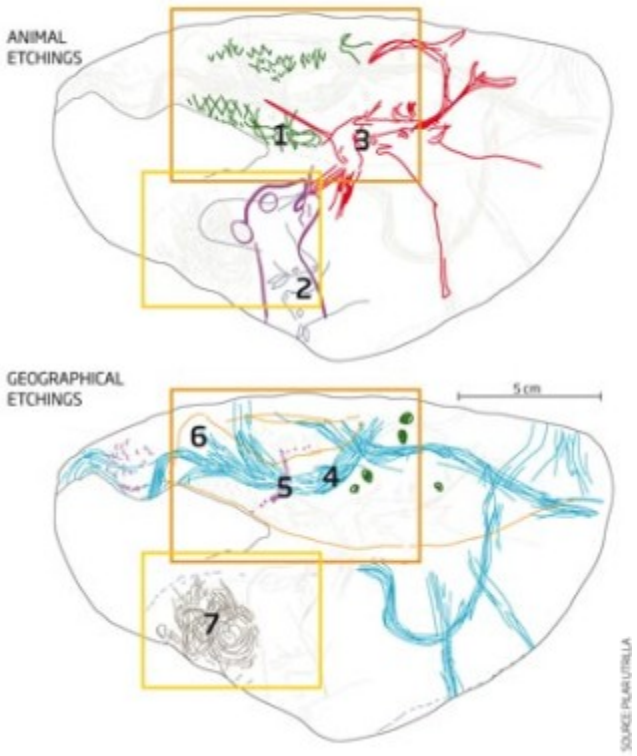
"The interpretation is, of course, pure speculation, as with all other such claims for Ice Age maps," says Bahn. "On the other hand, it would be extremely surprising if these people did not produce rough maps. They were as intelligent as we are and were constantly moving around the landscape." He agrees the stone is the best bet for a prehistoric western European map so far.

Set in stone

According to Pilar Utrilla's team this hand-sized rock is a prehistoric hunting map. Others believe it could be a spiritual guide or just an artistic scribble



Etchings describe animals and landscape: ibex (1), deer (2 and 3), a river (4) and a river crossing (5), a mountainous peak (6), and flood plains (7)



Turn left at the circular scratch (Image: Pilar Utrilla)

Others take issue with this interpretation. According to Jill Cook, head of the prehistory division at the British Museum in London, hundreds of similar etchings have been found sprinkled across Europe.

"Multiple lines positioned over animal figures is not unusual in slabs of this period. We haven't traditionally considered them to be maps." She also doesn't believe humans at the time had any need for maps (see next week's issue of New Scientist). "Their intimacy and knowledge of the landscape, including the location of individual trees and plants, would be such that maps would be less vital to them. On the whole, art of this period doesn't include landscape elements - no trees, rivers or hills - so this interpretation is very brave," she told New Scientist.

Archaeologist Jean Clottes, an expert for the International Council on Monuments and Sites, agrees that prehistoric humans probably had excellent mental maps to help them navigate. He has an alternative explanation for the engravings. Clottes believes that instead of connecting the artist to the physical world, they may have acted as a bridge to another, spiritual world. "For these people, their landscape was likely sacred. A map might not have helped them go from one place to another, but instead could have marked the places of very significant sacred places."

Maps through the millennia

There's no doubt our ancestors relied on maps. Here are some of the oldest known examples.

** The oldest map found in Europe, discovered in Pavlov in the Czech Republic, is about 25,000 years old. It depicts a mountain, river, valleys and routes around the region.*

** A schematic 6200-year-old drawing of Çatalhöyük in Turkey may be the oldest known city map.*

** The oldest known map of the world dates to 600 BC. It is inscribed on a clay tablet discovered in the city of Sippar in southern Iraq, is centred around Babylon and shows the world as a circle surrounded by "bitter water": the salty sea.*

** The oldest complete star atlas, measuring 2 metres across, was discovered in China in 1907. It dates from the 7th century AD and marks the position of 1339 stars, including clearly recognisable groups such as Orion and the big dipper.*

Women often opt to surgically remove their breasts, ovaries to reduce cancer risk

PHILADELPHIA – Many women at high risk for breast or ovarian cancer are choosing to undergo surgery as a precautionary measure to decrease their cancer risk, according to a report in Cancer Epidemiology, Biomarkers & Prevention, a journal of the American Association for Cancer Research.

"Women have their breasts or ovaries removed based on their risk. It does not always happen immediately after counseling or a genetic test result and can take more than seven years for patients to decide to go forward with surgery," said lead researcher D. Gareth Evans, M.D. Evans is a consultant in clinical genetics at the Genesis Prevention Center, University Hospital of South Manchester NHS Trust and a professor at the University of Manchester, United Kingdom.

Evans and colleagues assessed the increase in risk-reduction surgery among women with breast cancer and evaluated the impact of cancer risk, timing and age.

Rate of increase was measured among 211 women with known unaffected BRCA1 or BRCA2 mutation carriers. BRCA1 and BRCA2 are hereditary gene mutations that indicate an increased risk for developing breast cancer. Additionally, more than 3,500 women at greater than 25 percent lifetime risk of breast cancer without mutations also had a documented increase in risk-reduction surgery.

Women who had a biopsy after undergoing risk evaluation were twice as likely to choose a risk-reducing mastectomy. Forty percent of the women who were mutation carriers underwent bilateral risk-reducing mastectomy; 45 percent had bilateral risk-reducing salpingo-oophorectomy (surgical removal of ovaries). These surgeries are widely used by carriers of BRCA1 and BRCA2 gene mutations to reduce the risk for breast and ovarian cancer.

Evaluated by gene type, bilateral risk-reducing salpingo-oophorectomy was more common in women who were BRCA1 gene carriers - 52 percent had the surgery compared with 28 percent of the women who were BRCA2 gene carriers. "We found that older women were much less likely to have a mastectomy, but were more likely to have their ovaries removed," said Evans.

Most of the women, specifically those aged 35 to 45 years, opted for surgery within the first two years after the genetic mutation test, but some did not make a decision until seven years later.

"This is a very interesting study. It fleshes out some of what we know about adoption of risk reduction strategies in high-risk women who have participated in a very comprehensive and well thought-out genetic counseling, testing and management program," said Claudine Isaacs, M.D., an associate professor of medicine and co-director of the Fisher Center for Familial Cancer Research, Lombardi Comprehensive Cancer Center at Georgetown University.

BRCA1 and BRCA2 mutation carriers have a very high lifetime risk of cancer, and for BRCA1 carriers there are unfortunately no clearly proven non-surgical prevention strategies, according to Isaacs. These women

face a 50 to 85 percent lifetime risk of breast cancer, and mastectomy is currently the most effective prevention method available.

The findings confirm the expectations that when a woman has a biopsy, even if benign, most are more likely to opt for risk-reduction surgery.

"Screening should be conducted at a place with expertise in an effort to minimize false-positive results, which often lead to biopsy. This will minimize the anxiety that comes along with such a diagnosis. Patients should consult with an expert in advance and stay in contact with them to see how the science may be changing over time," she advised. "This is an ongoing conversation that needs to be addressed and individualized for each patient."

Likewise, Evans suggested that additional studies are needed to help evaluate the communication efforts and methods between doctors and/or counselors and women at risk for breast cancer. Questions to be raised should include how is the communication method occurring, are the doctors sympathetic and is there an ongoing dialogue?

"Careful risk counseling does appear to influence women's decision for surgery although the effect is not immediate," the researchers wrote.

The mission of the American Association for Cancer Research is to prevent and cure cancer. Founded in 1907, AACR is the world's oldest and largest professional organization dedicated to advancing cancer research. The membership includes more than 28,000 basic, translational and clinical researchers; health care professionals; and cancer survivors and advocates in the United States and nearly 90 other countries. The AACR marshals the full spectrum of expertise from the cancer community to accelerate progress in the prevention, diagnosis and treatment of cancer through high-quality scientific and educational programs. It funds innovative, meritorious research grants. The AACR Annual Meeting attracts more than 17,000 participants who share the latest discoveries and developments in the field. Special conferences throughout the year present novel data across a wide variety of topics in cancer research, treatment and patient care. The AACR publishes six major peer-reviewed journals: Cancer Research; Clinical Cancer Research; Molecular Cancer Therapeutics; Molecular Cancer Research; Cancer Epidemiology, Biomarkers & Prevention; and Cancer Prevention Research. The AACR also publishes CR, a magazine for cancer survivors and their families, patient advocates, physicians and scientists. CR provides a forum for sharing essential, evidence-based information and perspectives on progress in cancer research, survivorship and advocacy.

Surface features on Titan form like Earth's, but with a frigid twist

"It is really surprising how closely Titan's surface resembles Earth's," says Rosaly Lopes, a planetary geologist at the Jet Propulsion Laboratory (JPL) in Pasadena, California, who is presenting the results on Friday, 7 August. "In fact, Titan looks more like the Earth than any other body in the Solar System, despite the huge differences in temperature and other environmental conditions."

The joint NASA/ESA/ASI Cassini-Huygens mission has revealed details of Titan's geologically young surface, showing few impact craters, and featuring mountain chains, dunes and even "lakes". The RADAR instrument on the Cassini orbiter has now allowed scientists to image a third of Titan's surface using radar beams that pierce the giant moon's thick, smoggy atmosphere. There is still much terrain to cover, as the aptly named Titan is one of the biggest moons in the Solar System, larger than the planet Mercury and approaching Mars in size.

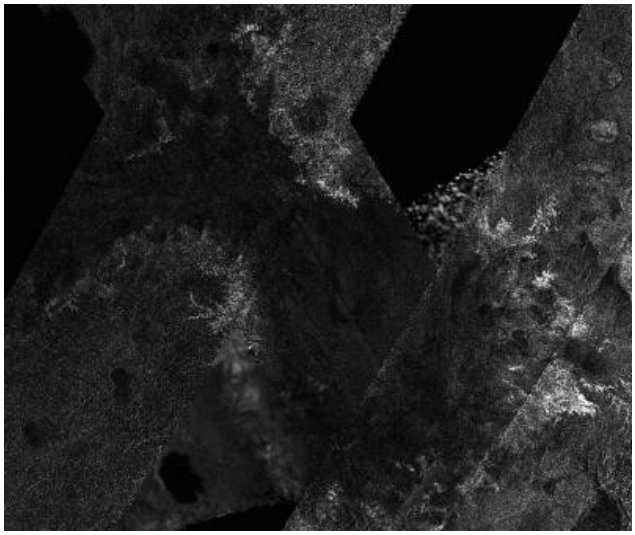
Titan has long fascinated astronomers as the only moon known to possess a thick atmosphere, and as the only celestial body other than Earth to have stable pools of liquid on its surface. The many lakes that pepper the northern polar latitudes, with a scattering appearing in the south as well, are thought to be filled with liquid hydrocarbons, such as methane and ethane.

"With an average surface temperature hovering around -180 °C, water cannot exist on Titan except as deep-frozen ice as strong as rock," Lopes says. On Titan, methane takes water's place in the hydrological cycle of evaporation and precipitation (rain or snow) and can appear as a gas, a liquid and a solid. Methane rain cuts channels and forms lakes on the surface and causes erosion, helping to erase the meteorite impact craters that pockmark most other rocky worlds, such as our own Moon and the planet Mercury.

Other new research presented at the IAU General Assembly points to current volcanic activity on Titan, but instead of scorching hot magma, scientists think these "cryovolcanoes" eject cold slurries of water-ice and ammonia. Scientists have spotted evidence for these outflows using another Cassini instrument called the Visual and Infrared Mapping Spectrometer (VIMS). This device can gather the infrared light from the Sun that is reflected back by Titan's surface after passing through its atmosphere, giving clues about the identity of the chemical compounds found on Titan's surface.

VIMS had previously detected an area, called Hotei Regio, with a varying infrared signature, suggesting the temporary presence of ammonia frosts that subsequently dissipated or were covered over. Although the ammonia does not stay exposed for long, models show that it exists in Titan's interior, indicating that a process is at work delivering ammonia to the surface. RADAR imaging has indeed found structures that resemble terrestrial volcanoes near the site of suspected ammonia deposition.

At the IAU General Assembly, new infrared images of this region, with ten times the resolution of prior mappings, will be unveiled. "These new results are the next advance in this exploration process," says Robert M. Nelson, a senior research scientist, also at JPL, who presented a result on Wednesday, 5 August. "The images provide further evidence suggesting that cryovolcanism has deposited ammonia onto Titan's surface. It has not escaped our attention that ammonia, in association with methane and nitrogen, the principal species of Titan's atmosphere, closely replicates the environment at the time that life first emerged on Earth. One exciting question is whether Titan's chemical processes today support a prebiotic chemistry similar to that under which life evolved on Earth?"



Yet more terrestrial-type features on Titan include dunes formed by cold winds, and mountain ranges. These mountains might have formed tectonically when Titan's crust compressed as it went into a deep freeze, in contrast to the Earth's crust, which continues to move today, producing earthquakes and rift valleys on our planet.

This mosaic of image swaths from Cassini's Titan Radar Mapper, taken with the synthetic-aperture radar (SAR), features a large dark region several hundred kilometers across that differs in several significant ways from other potential lakes observed on Titan. It is not as dark to the radar as many lakes (including the lakes seen here), and the nature of the margin is unusual. It has many characteristics in common with lakes, including its channels and interior, yet its differences distinguish it from other similar features. At the top (north), the feature has characteristics of a shoreline, with round bay-like margins and channels that drain into it; at left (west) and right (east) it is rimmed by bright, feathery, branching channel-like structures, some of which extend for tens of kilometres. Within the dark feature some details can be seen, some of which seem to be extensions of the channels draining into the dark feature. The mosaic is near the south pole, centerd near 82 degrees south, 205 degrees west. **Credit: NASA/JPL**

Many Titan researchers hope to observe Titan with Cassini for long enough to follow a change in seasons. The new image released by JPL accompanying this release shows what appears to be a dried-out lake at Titan's south pole. Lopes thinks that the hydrocarbons there likely evaporated because this hemisphere is experiencing summer. When the seasons change in several years and summer returns to the northern latitudes, the lakes so common there may evaporate and end up pooling in the south.

This IAU General Assembly has personal significance for Lopes, as she was born and raised in Rio de Janeiro. From abroad and on periodic visits back to her home country, Lopes has encouraged young Brazilians to pursue careers in science and technology. "It's wonderful to be back again", Lopes says.

Clever rooks repeat ancient fable

By Rebecca Morelle Science reporter, BBC News

One of Aesop's fables may have been based on fact, scientists report.

In the tale, written more than 2,000 years ago, a crow uses stones to raise the water level in a pitcher so it can reach the liquid to quench its thirst. Now a study published in Current Biology reveals that rooks, a relative of crows, do just the same when presented with a similar situation.

The team says the study shows rooks are innovative tool-users, even though they do not use tools in the wild. Another paper, published in the journal Plos One, shows that New Caledonian crows - which like rooks, are a member of the corvid group, along with ravens, jackdaws, magpies and jays - can use three tools in succession to reach a treat.

Floating feast

The crow and the pitcher fable was used by Aesop to illustrate that necessity is the mother of invention. But until now, the morality tale was not thought to have a grounding in fact.

To investigate further, a team from the University of Cambridge and Queen Mary, University of London (QMUL) presented four captive rooks with a set-up analogous to the fable.

Aesop's rook: The birds raise the water by dropping stones into a tube so they can reach a floating worm

The birds were shown a clear tube containing a small amount of water. Floating upon it was an out-of-reach worm. And a pile of stones were positioned nearby.

Dr Nathan Emery, co-author of the paper, from QMUL, said: "The rooks have to put multiple stones in the tube until the worm floats to the top."

And the four birds did just that. Two, called Cook and Fry, raised the water-level enough to grab the floating feast the very first time that they were presented with the test, while Connelly and Monroe were successful on their second attempt.

Footage of the experiments shows the rooks first assessing the water level by peering at the tube from above and from the side, before picking up and dropping the stones into the water.

The birds were extremely accurate, using the exact number of stones needed to raise the worm to a height where they could reach it.

In another experiment, the rooks were presented with a similar scenario. This time they were given a combination of small and large stones.

Overall, Dr Emery told BBC News, the rooks opted for the larger ones, raising the worm to the top of the tube more quickly. He said: "They are being as efficient as possible."

And when given a choice between a tube filled with water and another filled with sawdust, the birds were more likely to opt for the liquid-filled tube.

The researchers say their findings suggest that Aesop's ancient fable may have been based on fact.

They said: "In folklore, it is rarely possible to know with certainty which corvid is being referred to.

"Hence, Aesop's crow might have easily been Aesop's rook."

'No surprise'

Earlier this year, the same team revealed that rooks were able to use different tools to solve a variety of complex problems.

Dr Emery told BBC News: "I used to say, maybe two or three years ago, that everything they did surprised me. But nowadays, we've had so many startling findings that the rooks just don't surprise me that much any more. You almost expect them to do the cleverest thing."

The only other animals reported to have solved an Aesop-like problem are orangutans.

Christopher Bird, co-author on the paper, added: "Corvids are remarkably intelligent, and in many ways rival the great apes in their physical intelligence and ability to solve problems."

A different study published this week has also shed light on corvid intelligence.

A team at the University of Oxford found that New Caledonian crows were able to use three tools in succession to reach a reward.

These birds, which are found on the Pacific island of New Caledonia, use tools in the wild, crafting them from branches to pluck grubs from holes and crevices. But this study builds on their tool-using repertoire.

Captive crows were presented with several horizontal tubes. One of the tubes contained some out-of-reach food. The others contained long and medium-length hooks - but, again, these were all out of beak's reach. And a shorter hook-like tool was positioned nearby.

The researchers found that the birds picked up the short tool, then used this to grasp the medium-length tool, which they then employed to retrieve the longest tool from the tube. Finally, they were able to use this to drag out the tasty morsel.

Four out of seven of the birds tested were able to use three tools in the right order, the team said.

Professor Alex Kacelnik, an author on the paper from Oxford's Behavioural Ecology Group, said: "The essence of our paper is to try to understand the mental processes used by the animals to actually achieve their goals."

He said that the complexity of the task made it unlikely that the crows were solving the problem using trial and error. He added: "We are aware that the animals probably do it by putting together, in creative ways, things that they have learned individually."

Researchers believe that an ancient ancestor of the corvids might have evolved the capacity to use tools, and that all members of the corvid family may have this innate ability.

However, only New Caledonian crows draw upon it in the wild, potentially because of ecological pressures.

Observatory

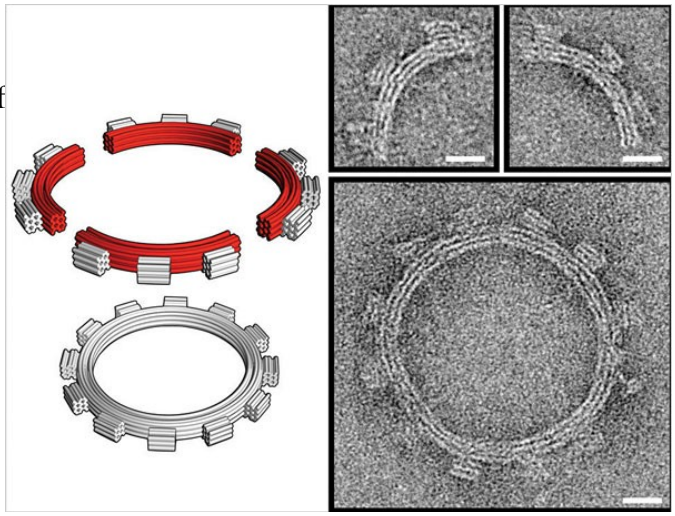
Scientists Use Curvy DNA to Build Molecular Parts

By HENRY FOUNTAIN

You can’t build a machine without parts. That’s true for large machines like engines and pumps, and it’s true for the tiniest machines, the kind that scientists want to build on the scale of molecules to do work inside the body.

Researchers have taken a step toward creating parts for molecular machines, out of DNA. In a paper in Science, Hendrik Dietz, Shawn M. Douglas and William H. Shih of the Dana Farber Cancer Institute and Harvard University describe a programmable technique for twisting and curving DNA into shapes.

Dr. Shih said the method used strands of DNA that self-assemble into rigid bundles, with the individual double helixes joined by strong crosslinks. Manipulating the base pairs in the helixes — using more or fewer of them between crosslinks — creates torque that causes the bundles to twist and bend in a specific direction. The researchers were able to control the degree of bending, and were even able to make a bundle bend back on itself.



A 12-tooth gear, about one-tenth of a micrometer in diameter, assembled from strands of DNA. **Science/AAAS**

The researchers built several structures, including a 12-toothed gear and a wire-frame ball. Dr. Shih said that while it was possible that a future molecular machine might use parts like these, the work was meant to demonstrate that "if you want to make a machine, you are going to need very precise fabrication ability."

The goal, he added, is to make objects that are far more complex, in order to eventually build a machine that could, say, deliver a tiny amount of a drug to a precise spot in the body.

Dr. Shih likened the work to the development of integrated circuits, where complexity has roughly doubled every 18 months for the past 40 years. "We're motivated to improve the technology," he said. "If you want to do amazing things, you are going to need to be able to build very complicated devices."

Quick Tests for the Flu Found Often Inaccurate

By ANDREW POLLACK

As the swine flu spreads, many doctors and hospitals are turning to rapid tests that can determine within minutes whether an anxious patient has the flu. Sales of such tests are soaring.

But the tests have a severe limitation: They may fail more than half the time to detect swine flu infections, according to newly published studies and to experts in medical testing.

The low sensitivity of the tests is becoming a concern to health authorities because a false negative reading might prompt a doctor not to prescribe antiflu drugs. It is also one of the big issues laboratory directors face as they prepare for what is expected to be a crush of flu testing this fall and winter. Numerous diagnostics companies are hoping to capitalize on demand for influenza testing.

The rapid tests "are missing a ton of flu," said Christine C. Ginocchio, director of the division of microbiology, virology and molecular diagnostics at the North Shore-Long Island Jewish Health System in Lake Success, N.Y.

For seasonal flu, experts have long known about the low detection ability of the rapid tests. The new studies suggest the tests are no better, and possibly worse, at detecting the swine flu strain now spreading around the world, known formally as the novel H1N1 virus.

In a study published recently in The Journal of Clinical Virology, Dr. Ginocchio found that one rapid test detected only 10 percent of the swine flu infections that could be picked up by a more sophisticated laboratory culture. A different rapid test detected 40 percent. (Dr. Ginocchio is a consultant to Luminex, a company that makes a more accurate but slower test.)

The federal Centers for Disease Control and Prevention said Thursday that in its own study, three rapid tests detected 40 to 69 percent of the swine flu cases. The rapid tests performed better on the seasonal flu, picking up as many as 80 percent of the cases.

Last week, the C.D.C. updated guidance urging doctors to be cautious in relying on the tests. "We're saying you need to understand the limitations of these tests," Dr. Timothy M. Uyeki, an author of the C.D.C. guidance, said in an interview. "The clinician should not base a decision to treat or not treat on the basis of a negative result."

But some doctors say there is no good substitute for the simplicity, speed and low cost of the rapid tests. Manufacturers of the tests say the products are helpful if used appropriately.

"When these tests are used properly, the performance is very, very good," said John D. Tamerius, senior vice president for clinical and regulatory affairs at Quidel, which describes itself as the leading maker of such tests.

He said the company's QuickVue flu test could detect 80 percent of infections if nasal samples were taken correctly and if the test was given early in the course of the disease, when more virus was present.

But in a letter to The New England Journal of Medicine in June, Navy researchers said the Quidel test detected only half the swine flu infections caught by a more sensitive technique. In the C.D.C. study, Quidel's test picked up 69 percent of the swine flu cases, the best performance of the three tests studied.

Spurred by flu test sales, Quidel's revenue from infectious disease testing rose 70 percent in the second quarter from a year earlier, to $16.1 million. Among the big buyers was Mexico, which had an early swine flu outbreak.

Quidel, of San Diego, is now manufacturing tests as fast as it can. The company's shares, which closed at $15.28 on Wednesday, have doubled since the flu outbreak started in April.

Other rapid tests makers include Inverness Medical Innovations, 3M, Thermo Fisher Scientific, Meridian Bioscience and Becton, Dickinson. With the exception of Meridian, these companies are much larger than Quidel and less dependent on flu tests.

Quidel estimates that about eight million rapid flu tests in total were sold in the United States in the 2007-8 flu season. The number is likely to jump this year.

More accurate tests are available but they generally require sophisticated laboratories. And results might not come for a day or more, making the tests of little use in deciding whether to prescribe drugs like Tamiflu, which are supposed to be started within 48 hours of the appearance of symptoms.

The rapid tests, by contrast, take only a few minutes to half an hour, and most can be done in the doctor's office or emergency room, without a laboratory. That is appealing to some doctors.

"When parents come in with a kid with fever, they want to know what the fever is from and is there something they can do about it," said Dr. Dorothy A. Levine, a pediatrician in Connecticut who uses the tests.

The rapid tests also cost only about $10 to $20, though some doctors might charge more, versus about $100 for a test using a sophisticated technique called the polymerase chain reaction, or P.C.R. While a negative result on a rapid test might not be reliable, a positive result, at least during flu season, usually does indicate a person has the flu.

The rapid tests do not tell if a patient has the swine flu. They say only if flu is present, or in some cases whether it is type A or type B influenza. The swine flu is type A, but so are many seasonal flu strains.

So more sophisticated tests, beside being used to double-check a negative rapid test result, are also needed to see if a positive test result is the swine flu.

Demand by patients to know if they had swine flu overwhelmed some public health and hospital laboratories in the spring, and some experts fear a repeat in the fall. "I definitely think there will be another crunch," said Rosemary Humes, senior adviser for scientific affairs at the Association of Public Health Laboratories.

The C.D.C. has developed and distributed its own test for swine flu that runs on equipment made by Life Technologies. But the agency says it would be costly and unnecessary to determine whether every flu case is swine flu.

Quest Diagnostics, the nation's largest clinical laboratory company, recently received an emergency authorization from the Food and Drug Administration to distribute a swine flu test to hospitals and other laboratories.

Luminex and Prodesse also sell tests to hospital laboratories that detect flu, though they do not specifically test for the swine flu. Because of the pandemic, "business is extraordinary for us," said Andrew M. Shrago, chief marketing officer of Prodesse, a privately held company in Waukesha, Wis.

In May, the F.D.A. sent warning letters to Prodesse, Luminex and Becton, Dickinson, saying they were improperly claiming their tests were for swine flu. The companies removed the offending language from their Web sites. The tests from the C.D.C., Quest, Luminex and Prodesse use the P.C.R. technique, which can amplify minute amounts of the viral genes, making those tests highly sensitive.

The rapid tests are more like pregnancy tests. They use antibodies to detect a protein from the virus. If that protein is present, a colored stripe appears on the test strip. But even a nasal sample from a patient with the flu might not contain enough of the protein to register a positive result.

DxNA, a company in St. George, Utah, says it hopes to have a one-hour P.C.R. swine flu test approved for emergency use this winter. Enigma Diagnostics of Britain hopes to introduce a similar test in 2011.

High-Profile Death Brings Attention to High-Risk Drug

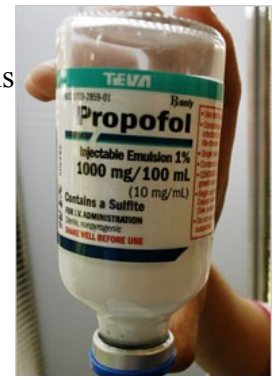
By PAM BELLUCK

As an anesthesiologist in a Nebraska hospital, he administered it to patients daily - propofol, a drug used to sedate millions of patients before surgery. Then one day he heard his colleagues discussing a medical article about propofol abuse.

"I thought, How the heck can you abuse propofol?" said the doctor, who asked not to be identified. "Then, in the back of my mind, I thought, I wonder what that feels like?" Soon, the doctor was injecting himself at home

to sleep, then to feel its mild euphoria, then because he could not stop. He would take home leftovers from his patients' surgical procedures — easy to do because propofol is not a controlled substance.

Propofol is a high-risk drug that Michael Jackson was given before he died, according to sources close to his family, who also said the singer's body showed signs of longtime drug use. The toxicology report concerning Mr. Jackson's death has been delayed as investigations expand.



While Mr. Jackson's apparent method of using the drug was unusual - with a private doctor in his home - researchers and addiction experts say propofol abuse is growing, particularly among those with medical access like the Nebraska doctor.

One afternoon, he recalled, his 9-year-old daughter came to wake him, saw an intravenous port in his leg and said, "Please tell me that isn't an IV." Last fall, after 15 injections in one night, the 38-year-old anesthesiologist dozed off while driving and hit a light pole, smashing his face on the windshield.

Propofol is the focus of inquiries into Michael Jackson's death. Fred Prouser/Reuters

Some experts say propofol abuse is spreading because unlike many prescription drugs, it is not a federally controlled substance. A 2007 survey of the country's 126 anesthesiology resident training programs found that 71 percent did not secure it in a pharmacy or track its dispensing.

Two years ago, a petition urged the Drug Enforcement Administration to restrict it as a controlled substance. A spokesman for the agency said it was still evaluating whether potential abuse outweighs the benefits of easy accessibility for doctors.

Propofol's benefits have made it one of the most widely used anesthetics. It wears off quickly, leaves no grogginess or nausea and is not believed to be physically addictive. A white liquid doctors refer to as "milk of amnesia," the drug is liked by abusers because it induces relaxation or sleep, can cause mild euphoria, sexual fantasies or sexual disinhibition upon waking and leaves the bloodstream so quickly it is difficult to detect.

But propofol can be extremely dangerous if not constantly monitored as it is in hospitals because it can slow breathing or lower blood pressure to the point of death. Its effects become compounded by other drugs in a person's system. Abusers who inject it often pass out instantly, sometimes getting injured; the Nebraska doctor said he fell once and "cut my chin open." He also started "talking gibberish" and "didn't remember doing certain things."

At Talbott Recovery Campus in Atlanta, an addiction treatment program, medical professionals who listed propofol among the drugs they were taking grew to 27 in 2008 from 8 in 2006, or 8 percent of those in the program, said Dr. Paul H. Earley, Talbott's medical director.

"I think the number of deaths is well above what's been reported," said Dr. Robert R. Kirby, an emeritus professor of anesthesiology at the University of Florida College of Medicine, and a co-author of a recent journal article on propofol abuse.

The 2007 survey found 18 percent of the training programs reported cases of propofol abuse among employees or trainees, including seven deaths. While the numbers were small compared with other prescription drugs, the results were significantly higher than 10 years earlier.

Using propofol as a home sleep aid - as it might have been administered to Mr. Jackson - would be "kind of like me using chemotherapy so I don't have to shave my head," said Dr. John F. Dombrowski, director of the Washington Pain Center and a board member of the American Society of Anesthesiologists.. "You'd never do that."

AstraZeneca, which makes branded propofol called Diprivan, says on its packaging that self-administration has rarely resulted in death and suggests restricted access.

Some cases of nonmedical abuse have been recorded, including one man who reportedly bought propofol on eBay. And the Nebraska doctor saw people dripping it from an IV a decade ago at a rave party. Others use a syringe for quick bursts of relaxation or instant naps between long, stressful hospital shifts.

"Someone can go to a bathroom, inject a small amount and recover five minutes later," Dr. Kirby said. One doctor-in-training at an East Coast hospital injected himself up to 100 times a day to relieve "his stress, his loneliness, boredom," said Dr. Paul E. Wischmeyer, a professor of anesthesiology at the University of Colorado, Denver, School of Medicine, who conducted the 2007 survey.

When he could not find it on hospital carts, he would reach into boxes of needles discarded during surgery with "remaining propofol in it and stick himself with those," Dr. Wischmeyer said, adding that the man risked contamination with patients' infections.

Dr. Earley said people drawn to propofol seem to have histories of "physical or sexual trauma," which, he said, "makes sense because the drug really produces this dissociative state - you're disconnected from

yourself." Dr. Omar S. Manejwala, associate medical director of the Farley Center, an addiction treatment program in Virginia where propofol cases are increasing, said addiction is possible and "more complex to treat because there are other co-occurring conditions like post-traumatic stress disorder."

Even in hospitals with controls, abuse can occur. Last year, a nurse in Gainesville, Fla., was convicted of killing a 24-year-old college student in 2005 with propofol injections.

Introduced about 20 years ago, propofol quickly "revolutionized" medicine, Dr. Dombrowski said, replacing sodium pentathol, whose side effects included nausea. Propofol is used for colonoscopies, surgery on hips and broken bones and plastic surgery, where Mr. Jackson might have been given it.

Dr. Ken Elmassian, an anesthesiologists' society board member and a physician at Ingham Regional Medical Center in Lansing, Mich., said patients had begun paying attention to the anesthetic they were getting, saying, "'Oh, you mean the drug that Michael Jackson got?' "

Ultimately, without proper training, it is virtually impossible to gauge the right amount to use.

"You can be a little floaty and high, followed by being asleep, followed by stopping breathing, and the window between those stages is a very small quantity of the drug, and it's not predictable," Dr. Earley said. "Using it by yourself is Russian roulette."

After his car crash, the Nebraska anesthesiologist, a father of four, spent 90 days at the Talbott addiction center and was disciplined by his state medical board. He was allowed to return to administering propofol in the operating room two months ago. He is monitored by counselors and takes daily drug tests, although propofol, experts point out, leaves the system too quickly for detection. "I have these big thoughts that pop up - 'Oh, that would feel relaxing' - but never a craving like I want to go home and use that," he said.

Still, he sees its use among other doctors. Just a week after returning from rehab, he attended the funeral of a colleague "I never would have dreamed was using it," the doctor said. "He had overdosed on propofol."

The Pain of Being a Redhead

By Tara Parker-Pope

Nobody likes going to the dentist, but redheads may have good reason.

A growing body of research shows that people with red hair need larger doses of anesthesia and often are resistant to local pain blockers like Novocaine. As a result, redheads tend to be particularly nervous about dental procedures and are twice as likely to avoid going to the dentist as people with other hair colors, according to new research published in The Journal of the American Dental Association.

Researchers believe redheads are more sensitive to pain because of a mutation in a gene that affects hair color. In people with brown, black and blond hair, the gene, for the melanocortin-1 receptor, produces melanin. But a mutation in the MC1R gene results in the production of a substance called pheomelanin that results in red hair and fair skin.

The MC1R gene belongs to a family of receptors that include pain receptors in the brain, and as a result, a mutation in the gene appears to influence the body's sensitivity to pain. A 2004 study showed that redheads require, on average, about 20 percent more general anesthesia than people with dark hair or blond coloring. And in 2005, researchers found that redheads are more resistant to the effects of local anesthesia, such as the numbing drugs used by dentists.

The mutation in the MC1R gene also occurs in brunettes, although it's less common. In the latest study, the researchers tested for the MC1R gene variant, finding it in 65 of 67 redheads and in 20 of 77 people with brown or black hair. The participants were surveyed about dental-care anxiety, fear of dental pain and whether they avoid going to the dentist.

People with the MC1R gene variant had more dental care–related anxiety and fear of dental pain than those without the gene variant. And they were more than twice as likely to avoid dental care.

Dr. Daniel I. Sessler, an anesthesiologist and chairman of the department of outcomes research at the Cleveland Clinic, said he began studying hair color after hearing so many colleagues speculate about redheads requiring more anesthesia.

"The reason we studied redheads in the beginning, it was essentially an urban legend in the anesthesia community saying redheads were difficult to anesthetize," Dr. Sessler said. "This was so intriguing we went ahead and studied it. Redheads really do require more anesthesia, and by a clinically important amount."

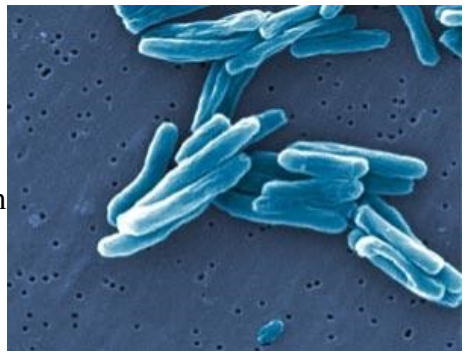
After publishing research on the topic, Dr. Sessler began hearing from redheads who complained about problems with dental pain and fear about going to the dentist. He said that when someone with red hair is considering a dental or other procedure requiring an anesthetic, they should talk to their doctor about the high probability that they are resistant to anesthetics.

"Because they're resistant, many redheads have had bad experiences," Dr. Sessler said. "If they go to the dentist or have a cut sutured, they'll need more local anesthetic than other people."

Mini-magnet test makes things sticky for TB

TUBERCULOSIS can now be diagnosed in just 30 minutes, using magnetic nanoparticles which identify Mycobacterium tuberculosis in sputum, even at very low concentrations.

TB is normally diagnosed by first spotting the bacteria in sputum under a microscope, and then sending the suspect samples away for confirmation. This involves growing larger colonies of the bacteria, which can take up to two weeks, delaying treatment and risking continued spread of the disease.



The new test, developed by Ralph Weissleder of Harvard Medical School, gives the answer in half an hour. Doctors can simply add the sputum to a solution containing nanoparticles with an iron core encased in iron oxide. Each nanoparticle is loaded with antibodies that encourage any TB-causing bacteria in the sputum to bind to it (Angewandte Chemie, DOI: 10.1002/anie.200901791).

TB-causing bacteria are now quicker to spot **(Image: CDC/Phanie/Rex Features)**

The solution is fed through a lab-on-a-chip which blocks and concentrates the nanoparticles that have bacteria attached to them but lets the other nanoparticles through. Then a small magnetic scanner encircling the chip registers the presence of bacteria-laden nanoparticles.

Skin growths saved poisoned Ukrainian president

* 17:46 07 August 2009 **by Andy Coghlan**

Benign skin growths that erupted on the face of Ukrainian president Victor Yushchenko helped save his life after he was poisoned with dioxin five years ago.

That's the verdict of doctors who have treated and monitored Yushchenko since an unknown assassin made the attempt on his life by lacing his soup with dioxin during a dinner in Kiev on 5 September 2004.

It now turns out that the lumps that grew on his face and body as a result probably saved his life by isolating the dioxin away from his vital, internal organs. They also helped to detoxify the poison, known chemically as TCDD (2,3,7,8-tetrachlrodibenzo-p-dioxin), by producing powerful enzymes called cytochrome p450s that are normally confined to the liver.

Detoxifying organ **(Image: AFP / Getty)**

'Detoxifying organ'

The growths are rearrangements of skin, created from skin stem cells. "A new organ was created out of normal structures of the skin, and the tissue expressed very high levels of dioxin-metabolizing enzymes," says Jean Saurat, the dermatologist heading the team which treated Yushchenko at the Swiss Centre for Human Applied Toxicology in Geneva. "They were made to detoxify the dioxin."

"A hamartoma is a new organisation of normal cells that simply organise themselves differently," says Saurat. "So skin can be regarded as a detoxifying organ," he says.

Saurat says that at the start of treatment, Yushchenko had concentrations of TCDD 50,000 times higher than those typically found in people.

Fat stores

Saurat declined to specify details of how his team treated Yushchenko, saying these will be disclosed in a forthcoming paper.

However, the study released this week reveals that the treatment involved the anti-obesity drug orlistat, and olestra, a zero-calorie, indigestible fat product developed but rejected for use in food because it absorbed vitamins on its way through the gut, and caused "anal leakage" in some consumers. Dioxin is known to be stored in fat. Saurat said Olestra was used early on, but was not the main component of the treatment.

By monitoring concentrations of dioxin in blood, fatty tissue, faeces, skin, urine and sweat, Saurat established that about 60 per cent of the dioxin was excreted unchanged, mainly in the faeces. It took about 15 months for half of the contaminant to be excreted.

"He's not completely clean yet, but we've got more than 95 per cent of it out now," says Saurat.

Measurements of 17 different types of dioxin showed that all except the TCDD were at concentrations expected in the general population, proving that he was poisoned with pure TCDD.

'Strong constitution'

Saurat says that if he'd died early on – before the skin lesions became apparent – the source of his poisoning may never have been known. He says that it was three months before he received treatment, and was only saved by his strong constitution.

"God knows what would've happened if we didn't treat him," says Saurat. "When he first came in, he was very, very ill, and he might have died from poisoning, but he excreted a lot of dioxin early on through vomiting and diarrhoea," he says.

The skin lesions are still there, but less severe. "His skin will still need special care," says Saurat, adding that the data from the case will be invaluable for treating and detecting milder cases of dioxin poisoning or contamination. ***Journal reference:*** *The Lancet (DOI: 10.1016/S0140-6736(09)60912-0)*

Renowned canine researcher puts dogs' intelligence on par with 2-year-old human

Border collies are brightest

TORONTO – Although you wouldn't want one to balance your checkbook, dogs can count.

They can also understand more than 150 words and intentionally deceive other dogs and people to get treats, according to psychologist and leading canine researcher Stanley Coren, PhD, of the University of British Columbia. He spoke Saturday on the topic "How Dogs Think" at the American Psychological Association's 117th Annual Convention.

Coren, author of more than a half-dozen popular books on dogs and dog behavior, has reviewed numerous studies to conclude that dogs have the ability to solve complex problems and are more like humans and other higher primates than previously thought.

"We all want insight into how our furry companions think, and we want to understand the silly, quirky and apparently irrational behaviors [that] Lassie or Rover demonstrate," Coren said in an interview. "Their stunning flashes of brilliance and creativity are reminders that they may not be Einsteins but are sure closer to humans than we thought."

According to several behavioral measures, Coren says dogs' mental abilities are close to a human child age 2 to 2.5 years.

The intelligence of various types of dogs does differ and the dog's breed determines some of these differences, Coren says. "There are three types of dog intelligence: instinctive (what the dog is bred to do), adaptive (how well the dog learns from its environment to solve problems) and working and obedience (the equivalent of 'school learning')."

Data from 208 dog obedience judges from the United States and Canada showed the differences in working and obedience intelligence of dog breeds, according to Coren. "Border collies are number one; poodles are second, followed by German shepherds. Fourth on the list is golden retrievers; fifth, dobermans; sixth, Shetland sheepdogs; and finally, Labrador retrievers," said Coren.

As for language, the average dog can learn 165 words, including signals, and the "super dogs" (those in the top 20 percent of dog intelligence) can learn 250 words, Coren says. "The upper limit of dogs' ability to learn language is partly based on a study of a border collie named Rico who showed knowledge of 200 spoken words and demonstrated 'fast-track learning,' which scientists believed to be found only in humans and language learning apes," Coren said.

Dogs can also count up to four or five, said Coren. And they have a basic understanding of arithmetic and will notice errors in simple computations, such as 1+1=1 or 1+1=3.

Four studies he examined looked how dogs solve spatial problems by modeling human or other dogs' behavior using a barrier type problem. Through observation, Coren said, dogs can learn the location of valued items (treats), better routes in the environment (the fastest way to a favorite chair), how to operate mechanisms (such as latches and simple machines) and the meaning of words and symbolic concepts (sometimes by simply listening to people speak and watching their actions).

During play, dogs are capable of deliberately trying to deceive other dogs and people in order to get rewards, said Coren. "And they are nearly as successful in deceiving humans as humans are in deceiving dogs."

Extinction hits 'whole families'

By Victoria Gill Science reporter, BBC News

Whole "chunks of life" are lost in extinction events, as related species vanish together, say scientists.

A study in the journal Science shows that extinctions tend to "cluster" on evolutionary lineages - wiping out species with a common ancestor.

The finding is based on an examination of past extinctions, but could help current conservation efforts.

Researchers say that this phenomenon can result in the loss of an entire branch of the "tree of life".

The message for modern conservation, say the authors, is that some groups are more vulnerable to extinction than others, and the focus should be on the lineages most at risk.

Lead researcher Kaustuv Roy, a biologist from the University of California, San Diego, focused on marine bivalves - including clams, oysters and mussels. The fossil record for these creatures dates back almost 200 million years.

By tracing this documented timeline of evolution and extinction, the team was able to see the effects of "background extinctions" as well as the mass extinctions, such as the one around 65 million years ago during which the dinosaurs finally died out.

Many species have become extinct during the relatively stable periods between those global calamities.

But even during such quiet periods, the team found that extinctions tended to cluster into evolutionary families - with closely-related species of clams vanishing together more often than would be predicted by chance.

Richard Grenyer, a biologist from Imperial College London, who was not involved in the study, told BBC News that by going "way back into the fossil record" this study provided important evidence of the patterns of extinction.

"Big groups of organisms tend to be similar to one another," he explained. "Look at the large cats for example."

But genetic similarities also mean, said Dr Grenyer, that "a bad effect that affects one of them, will likely affect all of them".

"It's like a casino of extinctions, with the odds rigged against certain groups."

Life's library

According to this pattern, the study's authors point out, extinctions are likely to eliminate entire branches of the evolutionary tree.

Professor Roy said: "If you have whole lineages more vulnerable than others, then very soon, even with relatively moderate levels of extinction, you start to lose a lot of evolutionary history."

Julie Lockwood, an ecologist from Rutgers University in New Jersey, US, who did not take part in this study, explained that because extinction events "hit certain lineages extremely hard... we lose whole chunks of life."

"There are examples of modern species where the same thing is happening," she told BBC News.

"In seabirds for example, the same drivers - climatic change and habitat loss - are threatening whole groups of species."

Richard Grenyer likened this loss to a fire in a library.

"Because whole sections are lost - the whole of the physics section, or all of the romantic fiction, the overall loss is much worse than if you randomly burned every 400th book."

But Dr Grenyer said that this evidence could help to drive more focused, and therefore more effective conservation efforts.

"We can use this information," he said.

"It doesn't make the conservation of individual species any easier, but if we know the sorts of things that affect tigers, we can infer conservation biology about the tiger's close relatives."