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Salt seeds clouds in the Amazon rainforest

Berkeley Lab scientists at the Advanced Light Source help track down the sources of condensation nuclei for mist and clouds in the Amazon rainforest

It's morning, deep in the Amazon jungle. In the still air innumerable leaves glisten with moisture, and fog drifts through the trees. As the sun rises, clouds appear and float across the forest canopy ... but where do they come from? Water vapor needs solid surfaces to condense on. Airborne particles are the seeds of liquid droplets in fog, mist, and clouds.

To learn how aerosol particles form in the Amazon, Mary Gilles of the Chemical Sciences Division at the U.S. Department of Energy's Lawrence Berkeley National Laboratory (Berkeley Lab) and David Kilcoyne of the Lab's Advanced Light Source (ALS) worked with Christopher Pöhlker of Germany's Max Planck Institute for Chemistry (MPIC) as part of an international team of scientists led by MPIC's Meinrat Andreae and Ulrich Pöschl. They analyzed samples of naturally formed aerosols collected above the forest floor, deep in the rainforest.

Combined with results from other facilities, the ALS analysis provided essential clues to the evolution of fine particles around which Amazon clouds and fog condense, beginning with chemicals produced by living organisms. The team found that among the most important initial triggers of the process are potassium salts.

Dissecting invisible aerosols

At ALS beamline 5.3.3.2, the researchers performed scanning transmission x-ray microscopy (STXM) to determine the near-edge x-ray absorption fine structure (NEXAFS) of particles collected during the wet season in the remote, pristine forest northeast of Manaus, Brazil.

"Through absorption of soft x-rays by an atom's core electrons, and subsequent emission of photons, the identity and exact location of the elements in the aerosol samples can be identified," says Kilcoyne. "The essence of STXM is that it not only tells you if carbon is present but how this carbon is bound to other elements within the aerosol particles. This allows us to distinguish between soot, which is graphitic, and organic carbon."

The researchers found three different types of organic aerosol particles, all similar to laboratory-generated reference samples: oxidation products based on precursor chemicals emitted in the gas phase by trees, including terpenes (the major component of turpentine) from tree resin, and isoprene, another organic compound abundantly released through leaves.

"In the beginning we focused on the carbon, oxygen, and nitrogen contents of the organic materials," says Pöhlker. "But then, to our surprise, we found very high potassium levels, up to 20 percent." The 77 Amazonian aerosol samples were remarkable for the strong signal of potassium, in the form of salts, in all but three of them. The samples were on the scale of mere millionths or billionths of a meter. The smaller the aerosol, the greater the proportion of potassium – those collected early in the morning were the smallest and richest in potassium. Larger particles contained more organic material but not more potassium. These facts suggest that potassium salts generated during the night acted as seeds for gas-phase products to condense onto, forming aerosols of different kinds.

"Biomass burning is also a rich source for potassium-containing aerosols in forested regions, but potassium from forest fires is correlated with the presence of soot, a graphitic form of carbon," Gilles says. "Before and during the collection period there were no documented fires that could have affected the biosphere where the samples were collected, and no evidence of soot was observed in the samples. Hence the source of potassium could only have been natural forest organisms."

Prime suspect

Fungal spores in the larger aerosol samples pointed to the prime suspect. Some fungi launch spores by building up water pressure through osmosis in sacs (asci) that contain the spores; when the pressure is great enough, the ascus bursts and squirts the spores into the air, along with fluid containing potassium, chloride, and sugar alcohol. Other fungi fire "ballistospores" when water vapor in the atmospheres condenses and causes a sudden release of restraining surface tension, also ejecting potassium, sodium, phosphates, sugars, and sugar alcohol. Other biogenic mechanisms also release salts into the early morning mists that cover the forest, including salts dissolved in water by transpiration during the day and, at night, the oozing of sap rich in sugars, minerals, and potassium from the edges of leaves.

Thus invisibly tiny grains of potassium salts, generated by natural plants and other living things at night and early in the morning, play a key role in the formation of aerosols in the rainforest.

Terpenes and isoprenes are primarily released in the gas phase by plants in the jungle, and once in the atmosphere they react with water, oxygen, and organic, compounds, acids, and other chemicals exuded by

indigenous plants. These reaction products are less volatile and initiate the condensation within the low-lying forest biosphere. Since the smallest particles are typically the most important in condensation, potassium salts fill the role. As the day goes on, organic gas-phase products continue to condense and the particles continue to grow. Throughout the rainy season the cloud cover, precipitation, water cycle, and finally the climate of the Amazon basin and beyond can be traced back to salts from fungi and other plants in the undisturbed jungle, providing the precursors of natural cloud-condensation nuclei and directly influencing how fog and clouds form and evolve in the rainforest.

"Biogenic potassium salt particles as seeds for secondary organic aerosol in the Amazon," by Christopher Pöhlker, Kenia T. Wiedemann, Bärbel Sinha, Manabu Shiraiwa, Sachin S. Gunthe, Mackenzie Smith, Hang Su, Paulo Artaxo, Qi Chen, Yafang Cheng, Wolfgang Elbert, Mary K. Gilles, Arthur L. D. Kilcoyne, Ryan C. Moffet, Markus Weigand, Scot T. Martin, Ulrich Pöschl, and Meinrat O. Andreae, appears in the August 31, 2012 issue of Science and is available online at http://www.sciencemag.org/content/337/6098/1075.abstract.

http://www.eurekalert.org/pub_releases/2012-09/jaaj-ssa090612.php

Study suggests acupuncture may be better than no acupuncture, sham acupuncture for chronic pain

Analysis of randomized controlled trials suggests acupuncture may be better than no acupuncture or sham acupuncture for the treatment of some chronic pain

CHICAGO – An analysis of patient data from 29 randomized controlled trials suggests that acupuncture may be better than no acupuncture or sham acupuncture for the treatment of some chronic pain, according to a report published Online First by Archives of Internal Medicine, a JAMA Network publication.

Acupuncture, the practice of inserting and stimulating needles at specific points on the body, is widely used for chronic pain, although controversy remains about its value, according to the study background.

The individual patient data meta-analyses conducted by Andrew J. Vickers, D.Phil., of Memorial Sloan-Kettering Cancer Center, New York, and colleagues used data from previously published randomized controlled trials (RCTs) with a total of 17,922 patients from the United States, United Kingdom, Germany, Spain and Sweden. Researchers sought to determine the effect size of acupuncture for some chronic pain conditions.

"We found acupuncture to be superior to both no-acupuncture control and sham acupuncture for the treatment of chronic pain," the authors comment. "Although the data indicate that acupuncture is more than a placebo, the differences between true and sham acupuncture are relatively modest, suggesting that factors in addition to the specific effects of needling are important contributors to therapeutic effects." Sham acupuncture in the trials included needles inserted superficially, devices with needles that retracted into the handle rather than penetrating the skin, and non-needle approaches such as deactivated electrical stimulation or detuned laser, according to the study.

The authors report that patients receiving acupuncture had less pain with scores that were 0.23, 0.16 and 0.15 SDs (standard deviations) lower than sham controls for back and neck pain, osteoarthritis and chronic headaches, respectively. The effect sizes in comparison to no-acupuncture controls were 0.55, 0.57 and 0.42 SDs, according to the study results. "Our results from individual patient data meta-analyses of nearly 18,000 randomized patients in high-quality RCTs provide the most robust evidence to date that acupuncture is a reasonable referral option for patients with chronic pain," the authors conclude.

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Commentary: Needling the Status Quo

In a commentary, Andrew L. Avins, M.D., M.P.H., of Kaiser-Permanente, Northern California Division of Research, Oakland, writes: "The relationship between conventional allopathic medical care and the world of complementary and alternative medicine (CAM) remains ambiguous."

"At the end of the day, our patients seek our help to feel better and lead longer and more enjoyable lives. It's ideal to understand the mechanism of action, which carries the potential for developing more and better interventions. But the ultimate questions is: does this intervention work (or, more completely, do its benefits outweigh its risks and justify its costs)?" Avins continues. "At least in the case of acupuncture, Vickers et al have provided some robust evidence that acupuncture seems to provide modest benefits over usual care for patients with diverse sources of chronic pain. Perhaps a more productive strategy at this point would be to provide whatever benefits we can for our patients, while we continue to explore more carefully all mechanisms of healing," Avins concludes.

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http://www.eurekalert.org/pub_releases/2012-09/tyn-pds083112.php

Preclinical data shows 100 percent prevention and treatment of influenza with engineered human antibody

Oral presentation at ICAAC 2012 on lead candidate from company's novel drug design platform

Cambridge, MA - Visterra, Inc., developer of novel therapeutics to treat major diseases, today announced the presentation of positive data from a preclinical study evaluating the efficacy of the company's lead product candidate, VIS410, a broadly protective, fully human monoclonal antibody being developed for influenza A infections. Data from preclinical studies were presented today at the 52nd Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC) in San Francisco. These data were also selected by ICAAC to be included in the public communication highlights for the meeting.

Developed using Visterra's innovative platform, VIS410 targets a site on influenza hemagglutinin (HA) that is present across all influenza A subtypes and is resistant to mutation development. VIS410 demonstrated broad neutralization against all influenza A strains tested in vitro, and provided potent and specific protection in mouse models against a lethal dose of influenza A virus, both prophylactically and therapeutically. In prophylactic studies, 100% of healthy non-infected mice who received a single dose of VIS410 survived subsequent infection with either H1N1 or H3N2 influenza A virus. In post-infection therapeutic studies, 100% of mice treated with a single dose of VIS410 survived a lethal viral challenge of either H1N1 or H3N2 when antibody was administered up to 72 hours after infection.

"This data with VIS410 shows several ways that this drug candidate has promise for fighting influenza, including possible pandemic strains," said Donna Ambrosino, M.D., Chief Medical Officer of Visterra. "With VIS410, we have designed an antibody that targets the viral hemagglutinin protein (HA) to enable to healthy person or patient to prevent or treat an established infection. Secondly, we have designed VIS410 as an antibody that neutralizes both groups of viral strains for influenza A, Group 1 and Group 2 viruses, opening the potential for a single monoclonal antibody to provide protection from all influenza A strains."

The data on VIS410 were described in an oral presentation today titled "Design of a Broadly Neutralizing Antibody Targeting Influenza A." Utilizing a proprietary platform to identify novel targets and design drugs against these targets, Visterra has identified a unique conformational epitope on the stem region of the influenza hemagglutinin (HA) protein, mapped by peptide scanning, that is not only conserved across all influenza subtypes, but is also resistant to virus mutation. Using this protein engineering approach, the company designed >50 human antibodies that bind to and neutralize viruses from both Group 1 and Group 2, including an optimized candidate referred to as VIS410. VIS410 targets the identified conserved region with picomolar affinity and demonstrates good physiochemical attributes, including solubility, stability and specificity. In vitro, VIS410 demonstrates dose-dependent viral inhibition with an EC50 in the range of 0.3 – 7 ug/ml against all Group 1 and Group 2 virus strains tested. Mechanistic studies indicate that VIS410 inhibits HA fusion with the cell membrane, thereby intervening in an early step in the influenza infection cycle. At doses of 2.5 and 10 mg/kg in mouse models, VIS410 provides 100% protection from lethal challenge of H1N1 and H3N2, respectively. Furthermore, when the monoclonal antibody is administered up to 72 hours after infection, it is completely effective in treating the infection with 100% survival for both H1N1 and H3N2 virus subtypes.

"We are highly encouraged by these VIS410 results, which suggest that an antibody approach such as Visterra's may be a turning point in the development of a new universal approach for both seasonal and pandemic influenza," said Steven Brugger, CEO of Visterra. "This study confirms proof of concept for our proprietary platform to identify unique targets that guide the engineering of novel drugs that are designed to be highly effective in the prevention or treatment of infectious disease."

About Influenza

Influenza virus infection is one of the most common infectious diseases, typically causing mild to severe illness, which can sometimes lead to death. Influenza epidemics occur yearly during autumn and winter, resulting in about three to five million cases of severe illness, and about 250,000 to 500,000 deaths worldwide. Although the usual strains of influenza that circulate in the annual influenza cycle constitute a substantial public health concern, far more lethal influenza strains have emerged periodically leading to pandemics that kill millions of people. Of the different types of influenza virus, influenza A viruses can replicate and mutate very rapidly, typically involving more serious infections including recent pandemics: H1N1 caused the most deadly global pandemic Spanish flu in 1918, as well as the 2009 swine flu outbreak, H2N2 caused Asian flu in the late 1950s, and H3N2 caused the Hong Kong flu in the late 1960s.

At the general population level, the most effective way to prevent influenza or severe outcomes from the disease is vaccination. However, although safe and effective vaccines have been available and used for more than 60 years,

influenza viruses are constantly changing, and the annual vaccine is developed based on an estimation of the three most prominent strains each season. A monoclonal antibody, like VIS410, that is designed to neutralize all influenza A strains, offers potential for both prevention and treatment of seasonal influenza disease. Furthermore, during a pandemic with a new influenza strain, timely production and implementation of an effective vaccine that targets the pandemic strain is not feasible. However, a universally effective monoclonal antibody could be immediately available and would be utilized for prevention in containment strategies as well as treatment for those at highest risk. VIS410 is being developed for clinical studies and expected to enter the clinical stage over the next two years. Finally, the unique epitope that VIS410 targets also holds promise for the development of a universal vaccine. A universal vaccine or therapeutic that targets a common element in all strains of influenza would have significant worldwide impact on addressing both seasonal and pandemic influenza.

http://www.eurekalert.org/pub_releases/2012-09/tju-ped091012.php

Physician's empathy directly associated with positive clinical outcomes, confirms large study

Patients of doctors who are more empathic have better outcomes and fewer complications

PHILADELPHIA--Patients of doctors who are more empathic have better outcomes and fewer complications, concludes a large, empirical study by a team of Thomas Jefferson University and Italian researchers who evaluated relationships between physician empathy and clinical outcomes among 20,961 diabetic patients and 242 physicians in Italy.

The study was published in the September 2012 issue of Academic Medicine, and serves as a follow up to a smaller study published in the same journal in March 2011 from Thomas Jefferson University investigating physician empathy and its impact on patient outcomes. That study included 891 diabetic patients and 29 physicians and concluded similar findings: patients of physicians with high empathy scores had better clinical outcomes than patients of other physicians with lower scores.

"This new, large-scale research study has confirmed that empathic physician-patient relationships is an important factor in positive outcomes," said Mohammadreza Hojat, Ph.D., research professor, Department of Psychiatry and Human Behavior; and director, Jefferson Longitudinal Study of Medical Education in the Center for Research in Medical Education and Health Care at Jefferson Medical College. "It takes our hypothesis one step further. Compared to our initial study, it has a much larger number of patients and physicians, a different tangible clinical outcome, hospital admission for acute metabolic complications, and a cross-cultural feature that will allow for generalization of the findings in different cultures, and different health care systems."

Participants in this study were 20,961 diabetic patients from a population of over 284,000 adult patients in the Local Health Authority, Parma, Italy, enrolled with one of 242 primary care physicians.

Researchers used the Jefferson Scale of Empathy (JSE) – developed in 2001 as an instrument to measure empathy in the context of medical education and patient care. This validated instrument relies on the definition of empathy in the context of patient care as a predominately cognitive attribute that involves an understanding of patient's concerns, pain, and suffering, and an intention to help. The scale includes 20 items answered on a seven-point Likert-type scale (strongly agree = 7, strongly disagree = 1). The 242 physicians completed the JSE.

In the 2011 study, to measure how a physician's empathy impacted a diabetic patient's treatment outcomes, the researchers used the results of two medical tests: the hemoglobin A1c test and cholesterol levels measurements. They found a direct association between a higher physician JSE score and a better control of patients' hemoglobin A1c and cholesterol level.

Here, researchers sought a different tangible clinical outcome. The presence of acute metabolic complications among diabetic patients, including hyperosmolar state, diabetic ketoacides, and coma, for patients who were hospitalized in 2009 was used as the outcome measure. Acute metabolic complications were used because they require hospitalization, can develop rather quickly, and their prevention is more likely to be influenced by the primary care physicians.

A total of 123 patients were hospitalized because of acute metabolic complications in 2009. Results showed that physicians in the higher empathy score group had a lower rate of patients with acute metabolic complications. For example, physicians with higher empathy levels had 29 (out of 7,224) patients admitted to the hospital, whereas physicians with lower levels had 42 (out of 6,434) patients. There are many factors that add to the strength of the study. Firstly, because of universal health care coverage in Italy, there is no confounding effect of difference in insurance, lack of insurance or financial barriers to access care.

"What's more, this second study was conducted in a health care system in which all residents enroll with a primary care physician resulting in a better defined relationship between the patients and their primary care physicians than what exists in the United States," said co-author Daniel Z. Louis, Managing Director for the

Center for Research in Medical Education and Health Care and research associate professor of family and community medicine at JMC. "Italy has a lower rate of switching doctors, facilitating long-lasting physician patient relationships," added co-author Vittorio Maio, PharmD, M.S., MSPH, associate professor at the Jefferson School of Population Health.

According to the Centers for Disease Control and Prevention, over 25 million people in the U.S. population have been diagnosed with diabetes, with almost 700,000 hospitalizations per year. There are approximately 2 million new cases per year. Worldwide, the number of total cases jumps to 180 million.

"Results of this study confirmed our hypothesis that a validated measure of physician empathy is significantly associated with the incidence of acute metabolic complications in diabetic patients, and provide the much-needed, additional empirical support for the beneficial effects of empathy in patient care" said Dr. Hojat. "These findings also support the recommendations of such professional organizations as the Association of American Medical Colleges and the American Board of Internal Medicine of the importance of assessing and enhancing empathic skills in undergraduate and graduate medical education."

The study's other co-authors include Stefano Del Canale, M.D., Ph.D., research coordinator of the Local Health Authority of Parma; Xiaohong Wang, M.S., research programmer/analyst, Center for Research in Medical Education and Health Care at JMC; Giuseppina Rossi, M.D., head, Department of Development and Integration of Primary Care Services, Local Health Authority of Parma; and Joseph S. Gonnella, M.D., Founder and Director, Center for Research in Medical Education and Health Care.

http://www.sciencedaily.com/releases/2012/09/120910151054.htm

Pain Drug Can Kill Resistant Tuberculosis: Low Cost Drug Wipes out Drug Resistant TB, but May Not Reach Patients in Need

An off-patent anti-inflammatory drug that costs around two cents for a daily dose has been found to kill both replicating and non-replicating drug resistant tuberculosis

ScienceDaily - An off-patent anti-inflammatory drug that costs around two cents for a daily dose in developing countries has been found by researchers at Weill Cornell Medical College to kill both replicating and non-replicating drug resistant tuberculosis in the laboratory -- a feat few currently approved TB drugs can do, and resistance to those is spreading.

Their findings, published online by the Proceedings of the National Academy of Sciences, point to a potential new therapy for the more than 500,000 people worldwide whose TB has become resistant to standard drug treatments. But the researchers worry that the effective drug, oxyphenbutazone, may never be tested in TB clinical trials.

Weill Cornell's Dr. Carl Nathan and his research team found what they call the "completely surprising" ability of oxyphenbutazone to kill drug resistant TB after testing thousands of approved drugs against the bacteria. This repurposing of agents already on the market can lead to quicker testing for new uses. "This agent might help save lives if there was a way to test it in TB patients," says Dr. Nathan. Oxyphenbutazone went on the market as a patented drug for arthritis-like pain in the early 1950s, and lost its patent and market dominance by the 1970s.

"It is difficult today to launch clinical studies on a medication that is so outdated in the United States, that it is mainly used here in veterinary medicine to ease pain," says the study's senior author, Dr. Nathan, chairman of the Department of Microbiology and Immunology, the R.A. Rees Pritchett Professor of Microbiology, and the director of The Abby and Howard Milstein Program in the Chemical Biology of Infectious Disease at Weill Cornell. "No drug firm will pay for clinical trials if they don't expect to make a profit on the agent. And that would be the case for an off-patent drug that people can buy over the counter for pain in most of the world."

He adds that oxyphenbutazone, best known under the trademark name of Tandearil, does have some established toxicities, "and is not a drug you should take for aches and pains if a safer alternative is available." But the drug's major toxicities appear to be less frequent than the major side-effects of the drug regimens that are currently used to treat TB, he says.

Treating the TB that Hides

Mycobacterium tuberculosis is unusual among disease-causing bacteria in that it naturally infects just humans. One-third of the world's population is infected with TB, but the bacteria typically remain dormant in a person with a healthy immune system. Nonetheless, TB becomes active in enough people that it is the leading cause of death in humans from a bacterial infection. It is difficult to treat, and the bacteria can become resistant to therapy. TB treatment in a drug-sensitive patient takes six months, using a combination of agents. If the TB is sensitive to these first-line agents and the therapy is completed with full-strength, non-counterfeit drugs, up to 95 percent of patients can be cured.

However, if a patient's TB becomes resistant to these drugs, second-line agents are administered every day for two years or more. "These second-line drugs are often toxic and expensive, and are not readily available in developing countries, where most of the infections occur," Dr. Nathan says. Mortality in drug resistant TB patients can be as high as 80 percent.

A major issue in treating TB is that the bacteria can "hide out" in the body in a non-replicating form, even when a TB patient is undergoing treatment. To find agents that could attack non-replicating TB, Dr. Nathan's research team first identified four conditions that keep bacteria in that state within the human body: low oxygen, mild acidity, a fat instead of sugar to eat and a small amount of the natural defense molecule nitric oxide.

The research team replicated those conditions in the test tube and then methodically tested the effectiveness of thousands of agents against the bacteria. After testing 5,600 drugs, researchers found oxyphenbutazone.

Researchers then delved into the mechanism by which oxyphenbutazone kills TB and found that the conditions that allow the bacterium to remain dormant modify the drug to the point that it starts reacting against both non-replicating and replicating TB. "When this happens, TB can't defend itself and dies," Dr. Nathan says.

But the researchers were unable to test oxyphenbutazone in mice, because the animals metabolize the drug to an inactive form far faster than humans.

"This makes testing the drug for TB use in humans problematic since the FDA requires preclinical animal testing studies for safety and efficacy," Dr. Nathan says. "Yet there is a long track record of oxyphenbutazone's relatively safe use in hundreds of thousands of people over decades."

Dr. Nathan and his team are continuing their research, testing hundreds of thousands of compounds for their action against TB. His team has already found another approved drug, nitazoxanide, to be effective against the bacteria, publishing his findings in 2009.

Nitazoxanide, a drug with an excellent safety record, is still on patent for use against some infections caused by other microbes. Discussions have been held about testing it in TB, Dr. Nathan says, but have stalled because of the same problem as oxyphenbutazone. The drug is metabolized so quickly in mice that it cannot be tested against experimental TB in that species.

For both oxyphenbutazone and nitazoxanide, Dr. Nathan argues that the requirement for testing in animals with experimental TB should be waived, because these agents work against TB in the test tube, have already been used with relative safety in people and might address an urgent need for treatment of a contagious disease with high mortality and few other treatment options.

This research was supported by the Tuberculosis Drug Accelerator Program of the Bill and Melinda Gates Foundation and the Abby and Howard P. Milstein Program in Chemical Biology of Infectious Disease.

Co-authors of the study include: Dr. Ben Gold, Dr. Maneesh Pingle, Julia Roberts, Dr. Mark Rundell, Dr. Thulasi Warrier, Dr. Aditya Venugopal, Dr. Crystal Darby, Xiuju Jiang, Dr. J. David Warren, Amy Cunningham-Bussel, Poonam Rath, Tamutenda Chidawanyika, Dr. Selin Somersan and Dr. W. Clay Bracken from Weill Cornell; Dr. Steven J. Brickner of S. J. Brickner Consulting; Dr. Ouathek Ouerfelli and Dr. Nilesh Shah from Memorial Sloan–Kettering Cancer Center; Dr. Eric L. Nuermberger from Johns Hopkins Hospital; and Dr. Joseph Fernandez, Ronald Realubit, Dr. J. Fraser Glickman, and Dr. Haiteng Deng from The Rockefeller University.

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http://www.sciencenews.org/view/generic/id/344785/title/Anti-inflammatories_tied_to_cardiac_risk_

Anti-inflammatories tied to cardiac risk

Heart attack survivors using certain painkillers are more likely to die or suffer another event

By Nathan Seppa

People who have survived a heart attack seem to increase their risk of having another one, or of dying, by taking common painkillers called NSAIDs, a popular class of drugs that includes ibuprofen.

The unsettling link between non-steroidal anti-inflammatory drugs and heart attack risk is not new. The American Heart Association released guidelines in 2007 discouraging the use of any NSAIDs among people with a history of cardiovascular disease. Researchers in Denmark now bolster that link with the largest study to date of NSAID use in heart patients. The findings appear September 10 in Circulation.

In conducting the analysis, the scientists mined a huge database to identify every first-time heart attack in people 30 years old or older that occurred in the country between 1997 and 2009, nearly 100,000 people in all. The researchers then cross-checked this information with death records, subsequent heart attacks and NSAID prescriptions. (Most NSAIDs in Denmark are prescribed.) About 44 percent of people were prescribed an

NSAID during the five years following a first heart attack. Compared with people who didn't get NSAIDs via prescription, those who did were 63 percent more likely to die over the next five years and 41 percent more likely to die specifically of a heart problem or to have another heart attack.
"This is the biggest study, no question, in terms of numbers and completeness," to address the NSAID/heart risk question, says Vibeke Strand, a rheumatologist at Stanford University School of Medicine.
While the study shows that NSAIDs as a group seem to boost heart attack risk, certain NSAIDs, such as diclofenac (Voltaren), appear worse than others. While the drug is sold by prescription only in the United States and Denmark, it is offered over the counter in other parts of Europe, says study coauthor Anne-Marie Schjerning Olsen, a physician at the University of Copenhagen. "I think it's a huge problem," she says.
Ibuprofen, which is marketed as Advil and Motrin, seemed to impart a consistent risk as well. The apparent risk from naproxen, sold as Aleve, was equivocal in these data, particularly after a patient had gotten past the first year post–heart attack.
Strand says the researchers have compiled "very impressive data." But she notes that the researchers were unable to track use of aspirin, which is sold over the counter in Denmark. Daily low-dose aspirin limits heart attacks by reducing the blood's clotting ability. "If you don't take aspirin regularly, or if you take it simultaneously with NSAIDs, you lose that aspirin benefit," Strand says. NSAIDs bind to the same molecular pocket on blood platelets as aspirin does, crowding out the aspirin. While NSAIDs have some ability to limit clotting caused by platelet aggregation, this capacity fades as the drugs wear off, she notes. In contrast, when aspirin binds to a platelet, its effect is irreversible, which is how daily aspirin suppresses stickiness in the population of platelets even as they are replenished.
"Some people think that if they are taking NSAIDs, they don't need aspirin," Strand says. "That's absolutely wrong." Patients who need NSAIDs for pain or inflammation, yet who have risk factors for heart disease, should take aspirin at least a few hours before taking an NSAID, she says.
Reducing aspirin's protective effect might explain part of why NSAIDs seem to add to heart risk. NSAIDs have also been linked to increased blood pressure and atrial fibrillation, a heart rhythm disorder.

http://www.eurekalert.org/pub_releases/2012-09/jaaj-ofa090612.php

Omega-3 fatty acid supplementation not associated with lower risk of major CVD events

Supplementation with omega-3 polyunsaturated fatty acids was not associated with a lower risk of all-cause death, cardiac death, sudden death, heart attack, or stroke

CHICAGO – In a study that included nearly 70,000 patients, supplementation with omega-3 polyunsaturated fatty acids was not associated with a lower risk of all-cause death, cardiac death, sudden death, heart attack, or stroke, according to an analysis of previous studies published in the September 12 issue of JAMA.
"Treatment with marine-derived omega-3 polyunsaturated fatty acids (PUFAs) for the prevention of major cardiovascular adverse outcomes has been supported by a number of randomized clinical trials (RCTs) and refuted by others. Although their mechanism of action is not clear, their postulated effect on cardiovascular outcomes may be due to their ability to lower triglyceride levels, prevent serious arrhythmias, or even decrease platelet aggregation and lower blood pressure. Current guidelines issued by major societies recommend their use, either as supplements or through dietary counseling, for patients after myocardial infarction [MI; heart attack], whereas the U.S. Food and Drug Administration has approved their administration only as triglyceride-lowering agents in patients with overt hypertriglyceridemia, and some (but not all) European national regulatory agencies have approved the omega-3 administration for cardiovascular risk modification. The controversy stemming from the varying labeling indications causes confusion in everyday clinical practice about whether to use these agents for cardiovascular protection," according to background information in the article.
Evangelos C. Rizos, M.D., Ph.D., of the University Hospital of Ioannina, Ioannina, Greece, and colleagues performed a large-scale synthesis of the available randomized evidence by conducting a systematic review and meta-analysis to determine the association between omega-3 PUFAs and major cardiovascular outcomes.
Of the 3,635 citations retrieved, 20 studies with 68,680 randomized patients were included, reporting 7,044 deaths, 3,993 cardiac deaths, 1,150 sudden deaths, 1,837 heart attacks, and 1,490 strokes. Analysis indicated no statistically significant association with all-cause mortality, cardiac death, sudden death, heart attack, and stroke when all supplement studies were considered.
"In conclusion, omega-3 PUFAs are not statistically significantly associated with major cardiovascular outcomes across various patient populations. Our findings do not justify the use of omega-3 as a structured intervention in everyday clinical practice or guidelines supporting dietary omega-3 PUFA administration. Randomized evidence will continue to accumulate in the field, yet an individual patient data meta-analysis

would be more appropriate to refine possible associations related to, among others, dose, adherence, baseline intake, and cardiovascular disease risk group," the authors conclude.

Editor's Note: All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Dr. Elisaf reported having given talks, attended conferences, and participated in trials sponsored by industry not associated with those that manufacture or market omega-3 supplements.

http://www.eurekalert.org/pub_releases/2012-09/ip-vca091112.php

Vitamin C and beta-carotene might protect against dementia

Study examines the influence of antioxidants on the pathogenesis of Alzheimer's disease

Forgetfulness, lack of orientation, cognitive decline… about 700, 000 Germans suffer from Alzheimer's disease (AD). Now researchers from the University of Ulm, among them the Epidemiologist Professor Gabriele Nagel and the Neurologist Professor Christine von Arnim, have discovered that the serum-concentration of the antioxidants vitamin C and beta-carotene are significantly lower in patients with mild dementia than in control persons. It might thus be possible to influence the pathogenesis of AD by a person's diet or dietary antioxidants. 74 AD-patients and 158 healthy controls were examined for the study that has been published in the "Journal of Alzheimer's Disease" (JAD).

AD is a neurodegenerative disease: Alterations in the brain caused by amyloid-beta-plaques, degeneration of fibrillae and a loss of synapses are held responsible for the characteristic symptoms. Oxidative stress, which constrains the exploitation of oxygen in the human body, is suspected to promote the development of AD. Whereas so called antioxidants might protect against neurodegeneration. In their study, the researchers have investigated whether the serum-levels of vitamin C, vitamin E, beta-carotene as well as lycopene and coenzyme Q10 are significantly lower in the blood of AD-patients. "In order to possibly influence the onset and development of Alzheimer's disease, we need to be aware of potential risk factors", says Gabriele Nagel. Participants were recruited from the cross-sectional study IMCA ActiFE (Activity and Function in the Elderly in Ulm) for which a representative population-based sample of about 1,500 senior citizens has been examined. The 65 to 90 years old seniors from Ulm and the surrounding area underwent neuropsychological testing and answered questions regarding their lifestyle. What is more, their blood has been examined and their body mass index (BMI) was calculated. For the present study, scientists have compared 74 patients with mild dementia (average age 78.9 years) with a control group consisting of 158 healthy, gender-matched persons of the same age. Results are quite interesting: The concentration of vitamin C and beta-carotene in the serum of AD-patients was significantly lower than in the blood of control subjects. Whereas no such difference between the groups could be found for the other antioxidants (vitamin E, lycopene, coenzyme Q10). Potential confounding factors such as education, civil status, BMI, consumption of alcohol and tobacco have been considered in the statistical analysis. Nevertheless, additional parameters such as the storage and preparation of food as well as stressors in the life of participants might have influenced the findings. Therefore, results need to be confirmed in prospective surveys. "Longitudinal studies with more participants are necessary to confirm the result that vitamin C and beta-carotene might prevent the onset and development of Alzheimer's disease", says Gabriele Nagel. Vitamin C can for example be found in citrus fruits; beta-carotene in carrots, spinach or apricots.

The study has been supported by the Ministry of Science, Research and the Arts of Baden-Württemberg (as part of the Geriatric Competence Center Ulm) and by the European Union. Further authors from the University of Ulm comprise Professor Albert Ludolph (Director of the Department of Neurology) and Professor Matthias Riepe, Department of Psychiatry and Psychotherapy II, as well as Professor Richard Peter and Florian Herbolsheimer (Institute of Epidemiology and Medical Biometry). Professor Thorsten Nikolaus (Geriatric Competence Center Ulm) and Professor Hans Biesalski (University of Hohenheim) have also contributed to the study.

http://www.eurekalert.org/pub_releases/2012-09/vt-bcr091012.php

Breast cancer risks acquired in pregnancy may pass to next 3 generations

Chemicals or foods that raise estrogen levels during pregnancy may increase cancer risk in daughters, granddaughters, and even great-granddaughters, according to scientists from Virginia Tech and Georgetown University.

Pregnant rats on a diet supplemented with synthetic estrogen or with fat, which increases estrogen levels, produce ensuing generations of daughters that appear to be healthy, but harbor a greater than normal risk for mammary cancer, the researchers report in today's Nature Communications.

Although the findings have not yet been validated in humans, the study shows that environmental damage may be passed from one generation to the next not through genetic mutations, but through "epigenetic" alterations that influence how genomic information is decoded.

The research also raises hope that people who may be especially sensitive to carcinogens can be identified and novel prevention strategies can be employed before cancer strikes.

"We have shown for the first time that altered DNA methylations modulated by specific diet in normal development are heritable and transgenerational," said Yue "Joseph" Wang, the Grant A. Dove Professor of Electrical and Computer Engineering at Virginia Tech Research Center – Arlington. "We also identified key methylation alteration sites that may be involved or responsible for increased breast cancer risk, which may serve as novel biomarkers for scientists to develop novel and targeted prevention strategies."

The National Cancer Institute estimates that more than 226,000 women and more than 2,000 men will develop breast cancer in 2012, and nearly 40,000 people will die of the disease.

Two thirds of breast cancers that occur in families have no known genetic cause, according to Leena Hilakivi-Clarke, a professor of oncology at Georgetown Lombardi Comprehensive Cancer Center. The study shows what may be underlying the cancer are not genetic mutations, but inherited effects of maternal intake of high-fat diets and exposure to excess estrogen during pregnancy.

"It is becoming clear that the process of epigenetic signaling — which genes are expressed and which genes are silenced — is being affected by a mother's hormonal environment during pregnancy," said Hilakivi-Clarke, who has studied the effects of maternal diet on offspring in animals and humans for more than 20 years. "The early studies indicate in a normal pregnancy a woman may have more than 20 different estrogen levels, and the highest and the lowest all result in a healthy baby. The challenge has been to understand how something in fetal development can affect breast cancer risk more than 50 years later."

The study was led by Sonia de Assis, a postdoctoral researcher in Hilakivi-Clarke's laboratory at the Georgetown Lombardi Comprehensive Cancer Center at Georgetown University Medical Center.

Virginia Tech researchers developed mathematical models and machine-learning techniques to analyze the changes in DNA methylation status in the descending daughters to understand how increased cancer risk is transmitted without genetic mutation.

DNA methylation is a key process in normal development, allowing cells with the same genome to perform different functions by adding chemical groups to DNA to turn some genes on and some genes off.

Wang's group found that the descendants with increased risk had several hundred common DNA regions that were methylated differently than in a control group, providing statistically convincing evidence that breast cancer risk can be transmitted via epigenetic means.

"Ultimately, it may be possible to undo or prevent this harmful methylation and decrease the risk of breast cancer." Wang said. "A next step will be to study the timing of the intervention and the impacts of the methylation as it occurs in the early, middle or end of the pregnancy. The promising news is pharmacologic or other interventions may be able to reverse the harmful exposure."

This study was supported by the American Cancer Society (116602-PF-09-018-01-CNE) and the National Institutes of Health including the National Cancer Institute (R03 CA150040, RO1 CA069065, U54 CA100970, U54CA149147, P30 CA051668 and P30 CA054174), the National Institute of Environmental Sciences (RO1 ES017594), and the National Institute of General Medical Sciences (R21 GM085665).

http://www.eurekalert.org/pub_releases/2012-09/uot-uot091012.php

U of Toronto-led team induces high-temperature superconductivity in a semiconductor with Scotch tape

Paves way for quantum computing and improvements in energy efficiency

Issued by the UNIVERSITY OF TORONTO

September 10, 2012 - Under strict embargo by Nature Communications until Tuesday, September 11, 11 a.m. EST

An international team led by University of Toronto physicists has developed a simple new technique using Scotch poster tape that has enabled them to induce high-temperature superconductivity in a semiconductor for the first time. The method paves the way for novel new devices that could be used in quantum computing and to improve energy efficiency.

"Who would have thought simply sticking things together can generate entirely new effects?" said team leader and U of T physicist Ken Burch. High-temperature superconductors are materials that conduct electricity without heating up and losing energy at liquid nitrogen temperatures. They are currently in use for transmitting electricity with low loss and as the building blocks of the next generation of devices (quantum computers). However, only certain compounds of iron, copper and oxygen – or cuprates – reveal high-temperature superconducting properties. Cuprates were believed to be impossible to incorporate with semi-conductors, and so their real-world use has been severely limited as has the exploration of new effects they may generate. For example, observing the phenomenon of the proximity effect – wherein the superconductivity in one material generates superconductivity in an otherwise normal semi-conductor – has been difficult because the fundamental quantum mechanics require the materials to be in nearly perfect contact.

That's where the poster tape comes in. "Typically, junctions between semi-conductors and superconductors were made by complex material growth procedures and fabricating devices with features smaller than a human hair," explains Burch. "However the cuprates have a completely different structure and complex chemical make-up that simply can't be incorporated with a normal semiconductor."
So instead, the team used Scotch poster tape and glass slides to place high-temperature superconductors in proximity with a special type of semi-conductor known as a topological insulator. Topological insulators have captured world-wide attention from scientists because they behave like semi-conductors in the bulk, but are very metallic at the surface. The result was induced superconductivity in these novel semi-conductors: a physics first.

The U of T team members include Kenneth S. Burch, Alex Hayat, Parisa Zareapour, Shu Yang F. Zhao, Michael Kreshchuk, Achint Jain. All are members of the Department of Physics and Institute for Optical Sciences and Alex Hayat who holds an additional appointment with U of T's Centre for Quantum Information and Quantum Control. Other scientists collaborating on the project are: Sang-Wook Cheong, Daniel C. Kwok and Nara Lee of Rutgers University, G.D. Gu, Ahijun Xu and Zhijun Xu of Brookhaven National Laboratory and Robert Cava of Princeton.

The work was supported by the Natural Sciences and Engineering Research Council of Canada, the Canadian Foundation for Innovation, the Ontario Ministry for Innovation and the National Science Foundation.

http://www.eurekalert.org/pub_releases/2012-09/uom-gtp091112.php

Genetic test predicts risk for Autism

A team of Australian researchers, led by University of Melbourne has developed a genetic test that is able to predict the risk of developing Autism Spectrum Disorder, ASD.

Lead researcher Professor Stan Skafidas, Director of the Centre for Neural Engineering at the University of Melbourne said the test could be used to assess the risk for developing the disorder.
"This test could assist in the early detection of the condition in babies and children and help in the early management of those who become diagnosed," he said.
"It would be particularly relevant for families who have a history of Autism or related conditions such as Asperger's Syndrome," he said.
Autism affects around one in 150 births and is characterized by abnormal social interaction, impaired communication and repetitive behaviours.
The test correctly predicted ASD with more than 70 per cent accuracy in people of central European descent. Ongoing validation tests are continuing including the development of accurate testing for other ethnic groups.
Clinical neuropsychologist, Dr Renee Testa from the University of Melbourne and Monash University, said the test would allow clinicians to provide early interventions that may reduce behavioural and cognitive difficulties that children and adults with ASD experience.
"Early identification of risk means we can provide interventions to improve overall functioning for those affected, including families," she said.
A genetic cause has been long sought with many genes implicated in the condition, but no single gene has been adequate for determining risk.
Using US data from 3,346 individuals with ASD and 4,165 of their relatives from Autism Genetic Resource Exchange (AGRE) and Simons Foundation Autism Research Initiative (SFARI), the researchers identified 237 genetic markers (SNPs) in 146 genes and related cellular pathways that either contribute to or protect an individual from developing ASD.
Senior author Professor Christos Pantelis of the Melbourne Neuropsychiatry Centre at the University of Melbourne and Melbourne Health said the discovery of the combination of contributing and protective gene markers and their interaction had helped to develop a very promising predictive ASD test.
The test is based on measuring both genetic markers of risk and protection for ASD. The risk markers increase the score on the genetic test, while the protective markers decrease the score. The higher the overall score, the higher the individual risk.
"This has been a multidisciplinary team effort with expertise across fields providing new ways of investigating this complex condition," Professor Pantelis said.
The study was undertaken in collaboration with Professor Ian Everall, Cato Chair in Psychiatry and Dr Gursharan Chana from the University of Melbourne and Melbourne Health, and Dr Daniela Zantomio from Austin Health.
The next step is to further assess the accuracy of the test by monitoring children who are not yet diagnosed over an extended study.

The study has been published today in the journal Molecular Psychiatry

http://www.eurekalert.org/pub_releases/2012-09/uom-cb091112.php

'Mad Cow' blood test now on the horizon

Using newly available genetic sequencing scientists discovered cells infected with prions (the infectious agent responsible for these diseases) release particles which contain easily recognized 'signature genes'.

Associate Professor Andrew Hill — from the Department of Biochemistry and Molecular Biology at the Bio21 Institute — said these particles travel in the blood stream, making a diagnostic blood test a possibility.

"This might provide a way to screen people who have spent time in the UK, who currently face restrictions on their ability to donate blood," he said. "With a simple blood test nurses could deem a prospective donor's blood as healthy, with the potential to significantly boost critical blood stocks."

Mad Cow disease was linked to the deaths of nearly 200 people in Great Britain who consumed meat from infected animals in the late 1980s.

Since 2000, the Australia Red Cross Blood Service has not accepted blood from anybody who lived in the UK for more than six months between 1980 and 1996, or who received a blood transfusion in the UK after 1980.

The research is published in this week's Oxford University Press Nucleic Acids Research journal — http://nar.oxfordjournals.org/content/early/2012/09/08/nar.gks832.full.

Lead author Dr Shayne Bellingham said the breakthrough might also help detect other human neurodegenerative diseases, such as Alzheimer's and Parkinson's. "This is an exciting new field where we can test for conditions in the brain and throughout the body, without being invasive," he said.

The researchers' genetic testing focused on a form of cell discharge called exosomes.

If exosomes were infected with prions (the pathogen that causes Creutzfeldt-Jakob Disease and Bovine Spongiform Encephalopathy, commonly known as Mad Cow Disease) they were found to also carry a specific signature of small genes called microRNA's.

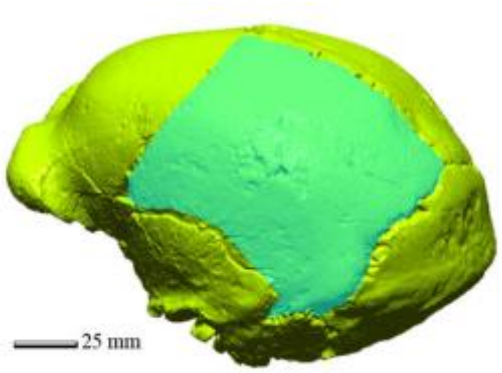
The research was undertaken at the University of Melbourne, with assistance from the Mental Health Research Institute of Victoria, the National Health and Medical Research Council and the Australian Research Council.

http://phys.org/news/2012-09-peking-isolated-population.html

Study: Peking Man an isolated population

Skull of latest inhabitant did increase in every direction as compared to the earliest inhabitant, but the shape remained relatively stable

(Phys.org)—Paleoanthropologists from the Institute of Vertebrate Paleontology and Paleoanthropology (IVPP), Chinese Academy of Sciences, used both traditional metrics and recently developed 3D scanning techniques to explore the morphological variations of Peking Man's skulls at Zhoukoudian Locality 1, and found that the skull of the latest inhabitant did increase in every direction as compared to the earliest inhabitant, but the shape remained relatively stable. The slow evolutionary rates derived from11 cranial measurements indicate Peking Man is an isolated population. Researchers reported in the latest issue of Acta Anthropologica Sinica 2012 (3).



3D laser scanning and the accurate measurement of parietal area (ZKD 3). Credit: XING Song

Peking Man is a collective name given to a group of hominid fossils found at Zhoukoudian in the suburbs of Beijing. Six skulls from Peking Man were discovered at Zhoukoudian Locality 1 since the official excavation in 1927.

In 1941, Pere Teilhard de Chardin emphasized the morphological stability of Homo erectus from Zhoukoudian throughout the 50 meters of sediments of Locality 1. He believed that not a single anatomical difference could be detected between the skull remains found at the very bottom of the deposit and those collected at the very top. This morphological stability was evidence of a slowness that characterized biological evolution whenever not obscured, disturbed or accelerated by the intrusive immigration of foreign elements.

This morphological stability was challenged when skull ZKD 5 was described which was estimated about 300,000 years younger than the skull ZKD 3 from the bottom deposits.

The morphological variations of skulls between the probable first and last inhabitants, represented by ZKD 3 and ZKD 5, were scaled by those between NJ 1 and NJ 2 skulls from Nanjing, whose owners probably spent the same duration as ZKD 3 and 5. After comparison, researchers found that the skull of the latest (or top)

inhabitant at Zhoukoudian Locality 1 increased in every direction as compared to the earliest (or bottom) inhabitant, while the shape somehow remained relatively stable after hundreds of thousand years of evolution. "We used 11 cranial measurements to determine evolutionary rates of Homo erectus from Zhoukoudian and Nanjing. The results show that biological evolutionary rate is very slow, compared with that of hominid from Nanjing. The Homo erectus crania from Zhoukoudian may represent an isolated population, and as a result, lacked evidence of gene flow from outside populations", said first author XING Song of the IVPP.
Journal reference: Acta Anthropologica Sinica

http://phys.org/news/2012-09-methane-mars-result-electrification-dust-devils.html

Methane on Mars may be result of electrification of dust-devils

Methane on Mars has long perplexed scientists

Methane on Mars has long perplexed scientists; the short-lived gas has been measured in surprising quantities in Mars' atmosphere over several seasons, sometimes in fairly large plumes. Scientists have taken this to be evidence of Mars being an 'active' planet, either geologically or biologically. But a group of researchers from Mexico have come up with a different – and rather unexpected – source of methane: dust storms and dust devils.

"We propose a new production mechanism for methane based on the effect of electrical discharges over iced surfaces," reports a paper published in Geophysical Research Letters, written by a team led by Arturo Robledo-Martinez from the Universidad Autónoma Metropolitana, Azcapotzalco, Mexico. "The discharges, caused by electrification of dust devils and sand storms, ionize gaseous CO2 and water molecules and their byproducts recombine to produce methane."

A Martian dust devil roughly 12 miles (20 kilometers) high captured on March 14, 2012 by the High Resolution Imaging Science Experiment (HiRISE) camera on NASA's Mars Reconnaissance Orbiter. Credit: **NASA/JPL-Caltech/UA**

In a laboratory simulation, they showed that that pulsed electrical discharges over ice samples in a synthetic Martian atmosphere produced about 1.41×1016 molecules of methane per joule of applied energy. The results of the electrical discharge experiment were compared with photolysis induced with UV laser radiation and it was found that both produce methane, although the efficiency of photolysis is one-third of that of the discharge.
The scientists don't rule out that methane may indeed come from other sources as well, but the way that dust devils and storms can quickly form means they can also quickly generate methane. "The present mechanism may be acting in parallel with other proposed sources but its main advantage is that it can generate methane very quickly and thus explain the generation of plumes," the team writes.
Methane on Mars may be result of electrification of dust-devils
Graph from the paper, 'Electrical discharges as a possible source of methane on Mars: Lab simulation'.
Methane has been observed in Mars' atmosphere since 1999, but in 2009, scientists studying the atmosphere of Mars over several Martian years with telescopes here on Earth announced they had found three regions of active release of methane over areas that had evidence of ancient ground ice or flowing water.
They observed and mapped multiple plumes of methane on Mars, one of which released about 19,000 metric tons of methane. The plumes were emitted during the warmer seasons—spring and summer—which is also when dust devils tend to form.
Methane on Mars is enticing because it only lasts a few hundred years in Mars' atmosphere, meaning it has to be continually replaced. And in the back of everyone's minds has been the possibility of some sort of Martian life producing it.
"Methane is quickly destroyed in the Martian atmosphere in a variety of ways, so our discovery of substantial plumes of methane … indicates some ongoing process is releasing the gas," said Dr. Michael Mumma of NASA's Goddard Space Flight Center in Greenbelt, Md in 2009. "At northern mid-summer, methane is released at a rate comparable to that of the massive hydrocarbon seep at Coal Oil Point in Santa Barbara, Calif."
The researchers in 2009 thought that the methane was being released from Mars' interior, perhaps because the permafrost blocking cracks and fissures vaporized, allowing methane to seep into the Martian air.

The unknown has been where the methane has been coming from; if it is being released from the interior, it could be produced by either geologic processes such as serpentinization, a simple water/rock reaction or biologic processes of microbes (or something bigger) releasing methane as a waste product.
But if dust devils and dust storms can also produce methane, the mystery becomes a little more mundane.
The new research by the team from Mexico also mentioned fissures in the surface, but for a different reason, saying that the electric field of dust devils is amplified by the topology of the soil: "The electrical field produced by a dust devil can not only overcome the weak dielectric strength of the Martian atmosphere, but also penetrate into cracks on the soil and so reach the ice lying at the bottom, with added strength, due to the topography of the terrain," the team wrote.
At a concentration of about 10 to 50 parts per billion by volume, methane is still a trace element in the Martian atmosphere, and indeed the sharp variations in its concentration that have been observed have been difficult to explain. Hopefully the research teams can coordinate follow-up observations of methane production during the dust devil and dust storm seasons on Mars.
More information: Robledo-Martinez, A., H. Sobral, and A. Ruiz-Meza (2012), Electrical discharges as a possible source of methane on Mars: Lab simulation, Geophys. Res. Lett., 39, L17202, doi:10.1029/2012GL053255.

http://bit.ly/QaTum2

Evolutionary trees of traditional medicine plants provide hints for drug-makers

How do we go about the business of "bioprospecting"?

There's a bizarre mindset that divides medicine into "natural" (made from plants; untainted by villainous pharmaceutical companies; delivered to your veins by forest animals) and everything else ("man-made" pills fashioned from profits and poisons). The reality, of course, is that many of the drugs used in our hospitals and pharmacies come from plants. Willow bark contains salicylic acid, the main ingredient in aspirin. Paclitaxel (taxol) was isolated from the bark of the Pacific yew tree; today, it is used to stop cancer cells from dividing. The rose periwinkle has given us vinblastine and vincristine, both used to treat leukaemia.
These examples scratch the surface of what the botanical world has given us, and what it might still offer. Of the tens of thousands of plants used in "traditional medicine", a piddling proportion has been tested for chemicals with medical benefits. How do we find the rest? How do we go about the business of "bioprospecting"? One solution is to tap the knowledge of indigenous populations, who still rely on plants for traditional medicine. When they get sick, how do they heal themselves?
But this approach has problems. Traditional use doesn't always imply an actual medical benefit, and the chosen plants might not yield interesting chemicals any more readily than the species around them. Many attempts to follow such leads have ended in the drug-development cul-de-sac. To make matters worse, collating traditional knowledge involves fieldwork and training, and is both expensive and time-consuming.
Meanwhile, the tools of molecular biology have become faster and cheaper. Companies can afford to gather large collections of plants, and screen their constituent chemicals en masse. Why filter them any further when you can test thousands of samples at once? But Haris Saslis-Lagoudakis from Imperial College London thinks that this scattershot approach to bioprospecting is a mistake. To him, traditional knowledge still has great value in honing our search for tomorrow's drugs.
He made his point by creating a family tree (a phylogeny) of over 20,000 plant species from New Zealand, Nepal, and the Cape of South Africa. Around 1,500 of these are used in traditional medicine and these, rather than being spread out throughout the family tree, are actually clustered in certain branches. The "hottest" branches contained 60 per cent more traditionally used plants that you'd expect if they were distributed randomly.
As one example among many, rushfoil (Croton) and physic nut (Jatropha) are close relatives form the spurge family, and are both used to treat malaria in Nepal. "We know that close relatives can share many of the chemical compounds they produce," says Saslis-Lagoudakis, "so our results suggest that the use of Croton and Jatropha to treat malaria is due to underlying shared chemistry between them."
Saslis-Lagoudakis also found that people tend to use related plants from the three continents to treat medical conditions that afflict the same organs. For example, members from the soapberry family (Sapindaceae) are used to treat digestive problems in New Zealand (Alectryon), Nepal (heartseed and Ceylon oak) and South Africa (jacket plum). Since these places are so distant, and their native floras are so radically different, it's likely the people there discovered the properties of their local plants independently.
To Saslis-Lagoudakis, these trends suggest that plants don't make their way into a healer's repertoire through superstition or chance. Instead, it's their medical properties – their bioactivity – that makes them useful. And

since drug manufacturers search for those same properties, the evolutionary relationships between traditionally used plants could help to guide their search.
But Michael Heinrich from University College London cautions that there could be other explanations for the results. Saslis-Lagoudakis thinks that the close relationships between traditionally used plants reflect their chemistry. Heinrich wonders if it reflects their "weediness". Weeds are more likely to be found and used, and families that are rich in weeds – such as daisies and mints – are a common part of traditional repertoires. "If you have to search for something to treat your diarrhoea, would you walk up to the Welsh mountains and try to get a rare endemic species or just use what grows in your backyards?" says Heinrich.
Still, it seems that bioprospectors are already on the path of using traditional knowledge, even if they're not aware of it. When Saslis-Lagoudakis listed all the plants that have yielded chemicals either already in use, or going through trials, he found that they're more likely to belong to groups being used in traditional medicine, and to the "hot" branches of his family tree.
Within these branches, question marks hang over more than 80 percent of species. They haven't been checked by bioprospecting companies, and many aren't being used by traditional healers. We have no idea what chemicals they contain, and Saslis-Lagoudakis writes that they "have high potential to deliver new medicines". He thinks that even in the era of cheap powerful molecular biology, traditional knowledge can make bioprospecting programmes more effective in three ways. They can tell us which conditions plants are used to treat, which could help to focus our tests. They can reveal which parts are used, and which organs can be ignored. And they can show how the plants are processed before being used, which "indicates how best to prepare a plant sample for testing."
"We hope our new methods in how traditional knowledge can be used to search for new drugs will direct bioprospectors back towards traditional medicine, and encourage more ethnobotanical fieldwork," he says. Heinrich agrees with the need for more fieldwork, especially in "the many understudied regions of the world, such as Southern Africa, New Zealand, and South and Central America". But he cautions that bioprospecting companies also take other considerations into account, like how different new compounds will be to existing ones, and how more effective they will be to existing gold standards. It's not just about the chemistry; it's about the applications too.
Reference: Saslis-Lagoudakis, Savolainen, Williamson, Forest, Wagstaff, Baral, Watson, Pendry and Hawkins. 2012. Phylogenies reveal predictive power of traditional medicine in bioprospecting. PNAS
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http://www.sciencedaily.com/releases/2012/09/120911172306.htm

Gene Linking Cataracts and Alzheimer's Disease Identified

In a recent study, investigators identified a gene linking age-related cataracts and Alzheimer's disease.

ScienceDaily - In a recent study, investigators at Boston University Schools of Medicine (BUSM) and Public Health (BUSPH) identified a gene linking age-related cataracts and Alzheimer's disease. The findings, published online in PLoS ONE, contribute to the growing body of evidence showing that these two diseases, both associated with increasing age, may share common etiologic factors.
Gyungah Jun, PhD, from the departments of medicine, ophthalmology and biostatistics at BUSM and BUSPH, served as the study's lead author. Lindsay A. Farrer, PhD, professor of medicine, neurology, ophthalmology, genetics & genomics, epidemiology and biostatistics and chief of the Biomedical Genetics Section at BUSM, was the study's senior author.
Using the Framingham Offspring Eye Study cohort, investigators looked at brain MRI findings on or after 10 years from the original eye exam and concluded that there was a significant correlation between a quantitative measure of cortical cataract and several Alzheimer's disease-related measures of brain degeneration, in particular volume of the temporal horn which is a brain structure that is progressively enlarged in patients with Alzheimer's disease. Another strong correlation in these same individuals, between cortical cataract formation and poorer performance on several cognitive tests administered at the time of the MRI scan, further supports this link.
With such a link not confounded by age or sex, the investigators then performed a genome-wide association study looking at nearly 190,000 single-nucleotide polymorphisms (SNPs), or DNA sequence variations. Three intronic (non-coding) SNPs in the gene encoding δ-catenin came to the fore. This protein is a key component in cell adherence and formation of cell junctional structures. Previously, δ-catenin was also implicated in brain and eye development, but not directly in either cataracts or Alzheimer's disease. To establish a more direct link of δ-catenin to Alzheimer's disease, the researchers transfected into neuronal cells δ-catenin bearing a mutation

near the location of the top-associated SNPs and observed a significant and specific increase in the toxic form of amyloid β, the protein that aggregates in Alzheimer brains and thought to be central to development of the disorder. In addition, the researchers found increased deposits of δ-catenin in lens tissue obtained from autopsy-confirmed Alzheimer's cases but not from subjects lacking Alzheimer's-associated neuropathology.
"Though much work remains to be done, a link between cataracts and Alzheimer's disease supports the idea of a systemic rather than brain-limited focus for processes leading to Alzheimer's disease," said Farrer. "This study gives hope that we are moving toward earlier diagnosis and new treatment targets for this debilitating disease."
Juliet Moncaster, PhD, from the department of psychiatry; Sudha Seshadri, MD from department of neurology and associate professor of the Framingham Heart Study; Jacqueline Buros, BS, from the department of medicine; Ann C. McKee, MD, from the departments of neurology, pathology and laboratory medicine, the Boston University Alzheimer's Disease Center, and the Bedford Veterans Administration Hospital; and Phillip A. Wolf, MD, of the departments of neurology, epidemiology and professor of the Framingham Heart Study of BUSM and BUSPH, contributed to this paper. Researchers from the University of Toronto, the Bedford Veterans Administration Hospital, the Universití Laval and the University of Cambridge also collaborated on this study.
This study was supported by grants from the National Institute on Aging for investigated-initiated projects (R01-AG025259, R01-AG33193, R01-AG081220, R01-AG16495, and R01-AG033040) and the Boston University Alzheimer Disease Center (P30-AG13846), National Institute of General Medical Science (R01-GM75986), Wellcome Trust, Medical Research Council, Canadian Institutes of Health Research, Alzheimer Society of Ontario, and Ontario Research Fund.
Gyungah Jun, Juliet A. Moncaster, Carolina Koutras, Sudha Seshadri, Jacqueline Buros, Ann C. McKee, Georges Levesque, Philip A. Wolf, Peter St. George-Hyslop, Lee E. Goldstein, Lindsay A. Farrer. δ-Catenin Is Genetically and Biologically Associated with Cortical Cataract and Future Alzheimer-Related Structural and Functional Brain Changes. PLoS ONE, 2012; 7 (9): e43728 DOI: 10.1371/journal.pone.0043728

http://www.wired.com/wiredscience/2012/09/ndm-icaac-3/

"Superbug" NDM-1 Found In US Cat (ICAAC 3)

The "Indian superbug" NDM-1 - actually a gene which encodes an enzyme which confers resistance to almost all known antibiotics - has been found for the first time in a pet

By Maryn McKenna

News from the ICAAC meeting: The "Indian superbug" NDM-1 — actually a gene which encodes an enzyme which confers resistance to almost all known antibiotics — has been found for the first time in a pet, somewhere in the United States.
When you consider the close contact we have with our pets — letting them lick us, smooching them on the head, allowing them to sleep on the bed — you'll understand why this could be such bad news.
The finding was announced by Dr. Rajesh Nayak, a research scientist with the Food and Drug Administration's National Center for Toxicological Research in Jefferson, Ark. (The research was carried out by Dr. Bashar Shaheen, a post-doc in Dr. Nayak's lab.) The gene (technically blaNDM) was found in isolates of E. coli that they received from Dr. Dawn Boothe of Auburn University — part of a project, Nayak said, in which Boothe receives bacterial samples from veterinary laboratories all over the United States. Of the 100 isolates they received from Boothe, six — all from a single animal — contained NDM-1.
A quick recap, in case NDM-1 is new to you: The gene and the enzyme it encodes were first identified in 2008 in Sweden, in a man of Indian origin who had gone home to India, was hospitalized, recovered, and then was hospitalized again in Sweden. The Klebsiella found in the man's urine was resistant to a huge array of drugs, including a last-resort category reserved for very serious infections that are known as carbapenems. The bacterium was susceptible to only two drugs, one old and toxic, the other new and not effective in all tissues of the body.
In 2009, bacteria containing the NDM-1 gene — which travels on several plasmids, pieces of DNA that can move easily between organisms — were found in the United Kingdom, and its Health Protection Agency put out a national alert. In 2010, bacteria containing NDM-1 were found in the United States for the first time, in three US residents living in three different states.
What the original patient, the US patients and most of the UK cases all had in common was ties to India and Pakistan: medical treatment (either emergencies or elective surgery), family ties, or travel back and forth. The identification of the gene with South Asia — the acronym stands for "New Delhi metallo-beta-lactamase" — ignited a political storm within India, with lawmakers claiming that alarm over the bug was motivated by Western jealousy of India's burgeoning medical-tourism industry. The furor got worse when the original researchers published studies of patients in South Asia, demonstrating that organisms containing the gene were not confined to hospitals but circulating widely in everyday life, and also analyses of water from New Delhi that showed the bug was moving through the water supply. Meanwhile, NDM-1 continued to spread, to more than a dozen countries so far.

The NDM-1 story has been long and contentious (my archive of posts is here), but from the first, two things have been clear. However the political battles fall out, medicine views the emergence of this gene as a catastrophe, because it edges organisms to the brink of being completely non-responsive to antibiotics, as untreatable as if the infections were contracted before the antibiotic era began. And because the gene resides in organisms that happily live in the gut without causing symptoms, NDM-1 has been a hidden catastrophe, crossing borders and entering hospitals without ever being detected.

And now, according to Shaheen and Nayak's finding, possibly entering households and families in the same covert manner.

I spoke to Nayak after his ICAAC presentation Tuesday. He said that very little is known about the source of the bacterial samples, including the identity of the family and the cat. "The reason why we don't know is these were not collected by us, and they were not collected by Dr. Boothe; they were collected by veterinarians," he said. "So a family comes in, says 'My cat is not feeling well,' and the veterinarian collects blood, urine, whatever, and sends them in. There is no history associated with them."

The timing of the sample is perplexing, he agreed. The isolates were received between 2008 and 2009 from the labs where vets sent them, meaning that the NDM-1 in the unknown cat was collected at the same time as the earliest recognition of the resistance factor in Europe, and at least a year before NDM-1 was perceived in the United States.

He emphasized that it isn't known whether the cat passed NDM-1 on to its family (or, conversely, whether the family were responsible for giving the bug to their pet). If that happened, it would not be the first time that bacterial traffic between pets and their humans has made one or the other sick. There is a long literature of MRSA passing back and forth between people and their cats and dogs, in some cases making the humans sick and in some cases making the animals very ill. (Coincidentally, this also was discussed at ICAAC by Dr. Tara Smith of University of Iowa, at almost the same time that Nayak was presenting his work.) And Nayak's group actually made the NDM-1 finding while following up two pieces of research they published last year about organisms in pets which had the resistance pattern ESBL — troubling, but still susceptible to carbapenems, and thus one step away from NDM-1.

"Carbapenem resistance is such an important issue," Nayak told me. "Carbapenems are the last line of defense. And companion animals are so close to humans; what if there is a transfer from one to another? It is possible, that is all I can say; it is a distinct possibility."

http://nyti.ms/R59HeG

Ceramic Fragments Point to Artistry in the Ice Age

New discoveries in Croatia suggest that ice age humans made evocative ceramic art far more regularly than once believed

By ALANNA MITCHELL

We know them best for their stone tools and intrepid mammoth hunting. But new discoveries in Croatia suggest that ice age humans made evocative ceramic art far more regularly than once believed.

Thirty-six fragments of fired clay, excavated in the Vela Spila cave on an island off the Adriatic coast, make up the second-largest collection found so far of the earliest human experiments with ceramic art. They are 15,000 to 17,500 years old — the first European evidence of ceramic art after the ice sheets stopped spreading.

The oldest and largest collection, made about 30,000 years ago and found in the Czech Republic, includes a famously corpulent nude figurine known as the Venus of Dolni Vestonice. Apart from that, little fired ceramic art remains from the time before the explosion of ceramic pot-making 10,000 years ago, after the ice sheets retreated and early humans settled down to farm.

That led paleontologists to believe that ceramic art was uncommon among the highly mobile people of the ice age. But Rebecca Farbstein, the University of Cambridge archaeologist who described the Croatian collection in a recent paper in the journal PLoS One, said the work was not so unusual after all.

"The history of ceramic technology is longer and more diverse than we originally thought," she said.

The most lifelike piece found at Vela Spila (the term is Croatian for big cave) is the tiny dark brown torso and foreleg of an animal, possibly a horse or deer, complete with a smooth, anatomically correct hole in its rear. But when the piece was uncovered in 2001, the team stuffed it into a bag without identification.

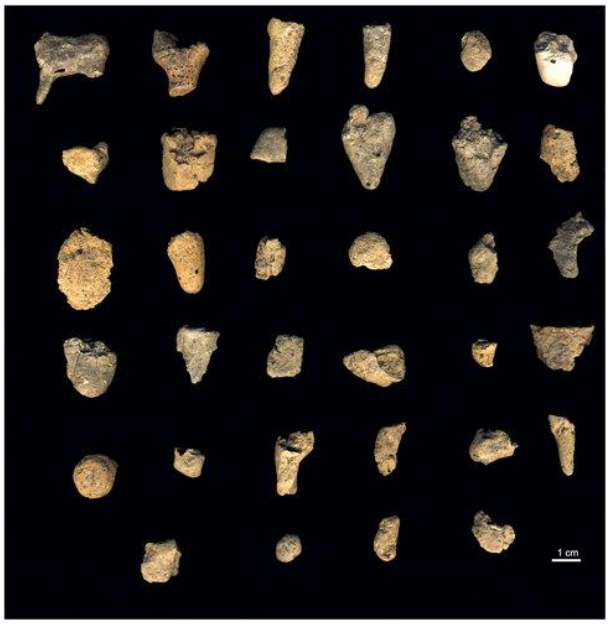
"It was overlooked because no one expected to find ceramics in the Paleolithic," Dr. Farbstein said.

Five years later, someone looked in the bag and realized what the figure was. When scientists went back to the cave that year to excavate further, they found the other 35 ceramic art pieces.

Olga Soffer, an emerita professor of anthropology at the University of Illinois who has worked on the Czech ceramics, said the find reinforced the idea that ceramic work - a major, complex technological breakthrough in human history — was invented for art rather than utility. In turn, that helps flesh out the modern understanding of how early human minds worked: more metaphor, less blood. "Life was lived by more than stone spear point," Dr. Soffer said. "It gets us away from the Hemingway, mega-macho male stuff."

Dr. Farbstein said her analysis of the Vela Spila findings suggested that the inhabitants of the cave independently developed their own form of ceramic art more than 10,000 years after the Czech invention.

The excavation revealed that ceramic art in the cave lasted for two and a half millenniums before vanishing from the archaeological record, only to reappear 8,000 years later. A handful of other sites nearby from the same ice age era are devoid of ceramics.



Ceramic shards from Vela Spila. **Farbstein, Radic, Brajkovic, Miracle**

There are similarities between the Czech and Croatian ceramics. In each case the figurines' limbs are made by pinching each pair together to form a single appendage, as if the legs or arms are glued together. One of the Croatian figurines is covered with bands of incisions, and the artist has etched a line between the joined back legs to represent two legs, as seen in some Czech pieces.

Tantalizingly, several of the Croatian pieces feature the imprint of a finger, perhaps left there when the artist tried to smooth wet clay. Again, some Czech pieces, including the Venus, have similar marks.

But the Czech figurines depict feet, while the Croatian ones do not. And while the Czech ceramics were made at outdoor hearths and were sometimes deliberately exploded, as if in a ritual, the Croatian ceramics were found in a cave with no hearth.

Other archaeologists who study the same period are unconvinced that the Vela Spila ceramics were a brand-new invention. Jiri Svoboda of the Institute of Archaeology of the Academy of Sciences of the Czech Republic, Brno, says it is also plausible that the Croatian artists learned from the Czechs.

"It seems that these people were doing very similar things, but 10,000 to 15,000 years later," he said from his excavation site at Dolni Vestonice, adding, "I would vote personally for continuity."

Dr. Soffer said it was possible that ceramic artworks were made in many places but not fired - or that the firing was not hot enough, so the ceramics were destroyed by time. She said finding out where the Croatian figurines' clay originated may help answer some questions.

The archaeological record is silent so far on a question that teases the imagination: What were the ceramics for? Could they have been as mobile as their makers, perhaps carried as tokens in the clothing of those hairy mammoth hunters?

http://www.sciencedaily.com/releases/2012/09/120912125832.htm

Popular Pain-Relieving Medicines Linked to Hearing Loss in Women

Headache? Back pain? At the first sign of pain, you might reach for a pain-relieving medicine to sooth your bodily woes.

ScienceDaily - Analgesics are the most frequently used medications in the United States and are commonly used to treat a variety of medical conditions.

But although popping a pill may make the pain go away, it may do some damage to your ears.

According to a study by researchers at Brigham and Women's Hospital (BWH), women who took ibuprofen or acetaminophen two or more days per week had an increased risk of hearing loss. The more often a woman took either of these medications, the higher her risk for hearing loss. Also, the link between these medicines and hearing loss tended to be greater in women younger than 50 years old, especially for those who took ibuprofen six or more days per week.

There was no association between aspirin use and hearing loss.

The study will be published in the September 15, 2012 issue of the American Journal of Epidemiology.

The researchers prospectively examined the relationship between frequency of aspirin, ibuprofen and acetaminophen use and risk of hearing loss among women in the Nurses' Health Study II.

Data from 62,261 women ages 31 to 48 years at baseline was studied. The women were followed for 14 years, from 1995 to 2009. Ten thousand and twelve women self-reported hearing loss.
Compared with women who used ibuprofen less than once per week, those who used ibuprofen 2 to 3 days per week had a 13 percent increased risk for hearing loss, while women who used the medication 4 to 5 days per week had a 21 percent increased risk. For those who used ibuprofen six or more days per week, the increased risk was 24 percent.
Compared with women who used acetaminophen less than once per week, women who used acetaminophen 2 to 3 days per week had an 11 percent increased risk for hearing loss, while women taking the medicine 4 to 5 days per week had a 21 percent increased risk.
"Possible mechanisms might be that NSAIDs may reduce blood flow to the cochlea -- the hearing organ -- and impair its function," said first study author Sharon G. Curhan, MD, BWH Channing Division of Network Medicine. "Acetaminophen may deplete factors that protect the cochlea from damage."
Curhan notes that although analgesics are widely available without a prescription, they are still medicines that carry potential side effects.
"If individuals find a need to take these types of medications regularly, they should consult with their health care professional to discuss the risks and benefits and to explore other possible alternatives," said Curhan.
Over 50 percent of American adults suffer from high-frequency hearing loss by the time they reach 60 years old. One-third of women in their 50s and nearly two-thirds in their 60s have experienced hearing loss.
According to the World Health Organization, adult-onset hearing loss is the sixth most common disease burden in high-income countries.
S. G. Curhan, J. Shargorodsky, R. Eavey, G. C. Curhan. Analgesic Use and the Risk of Hearing Loss in Women. American Journal of Epidemiology, 2012; DOI: 10.1093/aje/kws146

http://bit.ly/TWDnLu

Deaf gerbils are all ears thanks to stem cells

Deaf gerbils have recovered their hearing after human stem cells were injected into their ears.

18:00 12 September 2012 by Andy Coghlan

"It's a proof of concept, and it's important because for the first time we've shown stem cells can be used to repair the ear," says Marcelo Rivolta of the University of Sheffield, UK, and head of the team that treated the gerbils.
Spiral ganglion neurons in the ear convert mechanical sound vibrations into electrical signals that the brain interprets as sound.
When these neurons get damaged or die they can't be replaced. This results in a form of deafness called auditory neuropathy, which affects about a tenth of deaf people, possibly as many as 300,000 in the UK alone, says Rivolta.
Cochlear implants can correct the main form of deafness, which occurs when the cochlea loses hair cells that register sound by bending. But neurons can't be substituted except through an expensive, risky and invasive procedure to implant an electrode directly into the brain.
Now, Rivolta and his colleagues hope to develop much simpler treatments based on the so-called otic neural progenitor stem cells they made in the lab from human embryonic stem cells, the cells in embryos that can turn into all types of bodily tissues.

Restoring ganglion neurons

Rivolta's team injected about 50,000 of the otic neural progenitor cells into single ears of 18 gerbils. The animals' spiral ganglion neurons had been deliberately destroyed with a drug called ouabain, leaving them completely deaf. The stem cells were injected into the cochlea through a tiny, drilled hole.
Post mortems showed that the stem cells turned into specialised spiral ganglion neurons in the ear.
Within 10 weeks, about two-thirds of the animals had recovered some hearing. On average, the animals recovered about 46 per cent of their hearing, as measured by their ability to respond to sounds of varying volume.
"In people, this would mean going from only being able to hear a loud truck on the street to being able to hold a conversation," says Rivolta. However, he adds that considerably more work in animals is needed to refine the procedure – it will be years before it can be tested in people.
The team also produced cells similar to the hair cells that are damaged in the majority of deaf people, but Rivolta says much more work is needed to turn these into fully functional hair cells. "If we could replace hair cells, that would enable us to treat 80 to 90 per cent of all deaf people," he says.
Journal reference: Nature, DOI: 10.1038/nature.11415

http://www.eurekalert.org/pub_releases/2012-09/uocd-loo091312.php

Lack of oxygen in cancer cells leads to growth and metastasis

CD24 is a rational target in hypoxic cancers

It seems as if a tumor deprived of oxygen would shrink. However, numerous studies have shown that tumor hypoxia, in which portions of the tumor have significantly low oxygen concentrations, is in fact linked with more aggressive tumor behavior and poorer prognosis. It's as if rather than succumbing to gently hypoxic conditions, the lack of oxygen commonly created as a tumor outgrows its blood supply signals a tumor to grow and metastasize in search of new oxygen sources – for example, hypoxic bladder cancers are likely to metastasize to the lungs, which is frequently deadly. A University of Colorado Cancer Center study recently published in the journal Cancer Research details a mechanism by which these hypoxic conditions create aggressive cancer, with possible treatment implications for cancers including breast, ovarian, colorectal, pancreatic, prostate, bladder and other cancers.

"We've known that the protein HIF-1a is overexpressed in hypoxic tumors. And we've known that the cancer stem cell marker CD24 is overexpressed in many tumors. This study shows a link between the two – the HIF-1a of hypoxia creates the overexpression of CD24. And it's this CD24 that creates a tumor's aggressive characteristics of growth and metastasis," says Dan Theodorescu, MD, PhD, director of the University of Colorado Cancer Center and the paper's senior author.

Outgrowing the blood supply leads to tumor hypoxia, which leads to overexpression of HIF-1a, which signals the production of CD24, which makes tumors grow and metastasize. In addition to aggression, CD24 has also been shown to confer resistance to chemotherapy, allowing this small population of cells to regrow the tumor once chemotherapy ends, leading to relapse and disease progression.

"Now imagine we target CD24," Theodorescu says. "Either by removing a cell's ability to make CD24 or by killing cells marked by this protein, it's likely we could disarm this most dangerous population of cells."

Theodorescu and colleagues showed this by adjusting levels of HIF-1a and CD24 in cancer cell samples and animal models. With HIF-1a low and yet CD24 artificially high, cells retained the ability to grow and metastasize. With CD24 low and yet HIF-1a artificially high, cell survival and proliferation decreased.

"It seems CD24 overexpression in hypoxic cells drives growth and metastasis in these hypoxic tumors," Theodorescu says. "Now we have a rational target: CD24 for these hypoxic tumors."

http://www.eurekalert.org/pub_releases/2012-09/uoc--nsc091012.php

Neural stem cells regenerate axons in severe spinal cord injury

New relay circuits, formed across sites of complete spinal transaction, result in functional recovery in rats

In a study at the University of California, San Diego and VA San Diego Healthcare, researchers were able to regenerate "an astonishing degree" of axonal growth at the site of severe spinal cord injury in rats. Their research revealed that early stage neurons have the ability to survive and extend axons to form new, functional neuronal relays across an injury site in the adult central nervous system (CNS).

The study also proved that at least some types of adult CNS axons can overcome a normally inhibitory growth environment to grow over long distances. Importantly, stem cells across species exhibit these properties. The work will be published in the journal Cell on September 14.

The scientists embedded neural stem cells in a matrix of fibrin (a protein key to blood clotting that is already used in human neuron procedures), mixed with growth factors to form a gel. The gel was then applied to the injury site in rats with completely severed spinal cords.

"Using this method, after six weeks, the number of axons emerging from the injury site exceeded by 200-fold what had ever been seen before," said Mark Tuszynski, MD, PhD, professor in the UC San Diego Department of Neurosciences and director of the UCSD Center for Neural Repair, who headed the study. "The axons also grew 10 times the length of axons in any previous study and, importantly, the regeneration of these axons resulted in significant functional improvement."

In addition, adult cells above the injury site regenerated into the neural stem cells, establishing a new relay circuit that could be measured electrically. "By stimulating the spinal cord four segments above the injury and recording this electrical stimulation three segments below, we detected new relays across the transaction site," said Tuszynski.

To confirm that the mechanism underlying recovery was due to formation of new relays, when rats recovered, their spinal cords were re-transected above the implant. The rats lost motor function – confirming formation of new relays across the injury.

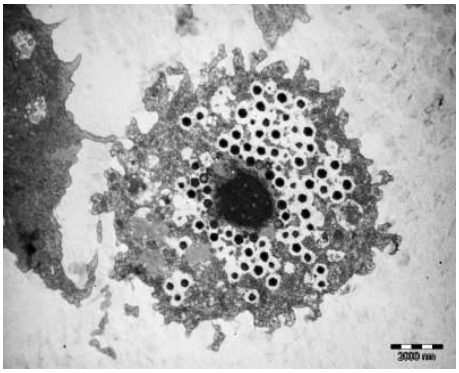
The grafting procedure resulted in significant functional improvement: On a 21-point walking scale, without treatment, the rats score was only 1.5; following the stem cell therapy, it rose to 7 – a score reflecting the animals' ability to move all joints of affected legs.
Results were then replicated using two human stem cell lines, one already in human trials for ALS. "We obtained the exact results using human cells as we had in the rat cells," said Tuszynski.
The study made use of green fluorescent proteins (GFP), a technique that had never before been used to track neural stem cell growth. "By tagging the cells with GFP, we were able to observe the stem cells grow, become neurons and grow axons, showing us the full ability of these cells to grow and make connections with the host neurons," said first author Paul Lu, PhD, assistant research scientist at UCSD's Center for Neural Repair. "This is very exciting, because the technology didn't exist before."
According to the researchers, the study makes clear that early-stage neurons can overcome inhibitors present in the adult nervous system that normally work to maintain the elaborate central nervous system and to keep cells in the adult CNS from growing aberrantly.
Additional contributors to the study include Yaozhi Wang, Lori Graham, Karla McHale, Mingyong Gao, Di Wu, John Brock, Armin Blesch, Ephron S. Rosenzweig, Binhai Zheng and James M. Conner, UCSD Department of Neurosciences; Leif A. Havton, UCLA Department of Neurology; and Martin Marsala, UCSD Department of Anesthesiology.
The work was supported by the Veterans Administration, National Institutes of Health (NS09881), Canadian Spinal Research Organization, The Craig H. Neilsen Foundation, and the Bernard and Anne Spitzer Charitable Trust.

http://www.eurekalert.org/pub_releases/2012-09/uoia-sog091312.php

Study of giant viruses shakes up tree of life

A new study of giant viruses supports the idea that viruses are ancient living organisms and not inanimate molecular remnants run amok

CHAMPAIGN, Ill. - A new study of giant viruses supports the idea that viruses are ancient living organisms and not inanimate molecular remnants run amok, as some scientists have argued. The study reshapes the universal family tree, adding a fourth major branch to the three that most scientists agree represent the fundamental domains of life. The new findings appear in the journal BMC Evolutionary Biology.



Giant viruses should be included reconstructions of the tree of life, researchers report in a new study. The mimivirus, shown here (small black hexagons) infecting an amoeba, is as big as some bacterial cells and shares some ancient protein structures with most organisms. **Professor Didier Raoult, Rickettsia Laboratory, La Timone, Marseille, France**

The researchers used a relatively new method to peer into the distant past. Rather than comparing genetic sequences, which are unstable and change rapidly over time, they looked for evidence of past events in the three-dimensional, structural domains of proteins. These structural motifs, called folds, are relatively stable molecular fossils that – like the fossils of human or animal bones – offer clues to ancient evolutionary events, said University of Illinois crop sciences and Institute for Genomic Biology professor Gustavo Caetano-Anollés, who led the analysis.
"Just like paleontologists, we look at the parts of the system and how they change over time," Caetano-Anollés said. Some protein folds appear only in one group or in a subset of organisms, he said, while others are common to all organisms studied so far. "We make a very basic assumption that structures that appear more often and in more groups are the most ancient structures," he said.
Most efforts to document the relatedness of all living things have left viruses out of the equation, Caetano-Anollés said. "We've always been looking at the Last Universal Common Ancestor by comparing cells," he said. "We never added viruses. So we put viruses in the mix to see where these viruses came from."
The researchers conducted a census of all the protein folds occurring in more than 1,000 organisms representing bacteria, viruses, the microbes known as archaea, and all other living things. The researchers included giant viruses because these viruses are large and complex, with genomes that rival – and in some cases exceed – the genetic endowments of the simplest bacteria, Caetano-Anollés said. "The giant viruses have incredible machinery that seems to be very similar to the machinery that you have in a cell," he said. "They have complexity and we have to explain why."
Part of that complexity includes enzymes involved in translating the genetic code into proteins, he said. Scientists were startled to find these enzymes in viruses, since viruses lack all other known protein-building machinery and must commandeer host proteins to do the work for them.
In the new study, the researchers mapped evolutionary relationships between the protein endowments of hundreds of organisms and used the information to build a new universal tree of life that included viruses. The

resulting tree had four clearly differentiated branches, each representing a distinct "supergroup." The giant viruses formed the fourth branch of the tree, distinct from bacteria, archaea and eukarya (plants, animals and all other organisms with nucleated cells). The researchers discovered that many of the most ancient protein folds – those found in most cellular organisms – were also present in the giant viruses. This suggests that these viruses appeared quite early in evolution, near the root of the tree of life, Caetano-Anollés said.

The new analysis adds to the evidence that giant viruses were originally much more complex than they are today and experienced a dramatic reduction in their genomes over time, Caetano-Anollés said. This reduction likely explains their eventual adoption of a parasitic lifestyle, he said. He and his colleagues suggest that giant viruses are more like their original ancestors than smaller viruses with pared down genomes.

The researchers also found more evidence that viruses are key "spreaders of information," Caetano-Anollés said. "The protein structures that other organisms share with viruses have a particular quality, they are (more widely) distributed than other structures," he said. "Each and every one of these structures is an incredible discovery in evolution. And viruses are distributing this novelty," he said. Most studies of giant viruses are "pointing in the same direction," Caetano-Anollés said. "And this study offers more evidence that viruses are embedded in the fabric of life."

The research team included graduate student Arshan Nasir; and Kyung Mo Kim, of the Korea Research Institute of Bioscience and Biotechnology.

The paper, "Giant Viruses Coexisted With the Cellular Ancestors and Represent a Distinct Supergroup Along With Superkingdoms Archaea, Bacteria and Eukarya," is available online.

http://bit.ly/Qv3zb3

Cholesterol Confusion: Researchers Closer to Understanding Which Forms of Cholesterol Can Really Hurt Us

A protein may turn good cholesterol bad and bad cholesterol lethal

By Thea Singer

We have been hearing for years that high-density lipoprotein (HDL)—the "good cholesterol"—may not be all it's cracked up to be. Now a new study shows that a certain subclass of HDL may actually be "bad," increasing the risk of coronary heart disease.

A small protein may be to blame. HDL with a small proinflammatory protein called apolipoprotein C-III (apoC-III) on its surface may nearly double the risk of heart disease in healthy men and women, according to Frank Sacks, professor of cardiovascular disease prevention at the Harvard School of Public Health and senior author on a paper in the April Journal of the American Heart Association.

Conversely, Sacks's study found, HDL without apoC-III may be especially heart-protective. A number of studies have shown that LDL (low-density lipoprotein)—the "bad cholesterol"—with apoC-III on its surface is particularly harmful, leading to higher incidence of plaque buildup in artery walls. Yet, Sacks says, this is the first large-scale prospective study with healthy subjects to show that apoC-III on HDL may have similar effects.

The scientists examined blood samples taken from 572 women in the Nurses' Health Study and from 699 men in the Health Professionals Follow-Up Study, two of the largest long-term investigations of factors that affect women's and men's health. Over 10 to 14 years of follow-up, they documented 634 cases of coronary heart disease, which they matched with control subjects for age, smoking status and the date blood was drawn. After adjusting for those and other lifestyle-based cardiovascular risk factors, they found a nearly twofold increase in risk for HDL with apoC-III. The men and women whose levels of HDL with apoC-III were in the top 20 percent had a 60 percent higher risk of developing heart disease than those in the bottom 20 percent.

Sacks says the techniques his team used to measure the levels of the two HDL subclasses, which Harvard is patenting, could lead to more precise tests to evaluate heart disease risk and treatment response.

Moreover, the findings, if replicated in his and others' ongoing studies, could spur development of drugs that target HDL subclasses, working to raise HDL without apoC-III and lower HDL with it. "The bottom line is, there's a lot more to be learned about HDL and how it acts," says Nilesh Samani of the University of Leicester in England and co-author of a paper that found raising HDL levels might not change heart disease risk.

http://www.sciencedaily.com/releases/2012/09/120913105008.htm

Cell Death Mystery Yields New Suspect for Cancer Drug Development

A mysterious form of cell death, coded in proteins and enzymes, led to a discovery by UNC researchers uncovering a prime suspect for new cancer drug development.

ScienceDaily - CIB1 is a protein discovered in the lab of Leslie Parise, PhD , professor and chair of the department of biochemistry at the University of North Carolina at Chapel Hill. The small calcium binding protein is found in all kinds of cells. Cassandra Moran, DO, was a pediatric oncology fellow at UNC prior to

accepting a faculty position at Duke University. She is interested in neuroblastoma, a deadly form of childhood brain cancer. While working in the Parise lab at UNC as a resident, she found that decreasing CIB1 in neuroblastoma cells caused cell death.
Cancer is a disease of uncontrolled cell growth, so the ability to cause cancer cell death in the lab is exciting to researchers -- but the UNC team couldn't figure out how it was happening.
Tina Leisner, PhD, a UNC research associate in biochemistry, picked up where Dr. Moran left off when she returned to her clinical training. "It was a mystery how loss of CIB1 was causing cell death. We knew that it wasn't the most common mechanism for programmed cell death, called apoptosis, which occurs when enzymes called caspases become activated, leading to the destruction of cellular DNA. These cells were not activating caspases, yet they were dying. It was fascinating, but frustrating at the same time," said Leisner.
What Dr. Leisner and her colleagues found, in the end, is that CIB1 is a master regulator of two pathways that cancer cells use to avoid normal mechanisms for programmed cell death. These two pathways, researchers believe, create "alternate routes" for cell survival and proliferation that may help cancer cells outsmart drug therapy. When one pathway is blocked, the other still sends signals downstream to cause cancer cell survival.
"What we eventually discovered is that CIB1 sits on top of two cell survival pathways, called PI3K/AKT and MEK/ERK. When we knock out CIB1, both pathways grind to a halt. Cells lose AKT signaling, causing another enzyme called GAPDH to accumulate in the cell's nucleus.Cells also lose ERK signaling, which together with GAPDH accumulation in the nucleus cause neuroblastoma cell death. In the language of people who aren't biochemists, knocking out CIB1 cuts off the escape routes for the cell signals that cause uncontrolled growth, making CIB1 a very promising drug target," said Dr. Parise.
This multi-pathway action is key to developing more effective drugs. Despite the approval of several targeted therapies in recent years, many cancers eventually become resistant to therapy.
"What is even more exciting," Leisner adds, "is that it works in completely different types of cancer cells. We successfully replicated the neuroblastoma findings in triple-negative breast cancer cells, meaning that new drugs targeted to CIB1 might work very broadly."
The team's findings were published in the journal Oncogene. In addition to Drs. Leisner, Moran and Parise, Stephen P. Holly, PhD, contributed to the research.
Research reported in this publication was supported by the National Heart, Lung and Blood Institute of the National Institutes of Health under awards number HL07149T32 and 5R01HL092544.
T M Leisner, C Moran, S P Holly, L V Parise. CIB1 prevents nuclear GAPDH accumulation and non-apoptotic tumor cell death via AKT and ERK signaling. Oncogene, 2012; DOI: 10.1038/onc.2012.408

http://bit.ly/PInWnw

Inferior lizard tails weaken hopes of regrowing limbs

THE regenerated tail of a lizard is not a perfect replica of the original, but a poor knock-off with a different anatomy.

13 September 2012 by Hannah Krakauer

The old ones are the best **(Image: Pete Oxford/FLPA)**

This finding raises the question of whether it will ever be possible to fully regenerate injured human limbs - despite optimistic claims to the contrary.
Rebecca Fisher of the University of Arizona College of Medicine in Phoenix and her colleagues discovered key anatomical differences when they looked at original and fully regenerated tails in the green anole lizard (Anolis carolinensis), which can "drop" its tail when caught by a predator and later grow another. Running through the new tail, for example, was a single long tube of cartilage rather than the chain link of vertebrae found in the original.
The muscles were different too. In place of shorter, variegated muscle fibres were long muscles stretching from tip to stump (The Anatomical Record, doi.org/jbp).
Both differences suggest that the regenerated tail would be less flexible, says Fisher, because neither the cartilage tube nor the long muscle fibres are capable of the fine control that comes with shorter muscles and lots of small joints between bones. Further functional studies should show what changes these might make to the lizard's agility.
Most intriguing to Fisher were the pores she noticed throughout the cartilage. A tail made of vertebrae has regular gaps that allow blood vessels and nerves to pass through. But the replacement cartilage, perhaps because it is all one piece, is peppered with small holes, which increase in number towards the tip of the tail. The pores only let blood vessels through - not nerves. New nerves either remain trapped within the cartilage

tube or spread a short distance from the stump and don't seem to reach the muscles and skin except right at the base of the tail (The Anatomical Record, doi.org/jbn).

Whether the findings will put a dampener on hopes of eventually regenerating human limbs remains to be seen. Jason Pomerantz, a regenerative medicine researcher at the University of California, San Francisco, says there are big implications in the differences between the regenerated structure and original. "Even in a context that we think of as a 'good' example of regeneration, the regenerated structure is not perfect and functioning as well as the original," he says. It highlights the challenge of regenerating a complicated structure, he adds.

Ellen Heber-Katz, a mammalian tissue regeneration specialist at the Wistar Institute in Philadelphia, Pennsylvania, is more optimistic. A range of animals can regenerate limbs or tails, and one lizard species may not reflect the capabilities of mammals, she says.

http://bit.ly/RWcKph

Conventional Forensic Theory on Order of Bugs That Feast on Corpses Upended

Beetles might precede blowflies (not vice versa, as forensic entomology has long suggested), a finding that could change time of death and other calculations made by crime-scene investigators

By Alaina G. Levine | Thursday, September 13, 2012 | 4

When a human body calls it quits, it can take as few as 30 seconds for blowflies to begin feasting on it. For the next several hours to days, a carnival of blowflies, other flies and beetles make the departed their personal bed-and-breakfasts. A determination of that succession of insects is one of the tools that crime-scene investigators (CSIs) use to estimate the postmortem interval (PMI), or the time elapsed since death.

Since the dawn of modern forensic science in the 19th century, the general belief has been that the order in which carrion-attending arthropods descend starts with blowflies, proceeds to maggots (from the fly eggs) and then moves on to beetles and other predators. Now a 27-year-old graduate student has determined that this is not always the case. Her research could represent a fly in the ointment (we could not resist) for the still burgeoning field of forensic entomology, in which scientists use bug evidence to help them solve crimes.

Entomologist Amanda Fujikawa of the University of Nebraska–Lincoln made her discovery while analyzing how the decomposition of mammal carcasses affects nearby ecosystems in Valentine National Wildlife Refuge in the Sandhills region in Nebraska, a unique prairie environment with grass-anchored sand dunes. She chose the area for its limited access. With only a few roads leading into the area, she was confident her experiments would not be interrupted. In late spring and midsummer, she placed dead rabbits and roadkill in various areas around the refuge and then set up traps to collect carrion insects as they were attracted to the carcasses. She soon noticed that beetles led the parade, not flies.

"It's too early to say if it's a game changer, as it could just be a geographic anomaly," Fujikawa says, but "the fact we saw it and don't know why is most important." Fujikawa's optimism that the research is noteworthy is shared by biologist Jeffrey D. Wells of Florida International University, who was not involved in the research. "It's quite a surprise from the standpoint of carrion ecology," he says. "This is the first example I've seen of carrion beetles behaving according to a different physical scale compared to the typical pattern. Carrion beetles, burying beetles in particular, often win the race to find and monopolize a very small mammal carcass such as a mouse. I've never seen this happen with a rabbit or larger dead mammal. For the forensic entomologist, this raises the possibility that beetles can delay or even eliminate the typical pattern of fly maggots on a corpse. One danger is that if this goes unrecognized, the entomologist might significantly underestimate the time since death."

Fujikawa's advisor Leon Higley, an insect ecologist, echoes this sentiment. "Amanda's work shows there's a lot more variability in insect succession issues" than previously thought, he says. "She is shaping our perceptions of how events actually occur with regard to decomposition."

The evidence also suggests that some postmortem interval estimates may be wrong. There is still much to learn and confirm in the discipline, Fujikawa says, adding: "We still don't have a basic understanding of the biology of maggot development on a carcass: how they respire, how their role in decomposition affects the ecosystem and what they are doing when they are not feeding."

Fujikawa is starting to fill in some of the field's blanks. Her master's thesis demonstrated that adult blowflies can alter the morphology of blood stains at crime scenes. When flies feed on blood, they change the dispersal pattern of the original pool. In addition, they may regurgitate the blood and defecate in a different location. If crime-scene investigators do not know what those little critters are up to, they might interpret a stain as part of the blood spatter when, in fact, it is insect regurgitation and defecation. This could lead them to make false assumptions relating to the scene and crime itself, such as angles and trajectories associated with the death.

Fujikawa has also discovered that insect feces fluoresce under a light source with a wavelength of 465 nanometers and an orange filter, whereas blood will not. This novel insight could be used by crime-scene investigators to distinguish blood spatter from bug activity. She published her research in journals that are used by law enforcement, such as the Journal of Forensic Sciences (see here and here), specifically so that they could easily access and utilize this information.

With a grant from the National Institute of Justice, Fujikawa is now focusing on how blowflies develop under different temperature conditions. This is a key piece of information needed to narrow down PMI since time of death is a calculation based on the age of maggots growing and grazing on a carcass. Fujikawa's research is the first comprehensive study of its kind, Higley says, adding, "I wouldn't be surprised if 50 to 60 years from now, [people] are still referring to her work."

http://phys.org/news/2012-09-chemist-synthesis-expensive-antimalarial-drug.html

Chemist develops new synthesis of most useful, yet expensive, antimalarial drug

Chemists at Indiana University have developed a new synthesis for artemisinin

In 2010 malaria caused an estimated 665,000 deaths, mostly among African children. Now, chemists at Indiana University have developed a new synthesis for the world's most useful antimalarial drug, artemisinin, giving hope that fully synthetic artemisinin might help reduce the cost of the live-saving drug in the future.

Effective deployment of ACT, or artemisinin-based combination therapy, has been slow due to high production costs of artemisinin. The World Health Organization has set a target "per gram" cost for artemisinin of 25 cents or less, but the current cost is about $2.40 per gram, and production of low-cost semi-synthetic artemisinin has yet to materialize.

"In 2005, the WHO claimed that the structure of artemisinin was too complex for cost-effective synthesis," said IU Bloomington College of Arts and Sciences chemistry professor Silas Cook. "We saw this as a natural challenge to the creativity and tenacity of organic chemists."

Published recently in the Journal of the American Chemical Society as "A Concise Synthesis of Artemisinin," Cook and postdoctoral co-author Chunyin Zhu report a succinct five-part process beginning with inexpensive cyclohexenone, an ideal feedstock available on metric-ton scale. Subsequent chemistry highlights several new reactions developed in the Cook group to enable this short, low-cost synthesis.

The result was the production of fully synthetic artemisinin on gram scale, greater than all previous total syntheses combined.

"The key to the ultimate success of synthetic artemisinin will be the large-scale production of the drug," Cook said. "As such, we had to completely rethink what qualified as suitable starting materials for this synthesis and invent new chemistry." The result was the use of readily available commodity chemicals in a process that was shorter than any other artemisinin total synthesis ever conducted.

The next challenge will be to move from gram-scale to kilogram-scale production, a process Cook may or may not be involved with.

"There is still work to be done. And we'd love to do it here, but the project has yet to attract outside funding," he said. "This is still in an experimental phase until you can scale up. We patented it, so the intellectual property rights are in place."

http://vitals.nbcnews.com/_news/2012/09/13/13843610-ebola-out-of-control-in-congo-who-says?lite

Ebola out of control in Congo, WHO says

An Ebola outbreak in Democratic Republic of Congo risks spreading to major towns if not brought under control soon, the World Health Organization said on Thursday.

By Reuters

The death toll has more than doubled since last week to 31, including five health workers. There is no treatment for Ebola, which is highly contagious and can cause internal bleeding. Depending on the strain, it kills between 50 percent and 90 percent of victims.

"The epidemic is not under control. On the contrary the situation is very, very serious," Eugene Kabambi, a WHO spokesman in Congo's capital Kinshasa, told Reuters by telephone.

"If nothing is done now, the disease will reach other places, and even major towns will be threatened," he said.

The disease has so far struck in the towns of Isiro and Viadana in Orientale province in the north east.

In August, 16 people in neighboring Uganda died from Ebola infections, although health experts said the two epidemics are not connected. They have blamed the Congolese outbreak on villagers eating contaminated meat in the forests that cover the region.

http://www.sciencedaily.com/releases/2012/09/120913162437.htm

'Mini' Stroke Can Cause Major Disability, May Warrant Clot-Busters

A transient ischemic attack, TIA or a "mini stroke," can lead to serious disability, but is frequently deemed by doctors too mild to treat

ScienceDaily - A transient ischemic attack, TIA or a "mini stroke," can lead to serious disability, but is frequently deemed by doctors too mild to treat, according to a study in the American Heart Association journal Stroke.

Patients with transient ischemic attack, TIA or "mini" stroke, are not typically given clot-busting drugs because the condition is considered too mild to treat. However, 15 percent of patients had some disability 90 days after a mini stroke. Some patients with minor stroke may benefit from clot-busting drug treatment.

"Our study shows that TIA and minor stroke patients are at significant risk of disability and need early assessment and treatment," said Shelagh Coutts, M.D., lead author of the study at Foothills Hospital in Calgary, Alberta, Canada. "We should be imaging patients earlier and be more aggressive in treating patients with thrombolysis if we can see a blockage no matter how minor the symptoms are."

Thrombolysis is a treatment used to dissolve dangerous clots and restore healthy blood flow to the brain. TIA and minor stroke patients don't typically receive this treatment because the condition is frequently not deemed serious enough to warrant it, researchers said. Among the 499 patients studied, 15 percent had at least minor disability 90 days after their original "mini stroke." Minor disability was defined as being unable to carry out previous activities, but capable of and handling personal affairs without assistance.

Computed tomography (CT) scans showed some "mini stroke" patients had narrowed blood vessels in the brain, and others reported ongoing or worsening symptoms. Those patients were more than twice as likely to have disability at 90 days. Coutts suggests that thrombolysis treatment should be considered in these patients.

Patients with type 2 diabetes had a similarly high risk of disability. Also, women were nearly twice as likely as men to be disabled 90 days after TIA.

"For every second after a mini stroke, the patient's brain may be losing oxygen -- possibly leading to a major event," Coutts said. "If a scan finds that you have a narrowing of a blood vessel in or outside of the brain, you are at a high risk of being disabled." Recurrent strokes posed the greatest threat to patients. Of those who had recurrent strokes, 53 percent were disabled, compared to 12 percent of patients without a recurrent stroke.

In 2009, the American Heart Association/American Stroke Association recommended immediate action and thorough testing for TIA -- much like the exams performed after a full-blown stroke. These exams can show blockage in a brain blood vessel, which can increase patients' risk of a subsequent, more serious event.

"The symptoms of a TIA -- abrupt onset of inability to move one side of your body, numbness on one side, dizziness and trouble walking -- may pass quickly," Coutts said. "But, if you experience them, you should immediately go to the hospital, where proper scans can be done. Based on these results we have started a trial in Canada giving clot busting drugs to patients with mild symptoms, but blocked blood vessels in the brain.

"If ignored, these symptoms can lead to death. This is not a benign disease."

Shelagh B. Coutts, Jayesh Modi, Shiel K. Patel, Heidi Aram, Andrew M. Demchuk, Mayank Goyal, and Michael D. Hill. What Causes Disability After Transient Ischemic Attack and Minor Stroke?: Results From the CT And MRI in the Triage of TIA and Minor Cerebrovascular Events to Identify High Risk Patients (CATCH) Study. Stroke, 2012; DOI: 10.1161/STROKEAHA.112.665141

http://www.sciencedaily.com/releases/2012/09/120913173025.htm

Stress Breaks Loops That Hold Short-Term Memory Together

Psychologists have revealed how stress can addle the mind, as well as how neurons help "remember" information in the first place

ScienceDaily - Stress has long been pegged as the enemy of attention, disrupting focus and doing substantial damage to working memory -- the short-term juggling of information that allows us to do all the little things that make us productive.

By watching individual neurons at work, a group of psychologists at the University of Wisconsin-Madison has revealed just how stress can addle the mind, as well as how neurons in the brain's prefrontal cortex help "remember" information in the first place.

Working memory is short-term and flexible, allowing the brain to hold a large amount of information close at hand to perform complex tasks. Without it, you would have forgotten the first half of this sentence while reading the second half. The prefrontal cortex is vital to working memory.

"In many respects, you'd look pretty normal without a prefrontal cortex," said Craig Berridge, UW-Madison psychology professor. "You don't need that part of the brain to hear or talk, to keep long-term memories, or to remember what you did as a child or what you read in the newspaper three days ago."

But without your prefrontal cortex you'd be unable to stay on task or modulate your emotions well.
"People without a prefrontal cortex are very distractible," Berridge said. "They're very impulsive. They can be very argumentative."
The neurons of the prefrontal cortex help store information for short periods. Like a chalkboard, these neurons can be written with information, erased when that information is no longer needed, and rewritten with something new.
It's how the neurons maintain access to that short-term information that leaves them vulnerable to stress. David Devilbiss, a scientist working with Berridge and lead author on a study published today in the journal PLoS Computational Biology, applied a new statistical modeling approach to show that rat prefrontal neurons were firing and re-firing to keep recently stored information fresh.
"Even though these neurons communicate on a scale of every thousandth of a second, they know what they did one second to one-and-a-half seconds ago," Devilbiss said. "But if the neuron doesn't stimulate itself again within a little more than a second, it's lost that information."
Apply some stress -- in the researchers' case, a loud blast of white noise in the presence of rats working on a maze designed to test working memory -- and many neurons are distracted from reminding themselves of … what was it we were doing again?
"We're simultaneously watching dozens of individual neurons firing in the rats' brains, and under stress those neurons get even more active," said Devilbiss, whose work was supported by the National Science Foundation and National Institutes for Health. "But what they're doing is not retaining information important to completing the maze. They're reacting to other things, less useful things."
Without the roar of white noise, which has been shown to impair rats in the same way it does monkeys and humans, the maze-runners were reaching their goal about 90 percent of the time. Under stress, the animals completed the test at a 65 percent clip, with many struggling enough to fall to blind chance.
Recordings of the electrical activity of prefrontal cortex neurons in the maze-running rats showed these neurons were unable to hold information key to finding the next chocolate chip reward. Instead, the neurons were frenetic, reacting to distractions such as noises and smells in the room.
The effects of stress-related distraction are well-known and dangerous.
"The literature tells us that stress plays a role in more than half of all workplace accidents, and a lot of people have to work under what we would consider a great deal of stress," Devilbiss said. "Air traffic controllers need to concentrate and focus with a lot riding on their actions. People in the military have to carry out these thought processes in conditions that would be very distracting, and now we know that this distraction is happening at the level of individual cells in the brain."
The researchers' work may suggest new directions for treatment of prefrontal cortex dysfunction.
"Based on drug studies, it had been believed stress simply suppressed prefrontal cortex activity," Berridge said. "These studies demonstrate that rather than suppressing activity, stress modifies the nature of that activity. Treatments that keep neurons on their self-stimulating task while shutting out distractions may help protect working memory."
Devilbiss DM, Jenison RL, Berridge CW. Stress-Induced Impairment of a Working Memory Task: Role of Spiking Rate and Spiking History Predicted Discharge. PLoS Computational Biology, 2012; 8 (9): e1002681 DOI: 10.1371/journal.pcbi.1002681

http://www.sciencedaily.com/releases/2012/09/120913173032.htm

No Evidence That Black Cohosh Relieves Menopause Symptoms

Many women coping with hot flashes and other distressing symptoms of menopause have turned to black cohosh supplements

ScienceDaily - Although many women coping with hot flashes and other distressing symptoms of menopause have turned to black cohosh supplements as a treatment alternative, a new review by The Cochrane Library finds no evidence that the herb is effective.
"I was a little surprised of the outcome of the review given the large number of perimenopausal women that use the herb across the globe for the management of menopausal symptoms, as well as the many manufacturers and therapists that promote the herb for this purpose," said lead reviewer Matthew Leach, Ph.D., a research fellow in the School of Nursing & Midwifery at the University of South Australia.
Leach and his co-reviewer evaluated 16 studies involving 2,027 menopausal women. Study participants used an average daily oral preparation of 40 mg of black cohosh for an average of 23 weeks. Treatments for randomly assigned comparison groups included using placeboes, hormone therapy, red clover, or antidepressants.

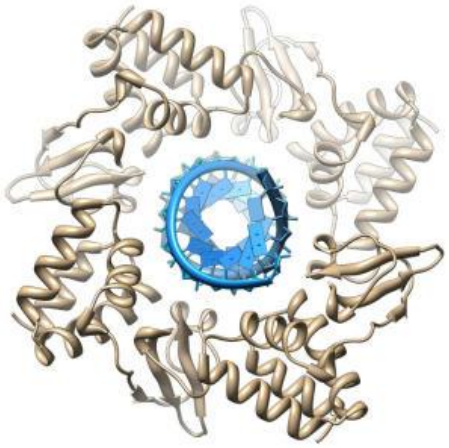
The reviewers found there was insufficient evidence to support the effectiveness of black cohosh for menopausal symptoms. There was no significant difference between it and the placebo groups in changing hot flash frequency. Compared to black cohosh, hormone therapy significantly reduced hot flash frequency.
"I have many women patients who have tried black cohosh," said Brent A. Bauer, M.D., director of the Complementary and Integrative Medicine Program at the Mayo Clinic in Minnesota. "I would say the response seems to roughly fall into three camps: those that get a pretty noticeable improvement in symptoms and continue to use it long term, those that get some improvement but not enough to get enthusiastic about it, and those that try it and perceive no benefit at all."
Matthew J Leach, Vivienne Moore. Black cohosh (Cimicifugaspp.) for menopausal symptoms. Cochrane Database of Systematic Reviews, 2012, Issue 9. Art. No.: CD007244 DOI: 10.1002/14651858.CD007244.pub2

http://www.sciencedaily.com/releases/2012/09/120913173320.htm

How Deadly Marburg Virus Silences Immune System: Breakthrough Findings Point to Targets for Drugs and Vaccines

Scientists at The Scripps Research Institute have determined the structure of a critical protein from the Marburg virus, a close cousin of Ebola virus

ScienceDaily -. These viruses cause similar diseases and are some of the deadliest pathogens on the planet, each killing up to 90 percent of those infected.
Described in the Sept. 13, 2012 publication of the journal PLoS Pathogens, the new research reveals how a key protein component of the Marburg virus, called VP35, blocks the human immune system, allowing the virus to grow unchecked. The structure provides a major step forward in understanding how the deadly virus works, and may be useful in the development of potential treatments for those infected.
"The immune system is designed to recognize certain hallmarks of virus infection," said Erica Ollmann Saphire, the Scripps Research scientist who led the effort. "When these are sensed, an immediate antiviral defense is launched. However, the Marburg and Ebola viruses mask the evidence of their own infection. By doing so, the viruses are able to replicate rapidly and overwhelm the patient's ability to launch an effective defense."



The Marburg virus VP35 protein (beige) surrounds the virus's double-stranded RNA (blue), masking it from immune system detection. (Credit: Image by Christina Corbaci, The Scripps Research Institute)

Deadly Outbreaks

Ebola virus outbreaks have occurred in the last month in both Uganda and the Democratic Republic of the Congo, while Marburg virus broke out in Angola in 2005 to 2006 and again in Uganda in 2007. The Angolan Marburg virus outbreak began in a pediatric ward and killed 88 percent of those it infected. The virus has since been imported into the United States (Colorado) and the Netherlands by tourists who had visited Africa.
There is currently no cure for Marburg hemorrhagic fever. The virus is spread when people come into contact with the bodily fluids of a person or animal who is already infected. The best treatment consists of administering fluids and taking protective measures to ensure containment, like isolating the patient and washing sheets with bleach.
Most people, however, die within two weeks of exposure from a combination of dehydration, massive bleeding, and shock. A smaller number of people have stronger and immediate immune responses against the virus and survive.

A New Roadmap for Defense

The breakthrough described in the PLoS Pathogens article explains a key reason why the viruses are so deadly and provides the necessary templates to develop drugs to treat the infection.
The study's lead author, Research Associate Shridhar Bale, explains that a key signature of Marburg virus infection is the double-stranded RNA that results from its replication inside cells. When human immune system proteins detect this virus-specific RNA, they sound an alarm to signal the rest of the immune system to respond. The new research describes how the VP35 protein of the Marburg virus binds to the viral double-stranded RNA and hides it to prevent the alarm from being sounded.
The new research also revealed a surprise. Images from the Marburg virus reveal the VP35 protein spirals around the double-stranded RNA, enveloping it completely. This is in contrast to previous images of the similar VP35 protein from Ebola virus that showed it only capping the ends of the RNA, leaving the center of the RNA helix exposed for possible recognition.

In addition to Ollmann Saphire and Bale, the article, "Marburg virus VP35 can both fully coat the backbone and cap the ends of dsRNA for interferon antagonism," was authored by Jean-Philippe Julien, Zachary A. Bornholdt, Michelle A. Zandonatti, Gerard J.A. Kroon, Christopher R. Kimberlin, Ian J. MacRae, and Ian A. Wilson of The Scripps Research Institute, and Peter Halfmann, John Kunert, and Yoshihiro Kawaoka of the University of Wisconsin.

Support for the research was provided by grants from the Burroughs Wellcome Fund and The Skaggs Institute for Chemical Biology at Scripps Research.

Bale S, Julien J-P, Bornholdt ZA, Kimberlin CR, Halfmann P, et al. Marburg Virus VP35 Can Both Fully Coat the Backbone and Cap the Ends of dsRNA for Interferon Antagonism. PLoS Pathog. PLoS Pathogens, 2012; 8(9): e1002916 DOI: 10.1371/journal.ppat.1002916

http://www.sciencedaily.com/releases/2012/09/120913203653.htm

Neural Implant Recovers Ability to Make Decisions, Monkey Study Shows

A key step towards recovering specific brain functions in sufferers of brain disease and injuries

ScienceDaily - Researchers have taken a key step towards recovering specific brain functions in sufferers of brain disease and injuries by successfully restoring the decision-making processes in monkeys.

By placing a neural device onto the front part of the monkeys' brains, the researchers, from Wake Forest Baptist Medical Centre, University of Kentucky and University of Southern California, were able to recover, and even improve, the monkeys' ability to make decisions when their normal cognitive functioning was disrupted.

The study, which has been published today (Sept. 14) in IOP Publishing's Journal of Neural Engineering, involved the use of a neural prosthesis, which consisted of an array of electrodes measuring the signals from neurons in the brain to calculate how the monkeys' ability to perform a memory task could be restored.

In the delayed match-to-sample task an image was flashed onto a screen and, after a delay, the monkeys were prompted to select the same image on the screen from a sampling which included 1-7 other images. Five monkeys (all rhesus, Macaca mulatta) were involved in the experiment and were trained for two years to perform to a 70-75 per cent proficiency in the task.

The movement of the monkeys' arms were tracked with a camera and translated to movements of the cursor on the screen; they were awarded with a drop of juice when they correctly matched an image.

The prosthesis was placed into two cortical layers -- L2/3 and L5 -- of the brain and recorded brain activity within structures known as minicolumns in the prefrontal cortex area.

Once it was confirmed that minicolumn communication between layers L2/3 and L5 was involved in decision making, it was suppressed by administering the dopamine-modifying drug, cocaine, to the monkeys. The task was performed again but this time the researchers deployed a 'multi-input multi-output nonlinear' (MIMO) model to stimulate the neurons that were used in the task.

"The MIMO model is a specific type of calculation which looks for the complex mathematical relationship between an input (L2/3) and an output (L5). In the case of neural activity, the output is typically the pattern of firing of individual neurons during the task.

"Inputs to that pattern may be blood flow, temperature, the electrical activity of other neurons, and even the prior electrical activity of the same cell," said lead author of the study Professor Robert Hampson.

By recording the inputs from layer L2/3 neurons, the MIMO model could predict the output of layer L5 neurons and thus, through the electrodes, electrically stimulate the same necessary L5 neurons. The results showed that the MIMO model was exceedingly effective in recovering performance of the task and was even able to improve performance under normal conditions.

"The reason the MIMO model was effective in improving performance in the task was because we specifically 'tuned' the model to analyze the firing of neurons that occurred when the animals correctly performed the behavioral task; the brain doesn't always produce the full 'correct' pattern on every trial," said senior author Professor Sam Deadwyler.

On the utilization of this method in the treatment of human brain conditions, Professor Deadwyler continued: "In the case of brain injury or disease where larger areas are affected, the system would record the inputs to that area from other areas and, when they occur, program the delivery of the appropriate output patterns to brain regions that normally receive signals from the injured area, thereby restoring lost brain function."

All animal procedures were reviewed and approved by the Institutional Animal Care and Use Committee of Wake Forest University, in accordance with U.S. Department of Agriculture, International Association for the Assessment and Accreditation of Laboratory Animal Care, and National Institutes of Health guidelines.

Robert E Hampson, Greg A Gerhardt, Vasilis Marmarelis, Dong Song, Ioan Opris, Lucas Santos, Theodore W Berger, Sam A Deadwyler. Facilitation and restoration of cognitive function in primate prefrontal cortex by a neuroprosthesis that utilizes minicolumn-specific neural firing. Journal of Neural Engineering, 2012; 9 (5): 056012 DOI: 10.1088/1741-2560/9/5/056012

http://www.eurekalert.org/pub_releases/2012-09/rb-lfw091412.php

Learning faster with neurodegenerative disease

Huntington's gene mutation carriers: Severity of the genetic mutation related to learning efficiency

People who bear the genetic mutation for Huntington's disease learn faster than healthy people. The more pronounced the mutation was, the more quickly they learned. This is reported by researchers from the Ruhr-Universität Bochum and from Dortmund in the journal Current Biology. The team has thus demonstrated for the first time that neurodegenerative diseases can go hand in hand with increased learning efficiency. "It is possible that the same mechanisms that lead to the degenerative changes in the central nervous system also cause the considerably better learning efficiency" says Dr. Christian Beste, head of the Emmy Noether Junior Research Group "Neuronal Mechanisms of Action Control" at the RUB.

Passive learning through repeated stimulus presentation

In a previous study, the Bochum psychologists reported that the human sense of vision can be changed in the long term by repeatedly exposing subjects to certain visual stimuli for short periods (we reported in May 2011, http://aktuell.ruhr-uni-bochum.de/pm2011/pm00136.html.de). The task of the participants was to detect changes in the brightness of stimuli. They performed better if they had viewed the stimuli passively for a while first. In the current study, the researchers presented the same task to 29 subjects with the genetic mutation for Huntington's disease, who, however, did not yet show any symptoms. They also tested 45 control subjects without such mutations in the genome. In both groups, the learning efficiency was better after passive stimulus presentation than without the passive training. Subjects with the Huntington's mutation, however, increased their performance twice as fast as those without the mutation.

Glutamate may have paradoxical effect

Degenerative diseases of the nervous system are based on complex changes. A key mechanism is an increased release of the neurotransmitter glutamate. However, since glutamate is also important for learning, in some cases it could lead to the paradoxical effect: better learning efficiency despite degeneration of the nerve cells.

Detecting differences in brightness under aggravated conditions

In each experimental run, the subjects saw two consecutive small bars on a computer screen that either had the same or different brightness. Sometimes, however, not only the brightness changed from bar one to bar two, but also the orientation of the bar (vertical or horizontal). "Normally, the distraction stimulus, i.e. the change in orientation, draws all the attention" Christian Beste explains. "But after the passive training with the visual stimuli, the distraction stimulus has no effect at all." The shift of attention from the non-relevant to the relevant properties of the stimulus was also visible in the electroencephalogram (EEG) in brain areas for early visual processing.

Better performance with stronger mutation

In Huntington's disease, a short segment of a gene is repeated. The number of repetitions determines when the disease breaks out. In the present study, a greater number of repetitions was, however, also associated with higher learning efficiency. "This shows that neurodegenerative changes can cause paradoxical effects" says Christian Beste. "The everyday view that neurodegenerative changes fundamentally entail deterioration of various functions can no longer be maintained in this dogmatic form."

C. Beste, E. Wascher, H.R. Dinse, C. Saft (2012): Faster perceptual learning through excitotoxic neurodegeneration, Current Biology, doi: 10.1016/j.cub.2012.08.012

http://www.sciencedaily.com/releases/2012/09/120914123812.htm

Surgery Has a More Profound Effect Than Anesthesia On Brain Pathology and Cognition in Alzheimer's

Post-operative cognitive decline is the loss of cognitive abilities, usually in older adults, in the days to weeks after surgery

ScienceDaily - A syndrome called "post-operative cognitive decline" has been coined to refer to the commonly reported loss of cognitive abilities, usually in older adults, in the days to weeks after surgery. In fact, some patients time the onset of their Alzheimer's disease symptoms from a surgical procedure. Exactly how the trio of anesthesia, surgery, and dementia interact is clinically inconclusive, yet of great concern to patients, their families and physicians.

A year ago, researchers at the Perelman School of Medicine at the University of Pennsylvania reported that Alzheimer's pathology, as reflected by cerebral spinal fluid biomarkers, might be increased in patients after surgery and anesthesia. However, it is not clear whether the anesthetic drugs or the surgical procedure itself was responsible. To separate these possibilities, the group turned to a mouse model of Alzheimer's disease.

The results, published online this month in the Annals of Surgery, shows that surgery itself, rather than anesthesia, has the more profound impact on a dementia-vulnerable brain.
The team, led by Roderic Eckenhoff, MD, Austin Lamont Professor of Anesthesia, exposed mice with human Alzheimer disease genes, to either anesthesia alone, or anesthesia and an abdominal surgery. The surgery was similar to appendectomy or colectomy, very common procedures in humans. They found that surgery causes a lasting increase in Alzheimer's pathology, primarily through a transient activation of brain inflammation. Also, a significant cognitive impairment persisted for at least 14 weeks after surgery compared to controls receiving anesthesia alone. Neither surgery nor anesthesia produced changes in normal non-transgenic animals.
"In the mice, there was a clear and persistent decrement in learning and memory caused by surgery as compared with inhalational anesthesia -- but only in the context of a brain made vulnerable by human Alzheimer-associated transgenes," notes Eckenhoff.
He also notes that at the time of surgery, the AD mice showed no outward symptoms of AD, despite having subtle evidence of ongoing neuropathology. "This timeline is analogous to both the age range and cognitive status of many of our patients presenting for a surgical procedure and suggests the window of vulnerability to surgery of the Alzheimer's brain extends into this pre-symptomatic period," says Eckenhoff. This period might be analogous to what is now called prodromal AD.
"On the other hand," cautions Maryellen Eckenhoff, PhD, a neuroscientist on the team, "the brain vulnerability seen in the AD mice may not translate well to people." The AD mice used, like all current mouse models of Alzheimer disease, more closely resemble the situation in familial Alzheimer disease, which constitutes only a small minority of patients. She points out that it is not yet clear whether results from AD mouse models will represent patients who eventually get late-onset, or "sporadic" Alzheimer disease. These mice are, however, the current standard of choice for screening new drugs and have yielded considerable insight into Alzheimer pathogenesis.
The mechanism linking surgery and the cognitive effects seems to be inflammation. An inflammatory process is well known to occur as a result of surgery, at least outside the central nervous system. How this inflammatory process gains access to the brain, and accelerates AD pathology in a persistent way is still unclear.
Postoperative cognitive decline has not been convincingly demonstrated to persist after three months in most people, and whether it predicts later dementia is still unclear. This study suggests that in the setting of a vulnerable brain, the cognitive deficits after surgery might be irreversible.
However, the finding that inflammation is the underlying mechanism, immediately suggests a strategy for mitigating injury. "Human studies will be needed to first confirm these findings and then begin to deploy anti-inflammatory strategies to minimize injury," adds Eckenhoff. "As a profession, doctors need to understand the long-term implications of our care, both positive and negative, and do all we can to delay the onset of dementia."
Co-authors, all from Penn, are Junxia X. Tang, Feras Mardini, Luke S. Janik, Sean T. Garrity, Rosie Q. Li, and Gulnaz Bachlani.
This study was funded by the National Institute on Aging (Grant AG031742) and the Austin Lamont Endowment Fund.
Junxia X. Tang, Feras Mardini, Luke S. Janik, Sean T. Garrity, Rosie Q. Li, Gulnaz Bachlani, Roderic G. Eckenhoff, Maryellen F. Eckenhoff. Modulation of Murine Alzheimer Pathogenesis and Behavior by Surgery. Annals of Surgery, 2012; DOI: 10.1097/SLA.0b013e318269d623

http://phys.org/news/2012-09-ceria-nanoparticles-lessen-ischemic.html

Ceria nanoparticles could lessen the damage from ischemic strokes

Researchers propose a new approach for treatment: Ceria nanoparticles could trap the reactive oxygen compounds that result from ischemia

Phys.org - The most common form of strokes are caused by a sudden reduction in blood flow to the brain (ischemia) that leads to an inadequate supply of oxygen and nutrients. These so-called ischemic strokes are one of the leading causes of death and disability in industrialized nations. If they are not immediately remedied by medical intervention, areas of the brain may die off. In the journal Angewandte Chemie, Korean researchers have now proposed a new approach for supplemental treatment: Ceria nanoparticles could trap the reactive oxygen compounds that result from ischemia and cause cells to die.
When blood flow to areas of the brain is restricted, reactive oxygen compounds like superoxide radical anions ($O_2^{\bullet -}$), hydrogen peroxide (H_2O_2), and hydroxyl radicals ($HO^{\bullet -}$) form and accumulate. These species cause oxidative damage and are responsible for tissue damage and cell death during a stroke. Nerve connections and neurovascular units are destroyed and the function of the brain in these areas stops. Despite various treatments that primarily combat the causes of reduced blood flow, such as thrombosis, there has been no way to protect

nerves from oxidative damage after an acute ischemic stroke. Seung-Hoon Lee, Taeghwan Hyeon, and their team at Seoul National University hope that nanoparticles made of ceria may represent a new approach for treatment.

Cells contain enzymes that can break down reactive oxygen species: superoxide dismutases, which convert superoxide anions to hydrogen peroxide; and catalase, which splits hydrogen peroxide. Ceria nanoparticles can do both. How does this work? The cerium in ceria crystals is present in the form of Ce4+. However, if the particle size is reduced to a few nanometers in diameter, some spots on the surface are missing oxygen atoms. These places have Ce3+ instead, which can easily be reduced back to Ce4+ and can reversibly bind oxygen.

The researchers treated cell cultures with a substance that increases the concentrations of reactive oxygen species, which leads to increased cell death. Treatment with cerium oxide nanoparticles drastically improved the cell survival rate. In animal trials, the researchers induced ischemic strokes in rats. Intravenously administered ceria nanoparticles considerably reduced the stroke volume and nerve damage. An optimized, carefully balanced dose is necessary, however.

Interestingly, the concentrations of ceria nanoparticles in the healthy areas of the brain were very low, while those in the ischemic areas were drastically elevated. The researchers speculate that the ceria nanoparticles can barely pass through the intact blood-brain barrier. However, the barrier is damaged in the ischemic areas, allowing the diseased areas of the brain to be reached and oxidative damage to be stopped.

More information: Taeghwan Hyeon, Ceria Nanoparticles that Protect against Ischemic Stroke, Angewandte Chemie International Edition, dx.doi.org/10.1002/anie.201203780

http://www.bbc.co.uk/news/science-environment-19598980

Conflict and 'boom-bust' explain humans' rapid evolution

What explains the extraordinarily fast rate of evolution in the human lineage over the past two million years?

By Paul Rincon Science editor, BBC News website, Gibraltar

A leading human origins researcher has come up with an idea that involves aggression between groups and the boom-bust cycles that have punctuated our spread into new environments.

Prof Ian Tattersall said there were few examples to rival the accelerated evolution that led to our species.

He was speaking at this year's Calpe conference in Gibraltar.

"However you slice it, evolution within this [human family] has been very rapid indeed," Prof Tattersall, from the American Museum of Natural History (AMNH) in New York, told the conference.

"I think it's fair to say that our species Homo sapiens and its antecedents have come much farther, much faster than any other mammalian group that has been documented in this very tight time-frame."

This phenomenon of accelerated evolution is known as "tachytely". Among our ancestors, brain size doubled between two million and one million years ago. Then it has almost doubled again between one million years and the present day. Along with the increase in brain size came a reduction in the size of the teeth and face along with other changes in the skull.

The increase in brain size seems to have coincided with a modern physique characterised by a linear shape, long legs and relatively narrow hips. These features can already be seen in the skeleton of the "Turkana boy" from Kenya, who lived about two million years ago.

This contrasts sharply with the short legs and long arms of the Turkana boy's antecedent "Lucy" (Australopithecus afarensis), who lived in Ethiopia about one million years earlier.

Radical shift

Such fast change is not seen among apes, and while Prof Tattersall acknowledges the importance of the move our ancestors made from a tree-dwelling, to a ground-dwelling existence - something which has not affected our primate cousins - he says it is not enough to explain what is observed.

"Clearly the definitive abandonment of dependence on trees... has to count as one of the most radical shifts in adaptive zone ever made by any vertebrate since the very first tetrapod heaved itself out of water and on to terra firma," he said.

"Under natural conditions, it is very hard to see how the initial invasion of a new ecozone by hominids could have so consistently driven rapid change over the long period of time that we're talking about."

Human culture was probably the special, consistently present ingredient that drove the continuing fast pace of change in our lineage after we left the forests, said Prof Tattersall, but not in the way that some other researchers have proposed.

Certain evolutionary psychologists have popularised a model in which culture and brain complexity spurred each other on to greater heights in humans.

But Prof Tattersall said the way our technology transformed in fits and starts, along with the way these changes were often separated from biological evolution, meant this idea was not as good a fit for what is seen in the archaeological and fossil records. Aggression between small, distinct human groups in the past is one of the major remaining agents of such changes, he said.
"Inter-group conflict would certainly have placed a premium on such correlates of neural function as planning and throwing," Prof Tattersall explained. "If we were somehow able to implicate conflict among groups as a selective agent for increasing intelligence within groups, this might explain the otherwise quite mystifying independent increases in brain size that we see in several different lineages within the genus Homo."
Such conflict could be seen as a form of predation. And, predation is regarded as a classic example of the "Red Queen" hypothesis whereby prey and predator become faster or more cunning in a self-reinforcing way.
Indeed, there are hints of such conflict from the sparse fossil record. A paper published this month in the Journal of Human Evolution suggested that ancient humans in northern Spain were engaged in inter-group cannibalism against another band of people.

Extreme swings

Culture, in the form of clothing, fire use and the construction of shelters, has allowed humans to expand into environments that their relatively frail bodies could not otherwise have coped with. But both culture and technology have their limits. And relatively good climatic conditions would have favoured population expansions. This made the artificially enlarged ancient human populations vulnerable to fragmentation when environmental conditions worsened.
During the onset of an Ice Age or a drought, human populations would have contracted, driving the remaining small, isolated human groups to diversify - developing different biological traits from one another.
The wild environmental fluctuations in Pleistocene times - from about 2.5 million to 11,000 years ago - would have provided the ideal conditions for this to happen, the AMNH professor of palaeoanthropology explained.
When conditions improved again, populations that had developed different characteristics would have come into contact again. This might have increased the likelihood of competition between distinct groups, but also allowed genetic novelties to spread that would not have arisen without the initial fragmentation.
Prof Tattersall refers to the phenomenon as the "ratchet effect" and pointed to the large variation in human fossils from the early Pleistocene in Africa as an example, which may support his hypothesis.
At the conference, Richard Wrangham from Harvard University offered an alternative view, questioning the role of conflict as a driver. He pointed out that human hunter-gatherers had similar rates of inter-group aggression to chimpanzees.
The Calpe '12 conference runs from 13-16 September in Gibraltar.

http://www.eurekalert.org/pub_releases/2012-09/iaft-ssb091212.php

Study shows breath analysis could help diagnose pulmonary nodules

In pilot study, authors recommend using larger cohort to validate results

DENVER – A pilot study, published in the October 2012 issue of the International Association for the Study of Lung Cancer's (IASLC) Journal of Thoracic Oncology, showed that breath testing could be used to discriminate between benign and malignant pulmonary nodules. The study looked at 74 patients who were under investigation for pulmonary nodules and attended a referral clinic in Colorado between March 2009 and May 2010.
Researchers from Israel and Colorado collected exhaled breath from each patient, analyzing the exhaled volatile organic compounds using gas chromatography with mass spectrometry and information from chemical nanoarrays, which have been developed by Prof. Hossam Haick and his colleagues in the Technion-Israel Institute of Technology. The patients also underwent a bronchoscopy, wedge resection and/or lobectomy, whichever was required for final diagnosis. Nodules that either regressed or remained stable over a 24-month period were considered benign. The two techniques accurately identified that 53 pulmonary nodules were malignant and 19 were benign. Furthermore, the nanoarrays method discriminated between adenocarcinoma and squamous cell carcinoma and between early versus advanced disease.
This kind of testing could help solve some of the problems computed tomography screening has created. While low-dose CT screening has reduced the mortality rate by 20 percent, many people have to undergo invasive procedures only to find out their pulmonary nodules are not cancerous. The false positive rate is 96 percent. This testing could serve as a secondary screener for patients who were found to have pulmonary nodules after CT screening.
Authors say, "the reported breath test in this study could have significant impact on reducing unnecessary inves¬tigation and reducing the risk of procedure-related morbid¬ity and costs. In addition, it could facilitate

faster therapeutic intervention, replacing time-consuming clinical follow-up that would eventually lead to the same intervention."

The leading authors of this work include Dr. Nir Peled, Meggie Hakim and IASLC member Dr. Hossam Haick. Co-authors include AISCL members Dr. Paul Bunn, Dr. York Miller, Dr. Fred Hirsch, Dr. Timothy Kennedy and Dr. John Mitchell.

http://www.scientificamerican.com/article.cfm?id=led-lightbulb-concerns

The Dark Side of LED Lightbulbs

LEDs contain lead, arsenic and a dozen other potentially dangerous substances

Dear EarthTalk: Are there health or environmental concerns with LED lightbulbs, which may soon replace compact fluorescents as the green-friendly light bulb of choice?—Mari-Louise, via e-mail

Indeed, LED (light emitting diode) lighting does seem to be the wave of the future right now, given the mercury content and light quality issues with the current king-of-the-hill of green bulbs, the compact fluorescent (CFL). LEDs use significantly less energy than even CFLs, and do not contain mercury. And they are becoming economically competitive with CFLs at the point of purchase while yielding superior quality lighting and energy bill savings down the line.

But LEDs do have a dark side. A study published in late 2010 in the journal Environmental Science and Technology found that LEDs contain lead, arsenic and a dozen other potentially dangerous substances. LEDs are touted as the next generation of lighting," says Oladele Ogunseitan, one of the researchers behind the study and chair of the University of California (UC)-Irvine's Department of Population Health & Disease Prevention. "But as we try to find better products that do not deplete energy resources or contribute to global warming, we have to be vigilant [about] toxicity hazards…."

Ogunseitan and other UC-Irvine researchers tested several types of LEDs, including those used as Christmas lights, traffic lights, car headlights and brake lights. What did they find? Some of the worst offenders were low-intensity red LEDs, which were found to contain up to eight times the amount of lead, a known neurotoxin, allowed by California state law and which, according to researchers, "exhibit significant cancer and noncancer potentials due to the high content of arsenic and lead." Meanwhile, white LEDs contain the least lead, but still harbor large amounts of nickel, another heavy metal that causes allergic reactions in as many as one in five of us upon exposure. And the copper found in some LEDs can pose an environmental threat if it accumulates in rivers and lakes where it can poison aquatic life.

Ogunseitan adds that while breaking open a single LED and breathing in its fumes wouldn't likely cause cancer, our bodies hardly need more toxic substances floating around, as the combined effects could be a disease trigger. If any LEDs break at home, Ogunseitan recommends sweeping them up while wearing gloves and a mask, and disposing of the debris — and even the broom — as hazardous waste. Furthermore, crews dispatched to clean up car crashes or broken traffic lights (LEDs are used extensively for automotive and traffic lighting) should wear protective clothing and handle material as hazardous waste. LEDs are currently not considered toxic by law and can be disposed of in regular landfills.

According to Ogunseitan, LED makers could easily reduce the concentrations of heavy metals in their products or even redesign them with truly safer materials, especially if state or federal regulators required them to do so. "Every day we don't have a law that says you cannot replace an unsafe product with another unsafe product, we're putting people's lives at risk," he concludes. "And it's a preventable risk."

Of course, we all need some kind of lighting in our lives and, despite their flaws, LEDs may still be the best choice regarding light quality, energy use and environmental footprint. That said, researchers are busy at work on even newer lighting technologies that could render even today's green choices obsolete.

CONTACT: UC-Irvine study, www.pubs.acs.org/doi/abs/10.1021/es101052q?prevSearch=irvine%2Bled.

http://blogs.scientificamerican.com/unofficial-prognosis/2012/09/15/but-who-will-the-doctor-confide-in/

But who will the doctor confide in?

Given the number of decisions doctors make on a daily basis, errors are inevitable. The problem is that there is no forum to talk about them.

By Ilana Yurkiewicz | September 15, 2012

He was a family practitioner. He had a good relationship with the couple, helping to deliver their first baby two years earlier. He was happy to learn the reason for their appointment was that were expecting another.

The second pregnancy could not have gone worse. Though she showed all the telltale signs and felt as though she was carrying a child, the four tests were consistent: No pregnancy. No pregnancy. No pregnancy. No pregnancy.

He knew the couple would be devastated. Mom's tears showed he was right.

It was only midway through the D and C to clean out her uterus that Dr. David Hilfiker came to the horrifying realization that the fetus inside had been alive.

A story like this could destroy a doctor's career. Editors at the *New England of Medicine*, the place where it was submitted, understood this well. That's why one of them called Hilfiker in the fall of 1983 to make sure he still wanted to go through with it. He did, and it was published in 1984.

Why did he do it? Why tell this story publicly, risking his practice and his reputation?

The case was deeply disturbing. But perhaps one of the most disturbing parts was that it was not unique. Hilfiker goes on in the piece to tell tales of other errors, from the severe to the more mundane. A boy whom he diagnosed with a dislocated foot but who actually had a severe case of compartment syndrome that required immediate surgery. A woman with chest pains whom he advised not to go to the emergency room, and who twenty minutes later went into cardiac arrest and died. Unnecessary hospital admissions that waste money and resources.

Given the number of decisions doctors make on a daily basis, he said, errors are inevitable. The problem is that there is no forum to talk about them.

"The medical profession simply seems to have no place for its mistakes. There is no permission given to talk about errors, no way of venting emotional responses. Indeed, one would almost think that mistakes are in the same category as sins: it is permissible to talk about them only when they happen to other people."

1984. What was the climate of medicine like?

When the piece went public, one hundred and fifty people were moved to write letters in response. But according to Hilfiker, among those only two were negative, questioning his ability as a doctor. The rest – many of them from other caregivers – expressed feelings of identification, of sympathy, and of praise. Letters from around the nation thanked Hilfiker for speaking out about something that was universally experienced but that never dared to be uttered.

Then there were others. In the moving piece "The day Joy died," Dr. Gary P. Brandeland speaks of the painful aftermath of a 1986 incident when a 21-year-old patient of his died because of an anesthesia mistake.

"For months afterward, I felt like I was being beaten with a baseball bat, physically and emotionally. Out of the 52 doctors in our clinic, only one, an ophthalmologist, asked me how I was doing. For everyone else, it was business as usual. This lack of support from colleagues was a surprise and a huge disappointment. I was treated like some kind of disease they might catch."

Another, a reflection piece by a doctor who trained in the 1980s and who preferred to remain anonymous:

"Early in our training we learned that doctors had a higher instance of alcoholism, drug abuse, suicide, marriage, break up and a lower life expectancy than the general population. In sharp contrast to other at risk groups, we were not offered any strategies to deal with these risks – it seemed that it was up to me."

Common themes are not difficult to find: a culture of expected perfection; no room to be open about mistakes; and the healing of physicians ignored.

Since the 1980s, there have been big movements in both reducing the number of errors doctors make and disclosing them to patients when they happen anyway. Things like checklists and electronic health records may accomplish the former, while research showing that the risk of litigation actually decreases with increasing disclosure encourages the latter. In 1999, the Institute of Medicine released "To Err is Human: Building A Safer Health System," which formulated specific recommendations for cutting down on preventable adverse events.

But there still remains the next step: a doctor recovering for him or herself.

We certainly ought to focus on reducing errors. But no matter how great the strides, mistakes will never vanish completely. Errors do not have to stem from gaps in competence to have consequences. Being tired or careless can lead to devastating outcomes. But so too can taking risks to help a patient.

"Don't expect to be perfect," an older doctor once advised me soberly. For doctors-in-training, the idea that we could someday be responsible for a major injury or death is an unbearable thought. We study hard and hope that will be enough. But we know in the back of our minds that it doesn't work that way.

We can't expect to never make mistakes. We can only prepare for how we will grapple with them.

2012.

When I first read Hilfiker's piece, I had two main reactions. One was appreciating the genuine and courageous character that shone through his writing. Two was thinking how foreign his world felt.

A few months ago, I wrote about a challenging patient encounter I experienced as a first-year medical student. I walked into a room on a general medicine ward and ended up in an emotional minefield I felt unequipped to navigate. My patient desperately needed help, but it was help I couldn't provide. I left shaken, worried that my visit had done more harm than good.

When I reported the case to my three preceptors, they were just as interested in how I was holding up emotionally as in how well I had gathered my patient's history of present illness. Each had words of wisdom on how to bounce back after an incident like that. I was able to discuss things I felt I did right and others I felt I did wrong. I received feedback on how to improve, without feeling judged.

The relationship went both ways. One time one of our preceptors told us about a difficult patient situation of her own that was causing her guilt, and she welcomed our thoughts on grappling with it. We were in a safe space that focused on improvement over perfection and that encouraged us to embrace our emotional impulses.

You could argue that as a student, I am expected to make mistakes, and that the "yoke of perfection" Hilfiker talks of does not yet apply to me. You could also argue that my experiences with these doctors are not universal, and that for every caregiver who welcomes the expression of emotions there remain others who eschew it as a sign of weakness. All this would be true.

But from my limited experiences in settings of care so far, there seems to a shift in climate away from what Hilfiker bemoaned. It is certainly not absolute. But we recognize today that doctors are human beings with feelings: feelings that will be damaged when things go wrong, and feelings that need outlets for healthy processing and healing. We recognize that we should be cultivating that type of openness, not stifling it. My education reflects that awareness. As patient safety activist Linda K. Kenney captured the change:

"Back in 2002, a literature search on physician/clinician support would turn up very little. Today, that same search would yield a tremendous amount on the subject. Physicians are more willing to speak more publicly about the emotional impact of these events."

I am grateful that "how are you feeling?" is a question not just for patients anymore. And I hope it continues. Because one day, I may make an error that falls in the category of more than mundane. I am terrified for that day. But if it comes, I pray I will be in an environment that cares for me so that I may be strong enough to care for the one I hurt, for my other patients – and for myself.

About the Author: *Ilana Yurkiewicz is a second year student at Harvard Medical School who graduated from Yale University with a B.S. in biology. She was a science reporter for The News & Observer in Raleigh, North Carolina via the AAAS Mass Media Fellowship and then went on to write for Science Progress in Washington, DC. She has an academic interest in bioethics, currently conducting ethics research at Harvard after previously interning at the Presidential Commission for the Study of Bioethical Issues. Follow on Twitter @ilanayurkiewicz.*

http://www.scientificamerican.com/podcast/episode.cfm?id=bird-seed-poisons-wild-birds-12-09-16

Bird Seed Poisons Wild Birds

To improve shelf life, Scotts Miracle-Gro used a pesticide toxic to birds in its bird seed. David Biello reports

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Birds face many man-made mortal threats: windows, cats, habitat destruction, even climate change. And now, there's poison—in their bird seed.

You see the Scotts Miracle-Gro Company had been in the habit of applying banned pesticides to its wild bird food products. In particular, the company applied a chemical known as Storcide II to its bird food despite a warning label for that product that reads "Storcide II is extremely toxic to fish and toxic to birds and other wildlife."

Why add a compound toxic to birds to food meant to be eaten by birds? Because Scott didn't want bugs infesting its bird food during storage.

By the time Scotts stopped adding the pesticide in March 2008, the company had sold some 70 million bags of adulterated bird food. The company also submitted false documents to the U.S. Environmental Protection Agency, distributed pesticides with misleading labels and distributed illegal pesticides. As a result, the EPA slapped the company with $12.5 million in criminal fines and civil penalties.

So when you put out new bird seed this winter, at least you won't be inadvertently poisoning any chirpers. Oh, and keep those cats inside too.

—David Biello

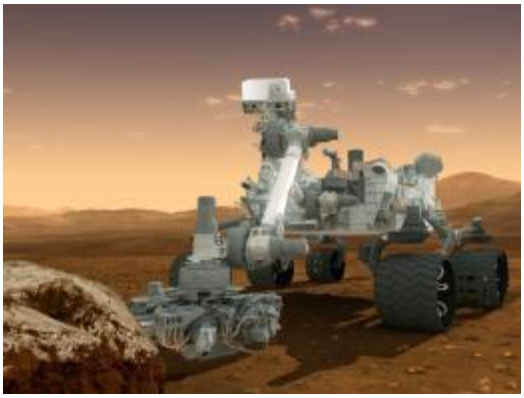
http://phys.org/news/2012-09-drill-bits-rover-contaminate-mars.html

Drill bits on rover could contaminate Mars

For all the hopes NASA has pinned on the rover it deposited on Mars last month, one wish has gone unspoken: Please don't find water.

Scientists don't believe they will. They chose the cold, dry equatorial landing site in Mars' Gale Crater for its geology, not its prospects for harboring water or ice, which exist elsewhere on the planet. But if by chance the rover Curiosity does find water, a controversy that has simmered at NASA for nearly a year will burst into the

open. Curiosity's drill bits may be contaminated with Earth microbes. If they are, and if those bits touch water, the organisms could survive.
The possible contamination of the drill bits occurred six months before the rover's launch last Nov. 26. The bits had been sterilized inside a box to be opened only after Curiosity landed on Mars.
But that changed after engineers grew concerned that a rough landing could damage the rover and the drill mechanism. They decided to open the box and mount one bit in the drill as a hedge to ensure success of one of the most promising scientific tools aboard Curiosity. The drill is to bore into rocks looking for clues that life could have existed on the planet. Even if a damaged mechanism couldn't load a drill bit, at least the rover would have one ready to go.
Under the agency's procedures, the box should not have been opened without knowledge of a NASA scientist who is responsible for guarding Mars against contamination from Earth. But Planetary Protection Officer Catharine Conley wasn't consulted. "They shouldn't have done it without telling me," she said. "It is not responsible for us not to follow our own rules."
Those rules required sterilization of any part of Curiosity that will touch the surface of the planet, including the drill bits and all six of the rover's wheels. The precaution was taken to preserve the ability to explore water or ice - even if the chances of finding it were remote.
Conley, a microbiologist, said she learned about the unsealing of the box shortly before the launch. By then, it was too late to fix.
Other NASA officials said the decision to open the box of drill bits was a calculated risk.
"Water or ice near the surface in Gale Crater was not a significant probability," said David Lavery, program executive for solar system exploration at NASA headquarters. "We weighed that against the risks of not having a bit mounted in the drill prior to launch, and the specter of not being able to drill any holes at all on Mars."
"Of course, there is always a possibility that Mars will surprise us," Lavery said.



This artist's concept features NASA's Mars Science Laboratory Curiosity rover, a mobile robot for investigating Mars' past or present ability to sustain microbial life. **Image credit: NASA/JPL-Caltech**

The box containing the bits was unsealed in a near-sterile environment, he said. Even so, the breach was enough to alter aspects of the mission and open a rift at NASA between engineers and planetary protection officials.
Curiosity was first proposed in 2004 under a mission category that would have allowed it to explore a region with ice and water. That category called for sterilizing portions of the spacecraft that would contact the surface of Mars to avoid contamination of moist areas where microbes - from Earth or from Mars - have the best chances of survival.
On Nov. 1, after learning that the drill bit box had been opened, Conley said she had the mission reclassified to one in which Curiosity could touch the surface of Mars "as long as there is no ice or water."
Conley's predecessor at NASA, John D. Rummel, a professor of biology at East Carolina University, said, partly in jest: "It will be a sad day for NASA if they do detect ice or water. That's because the Curiosity project will most likely be told, 'Gee, that's nice. Now turn around.' "
If water is found, Curiosity could still conduct tests from a distance with instruments including a laser and spectrometers.
About 250,000 bacterial spores throughout Curiosity are assumed to have survived the landing, officials said. Nearly all of them are believed to have perished within minutes of exposure to the harsh Martian conditions in Gale Crater - freezing temperatures, intense ultraviolet radiation and an atmosphere of mostly carbon dioxide.
But scientists have learned in recent years that some Earth life forms can live in space and in at least some of the conditions found on Mars. The European Space Agency discovered that lichens launched on a Russian Soyuz rocket in 2005 survived several days of full exposure to the vacuum of space and ultraviolet and cosmic radiation.
Just this year, Andrew Schuerger, a plant pathologist and expert on the survival of terrestrial microorganisms under Martian conditions, found a bacterium species capable of growing in conditions present on the surface of Mars, including air pressure of just seven millibars. Air pressure on Earth is 1,017 millibars at sea level.
NASA officials announced this week that one month into its two-year mission, Curiosity had made a scheduled pit stop while en route to Glenelg Intrigue, a tantalizing confluence of three types of terrain targeted for the first

drilling experiment. The pause allows scientists to run tests on the mechanical joints of the rover's robotic arm and surface sampler, or scoop, and other instruments designed to help crack Mars' mysteries.
Sometime next month, NASA scientists are expected to select a rock at Glenelg Intrigue and bore into it with the drill, which will then transfer small samples of powder from the rock into science instruments housed in the belly of the rover. Conley has no concerns that the experiment will contaminate the site because she believes any surviving organisms will die swiftly.
Fear of microbial contamination of the Martian environment long ago moved NASA and a United Nations space advisory committee to divide the planet's surface into areas based on the probability of encountering ice and water. The group also recommended sterilizing spacecraft destined for areas with ice and water.
Contaminating another planet is an ethical concern for scientists, as well as a practical one.
"We keep learning more and more about Mars and the amazing durability of life," said Bruce Betts, a spokesman for the Planetary Society in Pasadena. "So wouldn't it be tragic if some future expedition were to discover life on Mars only to discover later that it had actually discovered life from Earth?"