

Plants set stage for evolutionary drama

Oxygen increase triggered by vascular plants enabled the development of complex animals.

Joseph Milton

Plants made the evolution of large, complex animals such as predatory fish possible, a study of ocean sediments suggests. The findings, published in this week's Proceedings of the National Academy of Sciences¹, are the first empirical evidence to support a theory that there was a dramatic rise in oxygen levels in the Devonian period, 400 million years ago, and the first to indicate that the rise and spread of higher plants probably drove the increase.

"The evolution of vascular plants completely changed history, allowing a high concentration of oxygen in the atmosphere to be sustained. Eventually, that process led to higher animals such as ourselves," says Tais Dahl, an earth scientist at the University of Southern Denmark in Odense, who led the study.



Devonian fish Dunkleosteus, a predatory prehistoric fish of the late Devonian, was able to evolve because of the rise of higher plants. JAIME CHIRINOS / SCIENCE PHOTO LIBRARY

Dahl's team looked at the concentration of molybdenum and the ratios of its isotopes - atoms of the same element with different numbers of neutrons and different masses - in oceanic rocks for clues to the concentration of oxygen in the seas over time.

Molybdenum in sea water behaves in different ways, depending on the concentration of oxygen. In oxygenated water, the lighter of the two main molybdenum isotopes - ⁹⁵Mo and ⁹⁸Mo - is absorbed into the seabed, leaving the heavier isotope in solution. "Sea water gets lighter and heavier as a measure of the balance between oxic and anoxic conditions," says Tim Lyons, a geochemist at the University of California, Riverside.

Patterns of heavy and light molybdenum in sea water, reflecting oxygenation levels, are captured in deposited rocks called shales. By examining the shale strata, scientists can chart periods of low and high oxygenation in the history of the seabed and, by inference, in the oceans themselves. Levels of oxygenation in the oceans are assumed to reflect levels in the atmosphere.

Double increase

Dahl's study uncovered two periods when heavy molybdenum isotopes show up in the shale records, suggesting that oxygen levels increased in the Ediacaran period, about 560–550 million years ago, and again, more dramatically, during the Devonian, around 400 million years ago. This is the first evidence supporting the theory that oxygen levels increased substantially during the Devonian.

Scientists previously suspected that such an event took place, but their assumptions were based on geochemical models rather than hard evidence. Different models suggested different oxygen levels at the beginning of the Devonian episode.

Many researchers thought that the proportion of oxygen in the atmosphere during the earlier episode, which coincided with a radiation or rapid burst of evolution giving rise to many new species during the Ediacaran, had reached levels similar to today's - around 21%. But Dahl's study suggests that the radiation in the Ediacaran probably occurred in a low-oxygen environment, and that it was not until the rise of vascular plants - those with a circulatory system to transport nutrients - in the Devonian that oxygen levels rose to near-modern values.

Breathing easy

The rise of vascular plants led to the oxygenation of the atmosphere, because their photosynthesis pumped out oxygen while large amounts of organic matter, mainly plant tissues such as lignin, were buried both on land and at sea. Without the burial of organic matter, any excess oxygen created by photosynthesis is used up as it degrades. This created the right conditions for the evolution of large complex animals, which require high levels of oxygen to survive.

However, Tim Lenton, an Earth system scientist at the University of East Anglia in Norwich, UK, questions whether atmospheric conditions can be inferred directly from measurements of oceanic oxygenation.

"It is always tempting to say that when oceans are ventilated the oxygen in the atmosphere is going up, but that isn't necessarily the case," he says, adding that lowering the supply of nutrients in the ocean also increases oxygenation, as animal life respire less.

Dahl says that further sampling is required to confirm the paper's findings, but that "it looks very promising at this stage". "This event allowed higher organisms to evolve, dictating animal evolution. It could also give us an idea about life on other planets - what is the trigger, and what is paving the way from microbial life to something like ourselves," he says.

Circulating tumor cells can provide 'real-time' information on patient's current disease state

DENVER - Circulating tumor cells (CTCs) may be a promising alternative, noninvasive source of tumor materials for biomarker assessment, according to data presented at the Fourth AACR International Conference on Molecular Diagnostics in Cancer Therapeutic Development.

"The basic idea is that CTCs can provide real-time information about a patient's current disease state, acting as a 'liquid biopsy,'" said Siminder Kaur Atwal, Ph.D., senior research associate at Genentech. "They are much less invasive than tumor biopsies because they can be detected from a blood draw and don't require surgical intervention."

For this study, Atwal and colleagues compared the CTC capture efficiency of the Food and Drug Administration-approved CellSearch platform with two biochip platforms, using tumor cell lines spiked into whole blood. They tried to detect epidermal growth factor receptor (EGFR) protein expression in CTCs from patients with lung cancer and HER2 expression or amplification in CTCs in patients with metastatic breast cancer.

Under the tested conditions, CellSearch and the newer biochip platforms offered similar efficiency. Further, capture efficiency was dependent on EpCAM (epithelial cell adhesion molecule) expression.

"This may be a limitation in capturing CTCs from certain tumor types, notably triple-negative breast cancers," Atwal said.

Captured CTCs were amenable to biomarker analyses such as HER2 status, qRT-PCR for breast cancer subtype markers, KRAS mutation detection and EGFR staining by immunofluorescence, the researchers found. In patients with HER2-positive breast cancer, HER2 status in CTCs and tumor tissue generally correlated; however, in one patient subset, HER2 status changed from the primary tumor at diagnosis. This finding indicates that in some cases, CTCs may offer a real-time view of a patient's biomarker status that is different from diagnostic tissue, Atwal said.

Some improvements are necessary in CTC detection and capture before the technology can be generally useful in clinical biomarker analysis, Atwal said. Future studies will focus on evaluating different detection and capture methods with a particular emphasis on tumor types with a low EpCAM expression. In addition, future research will look for other biomarkers in CTCs to determine if they represent a patient's tumor, she said.

Biomarker panel identifies prostate cancer with 90 percent accuracy

DENVER - Researchers in England say they have discovered a set of biomarkers that can distinguish prostate cancer from benign prostate disease and healthy tissue with 90 percent accuracy. This preliminary data, if validated in larger ongoing studies, could be developed into a serum protein test that reduces the number of unnecessary biopsies and identifies men who need treatment before symptoms begin.

The researchers, from Oxford Gene Technology (OGT) and its subsidiary, Sense Proteomic, Ltd., presented their findings at the Fourth AACR International Conference on Molecular Diagnostics in Cancer Therapeutic Development.

"This pilot study shows the potential for a new diagnostic test for prostate cancer. The measure of clinical specificity - the measure of false positives - is much improved in this study compared to that seen with the current prostate specific antigen and digital rectal examination test procedures used in diagnosis of prostate cancer," said John Anson, Ph.D., vice president of biomarker discovery at OGT.

Prostate cancer caused an estimated 258,000 deaths worldwide in 2008, and is the second most common cause of cancer deaths in males in the United States with approximately 32,000 deaths estimated for 2010. The most effective screening tests now available are based on a single biomarker, prostate specific antigen (PSA). PSA, however, is known to have a specificity of less than 50 percent, which generates high false positive rates, resulting in many unnecessary surgical and radiotherapy procedures, Anson said.

The researchers developed a "functional protein" microarray to detect autoantibodies in prostate cancer serum samples. By identifying the antigens to which these autoantibodies are raised, these autoantibodies can be used as biomarkers of disease.

Although more commonly linked to autoimmune diseases, the immune system also produces autoantibodies in response to other diseases, including cancer, due to pathological changes that occur during the course of the disease.

"The appearance of autoantibodies may precede disease symptoms by many years," Anson said. "This means that autoantibody-based diagnostic tests can enable presymptomatic and early diagnosis of disease. Early diagnosis of cancer, especially aggressive forms, could significantly increase cure rates."

The researchers developed a microarray of 925 proteins, and then used blood samples to test arrays. They compared the results from 73 samples from patients diagnosed with prostate cancer to 60 samples from a control group of cancer-free individuals to find proteins on the arrays that were bound by autoantibodies present in the blood samples.

Panels of up to 15 biomarkers were identified that distinguished prostate cancer from both benign prostate disease and healthy tissue. The researchers are now testing the biomarker panel in 1,700 samples drawn from prostate cancer patients, cancer-free controls, and patients with other cancers or with other prostate diseases. Identifying prostate cancer from other prostate disease will be the real test of the biomarker panel, according to Anson.

"The latter can present similar symptoms to prostate cancer and can, in many cases, raise PSA levels and trigger a biopsy. OGT expects its biomarker panel to discriminate between prostate cancer and these 'interfering' diseases," said Anson.

In addition to prostate cancer, OGT's "functional protein" microarray can be applied to discover biomarker panels and ultimately develop better diagnostic tests for other cancers and autoimmune diseases. Early results in systemic lupus erythematosus and non-small cell lung cancer are encouraging.

Heartbreak puts the brakes on your heart

Social rejection isn't just emotionally upsetting; it also upsets your heart. A new study finds that being rejected by another person makes your heart rate drop for a moment. The study is published in *Psychological Science*, a journal of the Association for Psychological Science.

Research has shown that the brain processes physical and social pain in some of the same regions. Bregtje Gunther Moor, Eveline A. Crone, and Maurits W. van der Molen of the University of Amsterdam and Leiden University in the Netherlands wanted to find out how social pain affects you physically.

For the study, volunteers were asked to send the researchers a photograph of themselves. They were told that for a study on first impressions, students at another university would look at the photo to decide whether they liked the volunteer. This was just a cover story for the real experiment. A few weeks later, each volunteer came to the laboratory, had wires placed on their chest for an electrocardiogram, and looked at a series of unfamiliar faces - actual students from another university. For each face, the volunteer was asked to guess whether that student liked them. Then they were told whether the person actually "liked" them or not - although this was merely a computer-generated response.

Each participant's heart rate fell in anticipation before they found out the person's supposed opinion of them. Heart rate was also affected after they were told the other person's opinion - if they were told the other student didn't like them, the heart dropped further, and was slower to get back up to the usual rate. The heart rate slowed more in people who expected that the other person would like them.

The results suggest that the autonomic nervous system, which controls such functions as digestion and circulation, gets involved when you're socially rejected. "Unexpected social rejection could literally feel 'heartbreaking,' as reflected by a transient slowing of heart rate," the researchers write.

The Claim: Gargling With Salt Water Can Ease Cold Symptoms

By ANAHAD O'CONNOR

THE FACTS Nothing but time can cure the common cold, but a simple cup of salt water might ease the misery this winter.

A sore, itchy throat and respiratory congestion are some of the more common symptoms of a cold, and gargling with salt water seems to help for several reasons. A saline solution can draw excess fluid from inflamed tissues in the throat, making them hurt less, said Dr. Philip T. Hagen, editor in chief of the "Mayo Clinic Book of Home Remedies," which is due out in October. Dr. Hagen pointed out that gargling also loosens thick mucus, which can remove irritants like allergens, bacteria and fungi from the throat.

In a randomized study published in *The American Journal of Preventive Medicine* in 2005, researchers recruited almost 400 healthy volunteers and followed them for 60 days during cold and flu season. Some of the subjects were told to gargle three times a day. At the end of the study period, the group that regularly gargled had a nearly 40 percent decrease in upper respiratory tract infections compared with the control group, and when they did get sick, "gargling tended to attenuate bronchial symptoms," the researchers wrote.

Other studies have also found gargling helpful against sore throats and congestion.

According to the Mayo Clinic, for best results, dissolve half a teaspoon of salt in a full glass of warm water and gargle the solution for a few seconds before spitting it out. Adults who want a more palatable remedy against cough and sore throat can try mixing warm water with lemon and honey. No need to spit it out.

THE BOTTOM LINE Gargling with a saline solution can ease symptoms of a cold.

Migraine cause 'identified' as genetic defect

Scientists have identified a genetic defect linked to migraine which could provide a target for new treatments.

A flawed gene found in a family of migraine sufferers could help trigger the severe headaches, a study in Nature Medicine suggests.

Dr Zameel Cader of the University of Oxford said the discovery was a step forward in understanding why one in five people suffers from migraines. The World Health Organization rates it as a leading cause of disability.

A migraine is a severe, long-lasting headache usually felt as a throbbing pain at the front or on one side of the head. Some can have a warning visual disturbance, called an aura, before the start of the headache, and many people also have symptoms such as nausea and sensitivity to light during the headache itself.

Until now, the genes directly responsible for migraine have been unknown.

In this study, scientists including some from the Medical Research Council's Functional Genomics Unit at the University of Oxford found a gene known as TRESK was directly attributable as a cause of migraine in some patients.

'Activate' gene

The study found that if the gene does not work properly, environmental factors can more easily trigger pain centres in the brain and cause a severe headache.

The international team used DNA samples from families with common migraine to identify the defective gene.

Dr Aarno Palotie, from the Wellcome Trust Sanger Institute, said the breakthrough could eventually lead to new drugs which could switch off the pain of migraines. "It opens new avenues for planning new research which possibly could then lead to new treatments... but of course it's a long road."

Dr Cader, one of the MRC researchers involved in the study, said: "Previous studies have identified parts of our DNA that increase the risk in the general population, but have not found genes which can be directly responsible for common migraine. "What we've found is that migraines seem to depend on how excitable our nerves are in specific parts of the brain. "Finding the key player which controls this excitability will give us a real opportunity to find a new way to fight migraines and improve the quality of life for those suffering." He told the BBC's Today programme the research showed the defective gene in migraine patients was under-active, therefore causing the headaches.

"So what we want to do is find a drug that will activate the gene," he added.

Professor Peter Goadsby, trustee of The Migraine Trust, said: "The identification of a mutation in a gene for the potassium channel in a family with migraine with aura provides both a further important part of the puzzle in understanding the biology of migraine, and a novel direction to consider new therapies in this very disabling condition."

Cancer-fighting Viagra, the drug that keeps on giving

Jessica Hamzelou, reporter

The increasingly all-purpose wonder-drug Viagra has added another string to its bow - the drug has been shown to boost the actions of a chemotherapy drug while limiting its toxic side effects.

At the moment, many cancers are treated with doxorubicin - an antibiotic that kills off cells. The drug's action is usually limited by its dose, though, as it's pretty toxic. Patients can experience nasty side effects, including nausea, vomiting, mouth infections and damage to the heart.

Sildenafil - brand name Viagra - on the other hand, works by inhibiting an enzyme called PDE-5 that controls blood flow in the penis. When the enzyme's action is blocked, the blood vessel walls relax, allowing more blood flow. Researchers have already noted increased levels of PDE-5 in a number of cancers, including breast, colon, bladder and lung cancers. Another PDE-5 inhibitor - exisulind - has been found to inhibit tumour growth in colon cancer cells.

Rakesh Kukreja and his colleagues at Virginia Commonwealth University set about finding out what effect sildenafil might have in prostate cancer when combined with doxorubicin. The team found the drug boosted the anti-tumour effects of doxorubicin in human prostate cancer cells and in live mice - causing more cell death while inhibiting tumour growth - although it had no effect on its own.

Viagra, which is already known to boost blood flow to the heart, also protected the mice's hearts from the effects of doxorubicin (Proceedings of the National Academy of Sciences, DOI: 10.1073/pnas.1006965107 (in press)).

"We believe sildenafil could be an excellent candidate for incorporation into cancer treatment protocols with the potential of enhancing the anti-tumour efficacy, while protecting the heart against both short term and long term damage from doxorubicin," Kukreja told The Telegraph.

In case you've forgotten Viagra's other purported benefits, the drug is already touted as speeding up jet lag recovery, boosting orgasms in depressed women, treating Crohn's disease and even cellulite.

'Hobbit' Was an Iodine-Deficient Human, Not Another Species, New Study Suggests

A new paper is set to re-ignite debate over the origins of so-called *Homo floresiensis* -- the 'hobbit' that some scientists have claimed as a new species of human.

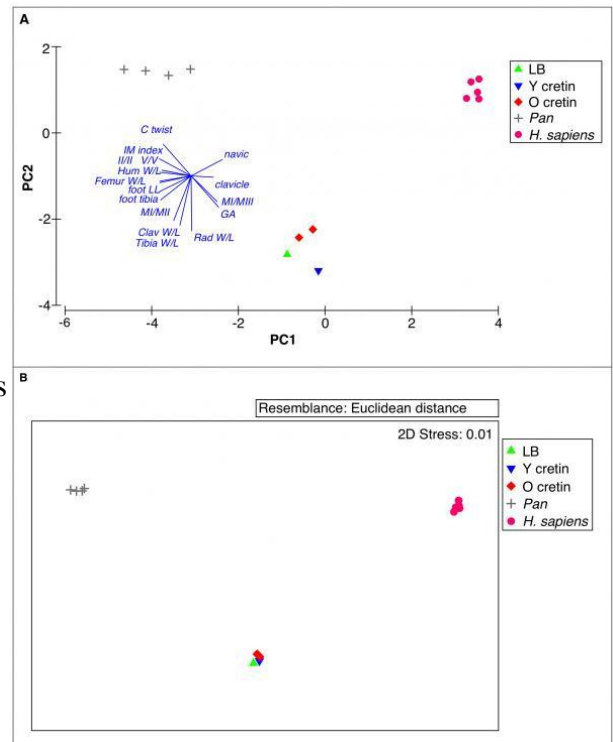
The University of Western Australia's Emeritus Professor Charles Oxnard and his colleagues, in a paper in PLoS ONE have reconfirmed, on the post-cranial skeleton, their original finding on the skull that *Homo floresiensis* in fact bears the hallmarks of humans -- *Homo sapiens* -- affected by hypothyroid cretinism.

The remains, allegedly as recent as 15,000 years, were discovered in 2003 in the Liang Bua caves on the Indonesian island of Flores by archaeologists seeking evidence of the first human migration from Asia to Australia.

When Professor Oxnard and fellow Australian researchers suggested in a 2008 paper that the skull showed evidence of endemic dwarf cretinism resulting from congenital hypothyroidism and were not a new species of human, their claim caused controversy.

In order to test their thesis, in their new paper Professor Oxnard and his team summarised data on the rest of the skeleton and mathematically compared the bones of cretins in relation to chimpanzees, unaffected humans and *H. floresiensis*. They used two methods with different statistical bases: principal components analyses (PCA) and non-metric multi-dimensional scaling (MDS).

Their work confirms the close grouping of *H. floresiensis* with the hypothyroid cretins, and the clear separation from both modern humans and from chimpanzees. This leads them to conclude that the Liang Bua remains were indeed most likely cretins from a population of unaffected *H. sapiens*. They have, further, provided a series of predictions for the further testing of the cretin hypothesis.



Multivariate analyses of quantitative features of *Homo floresiensis* in relation to cretins, unaffected humans and chimpanzees. Individuals are represented for each specimen by the coloured symbols above: *H. floresiensis* (LB), young adult cretins (Y cretin), older cretins (O cretin), *H. sapiens*, and *P. troglodytes* (Pan). Vectors are shown for each variable analyzed in the study. The direction of each vector indicates the association with each axis and the length indicates the strength of the association. (Credit: Charles Oxnard, Peter J. Obendorf, Ben J. Kefford. Post-Cranial Skeletons of Hypothyroid Cretins Show a Similar Anatomical Mosaic as *Homo floresiensis*. PLoS ONE, 2010; 5 (9): e13018 DOI: 10.1371/journal.pone.0013018)

"This is consistent with recent hypothyroid endemic cretinism throughout Indonesia, including the nearby island of Bali," Professor Oxnard said. "Cretinism is caused by various environmental factors including iodine deficiency -- a deficiency which would have been present on Flores at the period to which the dwarfed Flores fossils are dated."

Professor Oxnard has received the Charles R. Darwin Award for Lifetime Achievement in Physical Anthropology; was honoured as the dedicatee on a book *Shaping Primate Evolution*, Cambridge University Press; and was awarded the Chancellor's Medal of The University of Western Australia.

His co-authors in his most recent paper are Professor Peter Obendorf, School of Applied Sciences, RMIT University, Melbourne; and Professor Ben Kefford, Centre for Environmental Sustainability, Department of Environmental Sciences, University of Technology Sydney.

Garlic oil shows protective effect against heart disease in diabetes

Garlic has "significant" potential for preventing cardiomyopathy, a form of heart disease that is a leading cause of death in people with diabetes, scientists have concluded in a new study. Their report, which also explains why people with diabetes are at high risk for diabetic cardiomyopathy, appears in ACS' bi-weekly Journal of Agricultural and Food Chemistry.

Wei-Wen Kuo and colleagues note that people with diabetes have at least twice the risk of death from heart disease as others, with heart disease accounting for 80 percent of all diabetes-related deaths. They are especially vulnerable to a form of heart disease termed diabetic cardiomyopathy, which inflames and weakens the heart's muscle tissue. Kuo's group had hints from past studies that garlic might protect against heart disease in general and also help control the abnormally high blood sugar levels that occur in diabetes. But they realized that few studies had been done specifically on garlic's effects on diabetic cardiomyopathy.

The scientists fed either garlic oil or corn oil to laboratory rats with diabetes. Animals given garlic oil experienced beneficial changes associated with protection against heart damage. The changes appeared to be associated with the potent antioxidant properties of garlic oil, the scientists say, adding that they identified more than 20 substances in garlic oil that may contribute to the effect. "In conclusion, garlic oil possesses significant potential for protecting hearts from diabetes-induced cardiomyopathy," the report notes.

ARTICLE FOR IMMEDIATE RELEASE *"Cardiac Contractile Dysfunction and Apoptosis in Streptozotocin-Induced Diabetic Rats Are Ameliorated by Garlic Oil Supplementation"*

<http://pubs.acs.org/stoken/presspac/presspac/full/10.1021/jf101606s>

UT MD Anderson study finds women treated for breast cancer while pregnant have improved survival

HOUSTON - Long associated with a worse outcome, researchers at The University of Texas MD Anderson Cancer Center have discovered that women treated for breast cancer while pregnant, in fact, have improved disease-free survival and a trend for improved overall survival compared to non-pregnant women treated for the disease.

Jennifer Litton, M.D., assistant professor in MD Anderson's Department of Breast Medical Oncology, presented the findings in a poster discussion session at the 2010 Breast Cancer Symposium.

"Until now, older registry studies showed that breast cancer patients treated while pregnant had a worse outcome. However, in the past, these patients weren't always treated consistently with standard of care chemotherapy and often delayed their therapy until after delivery." said Litton, the study's first and corresponding author. "Given MD Anderson's experience in treating pregnant patients and our registry, we were able to look at these women treated by the same physicians, at the same institution, with the same standard of care."

In 1992, Richard Theriault, D.O., professor in the Department of Breast Medical Oncology, opened the first protocol examining a chemotherapeutic regimen for the management of these patients. He later published seminal studies proving that the regimen was safe for both pregnant mother and unborn child; it has since been adopted as the standard of care. MD Anderson has the oldest, active prospective registry in the world following the health of pregnant breast cancer patients and their children.

For the single institution, case-controlled study, Litton and her colleagues identified 75 women treated for breast cancer while pregnant. Using the institution's tumor registry and Department of Breast Medical Oncology database, the cases were compared to 150 non-pregnant breast cancer patients. Cases and controls were all treated at MD Anderson 1989 -2008, and were matched based on stage, age and year of diagnosis. Women who gave birth within one year of diagnosis were excluded from the comparison group.

All received the standard chemotherapy regimen - 5-fluorouracil, doxorubicin and cyclophosphamide (FAC); pregnant patients started therapy after completing their first trimester. Both groups received additional therapies as clinically indicated, with the pregnant women receiving those treatments after giving birth. The median follow-up was 4.16 years.

The researchers found a statistically significant five-year disease-free survival of 73.94 percent in pregnant women, compared to 55.75 percent in the non-pregnant patients. Although not statistically significant, overall survival was also higher in the cases than the controls: 77.42 percent and 71.86 percent, respectively.

"From this data set and our study, we are not sure why our pregnant breast cancer patients had better outcomes than those who were not," said Litton. "Is there something biological in the milieu of pregnancy that changes the response to chemotherapy? Or were these patients treated more aggressively?"

The reasons for the disease-free and overall survival discrepancy are still unknown, said Litton, and understanding their findings is of research priority.

"MD Anderson has a long history of being at the forefront of treating pregnant women for breast cancer, and, through our research, we've found it safe for both mother and child, and ultimately developed the standard of care," said Theriault, the study's senior author. "Now, when we are counseling breast cancer patients who are pregnant, we can say that they should have every expectation that they will do as well as our non-pregnant patients, and that they should start their treatment in the second or third trimester without delay."

In addition to Litton and Theriault, other authors on the all-MD Anderson study include: Gabriel Hortobagyi, M.D., professor and chair of the Department of Breast Medical Oncology; Karin Hahn, M.D., associate professor, Department of General Oncology; George Perkins, M.D., associate professor, Department of Radiation Oncology; Lavinia Middleton, M.D., professor, Department of Pathology; Ana Gonzalez-Angulo, associate professor, Departments of Breast Medical Oncology and Systems Biology; Shana Palla and Carla Warneke, both Department of Biostatistics.

The study was funded by the Wolff-Toomim Foundation.

Newly discovered planet may be first truly habitable exoplanet

Discovery suggests our galaxy may be teeming with potentially habitable planets

SANTA CRUZ, CA--A team of planet hunters led by astronomers at the University of California, Santa Cruz, and the Carnegie Institution of Washington has announced the discovery of an Earth-sized planet (three times the mass of Earth) orbiting a nearby star at a distance that places it squarely in the middle of the star's "habitable zone," where liquid water could exist on the planet's surface. If confirmed, this would be the most Earth-like exoplanet yet discovered and the first strong case for a potentially habitable one.

To astronomers, a "potentially habitable" planet is one that could sustain life, not necessarily one that humans would consider a nice place to live. Habitability depends on many factors, but liquid water and an atmosphere are among the most important.

"Our findings offer a very compelling case for a potentially habitable planet," said Steven Vogt, professor of astronomy and astrophysics at UC Santa Cruz. "The fact that we were able to detect this planet so quickly and so nearby tells us that planets like this must be really common."

The findings are based on 11 years of observations at the W. M. Keck Observatory in Hawaii. "Advanced techniques combined with old-fashioned ground-based telescopes continue to lead the exoplanet revolution," said Paul Butler of the Carnegie Institution. "Our ability to find potentially habitable worlds is now limited only by our telescope time."

Vogt and Butler lead the Lick-Carnegie Exoplanet Survey. The team's new findings are reported in a paper to be published in the *Astrophysical Journal* and posted online at arXiv.org. Coauthors include associate research scientist Eugenio Rivera of UC Santa Cruz; associate astronomer Nader Haghighipour of the University of Hawaii-Manoa; and research scientists Gregory Henry and Michael Williamson of Tennessee State University.

The paper reports the discovery of two new planets around the nearby red dwarf star Gliese 581. This brings the total number of known planets around this star to six, the most yet discovered in a planetary system other than our own solar system. Like our solar system, the planets around Gliese 581 have nearly circular orbits.

The most interesting of the two new planets is Gliese 581g, with a mass three to four times that of the Earth and an orbital period of just under 37 days. Its mass indicates that it is probably a rocky planet with a definite surface and that it has enough gravity to hold on to an atmosphere, according to Vogt.

Gliese 581, located 20 light years away from Earth in the constellation Libra, has a somewhat checkered history of habitable-planet claims. Two previously detected planets in the system lie at the edges of the habitable zone, one on the hot side (planet c) and one on the cold side (planet d). While some astronomers still think planet d may be habitable if it has a thick atmosphere with a strong greenhouse effect to warm it up, others are skeptical. The newly discovered planet g, however, lies right in the middle of the habitable zone.

"We had planets on both sides of the habitable zone--one too hot and one too cold--and now we have one in the middle that's just right," Vogt said.

The planet is tidally locked to the star, meaning that one side is always facing the star and basking in perpetual daylight, while the side facing away from the star is in perpetual darkness. One effect of this is to stabilize the planet's surface climates, according to Vogt. The most habitable zone on the planet's surface would be the line between shadow and light (known as the "terminator"), with surface temperatures decreasing toward the dark side and increasing toward the light side. "Any emerging life forms would have a wide range of stable climates to choose from and to evolve around, depending on their longitude," Vogt said.

The researchers estimate that the average surface temperature of the planet is between -24 and 10 degrees Fahrenheit (-31 to -12 degrees Celsius). Actual temperatures would range from blazing hot on the side facing the star to freezing cold on the dark side.

If Gliese 581g has a rocky composition similar to the Earth's, its diameter would be about 1.2 to 1.4 times that of the Earth. The surface gravity would be about the same or slightly higher than Earth's, so that a person could easily walk upright on the planet, Vogt said.

The new findings are based on 11 years of observations of Gliese 581 using the HIRES spectrometer (designed by Vogt) on the Keck I Telescope at the W. M. Keck Observatory in Hawaii. The spectrometer allows precise measurements of a star's radial velocity (its motion along the line of sight from Earth), which can reveal the presence of planets. The gravitational tug of an orbiting planet causes periodic changes in the radial velocity of the host star. Multiple planets induce complex wobbles in the star's motion, and astronomers use sophisticated analyses to detect planets and determine their orbits and masses.

"It's really hard to detect a planet like this," Vogt said. "Every time we measure the radial velocity, that's an evening on the telescope, and it took more than 200 observations with a precision of about 1.6 meters per second to detect this planet."

To get that many radial velocity measurements (238 in total), Vogt's team combined their HIRES observations with published data from another group led by the Geneva Observatory (HARPS, the High Accuracy Radial velocity Planetary Search project).

In addition to the radial velocity observations, coauthors Henry and Williamson made precise night-to-night brightness measurements of the star with one of Tennessee State University's robotic telescopes. "Our brightness measurements verify that the radial velocity variations are caused by the new orbiting planet and not by any process within the star itself," Henry said.

The researchers also explored the implications of this discovery with respect to the number of stars that are likely to have at least one potentially habitable planet. Given the relatively small number of stars that have been carefully monitored by planet hunters, this discovery has come surprisingly soon.

"If these are rare, we shouldn't have found one so quickly and so nearby," Vogt said. "The number of systems with potentially habitable planets is probably on the order of 10 or 20 percent, and when you multiply that by the hundreds of billions of stars in the Milky Way, that's a large number. There could be tens of billions of these systems in our galaxy."

This research was supported by grants from the National Science Foundation and NASA.

Study finds first direct evidence that ADHD is a genetic disorder Children with ADHD have more missing or duplicated segments of DNA

Research published today provides the first direct evidence that attention-deficit/hyperactivity disorder (ADHD) is a genetic condition. Scientists at Cardiff University found that children with ADHD were more likely to have small segments of their DNA duplicated or missing than other children.

The study also found significant overlap between these segments, known as copy number variants (CNVs), and genetic variants implicated in autism and schizophrenia, proving strong evidence that ADHD is a neurodevelopmental disorder – in other words, that the brains of children with the disorder differ from those of other children.

The research, published today in the journal *The Lancet*, was largely funded by the Wellcome Trust, with additional support from Action Medical Research, the Medical Research Council and the European Union.

"We hope that these findings will help overcome the stigma associated with ADHD," says Professor Anita Thapar. "Too often, people dismiss ADHD as being down to bad parenting or poor diet. As a clinician, it was clear to me that this was unlikely to be the case. Now we can say with confidence that ADHD is a genetic disease and that the brains of children with this condition develop differently to those of other children."

ADHD is one of the most common mental health disorders in childhood, affecting around one in 50 children in the UK. Children with ADHD are excessively restless, impulsive and distractible, and experience difficulties at home and in school. Although no cure exists for the condition, symptoms can be reduced by a combination of medication and behavioural therapy.

The condition is highly heritable – children with ADHD are statistically more likely to also have a parent with the condition and a child with an identical twin with ADHD has a three in four chance of also having the condition. Even so, until now there has been no direct evidence that the condition is genetic and there has been much controversy surrounding its causes, which some people have put down to poor parenting skills or a sugar-rich diet.

The team at Cardiff University analysed the genomes of 366 children, all of whom had been given a clinical diagnosis of ADHD, against over 1,000 control samples in search of variations in their genetic make-up that were more common in children with the condition.

"Children with ADHD have a significantly higher rate of missing or duplicated DNA segments compared to other children and we have seen a clear genetic link between these segments and other brain disorders," explains Dr Nigel Williams. "These findings give us tantalising clues to the changes that can lead to ADHD."

The researchers found that rare CNVs were almost twice as common in children with ADHD compared to the control sample – and even higher for children with learning difficulties. CNVs are particularly common in disorders of the brain.

There was also significant overlap between CNVs identified in children with ADHD and regions of the genome which are known to influence susceptibility to autism and schizophrenia. Whilst these disorders are currently thought to be entirely separate, there is some overlap between ADHD and autism in terms of symptoms and learning difficulties. This new research suggests there may be a shared biological basis to the two conditions.

The most significant overlap was found at a particular region on chromosome 16 which has been previously implicated in schizophrenia and other major psychiatric disorders and spans a number of genes including one known to play a role in the development of the brain .

"ADHD is not caused by a single genetic change, but is likely caused by a number of genetic changes, including CNVs, interacting with a child's environment," explains Dr Kate Langley. "Screening children for the CNVs that we have identified will not help diagnose their condition. We already have very rigorous clinical assessments to do just that."

Dr John Williams, Head of Neuroscience and Mental Health at the Wellcome Trust, which has supported Professor Thapar's work for ten years, says: "These findings are testament to the perseverance of Professor Thapar and colleagues to prove the often unfashionable theory that ADHD is a brain disorder with genetic links. Using leading-edge technology, they have begun to shed light on the causes of what is a complex and often distressing disorder for both the children and their families."

National study finds strong link between diabetes and air pollution **Findings unchanged after adjustment for obesity and other diabetes risk factors**

Boston, Mass. -- A national epidemiologic study finds a strong, consistent correlation between adult diabetes and particulate air pollution that persists after adjustment for other risk factors like obesity and ethnicity, report researchers from Children's Hospital Boston. The relationship was seen even at exposure levels below the current EPA safety limit.

The report, published in the October issue of *Diabetes Care*, is among the first large-scale population-based studies to link diabetes prevalence with air pollution. It is consistent with prior laboratory studies finding an increase in insulin resistance, a precursor to diabetes, in obese mice exposed to particulates, and an increase in markers of inflammation (which may contribute to insulin resistance) in both the mice and obese diabetic patients after particulate exposure.

Like the laboratory studies, the current study focused on fine particulates of 0.1-2.5 nanometers in size (known as PM_{2.5}), a main component of haze, smoke and motor vehicle exhaust. The investigators, led by John Pearson and John Brownstein, PhD, of the Children's Hospital Informatics Program, obtained county-by-county data on PM_{2.5} pollution from the Environmental Protection Agency (EPA), covering every county in the contiguous United States for 2004 and 2005.

They then combined the EPA data with data from the Centers for Disease Control (CDC) and the U.S. Census to ascertain the prevalence of adult diabetes and to adjust for known diabetes risk factors, including obesity, exercise, geographic latitude, ethnicity and population density (a measure of urbanization).

"We wanted to do everything possible to reduce confounding and ensure the validity of our findings," says Pearson, the study's first author.

In all analyses, there was a strong and consistent association between diabetes prevalence and PM_{2.5} concentrations. For every 10 µg/m³ increase in PM_{2.5} exposure, there was a 1 percent increase in diabetes prevalence. This finding was seen in both 2004 and 2005, and remained consistent and significant when differing estimates of PM_{2.5} exposure were used.

"We didn't have data on individual exposure, so we can't prove causality, and we can't know exactly the mechanism of these peoples' diabetes," acknowledges Brownstein. "But pollution came across as a significant predictor in all our models."

Even among counties falling within EPA limits for exposure, those with highest versus the lowest levels of PM_{2.5} pollution had a more than 20 percent increase in diabetes prevalence, which remained after controlling for diabetes risk factors.

"From a policy perspective, the findings suggest that the current EPA limits on exposure may not be adequate to prevent negative public health outcomes from particulate matter exposure," Brownstein says.

"Many environmental factors may contribute to the epidemic of diabetes in the United States and worldwide," notes Allison Goldfine, MD, head of clinical research at the Joslin Diabetes Center and a coauthor on the study.

"While a lot of attention has correctly been attributed to caloric excess and sedentary behaviors, additional factors may provide novel approaches to diabetes prevention."

Based on their findings, the researchers call for more study of environmental factors in diabetes, including basic research on the inflammatory mechanisms in diabetes and the role of PM_{2.5}.

"We would like to access better individual-level data on diabetes and exposure," adds Brownstein. "We also have an interest in investigating this finding internationally where standards may be less stringent."

The study was funded by the National Center for Biomedical Computing of the National Institutes of Health.

Notre Dame and Wyoming scientists genetically engineer silkworms to produce artificial spider silk

A research and development effort by the University of Notre Dame, the University of Wyoming, and Kraig Biocraft Laboratories, Inc. has succeeded in producing transgenic silkworms capable of spinning artificial spider silks. "This research represents a significant breakthrough in the development of superior silk fibers for both medical and non-medical applications," said Malcolm J. Fraser Jr., a Notre Dame professor of biological sciences. "The generation of silk fibers having the properties of spider silks has been one of the important goals in materials science."

Natural spider silks have a number of unusual physical properties, including significantly higher tensile strength and elasticity than naturally spun silkworm fibers. The artificial spider silks produced in these transgenic silkworms have similar properties of strength and flexibility to native spider silk.

Silk fibers have many current and possible future biomedical applications, such as use as fine suture materials, improved wound healing bandages, or natural scaffolds for tendon and ligament repair or replacement. Spider silk-like fibers may also have applications beyond biomedical uses, such as in bulletproof vests, strong and lightweight structural fabrics, a new generation athletic clothing and improved automobile airbags.

Until this breakthrough, only very small quantities of artificial spider silk had ever been produced in laboratories, but there was no commercially viable way to produce and spin these artificial silk proteins. Kraig Biocraft believed these limitations could be overcome by using recombinant DNA to develop a biotechnological approach for the production of silk fibers with a much broader range of physical properties or with pre-determined properties, optimized for specific biomedical or other applications.

The firm entered into a research agreement with Fraser, who discovered and patented a powerful and unique genetic engineering tool called "piggyBac". PiggyBac is a piece of DNA known as a transposon that can insert itself into the genetic machinery of a cell. "Several years ago, we discovered that the piggyBac transposon could be useful for genetic engineering of the silkworm, and the possibilities for using this commercial protein production platform began to become apparent."

Fraser, with the assistance of University of Wyoming researcher Randy Lewis, a biochemist who is one of the world's foremost authorities on spider silk, and Don Jarvis, a noted molecular geneticist who specializes in insect protein production, genetically engineered silkworms in which they incorporated specific DNAs taken from spiders. When these transgenic silkworms spin their cocoons, the silk produced is not ordinary silkworm silk, but, rather, a combination of silkworm silk and spider silk. The genetically engineered silk protein produced by the transgenic silkworms has markedly improved elasticity and strength approaching that of native spider silk.

"We've also made strides in improving the process of genetic engineering of these animals so that the development of additional transgenics is facilitated," Fraser said. "This will allow us to more rapidly assess the effectiveness of our gene manipulations in continued development of specialized silk fibers." Since silkworms are already a commercially viable silk production platform, these genetically engineered silkworms effectively solve the problem of large scale production of engineered protein fibers in an economically practical way.

"Using this entirely unique approach, we have confirmed that transgenic silkworms can be a potentially viable commercial platform for production of genetically engineered silk proteins having customizable properties of strength and elasticity," Fraser said. "We may even be able to genetically engineer fibers that exceed the remarkable properties of native spider silk."

The genetic engineering breakthrough was announced today (Sept. 29) by Fraser, Lewis and Kraig Biocraft CEO Kim Thompson at a press conference on the Notre Dame campus.

Less than half of essential workers willing to report to work during a serious pandemic 12 percent of workers would choose to quit or retire rather than report for work

Although first responders willingly put themselves in harm's way during disasters, new research indicates that they may not be as willing - if the disaster is a potentially lethal pandemic.

In a recent study, researchers at Columbia University's Mailman School of Public Health found that more than 50% of the first responders and other essential workers they surveyed might be absent from work during a serious pandemic, even if they were healthy.

The study, reported online in the October issue of the Journal of Occupational and Environmental Medicine, involved over 1100 workers recruited from six essential workgroups, all located in the New York metropolitan area. The workgroups included hospital employees, police and fire department personnel, emergency medical services workers, public health workers, and correctional facility officers.

The researchers found that while 80% of the workers would be able (i.e., available) to report to duty, only 65% were willing. Taken together, less than 50% of these key workers were both willing and able to report to

duty. According to the lead author, Dr. Robyn Gershon, Professor of Clinical Sociomedical Sciences and Associate Dean for Research Resources at Columbia University's Mailman School of Public Health, and Faculty Affiliate at Columbia University's National Center for Disaster Preparedness, "these data indicate that non-illness related shortfalls among essential workers could be substantial."

In anonymous surveys, workers reported on their willingness to work during a serious pandemic; the percent willing ranged from a high of 74% (public health workers) to a low of 56% (correctional workers). The researchers found that motivation to work during a serious pandemic was associated with workplace safety measures and trust in the employer's ability to protect workers from harm. Workers were also more willing to report to duty if their employer provided them with respirators and pandemic vaccine and had an established pandemic plan. Willingness was also tied to past experience; essential workers who had responded to a previous disaster were significantly more willing to report during a pandemic.

The researchers found that workers' ability or availability to work during a serious pandemic was closely linked to their personal obligations. Referred to as "dilemmas of loyalty," otherwise healthy essential workers might stay at home to care for sick family members or their children - if schools are closed. Organizational policies and programs that help workers meet their personal obligations will also increase workers' ability to work. "Even something as simple as ensuring that workers can communicate with their families while they are on duty, can have a big impact on both ability and willingness," reports Dr. Gershon.

Even though the Centers for Disease Control and Prevention (CDC) made workplace pandemic planning and training materials readily available, the Columbia study did not find much evidence of preparedness. Only a small proportion of the workers (9%) were aware of their organization's pandemic plans, and only 15% had ever received pandemic influenza training at work. As Dr. Gershon notes, "the study findings suggest that these preparedness steps are important in building worker trust. Workers who trust that their employers can protect them during a communicable disease outbreak will be significantly more likely to come to work and perform their jobs— jobs that are vital to the safety, security and well-being of the entire community."

To help ensure adequate staffing levels, employers should focus preparedness efforts on worker protection and the development of policies that facilitate the attendance of healthy workers. The authors suggest a number of relatively straightforward strategies that employers can take to support employees' response during pandemic outbreaks. These include:

- * Prepare a plan to quickly and easily vaccinate essential workers and their families, so that when a vaccine is available it can be readily distributed.

- * Discuss respiratory protection needs with public health officials. They can provide guidance on the need, feasibility, and use of these safety devices.

Guidance on planning is available from CDC-funded Preparedness and Emergency Response Learning Centers, such as the one at Columbia University's National Center for Disaster Preparedness.

Free radicals can be anti-aging - says new research

A major blow to the free radical theory of aging, which had lead the research in aging for more than 50 years and fuels a multimillionaire anti-aging industry has just been published by Portuguese scientists from the University of Minho. According to the theory, free radicals provoke oxidative damage and this is the cause of aging. The new work, however, shows that not only is possible to slow down aging in cells with high levels of oxidation but more, that a free radical (H₂O₂) is behind the high longevity seen with low caloric diets (a well known method to increase lifespan) turning upside down the way we see anti-aging therapy and research with major implications for the field. But the results, now published in the journal Proceedings of the National Academy of Sciences(1), will also affect the study of phenomena as diverse as inflammation, Alzheimer's disease or cell survival, all processes where free radicals are known to have a role.

So modern medicine is now more than ever able to treat disease and extend life. This is only an advantage, however, if the new lease of life is a healthy and active one. Millions of pounds of potential anti-aging products rest on the possibility of slow down the signs of old age and the free radical theory of aging – by suggesting a possible explanation to the basic chemical processes behind growing old – already has aging-worried individuals all over the world sustaining a multimillionaire industry of anti-aging anti-oxidant products. After all everyone knows that free radicals are bad and antioxidants are good. But are they really?

Free radicals are atoms with unpaired electrons what makes them extremely unstable and prone to donate or grab electrons from other molecules, causing oxidative damage in the process. This is usually not a problem in healthy individuals as the body's anti-oxidants are enough to keep radicals at bay but things like aging, smoking and pollution seem to increase the production and accumulation of radicals. And this is, according to the free radical theory of aging, the reason why aging (and an unhealthy life style) comes with fast deterioration of tissues and organs that creates disease and, eventually, death.

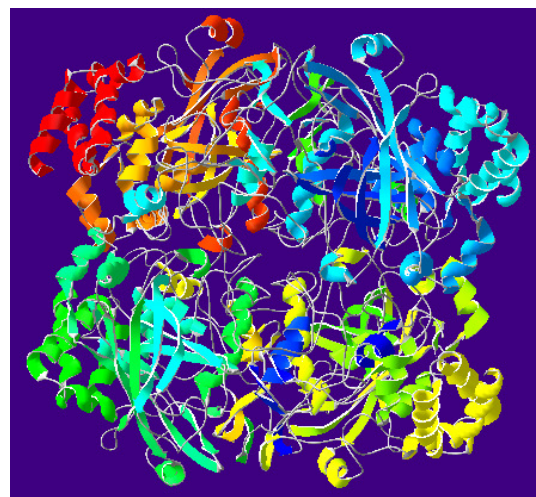
Scientific research however does not seem to be able to prove this. Although we know that free radicals are toxic and there is, in fact, experimental work supporting the free radical theory of aging, more and more results suggest that the theory is, at the very best, incomplete. Examples that do not fit go from long-lived mole rats (lasting an extraordinary 28 years) with much higher levels of oxidative damage than other rats living 10 times less, to the discovery that H₂O₂ - one of the main free radicals believed to cause aging – seems to be involved in the chemistry behind cell survival.

In an attempt to understand these apparent contradictions Paula Ludovico's group from the University of Minho and colleagues studied the yeast *Saccharomyces cerevisiae* under a low-caloric diet. These diets (if not extreme) slow down aging, making the organism live longer, although exactly how this happens is not very clear. They are also particularly interesting for this study as the longer life span can be accompanied by high levels of oxidative damage in an apparent contradiction of the free radical theory. Ludovico's plan was to look at the two most important radicals linked to aging – oxygen peroxide (H₂O₂) and superoxide anions (O₂⁻) – see how they changed under the diet, and also their link to oxidative damage.

But when the researchers looked for signs of free radicals as the yeast lived longer they were startled by something unexpected –free radicals levels within the yeast actually increased together with lifespan. They also saw that inactivation of two anti-oxidant proteins called catalases, which are specific for H₂O₂ – so resulting in H₂O₂ accumulation within the yeast - was enough for *S. cerevisiae* live longer (even without diet). These two results actually suggested that H₂O₂ could be behind the increased longevity. To confirm this unexpected possibility the yeast was grown in H₂O₂ medium and in fact they went to live longer than usual, proving that this radical in fact could slow down aging. This is particularly interesting as other researchers have seen the same effect with human skin cells growing in H₂O₂ what suggests that the anti-aging H₂O₂ role is common to many different species.

With superoxide anions O₂⁻ (the other free radical linked to aging) the results were very different, however, and as the yeast longevity increased (due to either a low caloric diet or catalase inactivation) O₂⁻ disappeared. It was found that this occurred because H₂O₂ activated two anti-oxidant proteins, this time specific for O₂⁻ (called SOD), and, as H₂O₂ increased, O₂⁻ was neutralised.

So what about oxidative damage, which according to the free radical theory is directly responsible for aging? Again an unexpected result – in fact although long-lived yeast under a low caloric diet showed less signs of oxidative damage as they live longer (in agreement with the theory's predictions), the same was not true to those without catalases. In fact, in these yeasts, the exact opposite occurred with oxidative damage increasing as the yeast lived longer.



Molecular structure of catalase, the antioxidant specific for H₂O₂

So how can we explain the protective capacity of H₂O₂ when this radical is well known to be toxic, killing cells? According to the first author of the article, Ana Mesquita, and Ludovico the explanation is in a phenomenon called hormesis, where a substance normally toxic can have beneficial effects if used in low doses. Why this happens is not totally clear but it is suspected that small amounts of stress (like small amounts of H₂O₂) can activate the body's repair mechanisms without really provoking any damage so ending up having "bizarre" beneficial effects. In this case H₂O₂ is enough to activate the antioxidants specific for O₂⁻, slowing down the aging normally provoked by this radical.

In conclusion, Ludovico and colleagues' new work have a few crucial results - first that it is possible to have little oxidative damage despite having high levels of free radicals (H₂O₂ in yeast with a low caloric diet) and second, that high levels of oxidative damage can exist in long-living organisms (like it occurs in yeast without functional catalases). Finally, in discovery that puts up side down the way we see anti-aging therapy and research, they prove that a free radical (H₂O₂) can actually be anti-aging.

These results seriously challenge the free radical theory and introduce a totally new vision for the role of free radicals (at least H₂O₂) in the body, and no doubt will have important implications in the way aging processes are seen from now. After all, the free radical theory has guided investigations into the causes and consequences of aging for more than 50 years, while free radicals have been always considered the "bad guys". And while (most) radicals probably have a role in the deterioration that accompanies old age, the process (and the radicals' role) is no doubt much more complex than the simple equation – free radicals: oxidative damage: aging - that the free radical theory proposes.

Interestingly, Ludovico's results also suggest that H₂O₂ can be used as an anti-inflammatory since O₂- is known to participate in inflammation although this will need further research. Another interesting discovery is the fact that catalases appear as pro-aging in opposition to the current idea - behind much research - that these proteins can be used to slow down aging. Finally this new work might also explain why, contrary to what is expected by the radical theory, in some studies, anti-oxidants are shown to reduce longevity.

But would this affect the anti-oxidant industry? Most probably not. After all there was never any scientific evidence that dietary anti-oxidant supplements affected the body's free radicals levels (despite what the industry want us to believe), and, still, millions of people continue to buy this elusive promise of a new lease of life. In the end, it's all about hope (at least for now...)

The research was done in collaboration with three other laboratories: the Department of Molecular and Cellular Biology at the Roswell Park Cancer Institute, NY and also ICBAS and IBMC from the University of Porto, Portugal Article by Catarina Amorim <http://www.pnas.org/content/107/34/15123.abstract>

Research integrity: Sabotage!

Postdoc Vipul Bhrigu destroyed the experiments of a colleague in order to get ahead. It took a hidden camera to expose a surreptitious and malicious side of science.

Brendan Maher

It is sentencing day at Washtenaw County Courthouse, a drab structure of stained grey stone and tinted glass a few blocks from the main campus of the University of Michigan in Ann Arbor. Judge Elizabeth Pollard Hines has doled out probation and fines for drunk and disorderly conduct, shoplifting and other mundane crimes on this warm July morning. But one case, number 10-0596, is still waiting. Vipul Bhrigu, a former postdoc at the university's Comprehensive Cancer Center, wears a dark-blue three-buttoned suit and a pinched expression as he cups his pregnant wife's hand in both of his. When Pollard Hines calls Bhrigu's case to order, she has stern words for him: "I was inclined to send you to jail when I came out here this morning."

Bhrigu, over the course of several months at Michigan, had meticulously and systematically sabotaged the work of Heather Ames, a graduate student in his lab, by tampering with her experiments and poisoning her cell-culture media. Captured on hidden camera, Bhrigu confessed to university police in April and pleaded guilty to malicious destruction of personal property, a misdemeanour that apparently usually involves cars: in the spaces for make and model on the police report, the arresting officer wrote "lab research" and "cells". Bhrigu has said on multiple occasions that he was compelled by "internal pressure" and had hoped to slow down Ames's work. Speaking earlier this month, he was contrite. "It was a complete lack of moral judgement on my part," he said.

Bhrigu's actions are surprising, but probably not unique. There are few firm numbers showing the prevalence of research sabotage, but conversations with graduate students, postdocs and research-misconduct experts suggest that such misdeeds occur elsewhere, and that most go unreported or unpunished. In this case, the episode set back research, wasted potentially tens of thousands of dollars and terrorized a young student. More broadly, acts such as Bhrigu's - along with more subtle actions to hold back or derail colleagues' work - have a toxic effect on science and scientists. They are an affront to the implicit trust between scientists that is necessary for research endeavours to exist and thrive.

Despite all this, there is little to prevent perpetrators re-entering science. In the United States, federal bodies that provide research funding have limited ability and inclination to take action in sabotage cases because they aren't interpreted as fitting the federal definition of research misconduct, which is limited to plagiarism, fabrication and falsification of research data. In Bhrigu's case, administrators at the University of Michigan worked with police to investigate, thanks in part to the persistence of Ames and her supervisor, Theo Ross.

"The question is, how many universities have such procedures in place that scientists can go and get that kind of support?" says Christine Boesz, former inspector-general for the US National Science Foundation in Arlington, Virginia, and now a consultant on scientific accountability. "Most universities I was familiar with would not necessarily be so responsive."

First suspicions

Ames, an MD PhD student, first noticed a problem with her research on 12 December 2009. As part of a study on the epidermal growth factor receptor, a protein involved in some cancers, she was running a western blot assay to confirm the presence of proteins in a sample. It was a routine protocol. But when she looked at the blot, four of her six samples seemed to be out of order - the pattern of bands that she expected to see in one lane appeared in another. Five days later, it happened again. "I thought, technically it could have been my mistake, but it was weird that they had gone wrong in exactly the same way," says Ames. The only explanation, she reasoned, was that the labelled lids for her cell cultures had been swapped, and she immediately wondered whether someone was sabotaging her work. To be safe, she devised a workaround: writing directly on the bottoms of the culture dishes so that the lids could not be switched.

Next, Ames started having an issue with the western blots themselves. She saw an additional protein in the sample lanes, showing that an extra antibody was staining the blot. Once again, it could have been a mistake, but it happened twice. "I started going over to my fiancé's lab and running blots overnight there," she says. As the problems mounted, Ames was getting agitated. She was certain that someone was monkeying with her experiments, but she had no proof and no suspect. Her close friends suggested that she was being paranoid.

Some labs are known to be hyper-competitive, with principal investigators pitting postdocs against each other. But Ross's lab is a small, collegial place. At the time that Ames was noticing problems, it housed just one other graduate student, a few undergraduates doing projects, and the lab manager, Katherine Oravec-Wilson, a nine-year veteran of the lab whom Ross calls her "eyes and ears". And then there was Bhrigu, an amiable postdoc who had joined the lab in April 2009.

Bhrigu had come to the United States from India in 2003, and completed his PhD at the University of Toledo, Ohio, under cancer biologist James Trempe. "He was an average student," says Trempe. "I wouldn't say that he was a star in the lab, but there was nothing that would make me question the work that he did." Ross thought Bhrigu would be a good fit with her lab - friendly, talkative, up on current trends in the field. Ames says that she liked Bhrigu and at the time had little reason to suspect him. "He was one of the last people I would have suspected didn't like me," she says.

On Sunday 28 February 2010, Ames encountered what she thought was another attempt to sabotage her work. She was replacing the media on her cells and immediately noticed that something wasn't right. The cells were "just dripping off the plate", as if they'd been hit with something caustic. She pulled the bottle of medium out from the fume hood and looked at it. Translucent ripples, like those that appear when adding water to whisky, were visible in the dark red medium. When she sniffed it, the smell of alcohol was overpowering. This, she thought, was the proof she needed. "It was clearly not my mistake," says Ames.

She fired off an e-mail to Ross. "I just found pretty convincing evidence that somebody is trying to sabotage my experiments," she wrote. Ross came and sniffed the medium too. She agreed that it didn't smell right, but she didn't know what to think.

Lab investigation

Some people whom Ross consulted with tried to convince her that Ames was hitting a rough patch in her work and looking for someone else to blame. But Ames was persistent, so Ross took the matter to the university's office of regulatory affairs, which advises on a wide variety of rules and regulations pertaining to research and clinical care. Ray Hutchinson, associate dean of the office, and Patricia Ward, its director, had never dealt with anything like it before. After several meetings and two more instances of alcohol in the media, Ward contacted the department of public safety - the university's police force - on 9 March. They immediately launched an investigation - into Ames herself. She endured two interrogations and a lie-detector test before investigators decided to look elsewhere.

At 4:00 a.m. on Sunday 18 April, officers installed two cameras in the lab: one in the cold room where Ames's blots had been contaminated, and one above the refrigerator where she stored her media. Ames came in that day and worked until 5:00 p.m. On Monday morning at around 10:15, she found that her medium had been spiked again. When Ross reviewed the tapes of the intervening hours with Richard Zavala, the officer assigned to the case, she says that her heart sank. Bhrigu entered the lab at 9:00 a.m. on Monday and pulled out the culture media that he would use for the day. He then returned to the fridge with a spray bottle of ethanol, usually used to sterilize lab benches. With his back to the camera, he rummaged through the fridge for 46 seconds. Ross couldn't be sure what he was doing, but it didn't look good.

Zavala escorted Bhrigu to the campus police department for questioning. When he told Bhrigu about the cameras in the lab, the postdoc asked for a drink of water and then confessed. He said that he had been sabotaging Ames's work since February. (He denies involvement in the December and January incidents.)

Motives for misconduct

Misbehaviour in science is nothing new - but its frequency is difficult to measure. Daniele Fanelli at the University of Edinburgh, UK, who studies research misconduct, says that overtly malicious offences such as Bhrigu's are probably infrequent, but other forms of indecency and sabotage are likely to be more common. "A lot more would be the kind of thing you couldn't capture on camera," he says. Vindictive peer review, dishonest reference letters and withholding key aspects of protocols from colleagues or competitors can do just as much to derail a career or a research project as vandalizing experiments. These are just a few of the questionable



practices that seem quite widespread in science, but are not technically considered misconduct. In a meta-analysis of misconduct surveys, published last year (D. Fanelli PLoS ONE 4, e5738; 2009), Fanelli found that up to one-third of scientists admit to offences that fall into this grey area, and up to 70% say that they have observed them.

Some say that the structure of the scientific enterprise is to blame. The big rewards - tenured positions, grants, papers in stellar journals - are won through competition. To get ahead, researchers need only be better than those they are competing with. That ethos, says Brian Martinson, a sociologist at HealthPartners Research Foundation in Minneapolis, Minnesota, can lead to sabotage. He and others have suggested that universities and funders need to acknowledge the pressures in the research system and try to ease them by means of education and rehabilitation, rather than simply punishing perpetrators after the fact.

But did rivalry drive Bhrigu? He and Ames were collaborating on one of their projects, but they were not in direct competition. Chiron Graves, a former graduate student in Ross's lab who helped Bhrigu learn techniques, says that Ross is passionate but didn't put undue stress on her personnel. "The pressures that exist in the system as a whole are somewhat relieved in Theo's lab," says Graves, now an assistant professor running a teacher-education programme at Eastern Michigan University in Ypsilanti. "Her take was to do good science."

Bhrigu says that he felt pressure in moving from the small college at Toledo to the much bigger one in Michigan. He says that some criticisms he received from Ross about his incomplete training and his work habits frustrated him, but he doesn't blame his actions on that. "In any kind of workplace there is bound to be some pressure," he says. "I just got jealous of others moving ahead and I wanted to slow them down."

Crime and punishment

At Washtenaw County Courthouse in July, having reviewed the case files, Pollard Hines delivered Bhrigu's sentence. She ordered him to pay around US\$8,800 for reagents and experimental materials, plus \$600 in court fees and fines - and to serve six months' probation, perform 40 hours of community service and undergo a psychiatric evaluation.

But the threat of a worse sentence hung over Bhrigu's head. At the request of the prosecutor, Ross had prepared a more detailed list of damages, including Bhrigu's entire salary, half of Ames's, six months' salary for a technician to help Ames get back up to speed, and a quarter of the lab's reagents. The court arrived at a possible figure of \$72,000, with the final amount to be decided upon at a restitution hearing in September.

Before that hearing could take place, however, Bhrigu and his wife left the country for India. Bhrigu says his visa was contingent upon having a job. A new hearing has been scheduled for October in which the case for restitution will be heard alongside arguments that Bhrigu has violated his probation.

Ross, though, is happy that the ordeal is largely over. For the month-and-a-half of the investigation, she became reluctant to take on new students or to hire personnel. She says she considered packing up her research programme. She even questioned her own sanity, worrying that she was the one sabotaging Ames's work via "an alternate personality". Ross now wonders if she was too trusting, and urges other lab heads to "realize that the whole spectrum of humanity is in your lab. So, when someone complains to you, take it seriously."

She also urges others to speak up when wrongdoing is discovered. After Bhrigu pleaded guilty in June, Ross called Trempe at the University of Toledo. He was shocked, of course, and for more than one reason. His department at Toledo had actually re-hired Bhrigu. Bhrigu says that he lied about the reason he left Michigan, blaming it on disagreements with Ross. Toledo let Bhrigu go in July, not long after Ross's call.

Now that Bhrigu is in India, there is little to prevent him from getting back into science. And even if he were in the United States, there wouldn't be much to stop him. The National Institutes of Health in Bethesda, Maryland, through its Office of Research Integrity, will sometimes bar an individual from receiving federal research funds for a time if they are found guilty of misconduct. But Bhrigu probably won't face that prospect because his actions don't fit the federal definition of misconduct, a situation Ross finds strange. "All scientists will tell you that it's scientific misconduct because it's tampering with data," she says.

Still, more immediate concerns are keeping Ross busy. Bhrigu was in her lab for about a year, and everything he did will have to be repeated. Reagents that he used have been double-checked or thrown away. Ames says her work was set back five or six months, but she expects to finish her PhD in the spring.

For her part, Ames says that the experience shook her trust in her chosen profession. "I did have doubts about continuing with science. It hurt my idea of science as a community that works together, builds upon each other's work and collaborates." Nevertheless, she has begun to use her experience to help teach others, and has given a seminar about the experience, with Ross, to new graduate students. She says that the assistance she got from Ross and others helped her cope with the ordeal.

"It did help restore the trust," she says. "In a sense I was lucky that we could catch it."

Brendan Maher is Nature's biology features editor. [Download PDF](#)

Odds of Life on Newfound Earth-Size Planet '100 Percent,' Astronomer Says

By Jeanna Bryner LiveScience Managing Editor

An Earth-size planet has been spotted orbiting a nearby star at a distance that would make it not too hot and not too cold - comfortable enough for life to exist, researchers announced today (Sept. 29).

If confirmed, the exoplanet, named Gliese 581g, would be the first Earth-like world found residing in a star's habitable zone - a region where a planet's temperature could sustain liquid water on its surface.

And the planet's discoverers are optimistic about the prospects for finding life there.

"Personally, given the ubiquity and propensity of life to flourish wherever it can, I would say, my own personal feeling is that the chances of life on this planet are 100 percent," said Steven Vogt, a professor of astronomy and astrophysics at the University of California, Santa Cruz, during a press briefing today. "I have almost no doubt about it." His colleague, Paul Butler of the Carnegie Institution of Washington, in Washington, D.C., wasn't willing to put a number on the odds of life, though he admitted he's optimistic.

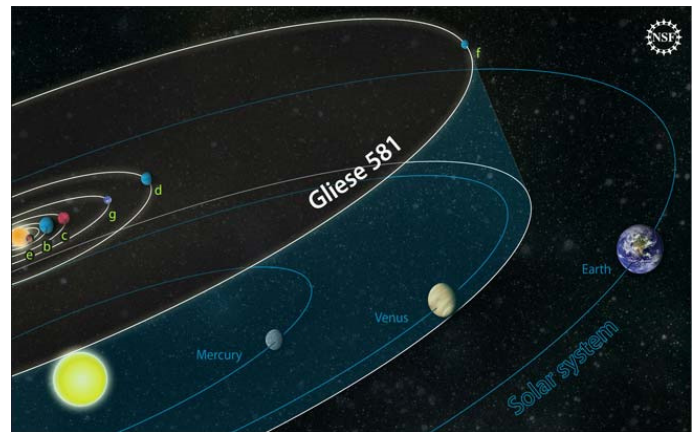
"It's both an incremental and monumental discovery," Sara Seager, an astrophysicist at the Massachusetts Institute of Technology, told SPACE.com. Incremental because the method used to find Gliese 581g already has found several planets most of the known planets, both super-Earths, more massive than our own world outside their stars' habitable zone, along with non-Earth-like planets within the habitable zone.

"It really is monumental if you accept this as the first Earth-like planet ever found in the star's habitable zone," said Seager, who was not directly involved in the discovery. Vogt, Butler and their colleagues will detail the planet finding in the *Astrophysical Journal*.

The newfound planet joins more than 400 other alien worlds known to date. Most are huge gas giants, though several are just a few times the mass of Earth.

Stellar tugs

Gliese 581g is one of two new worlds the team discovered orbiting the red dwarf star Gliese 581, bumping that nearby star's family of planets to six. The other newfound planet, Gliese 581f, is outside the habitable zone, researchers said. The star is located 20 light-years from Earth in the constellation Libra. One light-year is about 6 trillion miles (10 trillion km). Red dwarf stars are about 50 times dimmer than our sun. Since these stars are so much cooler, their planets can orbit much closer to them and still remain in the habitable zone.



The orbits of planets in the Gliese 581 system are compared to those of our own solar system. The Gliese 581 star has about 30 percent the mass of our sun, and the outermost planet is closer to its star than we are to the sun. The 4th planet, G, is a planet that could sustain life. Credit: Zina Deretsky, National Science Foundation

Estimates suggest Gliese 581g is 0.15 astronomical units from its star, close enough to its star to be able to complete an orbit in just under 37 days. One astronomical unit is the average distance between the Earth and sun, which is approximately 93 million miles (150 million km). The Gliese 581 planet system now vaguely resembles our own, with six worlds orbiting their star in nearly circular paths.

With support from the National Science Foundation and NASA, the scientists - members of the Lick-Carnegie Exoplanet Survey - collected 11 years of radial velocity data on the star. This method looks at a star's tiny movements due to the gravitational tug from orbiting bodies.

The subtle tugs let researchers estimate the planet's mass and orbital period, how long it takes to circle its star.

Gliese 581g has a mass three to four times Earth's, the researchers estimated. From the mass and estimated size, they said the world is probably a rocky planet with enough gravity to hold onto an atmosphere.

The planet is tidally locked to its star, so that one side basks in perpetual daylight, while the other side remains in darkness. This locked configuration helps to stabilize the planet's surface climate, Vogt said.

"Any emerging life forms would have a wide range of stable climates to choose from and to evolve around, depending on their longitude," Vogt said, suggesting that life forms that like it hot would just scoot toward the light side of that line while forms with polar-bear-like preferences would move toward the dark side.

Between blazing heat on the star-facing side and freezing cold on the dark side, the average surface temperature may range from 24 degrees below zero to 10 degrees Fahrenheit (minus 31 to minus 12 degrees Celsius), the researchers said.

Are you sure?

Supposedly habitable worlds have been found and later discredited, so what makes this one such a breakthrough? There's still a chance that further observations will dismiss this planet, also. But over the years, the radial velocity method has become more precise, the researchers point out in their journal article.

In addition, the researchers didn't make some of the unrealistic assumptions made in the past, Seager said.

For instance, another planet orbiting Gliese 581 (the planet Gliese 581c) also had been considered to have temperatures suitable for life, but in making those calculations, the researchers had come up with an "unrealistic" estimate for the amount of energy the planet reflected, Seager pointed out. That type of estimate wasn't made for this discovery. "We're looking at this one as basically the tip of the iceberg, and we're expecting more to be found," Seager said.

One way to make this a reality, according to study researchers, would be "to build dedicated 6- to 8-meter-class Automated Planet Finder telescopes, one in each hemisphere," they wrote.

The telescopes - or "light buckets" as Seager referred to them - would be dedicated to spying on the nearby stars thought to potentially host Earth-like planets in their habitable zones. The result would be inexpensive and probably would reveal many other nearby potentially habitable planets, the researchers wrote.

Beyond the roughly 100 nearest stars to Earth, there are billions upon billions of stars in the Milky Way, and with that in mind, the researchers suggest tens of billions of potentially habitable planets may exist, waiting to be found. Planets like Gliese 581g that are tidally locked and orbit the habitable zone of red dwarfs have a high probability of harboring life, the researchers suggest.

Earth once supported harsh conditions, the researchers point out. And since red dwarfs are relatively "immortal" living hundreds of billions of years (many times the current age of the universe), combined with the fact that conditions stay so stable on a tidally locked planet, there's a good chance that if life were to get a toe-hold it would be able to adapt to those conditions and possibly take off, Butler said.

Editor's Note: This story has been updated to correct an error in the paragraph stating that Mercury is tidally locked to the sun. While astronomers once thought that was the case, they no longer do.

Alien World Tour: The Exoplanets Around Star Gliese 581

By Mike Wall SPACE.com Senior Writer

The announcement Wednesday (Sept. 29) of two newfound alien planets circling the star Gliese 581 adds to the nearby solar system's intrigue, further cementing its status as a top candidate to harbor extraterrestrial life.

One of the two newly discovered planets, known as Gliese 581g, is a small, Earth-like world that likely lies within its star's habitable zone - the just-right range of distances that allow liquid water to exist.

Astronomers have now detected six planets orbiting Gliese 581, the most known to circle any star beyond our own sun. Here's a brief tour of the star and its planets, from the inside out:

Gliese 581: the mother star

Gliese 581 is a red dwarf located 20.5 light-years from Earth, in the constellation Libra. Like other red dwarfs, it's smaller and much dimmer than our sun. Scientists believe Gliese 581 is old - at least a few billion years - and relatively stable. Both are qualities conducive to the evolution of life, scientists have said.

Nearest planet

The nearest planet to the star is Gliese 581e, a rocky world nearly twice as massive as Earth. Gliese 581e is extremely close to its parent star - it completes an orbit every 3.15 days - so it's likely far too hot for life to have any chance of taking root. Gliese 581e is about 0.033 astronomical units from its parent star. One astronomical unit, or AU, is the average distance between the Earth and sun, about 93 million miles (150 million km).

Astronomers announced this planet's discovery in April 2009, and it's in the running for the lightest known extrasolar planet. So far, the only potential alien planet less massive than Gliese 581e is a world about 1.4 times the mass of Earth, but its existence - around a more distant star - has not yet been confirmed.

Next up: Gliese 581b

Traveling outward, the next planet is Gliese 581b, a Neptune-size alien world that's about 16 times as massive as Earth. This planet is still very close to the star, completing an orbit in 5.4 days. Astronomers first discovered this planet in December 2005, according to an extrasolar planet database maintained by NASA's Jet Propulsion Laboratory. Its average distance from the Gliese 581 star is about 0.041 AU.

Rocky world in third

Gliese 581c comes next. This is a rocky, smallish planet - about five Earth masses - that makes a full trip around the red dwarf every 15 days.

Astronomers once thought Gliese 581c might be in the habitable zone, but later observations suggested the planet is likely too hot to support liquid water or life. The planet is about 0.073 AU from its parent star.

Meet Gliese 581g

Unlike Gliese 581c, the newfound planet Gliese 581g looks much more hospitable. It is orbiting within the habitable zone of its parent star.

Gliese 581g is three to four times as massive as Earth, is most likely rocky, and may have an atmosphere, scientists say. It orbits about 0.146 AU from the central star. Liquid water could exist on some part of the planet's surface, which seems to have an average temperature between minus 24 and minus 10 degrees Fahrenheit (minus 31 to minus 12 degrees Celsius). Gliese 581g completes an orbit every 37 days or so.

Fifth planet is a super-Earth

The next planet in line is a so-called super-Earth, Gliese 581d, which is seven or eight times as massive as Earth and completes an orbit every 67 days. Though at first glance this planet appeared to be beyond the star's habitable zone, astronomers think it might just squeak in - computer models suggest a greenhouse effect could be warming its surface. It was discovered in April 2007 and orbits about 0.22 AU from its parent star.

Sixth planet on the outskirts

The outermost planet in the Gliese 581 system (that astronomers know about, anyway) is the newly discovered Gliese 581f, announced today. This planet is much farther away than the other five planets, zipping through space far outside the habitable zone, but it is still closer to its parent star than the Earth is to our sun.

The planet is about 0.76 AU from its parent star. Like all of the planets in the Gliese 581 system - and in our own solar system - Gliese 581f's orbit is nearly circular, scientists said.

New drug offers big relief for osteoarthritis pain

A phase II clinical trial of the first new type of drug for musculoskeletal pain since aspirin shows that it significantly reduces knee pain in osteoarthritis, the most common osteoarthritis pain, according to new research from Northwestern Medicine.

However, phase III trials of that drug, tanezumab, have been placed on clinical hold after 16 out of several thousand participants in the new trial developed progressively worsening arthritis and bone changes that required total joint replacements.

"The bottom line is this is a very effective drug for relieving pain; unfortunately, it appears some people go on to have their osteoarthritis progress more quickly," said Thomas Schnitzer, M.D., a rheumatologist and professor in the department of physical medicine and rehabilitation at Northwestern Medicine. "The long-term safety of tanezumab needs to be better understood."

Schnitzer is a principal investigator and lead author of a paper on the research, which will be published Aug. 26 in the *New England Journal of Medicine*. He also was an investigator on the phase III trial. The other lead author and principal investigator is Nancy Lane, M.D., a professor of internal medicine at UC Davis School of Medicine.

Tanezumab is the first new drug for general muscle or joint pain in over 100 years, Schnitzer said, noting nonsteroidals and COX inhibitors are a "fancy form of aspirin."

"It's very exciting to have a new approach to manage pain for osteoarthritis," he said. Other drugs currently used to treat pain have significant side effects -- bleeding, ulcers and an increase in heart attacks -- that limit their use. Anecdotally, tanezumab appears to provide greater pain relief than current drugs.

"The effects of tanezumab were remarkable," Lane said. "People on the drug went from having very limited activity to practically being on the dance floor. No medication available today has such dramatic results."

Schnitzer and Lane said the apparent worsening of certain patients' condition could be because tanezumab helped patients increase their activity and, as a result, put more stress on their diseased joints.

In the phase II study of 440 patients, treatment with tanezumab reduced knee pain during walking by 45 to 62 percent compared to 22 percent reduction in pain with a placebo. The pain scores were equal to or lower than those reported by patients during screening while taking their prior pain medication.

Schnitzer said the Food and Drug Administration (FDA) is examining data to decide how to proceed.

"The FDA may decide it's too dangerous overall or, rather, that there may be a specific patient population in which it should not be used or who need to be warned about possible serious side effects," he said.

The drug works by neutralizing or blocking Nerve Growth Factor (NGF), a molecule needed for normal development of the nervous system, but which also gets released when there is inflammation in the body. NGF stimulates nerve cells and triggers pain.

Nearly 27 million adults in the United States have osteoarthritis, according to the U.S. Department of Commerce, and about 40 percent suffer from knee osteoarthritis. The number of people with osteoarthritis is expected to rise as baby boomers reach retirement age and as the number of obese Americans increases. Half of all adults will develop symptoms in the knee at some point in their lives.

Evidence of Post-Stroke Brain Recovery Discovered

The world's largest study using neuroimaging of stroke patients struggling to regain ability to communicate finds that brain cells outside the damaged area can take on new roles.

Julius Fridriksson, a researcher at the University of South Carolina's Arnold School of Public Health, said the findings offer hope to patients of "chronic stroke," characterized by the death of cells in a specific area of the brain. The damage results in long-term or permanent disability.

"For years, we heard little about stroke recovery because it was believed that very little could be done," Fridriksson said. "But this study shows that the adult brain is quite capable of changing, and we are able to see those images now. This will substantially change the treatment for chronic-stroke patients."

The study, reported in the Sept. 15 issue of the Journal of Neuroscience, involved 26 patients with aphasia, a communication disorder caused by damage to the language regions in the brain's left hemisphere. Aphasia impairs a person's ability to process language and formulate speech.

About 35 percent of stroke patients have speech and/or communication problems. While many patients with aphasia regain some language function in the days and weeks after a stroke, scientists have long believed that recovery is limited after this initial phase. "Stroke is the leading cause of disability among adults, more than accidents or complications from Parkinson's or Alzheimer's diseases," said Fridriksson, director of the university's Aphasia Laboratory and an associate professor in the department of communication sciences and disorders.

"When someone has brain damage as a result of a stroke, the recovery is expected to be limited," he said. But Fridriksson's study shows that the brain can recover and that a patient's ability to communicate can improve.

Stroke patients underwent a functional magnetic resonance imaging test, also called fMRI, which measures brain activity. Patients received multiple MRI sessions before and after undergoing 30 hours of traditional speech therapy used to improve communication function in patients with aphasia.

By using fMRI - an imaging technique more improved and widely used in the past decade - Fridriksson was able to see the healthy areas of the brain that "take over" the functions of the areas damaged as a result of a stroke.

"The areas that are immediately around the section of the brain that was damaged become more 'plastic,' " Fridriksson said. "This 'plasticity,' so to speak, increases around the brain lesions and supports recovery. In patients who responded well with the treatment for anomia [difficulty in recalling words and names], their fMRI showed evidence that areas of the brain took over the function of the damaged cells."

The study found that patients who did not experience these changes did not have as improved a recovery, he said. This research lays the foundation for future studies of aphasia, including research on the use of low-current, electrical stimulation for the brain.

"Knowing where the brain has been damaged -- and the section that is taking over that function -- will enable us to better use electrical stimulation to promote recovery," said Fridriksson, the lead author of another paper published last month in the Journal of Neuroscience that examined the mapping of brain lesions that cause speech/communication impairment.

"It is believed that electrical currents to the brain will promote secretions of neurotransmitters that support brain plasticity," he said. "This could dramatically improve the quality of life for stroke patients."

New study finds groups demonstrate distinctive 'collective intelligence' when facing difficult tasks

Tendency to cooperate effectively is linked to the number of women in a group

CAMBRIDGE, Mass. -- When it comes to intelligence, the whole can indeed be greater than the sum of its parts. A new study co-authored by MIT, Carnegie Mellon University, and Union College researchers documents the existence of collective intelligence among groups of people who cooperate well, showing that such intelligence extends beyond the cognitive abilities of the groups' individual members, and that the tendency to cooperate effectively is linked to the number of women in a group.

Many social scientists have long contended that the ability of individuals to fare well on diverse cognitive tasks demonstrates the existence of a measurable level of intelligence in each person. In a study published Thursday, Sept. 30, in the advance online issue of the journal Science, the researchers applied a similar principle to small teams of people. They discovered that groups featuring the right kind of internal dynamics perform well on a wide range of assignments, a finding with potential applications for businesses and other organizations.

"We set out to test the hypothesis that groups, like individuals, have a consistent ability to perform across different kinds of tasks," says Anita Williams Woolley, the paper's lead author and an assistant professor at Carnegie Mellon's Tepper School of Business. "Our hypothesis was confirmed," continues Thomas W. Malone, a co-author and Patrick J. McGovern Professor of Management at the MIT Sloan School of Management. "We

found that there is a general effectiveness, a group collective intelligence, which predicts a group's performance in many situations."

That collective intelligence, the researchers believe, stems from how well the group works together. For instance, groups whose members had higher levels of "social sensitivity" were more collectively intelligent. "Social sensitivity has to do with how well group members perceive each other's emotions," says Christopher Chabris, a co-author and assistant professor of psychology at Union College in New York. "Also, in groups where one person dominated, the group was less collectively intelligent than in groups where the conversational turns were more evenly distributed," adds Woolley. And teams containing more women demonstrated greater social sensitivity and in turn greater collective intelligence compared to teams containing fewer women.

To arrive at their conclusions, the researchers conducted studies at MIT's Center for Collective Intelligence and Carnegie Mellon, in which 699 people were placed in groups of two to five. The groups worked together on tasks that ranged from visual puzzles to negotiations, brainstorming, games and complex rule-based design assignments. The researchers concluded that a group's collective intelligence accounted for about 40 percent of the variation in performance on this wide range of tasks.

Moreover, the researchers found that the performance of groups was not primarily due to the individual abilities of the group's members. For instance, the average and maximum intelligence of individual group members did not significantly predict the performance of their groups overall.

Only when analyzing the data did the co-authors suspect that the number of women in a group had significant predictive power. "We didn't design this study to focus on the gender effect," Malone says. "That was a surprise to us." However, further analysis revealed that the effect seemed to be explained by the higher social sensitivity exhibited by females, on average. "So having group members with higher social sensitivity is better regardless of whether they are male or female," Woolley explains.

Malone believes the study applies to many kinds of organizations. "Imagine if you could give a one-hour test to a top management team or a product development team that would allow you to predict how flexibly that group of people would respond to a wide range of problems that might arise," he says. "That would be a pretty interesting application. We also think it's possible to improve the intelligence of a group by changing the members of a group, teaching them better ways of interacting or giving them better electronic collaboration tools."

Woolley and Malone say they and their co-authors "definitely intend to continue research on this topic," including studies on the ways groups interact online, and they are "considering further studies on the gender question." Still, they believe their research has already identified a general principle indicating how the whole adds up to something more than the sum of its parts. As Woolley explains, "It really calls into question our whole notion of what intelligence is. What individuals can do all by themselves is becoming less important; what matters more is what they can do with others and by using technology."

"Having a bunch of smart people in a group doesn't necessarily make the group smart," concludes Malone. *In addition to Woolley, Malone and Chabris, the other co-authors were Alexander Pentland, the Toshiba Professor of Media Arts & Science at the MIT Media Lab; and Nada Hashmi, a doctoral candidate at MIT Sloan.*

Source: "Evidence for a collective intelligence factor in the performance of human groups" by Anita Williams Woolley, Christopher F. Chabris, Alexander Pentland, Nada Hashmi, and Thomas W. Malone. Science, 30 September, 2010.

Virus-like particles speed bacterial evolution

The exchange of genetic information among ocean bacteria has been greatly underestimated.

Amy Maxmen

In the ocean, genes can hop between bacteria with unexpected ease, thanks to strange virus-like particles that shuttle genes from one species to another¹. These particles, called gene-transfer agents (GTAs), insert DNA into bacterial genomes so frequently that gene transfer in the ocean may occur 1,000 to 100 million times more often than previously thought. This suggests that GTAs have had a powerful role in evolution.

"We know there's a lot of gene shuffling going on in bacteria, but nobody had come up with a good mechanism by which it happens," says John Paul, a marine microbiologist at the University of South Florida College of Marine Science in St Petersburg, and an author on the study that finally succeeded in uncovering a mechanism.



Coloured scanning electron micrograph (SEM) of a group of Rhodospirillum rubrum (R. rubrum) phototrophic bacteria (orange) Genes are shuttled between ocean bacteria many times faster than was previously thought.

EYE OF SCIENCE / SCIENCE PHOTO LIBRARY

GTAs, which harbour bits of their host's genome inside a protein coat, reside in bacterial genomes. When they exit, they take some of their host's genes with them. For 30 years, they have remained obscure objects of occasional study in the lab.

Paul's team engineered GTAs to contain a gene conferring antibiotic resistance. The researchers sealed these GTAs in bags filled with seawater collected from different coastal environments, and floated the bags in the ocean to mimic natural conditions as closely as possible. After incubation overnight, up to 47% of the bacteria living in the seawater-filled bags had incorporated the particles and their genetic contents into their genomes. The work is published today in *Science*¹.

"They're promiscuous little bastards," says Paul, pointing out that that the GTAs infected many different strains of ocean bacteria.

Ocean oddballs

"GTAs are very peculiar," says Eugene Koonin, an evolutionary biologist at the National Institutes of Health in Bethesda, Maryland. "Their only function seems to be transferring genes."

In bags near a coral reef in the Florida Keys, virus-like particles transferred genes to oceanic bacteria. An antibiotic-resistance gene spread rapidly to different bacteria inside a sealed plastic bag. Erich Bartels

Last year, Koonin and his colleagues examined genomic analyses of marine viruses and predicted GTAs to be major contributors to gene transfer in the ocean². He says that the current paper confirms his prediction by finding frequent GTA-mediated gene-transfer events in a marine microbial community.

Horizontal gene transfer — whereby genes are shuffled between organisms rather than passed down from parent to offspring — helps to explain how bacteria adapt rapidly to changing environments and can quickly acquire resistance to antibiotics. If one bacterium has a beneficial gene, that gene can spread horizontally to other bacteria in the population, increasing its frequency by improving the survival of those that carry it.

Horizontal gene transfer can also occur through direct cell–cell contact or by means of mobile genetic elements called plasmids, or by bacterial viruses — which often destroy the host upon departure. GTAs are virus-like, but they don't seem to take a toll on their host and, what's more, seem to efficiently shuttle genes between unrelated bacteria.

The team found exact copies of the antibiotic-resistance gene that the GTAs carried — a very unlikely finding had horizontal gene transfer occurred by another means. "We were absolutely amazed to see exact matches for the genes we put into the donor strain in different genera that are common in the marine environment," says co-author Lauren McDaniel, also at the University of South Florida College of Marine Science.

The authors chose to insert genes for resistance to the commonly-used lab antibiotic kanamycin for pragmatic reasons — its resistance can be easily detected by treating bacteria with the drug and seeing which ones survive — but Paul says there's no reason why GTAs wouldn't play a part in spreading clinically relevant types of antibiotic resistance.

Meanwhile, evolutionary biologist Jeffrey Townsend at Yale University in New Haven, Connecticut, says that this work stands out from other studies on this topic because the team measured the frequency of gene transfer in nature rather than inferring it through genetic analyses.

"People have had trouble tracking this down before, so this is a very important observation," he says. "In order to understand antibiotic resistance, pathogenicity, or the beneficial things that bacteria do for us, we need to understand how they evolve through horizontal gene transfer — knowing about this process can help us live in a world full of microbes."

References 1. McDaniel, L. D. et al. *Science* 330, 50 (2010). | Article | OpenURL | | ChemPort |

2. Kristensen, D. M., Mushegian, A. R., Dolja, V. V. & Koonin, E. V. *Trends Microbiol.* 18, 11-19 (2010).

Archaeologists shed new light on adaptability of modern humans' ancestors

A University of Otago-led archaeological investigation of campsites up to 50,000 years old in a remote highland valley of Papua New Guinea is revealing how highly adaptable the humans at the forefront of global colonisation were.

Otago anthropologist Professor Glenn Summerhayes and colleagues have just published findings in the leading journal *Science* indicating that, as early as 49,000 years ago, groups were regularly moving back and forth through extremely rugged territory to exploit rich plant food resources in Papua New Guinea's Ivane Valley, which is 2000 metres above sea level.

The archaeological work reveals campsites buried by volcanic ash where people made stone tools, hunted small animals and gathered the high energy nuts of the local Pandanus trees in conditions much colder than the present day. The sites were



occupied during a relatively warm phase of the last ice age - the Pleistocene - when New Guinea was joined to Australia as part of the continent of Sahul.

Professor Summerhayes, who led the team of archaeologists from Otago, Australia and Papua New Guinea, says the stone tools they found, known as waisted axes, suggest colonists were deliberately modifying the valley landscape, mostly likely to clear forest patches to promote the growth of useful plants such as Pandanus.

“Our findings paint a picture of a highly mobile society that quickly adapted to and survived in a radically different environment to the coastal regions they had recently arrived from. It is remarkable that this is occurring around 15,000 years before other modern humans would colonise Europe,” Professor Summerhayes says.

As well as using tools to engage in agro-forestry, state-of-the-art analysis of starch residues on the waisted axes suggest that yams were being brought to the valley as food supplies from the lower altitudes where they grew, he says. “All this is unprecedented evidence of careful, intentional colonisation over thousands of years, rather than people just wandering around foraging and moving on. These are unique footprints of humanity that challenge some current notions regarding at what stage humans can be truly said to have become ‘modern’ in their thinking and behaviour.”

The novel idea that Pleistocene peoples in Sahul were practising agro-forestry by opening up patches to promote growth of desired plants was first proposed two decades ago, on little if any evidence, by an ex-Otago staff archaeologist, Les Groube, based on his work at PNG’s coastal Huon Peninsula, he says.

“Our new evidence from the Ivane valley, including the presence of tools fit for this purpose, gels perfectly with his model,” Professor Summerhayes says.

Further residue and micro-wear analysis of the tools is currently being undertaken by Otago PhD Student Anne Ford in an attempt to gain solid evidence of the purposes to which they were put.

Provided by University of Otago

Poor kidney function linked to future heart and brain problems

People with impaired kidney function are at a higher risk of future stroke than people with normal kidney function, concludes a study published in the British Medical Journal today.

A second study, also published today, finds that even the earliest stages of chronic kidney disease are linked to a higher risk of coronary heart disease.

This study suggests that considering signs of early kidney disease, in addition to routinely measured risk factors such as blood pressure and blood cholesterol, modestly improves the identification of people at high risk of cardiovascular disease. It provides about half as much predictive gain as did history of diabetes or about a sixth as much as did history of smoking.

Doctors already know that chronic kidney disease and cardiovascular disease are linked. However, kidney disease often goes undiagnosed, because it is largely without symptoms, and the impact of kidney function on stroke is still unclear.

So, in the first study, researchers from Taiwan and the USA investigated the link between low glomerular filtration rate or GFR (the flow rate of fluid filtering through the kidneys) and risk of future stroke.

They analysed the results of 33 studies involving over 280,000 individuals and found that people with an estimated glomerular filtration rate (eGFR) of less than 60 ml/min/1.73m² (the normal range is 100-130 ml/min/1.73m²) had a 43% greater risk of future stroke than people with a normal eGFR. They also found that Asian people with a low eGFR were at higher risk of future stroke than their non-Asian counterparts.

Based on these findings, they conclude that a low eGFR should be seen as a marker for increased stroke risk, prompting doctors to start risk reduction strategies, such as blood pressure control and use of cholesterol lowering drugs, to avert future strokes, particularly in people of Asian race.

In the second study, UK and Icelandic researchers tracked 16,958 people living in Reykjavik over 24 years and found that even the earliest stages of chronic kidney disease were at increased risk of developing coronary heart disease. They found that assessment of chronic kidney disease in addition to conventional risk factors modestly improved coronary heart disease risk prediction. It provided about half as much predictive gain as did history of diabetes or about a sixth as much as did history of smoking.

The researchers also found a suggestive association between chronic kidney disease and increased risk of death from causes other than cardiovascular disease or cancer, recommending the need for further studies to investigate this link in more detail.

These findings are supported in an accompanying editorial, which says that the presence of chronic kidney disease should act as a "red flag" that triggers cardiovascular risk assessment and implementation of appropriate preventive strategies already shown to be effective in the general population.

Provided by British Medical Journal

Brain Chemical Finding Could Open Door to New Schizophrenia Drugs

New research has linked psychosis with an abnormal relationship between two signalling chemicals in the brain. The findings, published in tomorrow's edition of the journal *Biological Psychiatry*, suggest a new approach to preventing psychotic symptoms, which could lead to better drugs for schizophrenia.

Schizophrenia is one of the most common severe mental health conditions. Sufferers experience symptoms of psychosis -- an inability to distinguish between reality and imagination -- such as hallucinations and delusions. The condition tends to begin in the late teens or twenties, and usually persists for the rest of the sufferer's life.

Brain chemicals called neurotransmitters carry signals from one nerve cell to another. Research has linked schizophrenia with abnormally high levels of a neurotransmitter called dopamine in a region of the brain called the striatum. Drugs currently used to treat schizophrenia block the effects of dopamine in the brain. These drugs are not effective for all patients, and can have serious side effects.

The new pilot research, funded by the Medical Research Council (MRC), provides evidence that high levels of dopamine in people with psychotic symptoms occur as a consequence of changes in another brain chemical, glutamate. Glutamate-releasing cells in a brain region called the hippocampus connect to the striatum and influence the activity of dopamine-releasing cells. Drugs that interfere with glutamate signals in the brain might therefore be able to prevent psychotic symptoms in people with schizophrenia.

"Schizophrenia is a devastating illness that destroys the lives of people who are afflicted and those around them," said Dr James Stone of the Department of Medicine at Imperial College London, first author of the study. "At the moment, the drugs we have just aren't adequate. They don't help everybody, and they don't stop some of the most debilitating symptoms."

The researchers carried out brain scans on 16 people with an at-risk mental state for psychosis and 12 healthy volunteers, to measure the levels of glutamate and dopamine. In people with early signs of psychotic symptoms, there was a negative correlation between glutamate levels in the hippocampus and dopamine levels in the striatum area. There was a particularly marked correlation in the subjects who went on to develop psychosis later. There was no correlation in the healthy subjects.

"In healthy volunteers, there's no clear relationship between glutamate and dopamine, but in people with early signs of psychosis, we see this abnormal relationship," Dr Stone said. "This suggests that the signalling pathway between the hippocampus and the striatum is dysfunctional, and we might be able to treat this by targeting the glutamate system. If drugs that act on glutamate signalling can prevent psychotic symptoms, it would mean a real shift in the way that people are treated for schizophrenia."

"The next step will be to see if these results are confirmed in a larger group of people. There are already a number of promising drug candidates that interfere with glutamate signalling, so hopefully in a few years we'll be able to start testing new treatments for people with schizophrenia."

Professor Chris Kennard, chair of the MRC Neuroscience and Mental Health Board, said: "Studies like these are helping to unravel the complex mechanisms of psychiatric illness and bring us a step closer to more effective, targeted drugs for patients with schizophrenia. The MRC funds research like this in order to bring scientific findings from the lab bench to patient bedside, more quickly. If we can develop new drugs that prevent psychotic symptoms, it would mean a real benefit for patients with schizophrenia."

Story Source: The above story is reprinted (with editorial adaptations by ScienceDaily staff) from materials provided by Imperial College London, via EurekAlert!, a service of AAAS.

Journal Reference: 1. Stone. Altered Relationship Between Hippocampal Glutamate Levels and Striatal Dopamine Function in Subjects at Ultra High Risk of Psychosis. *Biological Psychiatry*, 2010; 68 (7): 599 DOI: 10.1016/j.biopsych.2010.05.034

Parkinson's disease: Excess of special protein identified as key to symptoms and possible new target for treatment with widely used anti-cancer drug imatinib

Johns Hopkins scientists have discovered that the over-activation of a single protein may shut down the brain-protecting effects of a molecule and facilitate the most common form of Parkinson's disease. The finding of this mechanism could lead to important new targets for drugs already known to inhibit it, thus controlling symptoms of the disorder, which affects about 1 million older Americans.

Previous research demonstrated that a protein called parkin protects brain cells by "tagging" certain toxic elements that are then destroyed naturally. It was also known that mutations in the gene that holds the code for parkin cause rare, familial forms of PD. However, parkin's role remained unclear in sporadic late-onset PD, the prevalence of which is increasing as the population ages.

Results of the new study, published Sept. 7 in the *Proceedings of the National Academy of Sciences (PNAS)* Online Early Edition, indicate that an over-activation of a protein called c-Abl– can shut down the activity of parkin and contribute to a build-up of toxic proteins that kill brain cells and enables the progression of PD.

C-Abl contributes to the regulation of cell death and is implicated in a host of diseases. It has already has proven to be a target for certain types of cancer-killing drugs, such as imatinib (Gleevec), the first drug designed to directly switch off a biochemical signal that directly targets a protein vital to cancer growth, says Ted Dawson, M.D., Ph.D., Leonard and Madlyn Abramson Professor in Neurodegenerative Diseases and scientific director of the Johns Hopkins Institute for Cell Engineering.

"Our new appreciation of c-Abl's role in sporadic PD suggests that we can give brain-permeable inhibitors of c-Abl to maintain parkin's normal protective function," Dawson says. "The testing of these already approved, well-tolerated drugs for a new use — as a neuro-protective treatment for PD — is a potentially exciting therapeutic arc that should be pursued."

The researchers first used a test called the Western blot to label certain proteins in neuron-like human cells in culture. They could see that c-Abl shut down the activity of parkin by measuring the levels of chemical tags on proteins that, in a healthy system, are marked for destruction. These "garbage" proteins, when overabundant, have been shown previously by Dawson's lab to be selectively toxic to neurons. When c-Abl was active, parkin's ability to tag those proteins was significantly decreased.

The team then incubated these cells with STI-571, a well-known c-Abl inhibitor marketed as imatinib or Gleevec. When compared to cultures not incubated with the compound, the inhibition of parkin's function by c-Abl was wholly prevented.

The c-Abl inhibitor, STI-571 was approved by the Food and Drug Administration in 2001 for the treatment of a cancer of white blood cells and in 2002 for the treatment of a rare form of stomach cancer. It works by blocking the activity of the abnormal c-Abl protein, which is much more active than the normal version. For a c-Abl inhibitor to be an effective treatment for Parkinson's disease, it would need to cross the blood-brain barrier, Dawson says.

Next, using a mouse which had been given drugs that cause Parkinson's-like traits, the team proved that when c-Abl is activated, parkin's function shuts down and as a result, garbage proteins accumulate and lead to a significant loss of neurons. The team also demonstrated that genetically altered mice in which c-Abl had been knocked out were protected against the same significant loss of neurons. They measured the loss of neurons by counting them: Wild-type (normal) mice lost about 8,000 neurons, while the genetically altered mice with the disabled c-Abl lost only about half that many.

Finally, the scientists turned to human brain tissue to look for evidence that c-Abl is a major regulator of parkin function. By comparing brain tissue of patients who died with Parkinson's disease with those who died of other causes, they established that when c-Abl shuts down Parkin, the "garbage" proteins accumulate and result is the death of neurons.

"With people living longer, lots more people are developing this common, debilitating neurological disorder," Dawson says, citing that one in 100 people are afflicted at the age of 60, and four times that many by the age of 80. "Now that we know the mechanism, it's important that we explore new, effective therapies that can slow or stop its progression."

The study was funded by the National Institutes of Health and the Bachmann Strauss Dystonia and Parkinson's Disease Foundation.

Authors of the study, in addition to Dawson, are Anthony J. Koleske of Yale University; and Han Seok Ko, Yunjong Lee, Joo-Ho Shin, Senthilkumar S. Karuppagounder, Bharathi Shrikanth Gadad, Olga Pletnikova, Juan C. Troncoso and Valina L. Dawson, all of Johns Hopkins University.

Key ingredient staves off marijuana memory loss ***Cannabis composition determines effects on the brain.*** **Arran Frood**

Smoking cannabis has long been associated with poor short-term memory, but a study now suggests that the strain of cannabis makes all the difference. In a test of short-term memory skills, only users of 'skunk'-type strains exhibited impaired recall when intoxicated, whereas people who smoked hashish or herbal cannabis blends performed equally well whether they were stoned or sober.

The findings suggest that an ingredient more plentiful in some types of marijuana than in others may help to reduce the memory loss that some users suffer.

The key difference between the types of cannabis is the ratio of two chemicals found in all strains. Tetrahydrocannabinol (THC) is the primary active ingredient, and is responsible for the effects associated with the classic 'high', including euphoria and giddiness but also anxiety and paranoia. The second chemical, cannabidiol, has more calming effects, and brain-imaging studies have shown that it can block the psychosis-inducing effects of THC². Skunk-type strains of cannabis contain a higher ratio of THC to cannabidiol than do hashish or herbal types.

Valerie Curran, a psychopharmacologist from University College London who led the latest study, says that if habitual users must partake they should be encouraged to use strains with higher levels of cannabidiol, rather than using skunk. She also argues that studying cannabidiol could provide insight into the mechanics of memory formation, and that it may have therapeutic benefits for disorders involving memory deficits. The findings are published in the *British Journal of Psychiatry* today¹.

marijuana leaf Levels of THC in 'skunk' marijuana are higher than in other varieties. Getty Images

Cannabis use has increased in recent years — almost as many 16–24-year-olds in the United Kingdom have tried as haven't, according to the 2008 report *Statistics on Drug Misuse* by the National Health Service — and concerns have been raised that increased levels of THC in 'skunk' varieties owing to aggressive plant breeding over the past decade are responsible for a rise in the number of young users displaying mild-to-severe cognitive impairment. However, links to a possible higher incidence and earlier onset of psychotic conditions such as schizophrenia remain controversial, as do associations with long-term psychological problems. Researchers suspect any effects of the drug on mental health could be a result of an increased ratio of THC to cannabidiol in cannabis, because levels of cannabidiol have not kept pace with rising THC concentrations.

Total recall

To test this hypothesis, Curran and her colleagues travelled to the homes of 134 volunteers, where the subjects got high on their own supply before completing a battery of psychological tests designed to measure anxiety, memory recall and other factors such as verbal fluency when both sober and stoned. The researchers then took a portion of the stash back to their laboratory to test how much THC and cannabidiol it contained.

The subjects were divided into groups of high (samples containing more than 0.75% cannabidiol) and low (less than 0.14%) cannabidiol exposure, and the data were filtered so that their THC levels were constant. Analysis showed that participants who had smoked cannabis low in cannabidiol were significantly worse at recalling text than they were when not intoxicated. Those who smoked cannabis high in cannabidiol showed no such impairment.

The results suggest that cannabidiol can mitigate THC's interference with memory formation. This is the first study in human to show such effects. One previous study, led by Aaron Ilan, a cognitive neuroscientist at the San Francisco Brain Research Institute in California, failed to find variations in cognitive effects with varying concentrations of cannabidiol³.

Ilan attributes the positive finding of Curran and her team to their more powerful methodology in analysing subjects' own smoking preferences. In the United States, government policy dictates that only marijuana provided by the National Institute on Drug Abuse can be used for research — and it "is notorious for being low in THC and of poor quality", says Ilan.

Lester Grinspoon, professor emeritus of psychiatry at Harvard Medical School in Boston, Massachusetts, who has studied the effects of marijuana on patients since 1967, says that Curran's study is important. "Cannabis with high cannabidiol levels will make a more appealing option for anti-pain, anti-anxiety and anti-spasm treatments, because they can be delivered without causing disconcerting euphoria," he says.

References 1. Curran, V. et al. *Br. J. Psychiat.* 197, 285-290 (2010).

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3. Ilan, A. B., Gevins, A., Coleman, M., ElSohly, M. A. & de Wit, H. *Behav. Pharmacol.* 16, 487-496 (2005).

Early Surgery After Hip Fractures Reduces Death, Study Finds

Performing early surgery on elderly hip fracture patients reduces the risk of death by 19%, found a study published in *CMAJ* (Canadian Medical Association Journal).

Hip fractures are associated with a mortality rate of 14 to 36% in the year following the fracture and can negatively affect a patient's independence and quality of life. Current guidelines recommend surgery within 24 hours of the break, although some physicians who favour delays believe it provides more time to prepare the patient and can decrease the risk of complications.

The researchers, from McMaster University and the University of Toronto, set out to determine the impact of early versus delayed surgery on death and postoperative complications. They looked at 16 observational studies with a total of 13, 478 patients aged 60 years and older. They found that surgery before 24 to 72 hours reduced the risk of death and may reduce the risk of postoperative pneumonia and pressure sores.

"Based on current evidence, surgery conducted before 24-72 hours is associated with reduced mortality and certain postoperative complications in elderly hip fracture patients," write Dr. Mohit Bhandari, McMaster University, with coauthors.

The authors recommend additional studies to better understand the effect of early surgery among elderly hip fracture patients.

Story Source: The above story is reprinted (with editorial adaptations by ScienceDaily staff) from materials provided by Canadian Medical Association Journal, via EurekAlert!, a service of AAAS.

Journal Reference: 1. Nicole Simunovic, P. J. Devereaux, Sheila Sprague, Gordon H. Guyatt, Emil Schemitsch, Justin Debeer, Mohit Bhandari. Effect of early surgery after hip fracture on mortality and complications: systematic review and meta-analysis. Canadian Medical Association Journal, 2010; DOI: 10.1503/cmaj.092220

How Injured Nerves Grow Themselves Back

Unlike nerves of the spinal cord, the peripheral nerves that connect our limbs and organs to the central nervous system have an astonishing ability to regenerate themselves after injury. Now, a new report in the October 1st issue of *Cell*, a Cell Press publication, offers new insight into how that healing process works.

"We know a lot about how various cell types differentiate during development, but after a serious injury like an amputation, nerves must re-grow," said Allison Lloyd of University College London. "They need a new mechanism to do that because the developmental signals aren't there."

That kind of regrowth isn't easy to pull off. Peripheral nerves are long cells; their nucleus is in the spinal cord and the axons that extend from them and relay nerve messages can reach all the way down a leg. "When a nerve gets cut, all the axons downstream degenerate," Lloyd said. Regrowth requires that the two ends somehow find their way back to each other through damaged tissue.

Scientists knew that Schwann cells were important to that process. Those cells are found wrapped around axons, where under normal circumstances they are rather "quiet" cells. All of that changes when an injury occurs; those Schwann cells de-differentiate back to a stem-cell-like state and play an important role in bridging the gap to repair damaged neurons.

"Schwann cells could sit on a nerve for years and then, at any point, switch states," Lloyd said. "They are quite unusual cells." (There are other examples of cells that can return to a stem-cell-like state, she said. For instance, cells in the liver and the endothelial cells that line blood vessels.)

But, the new study shows, the Schwann cells need help to repair the nerves properly. That help comes from a well-studied cell type known to play a role in wound healing: fibroblasts.

"This is a new role for fibroblasts," Lloyd said, an exciting find given that the cells are the type that grows when you place animal tissue in cell culture and have been very well studied as a result. "There is lots known about them, and they are always present at wounds. This shows that they act in a completely new way."

The fibroblasts send a signal to the Schwann cells, causing them to sort themselves into clumps, or cords, that make their way out of the nerve stump as a group. Those cords guide the regrowth of axons across the wound. Lloyd's team found that the response to the so-called ephrin-B signal issued by the fibroblasts depends on a factor called Sox2, best known for its central role in embryonic stem cells. Sox2 is also one of a handful of ingredients that can help reprogram adult cells to behave like embryonic stem cells.

Without the ephrin-B signal, Schwann cells fail to migrate in an organized fashion and the axons don't grow back properly.

Lloyd said the new findings might lead to ways to improve the repair of peripheral nerves, noting that the natural process isn't all that efficient. "It's not perfect, but if a hand is cut off and sewn back on, you can get some movement," Lloyd said. Her team is actively exploring ways to improve upon the natural nerve-healing mechanism now.

The researchers also have plans to investigate whether similar mechanisms might be involved in the movement and spread of cancers of the peripheral nervous system. "We don't know yet, but it wouldn't be surprising if this is relevant to the movement of other cells," Lloyd said.

The researchers include Simona Parrinello, MRC Laboratory for Molecular Cell Biology and the UCL Cancer Institute, University College London, London, UK; Iliaria Napoli, MRC Laboratory for Molecular Cell Biology and the UCL Cancer Institute, University College London, London, UK; Sara Ribeiro, MRC Laboratory for Molecular Cell Biology and the UCL Cancer Institute, University College London, London, UK; Patrick Wingfield Digby, MRC Laboratory for Molecular Cell Biology and the UCL Cancer Institute, University College London, London, UK; Marina Fedorova, MRC Laboratory for Molecular Cell Biology and the UCL Cancer Institute, University College London, London, UK; David B. Parkinson, University of Plymouth, Plymouth, UK; Robin D.S. Doddrell, University of Plymouth, Plymouth, UK; Masanori Nakayama, University of Munster, Munster, Germany; Ralf H. Adams, University of Munster, Munster, Germany; and Alison C. Lloyd, MRC Laboratory for Molecular Cell Biology and the UCL Cancer Institute, University College London, London, UK.

Story Source: The above story is reprinted (with editorial adaptations by ScienceDaily staff) from materials provided by Cell Press, via EurekAlert!, a service of AAAS.

Journal Reference: 1. Simona Parrinello, Iliaria Napoli, Sara Ribeiro, Patrick Wingfield Digby, Marina Fedorova, David B. Parkinson, Robin D.S. Doddrell, Masanori Nakayama, Ralf H. Adams, and Alison C. Lloyd. EphB Signaling Directs Peripheral Nerve Regeneration through Sox2-Dependent Schwann Cell Sorting. *Cell*, 2010; DOI: 10.1016/j.cell.2010.08.039

Experts Urge Making Cigarettes Non-Addictive a Research Priority

After a major review of scientific information, six leading tobacco research and policy experts have concluded that a nicotine reduction strategy should be an urgent research priority because of its potential to profoundly reduce the death and disease from tobacco use.

Their findings were published in the journal *Tobacco Control*.

According to this new report, reducing the amount of nicotine in cigarettes to non-addictive levels could have a significant public health impact on prevention and smoking cessation. Over time, the move could dramatically reduce the number of annual deaths related to cigarette smoking by decreasing adolescent experimentation with cigarettes preventing a progression to addiction, and by reducing dependence on tobacco among currently addicted smokers of all ages.

Dorothy Hatsukami, Ph.D., University of Minnesota Medical School, and Mitch Zeller, J.D., Pinney Associates in Bethesda, MD, led the overall effort as co-chairs of the National Cancer Institute's Tobacco Harm Reduction Network. They convened several meetings of researchers, policy makers, tobacco control advocates and government representatives that explored the science base for a nicotine reduction strategy.

Currently, about 44 million (or 20 percent) of adults in the United States smoke cigarettes. Other research cited by the authors had found that reducing nicotine to non-addictive levels could potentially reduce smoking prevalence to about 5 percent.

"Nicotine addiction sustains tobacco use. Quitting tobacco can be as difficult to overcome as heroin or cocaine addiction," said Hatsukami, director of the University of Minnesota's Tobacco Use Research Center and the Masonic Cancer Center's Cancer Control and Prevention Research Program "Reducing the nicotine in cigarettes to a level that is non-addicting could have a profound impact on reducing death and disability related to cigarettes and improving overall public health."

Hatsukami adds that studies to date have found that substantial reduction in nicotine in cigarettes does not lead to smokers smoking more lower-nicotine cigarettes because it is harder to compensate for very low nicotine intake.

"In addition, studies have shown a significantly lower number of cigarettes are smoked when low-nicotine cigarettes are used, resulting in eventual abstinence in a considerable number of smokers," she said.

"Imagine a world where the only cigarettes that kids could experiment with would neither create nor sustain addiction," Zeller said. "The public health impact of this would be enormous if we can prevent youthful experimentation from progressing to regular smoking, addiction, and the resulting premature disease and death later. Reducing the nicotine content in cigarettes may be a very effective way to accomplish this major impact," he added.

Hatsukami, Zeller, and their colleagues recommend engaging scientific, research and government agencies to conduct the necessary research and set priorities and goals as the next step toward determining the feasibility of a nicotine reduction approach.

This study was funded by the National Cancer Institute, National Institute on Drug Abuse and the American Legacy Foundation. Other authors of this paper include Drs. Kenneth Perkins (University of Pittsburgh), Mark LeSage (Minneapolis Medical Research Foundation and University Minnesota), David Ashley (formerly at the Centers for Disease Control and Prevention, now at the Food and Drug Administration), Jack Henningfield (Pinney Associates), Neal Benowitz (University of California, San Francisco), Cathy Backinger (National Cancer Institute).

Designer's Door Could Prove a Real Lifesaver in Earthquake Emergency

Research by a Kingston University MA student has led her to design a door which could be used as a shelter after an earthquake.

Younghwa Lee has been working on the project which, she hopes, could save hundreds of lives in countries where there is a risk of earthquakes. The MA Design: Product and Space student was motivated by the terrible loss of life in Haiti earlier this year to design a door, which can collapse so that it becomes a protective shelter.

"My starting point was the inherent strength of a door frame within a wall -- they often remain standing when many of the supporting walls fall down. Also there are more doors inside most homes than there are people so everyone in the house should be able to find a door," Younghwa, who is studying on the MA Design: Product and Space course, said.

Initially, Younghwa's door looks unremarkable but, in an emergency, it can swivel horizontally on a central pivot a little less than a metre above the ground. At the same time, the door folds horizontally so the bottom half of it remains on the ground, anchoring it to the floor and providing additional protection.

There is a small cabinet built into the door frame in which Younghwa has housed a wind-up torch, sachets of drinking water and medical supplies. "There should be enough room for two people to huddle under each door," she said.

The student, who came to Kingston from the South Korean capital Seoul in 2009, says it should take only five seconds to convert the door into a makeshift protective capsule. Younghwa decided to tackle the impact of a natural disaster while she was sitting, frustrated, at Seoul airport when her flight back to the United Kingdom was delayed by the cloud of volcanic ash earlier this year. With the catastrophe in Haiti occurring only a few months earlier, she decided to focus on earthquakes.

"Once an earthquake starts there are usually up to 15 seconds of relatively 'safe' vertical vibration before the destructive horizontal vibration starts," Younghwa explained. "The guidance for building occupants during an earthquake is to remain inside the building and take shelter under a strong table. My door is designed to be stronger and more stable than a table and -- as it isn't a flat surface -- most debris will slide off it."

Younghwa, 31, based her research on Istanbul as the US Geological Survey has estimated there is a 70 per cent chance the city will be hit by an earthquake measuring 7.6 on the richter scale before 2030, potentially killing as many as 150,000 people. She believes her doors could be inexpensively incorporated in many of the city's homes.

Kingston University's Design: Product and Space course leader Colin Holden said "Younghwa was brave to take on this kind of project because it would soon be very obvious if it didn't work. The principle of her final product is so simple and credible it makes you wonder why it doesn't already exist, and that's a rare achievement. I hope she pursues it further."