

<http://www.bbc.co.uk/news/health-22153318>

Beer taste excites male brain

Just a tiny taste of your favourite tipple can excite the brain and increase the urge to drink, even without any effect of alcohol - according to a study on 49 men.

By James Gallagher Health and science reporter, BBC News

The taste triggered the release of the brain's reward chemical, dopamine. The results of the study, published in the journal *Neuropsychopharmacology*, showed a greater effect in people with a family history of alcoholism. Experts said the family link was "surprising".

The men were placed in a brain scanner while small amounts of different drinks were sprayed into their mouths.

Taster

Researchers at the Indiana University School of Medicine, in the US, compared the effects of spraying water, a sports drink and the participant's favourite beer. Each was given 15ml of fluid over 15 minutes. It is enough to make a pint go round 38 people, so the scientists said the alcohol in the beer would have no effect on the body. The results showed that more dopamine was released in the brain after beer and the men were more likely to say they wanted to have an alcoholic drink.

Prof David Kareken said: "We believe this is the first experiment in humans to show that the taste of an alcoholic drink alone, without any intoxicating effect from the alcohol, can elicit this dopamine activity in the brain's reward centres." He suggested the more pronounced effect in men with a family history of alcoholism could be an inherited risk factor for alcoholism.

Prof Dai Stephens, from the University of Sussex, said: "These findings, though neatly done, and a first convincing demonstration in humans that a drink's flavour has such effects on the brain, are not particularly surprising as we have known for some time from animal studies that events conditioned to drug taking come to increase dopamine."

However, he said the family effect was surprising and raised questions about whether this "underlies the development of alcohol, and perhaps other drug abuse".

Peter Anderson, a professor of substance use, policy and practice at Newcastle University, said: "It is well known that all sorts of cues, including taste, smell, images, and habits raise desire for drinking. "This paper demonstrates that taste alone impacts on the brain functions associated with desire. This is not surprising - if taste increases desire, it has to impact on brain functions."

<http://www.sciencedaily.com/releases/2013/04/130415151434.htm>

Excess Vitamin E Intake Not a Health Concern, Study Suggests

No level of vitamin E in the diet or from any normal use of supplements should be a concern

Despite concerns that have been expressed about possible health risks from high intake of vitamin E, a new review concludes that biological mechanisms exist to routinely eliminate excess levels of the vitamin, and they make it almost impossible to take a harmful amount. No level of vitamin E in the diet or from any normal use of supplements should be a concern, according to an expert from the Linus Pauling Institute at Oregon State University. The review was just published in the *Journal of Lipid Research*.

"I believe that past studies which have alleged adverse consequences from vitamin E have misinterpreted the data," said Maret Traber, an internationally recognized expert on this micronutrient and professor in the OSU College of Public Health and Human Sciences. "Taking too much vitamin E is not the real concern," Traber said. "A much more important issue is that more than 90 percent of people in the U.S. have inadequate levels of vitamin E in their diet."

Vitamin E is an antioxidant and a very important nutrient for proper function of many organs, nerves and muscles, and is also an anticoagulant that can reduce blood clotting. It can be found in oils, meat and some other foods, but is often consumed at inadequate dietary levels, especially with increasing emphasis on low-fat diets.

In the review of how vitamin E is metabolized, researchers have found that two major systems in the liver work to control the level of vitamin E in the body, and they routinely excrete excessive amounts. Very high intakes achieved with supplementation only succeed in doubling the tissue levels of vitamin E, which is not harmful.

"Toxic levels of vitamin E in the body simply do not occur," Traber said. "Unlike some other fat-soluble vitamins such as vitamins A and D, it's not possible for toxic levels of vitamin E to accumulate in the liver or other tissues."

Vitamin E, because of its interaction with vitamin K, can cause some increase in bleeding, research has shown. But no research has found this poses a health risk. On the other hand, vitamin E performs many critical roles in optimum health. It protects polyunsaturated fatty acids from oxidizing, may help protect other essential lipids,

and has been studied for possible value in many degenerative diseases. Higher than normal intake levels may be needed for some people who have certain health problems, and smoking has also been shown to deplete vitamin E levels.

Traber said she recommends taking a daily multivitamin that has the full RDA of vitamin E, along with consuming a healthy and balanced diet.

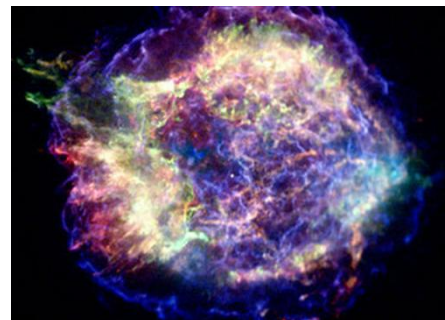
M. G. Traber. Mechanisms for the Prevention of Vitamin E Excess. The Journal of Lipid Research, 2013; DOI: 10.1194/jlr.R032946

<http://phys.org/news/2013-04-remnants-supernova-explosion-ancient-magnetotactic.html>

Remnants of supernova explosion found in ancient magnetotactic bacteria

First biological signature of an ancient supernova event, possibly linked to a specific exploding star

Phys.org - Back in 2004, German scientists discovered traces of supernova ejecta that had been deposited in the deep-sea ferromanganese crust of the Pacific Ocean. They dated the supernova event to 2.8 million years ago (Mya), using estimates from the decay of iron-60 radioisotope. They were also able to estimate the distance of the supernova event to 10 parsecs (pc) from our sun, based on the amount of iron-60 deposited. At the April 14th meeting of the American Physical Society, a Canadian scientist, Shawn Bishop, reported finding traces of iron-60 of supernova origin in the fossilized remains of a common bacteria.



Supernova Credit: NASA

By accurately dating the sediment cores in which the samples were found, Bishop appears to have discovered the first biological signature of an ancient supernova event, and may even be able to link it to a specific exploding star.

Bishop analyzed sample cores from strata roughly 100,000 years apart within deposits from 1.7 to 3.3 Mya. Iron-60 is not a product of any processes occurring here on earth, so any supply of it can be assumed to come from a non-terrestrial source. Bishop was able to extract out all the iron-60 of biological origin, and quantify it with a mass spectrometer. The amounts found were small, but they were enough to reliably date the sample to a period around 2.2 Mya. Other researchers, peripheral to the project, were then able to suggest a possible candidate star that dates to this period may lie in the Scorpius-Centaurus stellar association, roughly 130 pc (424 light-years) from the sun.

Iron-60 has a half-life of 2.6 million years, and makes an ideal clock for dating deposits on this timescale. It undergoes beta decay to form cobalt-60. A likely source for the iron concentrations in the deep-sea cores could be magnetotactic bacteria. These creatures incorporate crystals of magnetite (Fe₃O₄) in the form of long chains inside specialized organelles called magnetosomes. These organelles are used to sense the earth's magnetic field and possibly navigate in response to it. Magnetite-containing bacteria are today usually found in transition zones where oxygen-rich waters meet anoxic waters.

These discoveries paint a dramatic scene of supernova explosions raining down radioactive debris on the ancient earth. These deposits then filtered through the water where they also got incorporated into various iron-sulfide reactions, or manganese nodules still mined today. Many people might remember Howard Hughes' Glomar Explorer project, and the dramatic CIA efforts to find the wreck of the Soviet K-129 nuclear submarine. Mining the iron-rich manganese nodules was the convenient alibi the Glomar explorer used while it searched for the secret sub. Exploration of the deep links between the earth and its cosmic neighbors will undoubtedly continue to give tremendous insight into events both here and beyond.

More information: Abstract: X8.00002 : Search for Supernova ⁶⁰Fe in the Earth's Fossil Record, Bulletin of the American Physical Society, meetings.aps.org/Meeting/APR13/Event/192798

Approximately 2.8 Myr before the present our planet was subjected to the debris of a supernova explosion. The terrestrial proxy for this event was the discovery of live atoms of ⁶⁰Fe in a deep-sea ferromanganese crust. The signature for this supernova event should also reside in magnetite (Fe₃O₄) magnetofossils produced by magnetotactic bacteria extant at the time of the Earth-supernova interaction, provided the bacteria preferentially uptake iron from fine-grained iron oxides and ferric hydroxides. Using empirically derived microfossil concentrations in a deep-sea drill core, we deduce a conservative estimate of the ⁶⁰Fe fraction as ⁶⁰Fe/Fe = 3.6 × 10⁻¹⁵. This value sits comfortably within the sensitivity limit of present accelerator mass spectrometry (AMS) capabilities. This talk will detail the present status of our ⁶⁰Fe AMS search in magnetofossils and (possibly) show our initial results.

<http://www.technewsdaily.com/17766-could-life-be-older-than-earth-itself.html>

Could Life Be Older Than Earth Itself?

Applying a maxim from computer science to biology raises the intriguing possibility that life existed before Earth did and may have originated outside our solar system, scientists say.

Jillian Scharr, TechNewsDaily Staff Writer

Moore's Law is the observation that computers increase exponentially in complexity, at a rate of about double the transistors per integrated circuit every two years. If you apply Moore's Law to just the last few years' rate of computational complexity and work backward, you'll get back to the 1960s, when the first microchip was, indeed, invented.

Now, two geneticists have applied Moore's Law to the rate at which life on Earth grows in complexity - and the results suggest organic life first came into existence long before Earth itself.

Staff Scientist Alexei Sharov of the National Institute on Aging in Baltimore, and Theoretical Biologist Richard Gordon of the Gulf Specimen Marine Laboratory in Florida, took Moore's Law, replaced the transistors with nucleotides - the building blocks of DNA and RNA - and the circuits with genetic material, and did the math. The results suggest life first appeared about 10 billion years ago, far older than the Earth's projected age of 4.5 billion years.

So even if it's mathematically possible for life to have existed before Earth did, is it physically possible? Again, Sharov and Gordon said yes, it is. As our solar system was forming, pre-existing bacterial-like organisms, or even simple nucleotides from an older part of the galaxy, could have reached Earth by hitching an interstellar ride on comets, asteroids or other inorganic space debris - a theoretical process called panspermia.

The scientists' calculations are not scientific proof that life predates Earth - there's no way of knowing for sure that organic complexity increased at a steady rate at any point in the universe's history. Call it a thought exercise or an essay, rather than a theory, Sharov said. "There are lots of hypothetical elements to [our argument]... but to make a wider view, you need some hypothetical elements," Sharov told TechNewsDaily. Sharov and Gordon's idea raises other intriguing possibilities. For one, "life before earth" debunks the long-held science-fiction trope of the scientifically advanced alien species. If genetic complexity progresses at a steady rate, then the social and scientific development of any other alien life form in the Milky Way galaxy would be roughly equivalent to those of humans.

Sharov and Gordon's study draws a theoretical and practical parallel between the origin of life and the relationship between life and knowledge. Human evolution doesn't just occur in the genome; it occurs epigenetically, or within the mind, as technology, language and cultural memory all become more complex. "The functional complexity of organisms [is] encoded partially in the heritable genome and partially in the perishable mind," they explain in the paper.

By applying Moore's Law - a theory originally devised to explain technological development - to life, the geneticists aren't simplifying evolution; they're acknowledging its extraordinary complexity, they say. Although some may be skeptical of Sharov and Gordon's findings, the scientists stand by their conclusions. "Contamination with bacterial spores from space appears the most plausible hypothesis that explains the early appearance of life on Earth," they argue in the paper, which is published online in the preprint journal Arxiv. Sharov said that if he had to bet on it, he'd say "it's 99 percent true that life started before Earth - but we should leave 1 percent for some wild chance that we haven't accounted for."

The [full report is available](#) on Cornell University Library's online archives.

<http://nyti.ms/106VHPD>

Drug Makers Use Safety Rule to Block Generics

For decades, pharmaceutical companies have deployed an array of tactics aimed at preventing low-cost copies of their drugs from entering the marketplace. But federal regulators contend the latest strategy - which relies on a creative interpretation of drug safety laws - is illegal.

By KATIE THOMAS

The Federal Trade Commission recently weighed in on a legal case over the tactic involving the drug maker Actelion, and earlier this month a federal suit was filed in another case in Florida. "We definitely see this as a significant threat to competition," said Markus Meier, who oversees the commission's health care competition team.

The new approach is almost elegant in its simplicity: brand-name drug makers are refusing to sell their products to generic companies, which need to analyze them so they can create the copycat versions. Traditionally, the generic drug makers purchased samples from wholesalers. But because of safety concerns, an increasing number of drugs are sold with restrictions on who can buy them, forcing the generic manufacturers to ask the brand-name companies for samples. When they do, the brand-name firms say no.

Brand-name companies say they are protecting themselves - and patients - in case the drugs are somehow used improperly. They say no law requires one company to do business with another.

Advocates for generic drugs say the practice could limit access to the low-cost drugs, which they say have saved more than a trillion dollars over the last decade. They say the companies that have most aggressively pursued the tactic tend to be those with drugs that are nearing the end of their patent life.

Actelion, a Swiss company, is withholding samples of its flagship product, Tracleer, which treats a lung disorder. Its patent is set to expire in 2015. The company's other product in question, Zavesca, has a patent that expires later this year. Tracleer costs about \$79,000 a year, while Zavesca costs about \$229,000.

The issue has its roots in a 2007 law that allowed the Food and Drug Administration to require detailed safety programs for drugs with serious side effects or the potential for abuse. In many cases, those programs simply direct the company to educate doctors or patients about risks. But in other cases, they require that distribution be limited to approved pharmacists and health care providers.

About 70 drugs carry mandatory drug safety plans, and of those, 34 have more restrictive requirements, according to the F.D.A. Although the 2007 law said the programs should not be used to block development of generic drugs, brand-name companies said the language was vague and began restricting access to drug samples soon after it was passed.

In 2009, generic companies began complaining that Celgene had refused to sell them samples of Thalomid, the drug better known as thalidomide that is now used to treat cancer and leprosy, and a related drug, Revlimid. Lannett, a generic company, sued Celgene, claiming its practices were anticompetitive, and the case was settled. The trade commission and the Connecticut attorney general started investigations, which Celgene has said are still under way.

At least one company, Gilead Sciences, explicitly restricts access to samples. Pharmacies and other institutions that buy its drug Letairis, which treats a serious lung condition, must agree not to "use product in clinical trials or other studies without the prior written consent of Gilead Sciences," according to an order form sent to customers by Accredo, a specialty pharmacy that distributes Letairis for Gilead. A spokesman for Gilead declined to comment.

Brand-name manufacturers are also limiting access to drugs even when the government does not require it. In a federal lawsuit filed April 1 in Florida, Accord Healthcare, an Indian generics manufacturer, said the drug company Acorda refused to turn over samples of its multiple sclerosis drug Ampyra, even though there are no restrictions on its distribution.

In a letter to Accord from Acorda that was submitted to the United States District Court for the Southern District of Florida, in Fort Lauderdale, Acorda echoed other companies' positions and said it was under no obligation to sell its products to another manufacturer.

Apotex, a Canadian company, said the drug maker Novartis denied it access to Tasigna, a leukemia drug, until Apotex threatened to sue. Another company, Lundbeck, has so far declined to provide Apotex with samples of the drug Xenazine, which treats a movement disorder caused by Huntington's disease.

Julie Masow, a spokeswoman for Novartis, said Apotex ultimately purchased samples of Tasigna through the drug's sole distributor. She said the delay was the result of a misunderstanding, adding "generic companies are free to buy Novartis products through distribution channels."

Representatives of brand-name manufacturers say there are good reasons to restrict drugs to approved pharmacies or health care providers. Lundbeck said it sells Xenazine, also known as tetrabenazine, to a limited network of specialty pharmacies because it treats fewer than 25,000 people nationwide.

"Not many retail pharmacies would stock the product for so small a patient population," said Sally Benjamin Young, a spokeswoman for Lundbeck. She said Lundbeck was seeking guidance on the issue from regulators because "it is not clear under the applicable laws and regulations that Lundbeck is permitted to sell tetrabenazine to any person or entity without a prescription."

Some within the industry have been forthright about how these drug safety programs can be turned to a company's advantage. At a conference in 2010, one speaker delivered a presentation that listed "life cycle management options" as one benefit of such safety programs. "Life cycle management" is industry jargon for maximizing the length of a brand's patent life.

Representative Henry A. Waxman, Democrat of California, said Congress needed to remove the loophole that allows branded drug makers to deny generic manufacturers access to their products. "The purpose of these postmarket safety plans was to protect consumers from risky drugs, not to allow brand companies to thwart generic competition," said Mr. Waxman, who in 1984 co-wrote the landmark law expanding access to generic drugs.

But legislative efforts to require drug makers to sell samples to generic companies have failed twice, once during passage of the 2007 law, and last summer, when Congress reauthorized a user-fee program for drugs and medical devices. The language was removed from last year's bill after brand-name pharmaceutical companies lobbied against it, according to an industry lobbyist and legislative aides. A spokeswoman for the industry trade group, the Pharmaceutical Research and Manufacturers of America, declined to comment.

Without clarity from Congress or regulators, many are looking to the Actelion case, in which the company is asking the United States District Court in New Jersey to rule that it should not be forced to sell samples to Apotex and Roxane Laboratories. "This action concerns the fundamental right of a business to choose for itself with whom to deal and to whom to supply its products," Actelion said in legal filings.

Steve Giuli, the head of government affairs for the United States at Apotex, said the practice of denying access to samples was only the latest example of the brand-name industry's evolving efforts to prevent generic competition. "They just keep pulling things out of their playbook," he said. "You plug one up and they flip the page - and there's another one ready to go."

http://www.eurekalert.org/pub_releases/2013-04/uoc--ref041113.php

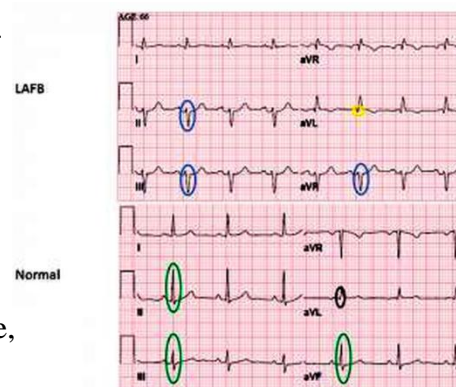
Routine EKG finding could signal serious heart problem

UC San Francisco-led team uncovers potential risks to cardiac condition previously thought benign

A common test that records the heart's electrical activity could predict potentially serious cardiovascular illness, according to a UC San Francisco-led study.

A cardiac condition called left anterior fascicular block (LAFB), in which scarring occurs in a section of the left ventricle, may not be as benign as currently thought and could increase the likelihood of heart failure, sudden cardiac death or atrial fibrillation.

In a study to be published on April 17 in the *Journal of the American Medical Association (JAMA)*, UCSF researchers and their colleagues at Wake Forest School of Medicine and the University of Washington, Seattle, analyzed data on 1,664 people over the age of 65 who were medically followed for 16 years.



This graphic compares LAFB vs. Normal EKG. Gregory Marcus/UCSF

The researchers selected those who had no evidence of cardiovascular disease from the National Institutes of Health-sponsored Cardiovascular Health Study. People with heart failure, high blood pressure or diabetes, or who had heart attacks, were excluded from the study sample.

"We then compared those with LAFB to those with a normal electrocardiogram (EKG)," said senior author Gregory Marcus, MD, an electrophysiologist with the UCSF Division of Cardiology and an associate professor in residence with the UCSF School of Medicine. "We found that those who had LAFB indeed had a higher risk of atrial fibrillation, congestive heart failure and death."

After adjusting for other potential confounding variables, LAFB posed a 57 percent greater risk for sudden cardiac death, an 89 percent greater risk for atrial fibrillation, and a 143 percent greater risk for heart failure. LAFB is a blockage of one of the electrical branches that delivers electrical signals to a part of the left ventricle, one of two chambers in the heart. Small studies suggest it is associated with fibrosis or scarring of the left ventricle, but the clinical ramifications of this have not been previously studied. It is unknown how many people LAFB affects.

"We now have come to realize that important cardiovascular diseases like atrial fibrillation, heart failure and maybe sudden cardiac death, are related to fibrosis of the left side of the heart," said Marcus, who sees cardiology patients at the UCSF Medical Center. "So we sought to test the hypothesis that LAFB, even in those people who are otherwise healthy, might be a readily available marker that any doctor can see on an EKG, of a propensity to left-heart fibrosis. And it therefore might predict those at risk for atrial fibrillation, heart failure and death."

There currently is no treatment for people with LAFB. However, this new finding potentially could open up a new area of research in cardiology, according to Marcus. "Currently there is a therapy for people with heart failure and a left bundle branch block using a special pacemaker called a biventricular pacemaker or cardiac resynchronization therapy," Marcus said. "So one question we have to explore is whether people with LAFB and heart failure, for example, might benefit from a specialized pacemaker."

Patients also can reduce their overall cardiovascular risk with lifestyle modifications, which include choosing a healthy diet, exercising regularly and eliminating tobacco products.

"This study may suggest that LAFB, even in the absence of known high blood pressure or diabetes, should be thought of as a cardiovascular risk factor," Marcus said. "Those patients with LAFB perhaps should be considered the same as someone with an established cardiovascular risk factors."

Co-authors include Mala Mandyam of the UCSF Division of Cardiology, Electrophysiology Section; Eric Vittinghoff, PhD, of the UCSF Department of Epidemiology and Biostatistics; Elsayed Z. Soliman, MD, of the Wake Forest School of Medicine; and Susan R. Heckbert, MD, PhD, of the University of Washington, Seattle.

This study was supported by the National Center for Research Resources, the National Center for Advancing Translational Sciences, and the Office of the Director, National Institutes of Health, through grant TL1 RR024129. This research was also supported by contracts HHSN268201200036C, N01HC85239, N01HC55222, N01HC85079, N01HC85080, N01HC85081, N01HC85082, N01HC85083, N01HC85086, and grants HL080295 and HL068986 from the National Heart, Lung, and Blood Institute (NHLBI), with additional contributions from the National Institute of Neurological Disorders and Stroke. Additional support was provided by grant AG023629 from the National Institute on Aging (NIA) and the Joseph Drown Foundation. Researchers reported no conflicts of interest to disclose.

http://www.eurekalert.org/pub_releases/2013-04/sumc-ssp041113.php

Stanford scientists pinpoint brain's area for numeral recognition

Precise anatomical coordinates of a brain "hot spot" that is preferentially activated when people view ordinary numerals

STANFORD, Calif. - Scientists at the Stanford University School of Medicine have determined the precise anatomical coordinates of a brain "hot spot," measuring only about one-fifth of an inch across, that is preferentially activated when people view the ordinary numerals we learn early on in elementary school, like "6" or "38."

Activity in this spot relative to neighboring sites drops off substantially when people are presented with numbers that are spelled out ("one" instead of "1"), homophones ("won" instead of "1") or "false fonts," in which a numeral or letter has been altered.

"This is the first-ever study to show the existence of a cluster of nerve cells in the human brain that specializes in processing numerals," said Josef Parvizi, MD, PhD, associate professor of neurology and neurological sciences and director of Stanford's Human Intracranial Cognitive Electrophysiology Program. "In this small nerve-cell population, we saw a much bigger response to numerals than to very similar-looking, similar-sounding and similar-meaning symbols.

"It's a dramatic demonstration of our brain circuitry's capacity to change in response to education," he added. "No one is born with the innate ability to recognize numerals."

The finding pries open the door to further discoveries delineating the flow of math-focused information processing in the brain. It also could have direct clinical ramifications for patients with dyslexia for numbers and with dyscalculia: the inability to process numerical information.

The cluster Parvizi's group identified consists of perhaps 1 to 2 million nerve cells in the inferior temporal gyrus, a superficial region of the outer cortex on the brain. The inferior temporal gyrus is already generally known to be involved in the processing of visual information.

The new study, which will be published April 17 in the *Journal of Neuroscience*, builds on an earlier one in which volunteers had been challenged with math questions. "We had accumulated lots of data from that study about what parts of the brain become active when a person is focusing on arithmetic problems, but we were mostly looking elsewhere and hadn't paid much attention to this area within the inferior temporal gyrus," said Parvizi, who is senior author of the study.

Not, that is, until fourth-year medical student Jennifer Shum, who also is doing research in Parvizi's lab, noticed that, among some subjects in the first study, a spot in the inferior temporal gyrus seemed to be substantially activated by math exercises. Charged with verifying that this observation was consistent from one patient to the next, Shum, the study's lead author, reported that this was indeed the case. So, Parvizi's team designed a new study to look into it further.

The new study relied on epileptic volunteers who, as a first step toward possible surgery to relieve unremitting seizures that weren't responding to therapeutic drugs, had a small section of their skulls removed and electrodes applied directly to the brain's surface. The procedure, which doesn't destroy any brain tissue or disrupt the brain's function, had been undertaken so that the patients could be monitored for several days to help attending neurologists find the exact location of their seizures' origination points. While these patients are bedridden in the hospital for as much as a week of such monitoring, they are fully conscious, in no pain and, frankly, a bit bored.

Over time, Parvizi identified seven epilepsy patients with electrode coverage in or near the inferior temporal gyrus and got these patients' consent to undergo about an hour's worth of tests in which they would be shown images presented for very short intervals on a laptop computer screen, while activity in their brain regions

covered by electrodes was recorded. Each electrode picked up activity from an area corresponding to about a half-million nerve cells (a drop in the bucket in comparison to the brain's roughly 100 billion nerve cells). To make sure that any numeral-responsive brain areas identified were really responding to numerals - and not just generic lines, angles and curves - these tests were carefully calibrated to distinguish brain responses to visual presentations of the classic numerals taught in Western schools, such as 3 or 50, as opposed to squiggly lines, letters of the alphabet, number-denoting words such as "three" or "fifty," and symbols that in fact were also numerals but - because they were drawn from the Thai, Tibetan and Devanagari languages - were extremely unlikely to be recognized as such by this particular group of volunteers.

In the first test, subjects were shown series of single numerals and letters - along with false fonts, in which the component parts of numerals or letters had been scrambled but defining curves and angles were retained, and the foreign-number symbols just described. A second test, controlling for meaning and sound, included numerals and their spelled-out versions (for instance, "1" and "one," or "3" and "three") and other words with the same sound or a similar one ("won" and "tree," respectively).

All of our brains are shaped slightly differently. But in almost the identical spot within each study subject's brain, the investigators observed a significantly larger response to numerals than to similar-shaped stimuli, such as letters or scrambled letters and numerals, or to words that either meant the same as the numerals or sounded like them.

Interestingly, said Parvizi, that numeral-processing nerve-cell cluster is parked within a larger group of neurons that is activated by visual symbols that have lines with angles and curves. "These neuronal populations showed a preference for numerals compared with words that denote or sound like those numerals," he said. "But in many cases, these sites actually responded strongly to scrambled letters or scrambled numerals. Still, within this larger pool of generic neurons, the 'visual numeral area' preferred real numerals to the false fonts and to same-meaning or similar-sounding words."

It seems, Parvizi said, that "evolution has designed this brain region to detect visual stimuli such as lines intersecting at various angles - the kind of intersections a monkey has to make sense of quickly when swinging from branch to branch in a dense jungle." The adaptation of one part of this region in service of numeracy is a beautiful intersection of culture and neurobiology, he said.

Having nailed down a specifically numeral-oriented spot in the brain, Parvizi's lab is looking to use it in tracing the pathways described by the brain's number-processing circuitry. "Neurons that fire together wire together," said Shum. "We want to see how this particular area connects with and communicates with other parts of the brain."

The study was funded by the National Institutes of Health (grant NS0783961), the Stanford NeuroVentures Program and the School of Medicine's Medical Scholars Research Program. Other co-authors were postdoctoral scholars Dora Hermes, PhD, Brett Foster, PhD, Mohammad Dastjerdi, PhD, and Jonathan Winawer, PhD; research assistant Vinitha Rangarajan; and neurosurgery resident Kai Miller, MD.

http://www.eurekalert.org/pub_releases/2013-04/tes-cod041513.php

Common osteoporosis drug slows formation of new bone

Study results suggest combination treatments may be needed to stop bone loss, fuel growth

Chevy Chase, MD—Although the drug zoledronic acid slows bone loss in osteoporosis patients, it also boosts levels of a biomarker that stops bone formation, according to a recent study accepted for publication in *The Endocrine Society's Journal of Clinical Endocrinology & Metabolism (JCEM)*.

Osteoporosis weakens bones and increases the risk patients will suffer fractures. The findings suggest combination therapy may be a more effective approach to battling this common condition.

"The key to effectively treating osteoporosis lies in increasing bone mass," said the study's lead author, Antonino Catalano, MD, PhD, of the University of Messina in Italy. "Zoledronic acid halts bone loss, but it also signals the body to stop forming new bone mass. The drug may need to be combined with other treatments to add bone mass."

The prospective intervention study followed the treatment of 40 postmenopausal women at an ambulatory care center. Half of the women received zoledronic acid, and half received a placebo. Levels of sclerostin – a biomarker that inhibits bone formation – increased among the participants who were treated with zoledronic acid. "The data points to an opportunity to increase bone mass by combining zoledronic acid with a drug that suppresses the resulting sclerostin's effect," Catalano said. "An innovative combination therapy using zoledronic acid and selective antibodies to block the sclerostin could simultaneously stop bone loss and encourage new bone formation. This is an important avenue for researchers to explore as they develop new osteoporosis treatments."

Other researchers working on the study include: N. Morabito, G. Basile, S. Brancatelli, D. Cucinotta and A. Lasco of the University of Messina.

The article, "Zoledronic Acid Acutely Increases Sclerostin Serum Levels in Women with Postmenopausal Osteoporosis," appears in the May 2013 issue of JCEM.

http://www.eurekalert.org/pub_releases/2013-04/miot-hso041713.php

Hop, skip or jump? Study says no to all of the above

The earliest stages of arthritis make cartilage more susceptible to damage from physical activities such as running or jumping

Written by Anne Trafton, MIT News Office

CAMBRIDGE, MA -- Osteoarthritis, which affects at least 20 percent of adults in the United States, leads to deterioration of cartilage, the rubbery tissue that prevents bones from rubbing together. By studying the molecular properties of cartilage, MIT engineers have now discovered how the earliest stages of arthritis make the tissue more susceptible to damage from physical activities such as running or jumping.

The findings could help researchers develop tests to diagnose arthritis earlier in patients at high risk for the disease and also guide engineers in designing replacement cartilage. The results also suggest that athletes who suffer traumatic knee injuries, such as a torn anterior cruciate ligament (ACL) — which gives them a greater chance of developing arthritis later in life — should be cautious when returning to their sport following surgery. "It's a clear signal to be careful of going right back out," says Alan Grodzinsky, an MIT professor of biological, electrical and mechanical engineering and senior author of a paper describing the findings in a recent issue of the *Biophysical Journal*. "Even though your knee may be stabilized, there's the possibility that deformation of cartilage at a high loading rate is still going to put it at risk."

Cartilage is packed with protein-sugar complexes known as aggrecans, each made of about 100 highly charged molecules called glycosaminoglycans (GAGs). Those molecules protect joints by absorbing water and causing the tissue to stiffen as pressure is applied.

"The cartilage is a stiff sponge, filled with fluid, and as we compress it, fluid has to percolate through these closely spaced GAG chains," Grodzinsky says. "The GAG chains provide resistance to flow, so the water can't get out of our cartilage instantly when we compress it. That pressurization at the nanoscale increases the stiffness of our cartilage to high-loading-rate activities."

The MIT team set out to investigate how the molecular structure of GAG generates this stiffening over such a wide range of activity — from sitting and doing nothing to running or jumping at high speed. To do this, they developed a new, highly sensitive type of atomic force microscopy (AFM), allowing them to measure how aggrecan reacts at the nanoscale to very high loading rates (the speeds at which forces are applied).

Conventional AFM, which generates high-resolution images by "feeling" the surface of a sample with a tiny probe tip, can also be used to subject samples to cyclic loading to measure their nanomechanical properties. But conventional AFM can apply only up to about 300 hertz (cycles per second). Hadi Tavakoli Nia, the lead author of the paper, and Iman Soltani Bozchalooi, both graduate students in mechanical engineering, developed a modified system that can apply much higher frequencies — up to 10 kilohertz, frequencies relevant to impact loading of joints.

'A very floppy sponge'

Using this system, the researchers compared normal cartilage and cartilage treated with an enzyme that destroys GAG chains, mimicking the initial stages of osteoarthritis. In this early phase, collagen, which gives cartilage its structure, is usually still intact. The researchers found that when exposed to very high loading rates — similar to what would be seen during running or jumping — normal cartilage was able to absorb fluid and stiffen normally. However, in the GAG-depleted tissue, fluid leaked out rapidly.

"That's what puts the collagen in trouble, because now this becomes a very floppy sponge, and if you load it at higher rates the collagen network can be damaged," Grodzinsky says. "At that point you begin an irreversible series of activities that can result in damage to the collagen and eventually osteoarthritis."

There is currently no good way to diagnose arthritis during those early stages, which are usually painfree. Many researchers are working to further improve magnetic resonance imaging (MRI) to test for loss of aggrecan, while others are looking for blood or urine markers. If such a test existed, it would be especially useful for monitoring patients who have experienced an acute knee injury. It is estimated that at least 12 percent of all osteoarthritis cases originated with a traumatic joint injury, Grodzinsky says.

Researchers in Grodzinsky's lab are now working to identify possible drugs that might halt the loss of aggrecan, as well as designing tissue scaffolds that could be implanted into patients who need cartilage-replacement surgery. The new AFM system should be useful for testing these scaffolds, to see if cells grown on the scaffold can produce the necessary tissue stiffening at high loading rates.

"These two aspects are really important: preventing cartilage degradation after injury and, if the cartilage is already damaged beyond its ability to be repaired, replacing it," Grodzinsky says.

Other authors of the paper are Yang Li, a graduate student in biological engineering; Lin Han, a former MIT postdoc; Han-Hwa Hung, a research specialist in biological engineering; Eliot Frank, a principal research engineer in biological engineering; Kamal Youcef-Toumi, a professor of mechanical engineering; and Christine Ortiz, a professor of materials science and engineering and MIT's dean for graduate education.

The research was funded by a Whitaker Foundation Fellowship, the National Science Foundation and the National Institutes of Health.

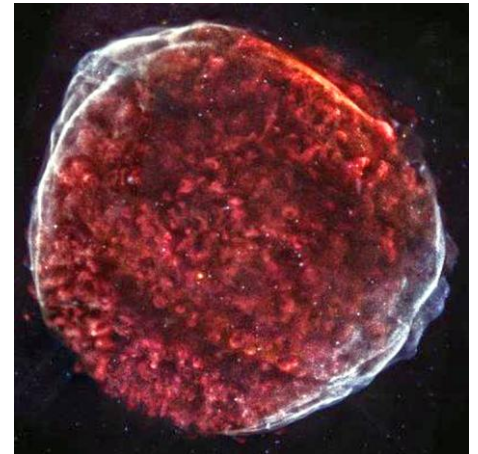
http://www.eurekalert.org/pub_releases/2013-04/cxc-xvo041713.php

X-ray view of a thousand-year-old cosmic tapestry

This year, astronomers around the world have been celebrating the 50th anniversary of X-ray astronomy. Few objects better illustrate the progress of the field in the past half-century than the supernova remnant known as SN 1006.

When the object we now call SN 1006 first appeared on May 1, 1006 A.D., it was far brighter than Venus and visible during the daytime for weeks. Astronomers in China, Japan, Europe, and the Arab world all documented this spectacular sight. With the advent of the Space Age in the 1960s, scientists were able to launch instruments and detectors above Earth's atmosphere to observe the Universe in wavelengths that are blocked from the ground, including X-rays. SN 1006 was one of the faintest X-ray sources detected by the first generation of X-ray satellites.

A new image of SN 1006 from NASA's Chandra X-ray Observatory reveals this supernova remnant in exquisite detail. By overlapping ten different pointings of Chandra's field-of-view, astronomers have stitched together a cosmic tapestry of the debris field that was created when a white dwarf star exploded, sending its material hurtling into space. In this new Chandra image, low, medium, and higher-energy X-rays are colored red, green, and blue respectively.



A long Chandra observation reveals the SN 1006 supernova remnant in exquisite detail. By overlapping 10 different pointings of Chandra's field-of-view, astronomers have stitched together a cosmic tapestry of the debris field that was created when a white dwarf star exploded, sending its material hurtling into space as seen from Earth over a millennium ago. In this new Chandra image, low, medium, and higher-energy X-rays are colored red, green, and blue respectively. Since SN 1006 belongs to the class of supernovas used to measure the expansion of the Universe, the new Chandra data provide insight into these important objects. NASA/CXC/Middlebury College/F.Winkler et al.

The new Chandra image provides new insight into the nature of SN1006, which is the remnant of a so-called Type Ia supernova. This class of supernova is caused when a white dwarf pulls too much mass from a companion star and explodes, or when two white dwarfs merge and explode. Understanding Type Ia supernovas is especially important because astronomers use observations of these explosions in distant galaxies as mileposts to mark the expansion of the Universe.

The new SN 1006 image represents the most spatially detailed map yet of the material ejected during a Type Ia supernova. By examining the different elements in the debris field - such as silicon, oxygen, and magnesium - the researchers may be able to piece together how the star looked before it exploded and the order that the layers of the star were ejected, and constrain theoretical models for the explosion.

Scientists are also able to study just how fast specific knots of material are moving away from the original explosion. The fastest knots are moving outward at almost eleven million miles per hour, while those in other areas are moving at a more leisurely seven million miles per hour. SN 1006 is located about 7,000 light years from Earth. The new Chandra image of SN 1006 contains over 8 days worth of observing time by the telescope. These results were presented at a meeting of High Energy Astrophysics Division of the American Astronomical Society in Monterey, CA.

This work involved Frank Winkler, from Middlebury College in Middlebury, VT; Satoru Katsuda from The Institute of Physical and Chemical Research (RIKEN) in Saitama, Japan; Knox Long from Space Telescope Science Institute in Baltimore, MD; Robert Petre from NASA -Goddard Space Flight Center (GSFC) in Greenbelt, MD; Stephen Reynolds from North Carolina State University in Raleigh, NC; and Brian Williams from NASA -GSFC in Greenbelt, MD.

NASA's Marshall Space Flight Center in Huntsville, Ala., manages the Chandra program for NASA's Science Mission Directorate in Washington. The Smithsonian Astrophysical Observatory controls Chandra's science and flight operations from Cambridge, Mass.

<http://phys.org/news/2013-04-diamonds-ancient-ocean-floor.html>

Did diamonds begin on the ancient ocean floor?

Findings suggest eclogitic diamonds originated as organic matter on the ancient sea floor

Phys.org - Geology professor Dan Schulze calls this singular gem from the remote Guaniamo region of Venezuela the "Picasso" diamond. The blue luminescent, high-resolution image of a diamond formed over a billion years ago reminds him of some paintings from Picasso's Blue Period. Like a cubist masterpiece, its striking irregular and anomalous features carry timeless secrets and yield new perspectives on life and the Earth's early history.

"A diamond is a time capsule. Anomalies in the chemical signature are the key to understanding the unusual conditions under which some diamonds were formed," says Schulze, an earth sciences professor in the Department of Chemical and Physical Sciences at U of T Mississauga.

Led by Schulze, an international team of scientists from Australia, Scotland, the United States and Venezuela discovered persuasive new evidence to support the idea that some diamonds, like Picasso, were formed from bacteria or algae on the ancient ocean floor. Their findings suggest these diamonds, known as eclogitic diamonds, originated as organic matter on the ancient sea floor, which was thrust down into the Earth's mantle by a geological process known as subduction. Attached to ocean floor rock deep beneath the surface, the organic carbon remnants were then transformed by extreme heat and pressure into diamonds.

The research is published in the April 2 issue of *Geology*.

Unlike the more common peridotitic diamonds, formed from inorganic carbon found deep in the Earth's mantle, the origins of eclogitic diamonds have been puzzling and controversial due to differences in their carbon signature. "Because diamonds are impermeable, they preserve inside themselves a record of the chemical and physical conditions that existed as they were formed," says Schulze, noting that tiny minerals trapped within the diamonds contain telltale clues to help solve the puzzle.

In their *Geology* study, Schulze and his colleagues deciphered this record by analyzing the oxygen composition of tiny garnet and silica grains encapsulated in eclogitic diamonds from mines in Venezuela, Australia and Botswana, and the carbon composition of the diamonds themselves. They observed a pattern of striking anomalies in the chemical signatures of both the mineral grains and diamonds that appear to explain how eclogite diamonds were formed.

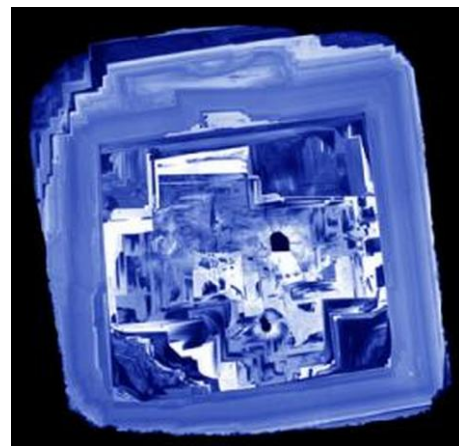
The silica grains in the Picasso diamond, for example, have a high oxygen composition that matches volcanic rock hydrothermally altered at low temperatures on the ancient sea floor, but is different from typical mantle material. "There is no other place on Earth where you get these values except on the ocean floor," says Schulze. The diamond itself has a low carbon composition similar to the remains of living organisms.

The same pattern of anomalies was consistently found in over 20 diamonds from three continents. "The simplest hypothesis is that the diamonds were formed from subducted organic materials. It's not just a local phenomenon. This is a geological process that was repeated worldwide in diamonds of different ages from three different locations," explains Schulze.

His research also sheds new light on the origins of two famous diamonds in the British Crown Jewels, the Cullinan I and Cullinan II. "There is a high probability that the Cullinan diamond, the largest gem-quality diamond ever found, is an eclogitic diamond made of biogenic material," he says. "But we'll never know for sure, as we can't get the diamonds for study!"

Life may have begun on the ancient sea floor and Schulze's research suggests many of the world's diamonds originated there too. "There are some people who will never believe this. But these findings will convert more skeptics to a hypothesis that's getting harder and harder to refute," he says.

http://www.eurekalert.org/pub_releases/2013-04/arrs-lop041013.php



Laser optics plus ultrasound imaging holds promise as a noninvasive test for prostate cancer

Multispectral photoacoustic imaging, which combines laser optics and ultrasound imaging technologies, can reliably distinguish between benign and malignant prostate tissue, a new study indicates.

Researchers at the University of Rochester looked at 42 prostatectomy specimens using the new imaging technique. Multispectral photoacoustic imaging, still in its infancy, predicted 25 out of 26 benign tissues correctly and 13 out of 16 malignant tissues correctly, said Dr. Vikram Dogra, lead author of the study.

Lipids, water, oxyhemoglobin and deoxyhemoglobin in the blood all respond to laser light, said Dr. Dogra. "By observing increases and decreases in these four things, we can tell if the tissue is malignant or benign, he said. "Deoxyhemoglobin is the biggest distinguisher between malignant and benign. If deoxyhemoglobin increases even slightly in intensity, the odds that the tissue is malignant increases dramatically," he said. Prostate cancer is the second leading cause of cancer death in American men. Transrectal ultrasound, the current gold standard to diagnose prostate cancer, has an overall success rate of about 70%, said Dr. Dogra. "Transrectal ultrasound is an invasive procedure and most men do not like it. There is a need for a new imaging technique," Dr. Dogra said. "We expect this technique to be clinically available in about five years," he added.

<http://www.sciencedaily.com/releases/2013/04/130418100150.htm>

Researchers Abuzz Over Caffeine as 'Cancer-Cell Killer'

Researchers from the University of Alberta are abuzz after using fruit flies to find new ways of taking advantage of caffeine's lethal effects on cancer cells - results that could one day be used to advance cancer therapies for people.

Previous research has established that caffeine interferes with processes in cancer cells that control DNA repair, a finding that has generated interest in using the stimulant as a chemotherapy treatment. But given the toxic nature of caffeine at high doses, researchers from the faculties of medicine and dentistry and science instead opted to use it to identify genes and pathways responsible for DNA repair.

"The problem in using caffeine directly is that the levels you would need to completely inhibit the pathway involved in this DNA repair process would kill you," said Shelagh Campbell, co-principal investigator. "We've come at it from a different angle to find ways to take advantage of this caffeine sensitivity."

Lead authors Ran Zhuo and Xiao Li, both PhD candidates, found that fruit flies with a mutant gene called melanoma antigen gene, or MAGE, appeared normal when fed a regular diet but died when fed food supplemented with caffeine.

On closer inspection, the researchers found that the mutant flies' cells were super-sensitive to caffeine, with the drug triggering "cell suicide" called apoptosis. Flies fed the caffeine-laden diet developed grossly disfigured eyes. Through this work, the research team identified three genes responsible for a multi-protein complex, called SMC5/SMC6/MAGE, which regulates DNA repair and the control of cell division. Neither process works properly in cancer cells.

Co-principal investigator Rachel Wevrick explains that this finding is significant because it means that scientists one day could be able to take advantage of cancer-cell sensitivity to caffeine by developing targeted treatments for cancers with specific genetic changes. Their results were published in the March issue of the peer-reviewed journal PLOS One.

"Unless you actually know what it is those proteins are doing in the first place to make a cell a cancer cell instead of a normal cell, it's hard to know what to do with that information," she says. "You need to know which genes and proteins are the really bad actors, how these proteins work and which of them work in a pathway you know something about where you can actually tailor a treatment around that information."

Along with Wevrick and Campbell as lead investigators, the project also included biological sciences professor Kirst King-Jones and medical geneticist Sarah Hughes. It's the type of research-intensive environment that benefits students who gain experience working with peers as part of a team, Wevrick says.

"The U of A has a reputation for co-operation, and that's not the case everywhere. People here are very willing to share their results and their successes, and work together."

The research was funded by the Cancer Research Society, the Canadian Institutes of Health Research and the Natural Sciences and Engineering Research Council of Canada.

Xiao Li, Ran Zhuo, Stanley Tiong, Francesca Di Cara, Kirst King-Jones, Sarah C. Hughes, Shelagh D. Campbell, Rachel Wevrick. The Smc5/Smc6/MAGE Complex Confers Resistance to Caffeine and Genotoxic Stress in Drosophila melanogaster. PLoS ONE, 2013; 8 (3): e59866 DOI: 10.1371/journal.pone.0059866

<http://www.wired.com/wiredscience/2013/04/super-earths-habitable-zone/>

3 New Exoplanets Might Have Right Temperature for Life

Scientists are reporting a bounty of new worlds that may be capable of sustaining life, with the discovery of three exoplanets slightly larger than Earth orbiting within their stars' habitable zone.

These findings come from NASA's Kepler spacecraft, a dedicated planet-hunting mission currently wrapping up four productive years in which it has spotted more than 100 planets outside our solar system. The telescope stares at about 150,000 stars simultaneously, watching for a tiny dip in their glow, which could indicate that a planet has passed in front and blocked their light. Though the majority of Kepler's discoveries are Jupiter-size worlds, the mission has lately been homing in on planets the size and temperature of our own, suggesting they may be good places to find life.

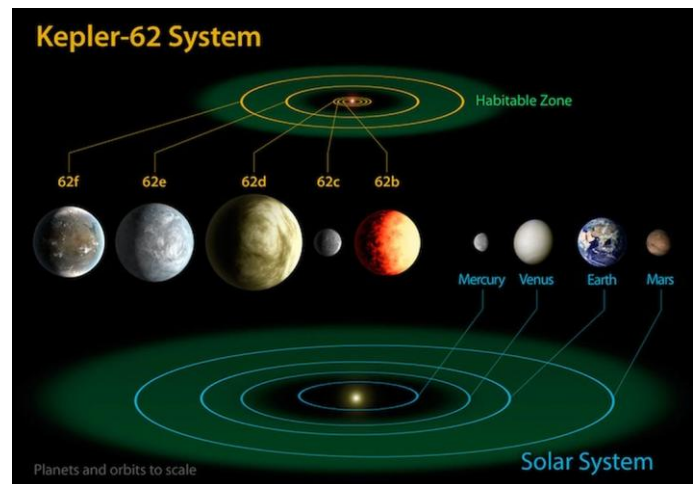
Two of the newly discovered potentially habitable exoplanets orbit the same star, Kepler-62, which is located about 1,200 light-years away. The system resembles our own, with five planets total, though the other three worlds are all too close to the star to contain life as we know it. The two farthest planets, Kepler-62e and Kepler-62f, have 1.6 and 1.4 times the radius of Earth and go around their parent star every 122 and 267 days, respectively. Because their parent star is only about two-thirds the size of our sun, the estimated surface temperatures of the two worlds is -3 degrees and -65 degrees Celsius.



The three newly discovered super-Earth exoplanets in comparison with our own world and the previous habitable zone record-holder, Kepler-22b. NASA/Ames/JPL-Caltech

While that sounds very chilly, the calculation doesn't take into account a potential atmosphere, which would act like a warm blanket, heating the planets up and possibly producing temperatures where liquid water could exist. There is a great deal of uncertainty with the new worlds and scientists are careful about drawing any conclusions. The Kepler team members don't know if the planets "have a rocky composition, an atmosphere, or water," they write in a paper available Apr. 18 in Science. Unless those properties can be found out, they "cannot determine whether [the exoplanets] are in fact habitable."

The other new world, reported today in The Astrophysical Journal, is called Kepler-69c. It takes 242 days to go around a star named Kepler-69 and has a radius about 1.7 times that of our own planet. Its surface temperature is estimated to be a balmy 27 degrees Celsius, basically beach-going weather. Given its size, it's unknown exactly how Earth-like conditions on its surface might be. Kepler has previously spotted an almost-Earth-size world in the habitable zone: Kepler-22b, sometimes called an ocean world. Scientists have speculated that it could be covered with liquid, but without more information they can't know for sure.



The five-planet system surrounding Kepler-62, showing how far they orbit from their parent star compared to the planets in our solar system. NASA/Ames/JPL-Caltech

Some researchers think that some of these Earth-sized worlds could be covered in vast oceans, though whether or not these oceans would be filled with water or other liquids is a matter of speculation. In their paper, the discoverers of Kepler-69c write that it "may be a water world and quite unlike any planet in our solar system."

http://www.eurekalert.org/pub_releases/2013-04/uomh-sst041813.php

Science surprise: Toxic protein made in unusual way may explain brain disorder **Study finds abnormal protein translation leads to Fragile X ataxia, a disorder seen in grandfathers of children with Fragile X syndrome**

ANN ARBOR, Mich. — A bizarre twist on the usual way proteins are made may explain mysterious symptoms in the grandparents of some children with mental disabilities.

The discovery, made by a team of scientists at the University of Michigan Medical School, may lead to better treatments for older adults with a recently discovered genetic condition.

The condition, called Fragile X-associated Tremor Ataxia Syndrome (FXTAS), causes shakiness and balance problems and is often misdiagnosed as Parkinson's disease. The grandchildren of people with the disease have a separate disorder called Fragile X syndrome, caused by problems in the same gene. The new discovery may also help shine light on that disease, though indirectly.

In a new paper published in the journal Neuron, the U-M-led team presents evidence that a toxic protein they've named FMRpolyG contributes to the death of nerve cells in FXTAS – and that this protein is made in a very unusual way.

Normally, DNA is transcribed into RNA, and then a part of the RNA is translated into a protein that performs its function in cells. Where this translation process starts on the RNA is usually determined by a specific sequence called a start codon.

The gene mutation that causes FXTAS is a repeated DNA sequence that is made into RNA but normally is not made into protein because it lacks a start codon. However, the investigators discovered that when this repeat expands, it can trigger protein production by a new mechanism known as RAN translation.

Corresponding author Peter Todd, M.D., Ph.D., notes that this unusual translation process appears to stem from a long chain of repeated DNA "letters" found in the genes of both grandparents and kids with Fragile X mutations. Todd is the Bucky and Patti Harris Professor in the U-M Department of Neurology

"Essentially, we've found that a sequence of DNA which shouldn't be made into protein is being made into protein – and that this causes a toxicity in nerve cells," he explains. "We believe that the protein forms aggregates, and that this is a major contributor to toxicity and symptoms in FXTAS."

The U-M group went on to show how this RAN translation occurs in FXTAS and demonstrated that blocking it prevents the repeat mutation from being toxic, suggesting a new target for future treatments.

Fragile X tremor/ataxia syndrome or FXTAS was only discovered a decade ago. It may affect as many as one in every 3,000 men and one in 20,000 women, who have a repeat mutation in the gene known as FMR1. However, these patients don't usually develop symptoms until late middle age, allowing them to pass the mutation on to their daughters, who can then have children where the DNA repeat that has grown much longer. In those children, especially in boys, it can cause severe intellectual disability and autism-like symptoms as the FMR1 gene shuts down and none of the normal protein is produced.

In fact, says Todd, it's often only after a child is diagnosed with Fragile X syndrome through genetic testing that their grandfather or grandmother finds out that their own symptoms stem from FXTAS. Doctors in U-M's Neurogenetics clinic for adults, and the Pediatric Genetics Clinic at U-M's C.S. Mott Children's Hospital, routinely work together to address the needs of Fragile X families.

"We have some treatments for the symptoms that FXTAS patients have, but we do not yet have a cure," says Todd, who regularly sees patients with FXTAS and related disorders. "Better treatments are needed – and this new discovery might help lead to novel strategies for clearing away or preventing the buildup of this toxic protein."

In addition, he says, the discovery that Fragile X ataxia results in part from RAN translation could have significance both for other diseases like amyotrophic lateral sclerosis (ALS, also called Lou Gehrig's disease) and certain forms of dementia that are caused by DNA repeats. It can also aid our understanding of basic biology. "This may represent a new way in which translational initiation events occur, and may have importance beyond this one disease," he notes. Further research on how RAN translation occurs, and why, is needed.

The idea that proteins can be created without a "start site" flies in the face of what most students of biology have learned in the last century. "In biology, we're finding that the rules we once thought were hard and fast have some wiggle room," Todd says.

In addition to Todd and co-corresponding author Henry L. Paulson, M.D., Ph.D. the Lucile Groff Professor of Neurology, the study's authors include Seok Yoon Oh, Amy Krans, Fang He, Michelle Frazer, Abigail J. Renoux, Kai-chun Chen, K. Matthew Scaglione from U-M Neurology; Chantal Sellier and Nicholas Charlet from France's Institut de Génétique et de Biologie Moléculaire et Cellulaire; Venkatesha Basrur and Kojo Elenitoba-Johnson from the U-M Department of Pathology; Jean P. Vonsattel and Elan D. Louis from Columbia University; Michael A. Sutton from the U-M Department of Physiology; J. Paul Taylor from St. Jude's Children's Hospital, and Ryan E. Mills from the U-M Department of Human Genetics.

The research was funded by NIH grants KNS069809A, RO1 NS038712, RO1 AG034228, and research funds from the Michigan Alzheimer's Disease Center.

http://www.eurekalert.org/pub_releases/2013-04/cumc-hlo041813.php

High levels of glutamate in brain may kick-start schizophrenia

Implications for early diagnosis and new treatment strategies

New York, NY - An excess of the brain neurotransmitter glutamate may cause a transition to psychosis in people who are at risk for schizophrenia, reports a study from investigators at Columbia University Medical Center (CUMC) published in the current issue of *Neuron*.

The findings suggest 1) a potential diagnostic tool for identifying those at risk for schizophrenia and 2) a possible glutamate-limiting treatment strategy to prevent or slow progression of schizophrenia and related psychotic disorders.

"Previous studies of schizophrenia have shown that hypermetabolism and atrophy of the hippocampus are among the most prominent changes in the patient's brain," said senior author Scott Small, MD, Boris and Rose Katz Professor of Neurology at CUMC. "The most recent findings had suggested that these changes occur very early in the disease, which may point to a brain process that could be detected even before the disease begins."

To locate that process, the Columbia researchers used neuroimaging tools in both patients and a mouse model. First they followed a group of 25 young people at risk for schizophrenia to determine what happens to the brain as patients develop the disorder. In patients who progressed to schizophrenia, they found the following pattern: First, glutamate activity increased in the hippocampus, then hippocampus metabolism increased, and then the hippocampus began to atrophy.

To see if the increase in glutamate led to the other hippocampus changes, the researchers turned to a mouse model of schizophrenia. When the researchers increased glutamate activity in the mouse, they saw the same pattern as in the patients: The hippocampus became hypermetabolic and, if glutamate was raised repeatedly, the hippocampus began to atrophy.

Theoretically, this dysregulation of glutamate and hypermetabolism could be identified through imaging individuals who are either at risk for or in the early stage of disease. For these patients, treatment to control glutamate release might protect the hippocampus and prevent or slow the progression of psychosis.

Strategies to treat schizophrenia by reducing glutamate have been tried before, but with patients in whom the disease is more advanced. "Targeting glutamate may be more useful in high-risk people or in those with early signs of the disorder," said Jeffrey A. Lieberman, MD, a renowned expert in the field of schizophrenia, Chair of the Department of Psychiatry at CUMC, and president-elect of the American Psychiatric Association. "Early intervention may prevent the debilitating effects of schizophrenia, increasing recovery in one of humankind's most costly mental disorders."

In an accompanying commentary, Bitu Moghaddam, professor of neuroscience and of psychiatry, University of Pittsburgh, suggests that if excess glutamate is driving schizophrenia in high-risk individuals, it may also explain why a patient's first psychotic episodes are often caused by periods of stress, since stress increases glutamate levels in the brain.

The other authors of "Imaging Patients with Psychosis and a Mouse Model Establishes a Spreading Pattern of Hippocampal Dysfunction and Implicates Glutamate as a Driver" are: Scott A. Schobel (CUMC, The New York State Psychiatric Institute (NYSPI), F. Hoffman–La Roche); Nashid H. Chaudhury (Yale University School of Medicine); Usman A. Khan (CUMC, SUNY Downstate Medical Center); Beatriz Paniagua (CUMC); Martin A. Styner (CUMC); Iris Asllani (CUMC); Benjamin P. Inbar (NYSPI); Cheryl M. Corcoran (CUMC, NYSPI); and Holly Moore (CUMC).

S.A. Schobel is currently a full-time employee of F. Hoffmann-La Roche, Ltd. Dr. Schobel's work on this study began when he was an assistant professor of clinical psychiatry at Columbia and prior to his employment at Roche. The remaining authors declare no financial or other conflicts of interest.

This research was supported by the Brain and Behavior Research Fund Young Investigator Grant, the Paul Janssen Fellowship in Translational Neuroscience Research, and NIMH K23MH090563 (S.A. Schobel); the National Center for Advancing Translational Sciences, NIH, through Grant Number U11 TR000040, formerly the National Center for Research Resources, Grant Number U11 RR024156 (S.A. Schobel; C.M.C.); NIMH K23MH066279 and R21MH086125 (C.M.C.); P40 HD03110 and U54 EB005149 (M.A.S, B.P.); the Sidney R. Baer, Jr. Foundation and P50 MH086385 (H.M.); the Broitman Foundation and 1R01MH093398-01 (S.A. Small); and the New York State Office of Mental Hygiene.

<http://phys.org/news/2013-04-pure-gold-nanoparticles-inhibit-fat.html>

Pure gold nanoparticles can inhibit fat storage

Gold nanoparticles can inhibit adipose storage and lead to accelerated aging and wrinkling, slowed wound healing and onset of diabetes

Phys.org - New research reveals that pure gold nanoparticles found in everyday items such as personal care products, as well as drug delivery, MRI contrast agents and solar cells can inhibit adipose (fat) storage and lead to accelerated aging and wrinkling, slowed wound healing and the onset of diabetes. The researchers, led by Tatsiana Mironava, a visiting assistant professor in the Department of Chemical and Molecular Engineering at Stony Brook University, detail their research, "Gold nanoparticles cellular toxicity and recovery: Adipose Derived Stromal cells," in the journal *Nanotoxicology*.

Together with co-author Dr. Marcia Simon, Professor of Oral Biology and Pathology at Stony Brook University, and Director of the University's Living Skin Bank, a world-class facility that has developed skin tissue for burn victims and various wound therapies, the researchers tested the impact of nanoparticles in vitro on multiple types of cells, including adipose (fat) tissue, to determine whether their basic functions were disrupted when exposed to very low doses of nanoparticles. Subcutaneous adipose tissue acts as insulation from heat and cold, functions as a reserve of nutrients, and is found around internal organs for padding, in yellow bone marrow and in breast tissue.

They discovered that the human adipose-derived stromal cells – a type of adult stem cells – were penetrated by the gold nanoparticles almost instantly and that the particles accumulated in the cells with no obvious pathway for elimination. The presence of the particles disrupted multiple cell functions, such as movement; replication (cell division); and collagen contraction; processes that are essential in wound healing.

According to the researchers, the most disturbing finding was that the particles interfered with genetic regulation, RNA expression and inhibited the ability to differentiate into mature adipocytes or fat cells. "Reductions caused by gold nanoparticles can result in systemic changes to the body," said Professor Mironava. "Since they have been considered inert and essentially harmless, it was assumed that pure gold nanoparticles would also be safe. Evidence to the contrary is beginning to emerge."

This study is also the first to demonstrate the impact of nanoparticles on adult stem cells, which are the cells our body uses for continual organ regeneration. It revealed that adipose derived stromal cells involved in regeneration of multiple organs, including skin, nerve, bone, and hair, ignored appropriate cues and failed to differentiate when exposed to nanoparticles. The presence of gold nanoparticles also reduced adiponectin, a protein involved in regulating glucose levels and fatty acid breakdown, which helps to regulate metabolism. "We have learned that careful consideration and the choice of size, concentration and the duration of the clinical application of gold nanoparticles is warranted," said Professor Mironava. "The good news is that when the nanoparticles were removed, normal functions were eventually restored."

"Nanotechnology is continuing to be at the cutting edge of science research and has opened new doors in energy and materials science," said co-author, Miriam Rafailovich, PhD, Chief Scientist of the Advanced Energy Center and Distinguished Professor of Materials Science and Engineering at Stony Brook. "Progress comes with social responsibility and ensuring that new technologies are environmentally sustainable. These results are very relevant to achieving these goals."

More information: "Gold nanoparticles cellular toxicity and recovery: Adipose Derived Stromal cells," Nanotoxicology, 2013. informahealthcare.com/doi/abs/10.3109/17435390.2013.769128

Abstract

Gold nanoparticles (AuNPs) are currently used in numerous medical applications. Herein, we describe their in vitro impact on human adipose-derived stromal cells (ADSCs) using 13 nm and 45 nm citrate-coated AuNPs. In their non-differentiated state, ADSCs were penetrated by the AuNPs and stored in vacuoles. The presence of the AuNPs in ADSCs resulted in increased population doubling times, decreased cell motility and cell-mediated collagen contraction. The degree to which the cells were impacted was a function of particle concentration, where the smaller particles required a sevenfold higher concentration to have the same effect as the larger ones. Furthermore, AuNPs reduced adipogenesis as measured by lipid droplet accumulation and adiponectin secretion. These effects correlated with transient increases in DLK1 and with relative reductions in fibronectin. Upon removal of exogenous AuNPs, cellular NP levels decreased and normal ADSC functions were restored. As adiponectin helps regulate energy metabolism, local fluctuations triggered by AuNPs can lead to systemic changes. Hence, careful choice of size, concentration and clinical application duration of AuNPs is warranted.

http://www.eurekalert.org/pub_releases/2013-04/uoc--qfe041813.php

Quest for edible malarial vaccine leads to other potential medical uses for algae

Can scientists rid malaria from the Third World by simply feeding algae genetically engineered with a vaccine?

That's the question biologists at UC San Diego sought to answer after they demonstrated last May that algae can be engineered to produce a vaccine that blocks malaria transmission. In a follow up study, published online today in the scientific journal Applied and Environmental Microbiology, they got their answer: Not yet, although the same method may work as a vaccine against a wide variety of viral and bacterial infections. In their most recent study, which the authors made freely available on the Applied and Environmental Microbiology website at <http://aem.asm.org/>, the researchers fused a protein that elicits an antibody response in mice against the organism that causes malaria, Plasmodium falciparum, which afflicts 225 million people worldwide, with a protein produced by the bacterium responsible for cholera, Vibrio cholera, that binds to intestinal epithelial cells. They then genetically engineered algae to produce this two-protein combination, or "fusion protein," freeze dried the algae and later fed the resulting green powder to mice. The researchers hypothesized that together these proteins might be an effective oral vaccine candidate when delivered using algae.

The result? The mice developed Immunoglobulin A (IgA) antibodies to both the malarial parasite protein and to a toxin produced by the cholera bacteria. Because IgA antibodies are produced in the gut and mucosal linings, they don't protect against the malarial parasites, which are injected directly into the bloodstream by mosquitoes. But their study suggests that similar fusion proteins might protect against infectious diseases that affect mucosal linings using their edible freeze-dried algae.

"Many bacterial and viral infections are caused by eating tainted food or water," says Stephen Mayfield, a professor of biology at UC San Diego who headed the study. "So what this study shows is that you can get a really good immune response from a recombinant protein in algae that you feed to a mammal. In this case, it

happens to be a mouse, but presumably it would also work in a human. That's really encouraging for the potential for algae-based vaccines in the future."

The scientists say bacterial infections caused by Salmonella, E. coli and other food and water-borne pathogens could be prevented in the future with inexpensive vaccines developed from algae that could be eaten rather than injected. "It might even be used to protect against cholera itself," said James Gregory, a postdoctoral researcher in Mayfield's lab and the first author of the paper. In his experiments with mice, he said, Immunoglobulin G (IgG) antibodies—which are found in blood and tissues—were produced against the cholera toxin, "but not the malaria antigen and we don't quite understand why."

Part of the difficulty in creating a vaccine against malaria is that it requires a system that can produce structurally complex proteins that resemble those made by the parasite, thus eliciting antibodies that disrupt malaria transmission. Most vaccines created by engineered bacteria are relatively simple proteins that stimulate the body's immune system to produce antibodies against bacterial invaders.

Three years ago, a UC San Diego team of biologists headed by Mayfield, who is also the director of the San Diego Center for Algae Biotechnology, a research consortium seeking to develop transportation fuels from algae, published a landmark study demonstrating that many complex human therapeutic proteins, such as monoclonal antibodies and growth hormones, could be produced by the common algae *Chlamydomonas*. That got Gregory wondering if complex malarial transmission blocking vaccine candidates could also be produced by *Chlamydomonas*. Two billion people live in malaria endemic regions, making the delivery of a malarial vaccine a costly and logistically difficult proposition, especially when that vaccine is expensive to produce. So the UC San Diego biologists set out to determine if this alga, an organism that can produce complex proteins very cheaply, could produce malaria proteins that would inhibit infections from malaria.

"It's too costly to vaccinate two billion people using current technologies," explained Mayfield. "Realistically, the only way a malaria vaccine will ever be used in the developing world is if it can be produced at a fraction of the cost of current vaccines. Algae have this potential because you can grow algae any place on the planet in ponds or even in bathtubs."

Collaborating with Joseph Vinetz, a professor of medicine at UC San Diego and a leading expert in tropical diseases who has been working on developing vaccines against malaria, the researchers showed in their earlier study, published in the open access journal PLoS ONE last May that the proteins produced by the algae, when injected into laboratory mice, made antibodies that blocked malaria transmission from mosquitoes.

The next step was to see if they could immunize mice against malaria by simply feeding the genetically engineered algae. "We think getting oral vaccines in which you don't have to purify the protein is the only way in which you can make medicines dramatically cheaper and make them available to the developing world," says Mayfield. "The Holy Grail is to develop an orally delivered vaccine, and we predict that we may be able to do it in algae, and for about a penny a dose. Our algae-produced malarial vaccine works against malarial parasites in mice, but it needs to be injected into the bloodstream."

Although an edible malarial vaccine is not yet a reality, he adds, "this study shows that you can make a pretty fancy protein using algae, deliver it to the gut and get IgA antibodies that recognize that protein. Now we know we have a system that can deliver a complex protein to the right place and develop an immune response to provide protection."

Mayfield is also co-director of the Center for Food & Fuel for the 21st Century, a new research unit that has brought together researchers from across the campus to develop renewable ways of improving the nation's food, fuel, pharmaceutical and other bio-based industries and is this week hosting a major symposium on the subject at the Institute of the Americas at UC San Diego.

Two other researchers in Mayfield's laboratory, Aaron Topol and David Doerner, participated in the research study, which was supported by grants from the San Diego Foundation, the California Energy Commission (500-10-039) and the National Science Foundation (CBET-1160184).

http://www.eurekalert.org/pub_releases/2013-04/ki-sss041913.php

Swedish study suggests reduced risk of dementia

Risk of developing dementia may have declined over the past 20 years

A new Swedish study published in the journal *Neurology* shows that the risk of developing dementia may have declined over the past 20 years, in direct contrast to what many previously assumed. The result is based on data from the SNAC-K, an ongoing study on aging and health that started in 1987.

"We know that cardiovascular disease is an important risk factor for dementia. The suggested decrease in dementia risk coincides with the general reduction in cardiovascular disease over recent decades", says Associate Professor Chengxuan Qiu of the Aging Research Center (ARC), established by Karolinska Institutet and Stockholm University. "Health check-ups and cardiovascular disease prevention have improved

significantly in Sweden, and we now see results of this improvement reflected in the risk of developing dementia."

Dementia is a constellation of symptoms characterized by impaired memory and other mental functions. After age 75, dementia is commonly due to multiple causes, mainly Alzheimer's disease and vascular dementia. In the current study, more than 3000 persons 75 years and older living in the central Stockholm neighborhood of Kungsholmen participated. Of the participants, 523 were diagnosed with some form of dementia. The key members of the research group have been essentially the same since 1987, including the neurologist responsible for the clinical diagnoses of dementia. All study participants were assessed by a nurse, a physician, and a psychologist.

The result shows the prevalence of dementia was stable in both men and women across all age groups after age 75 during the entire study period (1987-1989 and 2001-2004), despite the fact that the survival of persons with dementia increased since the end of the 1980s. This means that the overall risk of developing dementia must have declined during the period, possibly thanks to prevention and better treatment of cardiovascular disease. "The reduction of dementia risk is a positive phenomenon, but it is important to remember that the number of people with dementia will continue to rise along with the increase in life expectancy and absolute numbers of people over age 75", says Professor Laura Fratiglioni, Director of the Aging Research Center. "This means that the societal burden of dementia and the need for medical and social services will continue to increase. Today there's no way to cure patients who have dementia. Instead we must continue to improve health care and prevention in this area."

The study was funded by the Swedish Council for Working Life and Social Research (FAS), the Swedish Ministry of Health and Social Affairs, the Swedish Research Council, and Swedish Brain Power.

Publication: 'Twenty-year changes in dementia occurrence suggest decreasing incidence in central Stockholm, Sweden,' Chengxuan Qiu, Eva von Strauss, Lars Bäckman, Bengt Winblad, Laura Fratiglioni, published in the April 17, 2013, online issue of Neurology®, the medical journal of the American Academy of Neurology, doi: 10.1212/WNL.0b013e318292a2f9.

Read the abstract: <http://www.neurology.org/content/early/2013/04/17/WNL.0b013e318292a2f9.short>

<http://www.sciencedaily.com/releases/2013/04/130419132508.htm>

Intense, Specialized Training in Young Athletes Linked to Serious Overuse Injuries

Young athletes who specialize in one sport and train intensively have a significantly higher risk of stress fractures and other severe overuse injuries, even when compared with other injured athletes, according to the largest clinical study of its kind.

For example, young athletes who spent more hours per week than their age playing one sport – such as a 12-year-old who plays tennis 13 or more hours a week – were 70 percent more likely to experience serious overuse injuries than other injuries.

Loyola University Medical Center sports medicine physician Dr. Neeru Jayanthi presented findings during an oral podium research session April 19 at the American Medical Society for Sports Medicine (AMSSM) meeting in San Diego. The study is titled "Risks of Specialized Training and Growth in Young Athletes: A Prospective Clinical Cohort Study."

"We should be cautious about intense specialization in one sport before and during adolescence," Jayanthi said. "Among the recommendations we can make, based on our findings, is that young athletes should not spend more hours per week in organized sports than their ages."

Between 2010 and 20103, Jayanthi and colleagues at Loyola and Lurie Children's Hospital of Chicago enrolled 1,206 athletes ages 8 to 18 between who had come in for sports physicals or treatment for injuries. Researchers are following each athlete for up to three years.

There were 859 total injuries, including 564 overuse injuries, in cases in which the clinical diagnosis was recorded. The overuse injuries included 139 serious injuries such as stress fractures in the back or limbs, elbow ligament injuries and osteochondral injuries (injuries to cartilage and underlying bone). Such serious injuries can force young athletes to the sidelines for one to six months or longer.

The study confirmed preliminary findings, reported earlier, that specializing in a single sport increases the risk of overall injury, even when controlling for an athlete's age and hours per week of sports activity.

Among the study's other findings:

- Young athletes were more likely to be injured if they spent more than twice as much time playing organized sports as they spent in unorganized free play -- for example, playing 11 hours of organized soccer each week, and only 5 hours of free play such as pick-up games.
- Athletes who suffered serious injuries spent an average of 21 hours per week in total physical activity (organized sports, gym and unorganized free play), including 13 hours in organized sports. By comparison,

athletes who were not injured, participated in less activity – 17.6 hours per week in total physical activity, including only 9.4 hours in organized sports.

• Injured athletes scored 3.3 on researchers' six-point sports-specialization scale. Uninjured athletes scored 2.7 on the specialization scale. (On the sports specialization scale, an athlete is given one point for each of the following: Trains more than 75 percent of the time in one sport; trains to improve skill or misses time with friends; has quit other sports to focus on one sport; considers one sport more important than other sports; regularly travels out of state; trains more than eight months a year or competes more than six months per year. Jayanthi offers the following tips to reduce the risk of injuries in young adults:

- *Do not spend more hours per week than your age playing sports. (Younger children are developmentally immature and may be less able to tolerate physical stress.)*
- *Do not spend more than twice as much time playing organized sports as you spend in gym and unorganized play.*
- *Do not specialize in one sport before late adolescence.*
- *Do not play sports competitively year round. Take a break from competition for one-to-three months each year (not necessarily consecutively).*
- *Take at least one day off per week from training in sports.*

Jayanthi and colleagues at Loyola and Lurie Children's Hospital are planning a follow-up study to determine whether counseling recommendations on proper sports training can reduce the risk of overuse injuries in young athletes. The study is called TRACK – Training, Risk Assessment and Counseling in Kids.

"We will be testing our hypothesis that many of these serious injuries are potentially preventable," Jayanthi said. The current study was funded by two research grants from the American Medical Society for Sports Medicine. Jayanthi is a member of an AMSSM committee that is writing guidelines on preventing and treating overuse injuries in young athletes.

Jayanthi is Medical Director of Primary Care Sports Medicine at Loyola. He is an associate professor in the Departments of Family Medicine and Orthopaedic Surgery & Rehabilitation at Loyola University Chicago Stritch School of Medicine.

Co-authors of the study Lara Dugas, PhD, of Loyola's Department of Public Health Sciences and Cynthia LaBella, MD, and Brittany Patrick of Lurie Children's hospital. Loyola medical students and research assistants who assisted in the study are Dan Fisher, Courtney Pinkham, Erin Feller and Peter Linn.

The study was originally supported by Stritch School of Medicine's Student Training in Approaches to Research (STAR) program.

<http://phys.org/news/2013-04-grains-sand-ancient-supernova-meteorites.html>

Grains of sand from ancient supernova found in meteorites

It's a bit like learning the secrets of the family that lived in your house in the 1800s by examining dust particles they left behind in cracks in the floorboards.

Phys.org - By looking at specks of dust carried to earth in meteorites, scientists are able to study stars that winked out of existence long before our solar system formed. This technique for studying the stars – sometimes called astronomy in the lab—gives scientists information that cannot be obtained by the traditional techniques of astronomy, such as telescope observations or computer modeling.

Now scientists working at Washington University in St. Louis with support from the McDonnell Center for the Space Sciences, have discovered two tiny grains of silica (SiO₂; the most common constituent of sand) in primitive meteorites. This discovery is surprising because silica is not one of the minerals expected to condense in stellar atmospheres—in fact, it has been called 'a mythical condensate.'

Five silica grains were found earlier, but, because of their isotopic compositions, they are thought to originate from AGB stars, red giants that puff up to enormous sizes at the end of their lives and are stripped of most of their mass by powerful stellar winds. These two grains are thought to have come instead from a core-collapse supernova, a massive star that exploded at the end of its life.

Because the grains, which were found in meteorites from two different bodies of origin, have spookily similar isotopic compositions, the scientists speculate in the May 1 issue of *Astrophysical Journal Letters*, that they may have come from a single supernova, perhaps even the one whose explosion is thought to have triggered the formation of the solar system. A summary of the paper will also appear in the Editors' Choice compilation in the May 3 issue of *Science* magazine.

The first presolar grains are discovered

Until the 1960s most scientists believed the early solar system got so hot that presolar material could not have survived. But in 1987 scientists at the University of Chicago discovered miniscule diamonds in a primitive meteorite (ones that had not been heated and reworked). Since then they've found grains of more than ten other minerals in primitive meteorites.

Many of these discoveries were made at Washington University, home to Ernst Zinner, PhD, research professor in Physics at Washington University in St. Louis, who helped develop the instruments and techniques needed to study presolar grains (and the last author on the paper).

The scientists can tell these grains came from ancient stars because they have highly unusual isotopic signatures. (Isotopes are different atoms of the same chemical element that have a slightly different mass.)

Different stars produce different proportions of isotopes. But the material from which our solar system was fashioned was mixed and homogenized before the solar system formed. So all of the planets and the Sun have the pretty much the same isotopic composition, known simply as "solar."

Meteorites, most of which are pieces of asteroids, have the solar composition as well, but trapped deep within the primitive ones are pure samples of stars. The isotopic compositions of these presolar grains provide clues to the complex nuclear and convective processes operating within stars, which are poorly understood.

Even our nearby Sun is still a mystery to us; much less more exotic stars that are incomprehensibly far away. Some models of stellar evolution predict that silica could condense in the cooler outer atmospheres of stars but others predict silicon would be completely consumed by the formation of magnesium- or iron-rich silicates, leaving none to form silica.

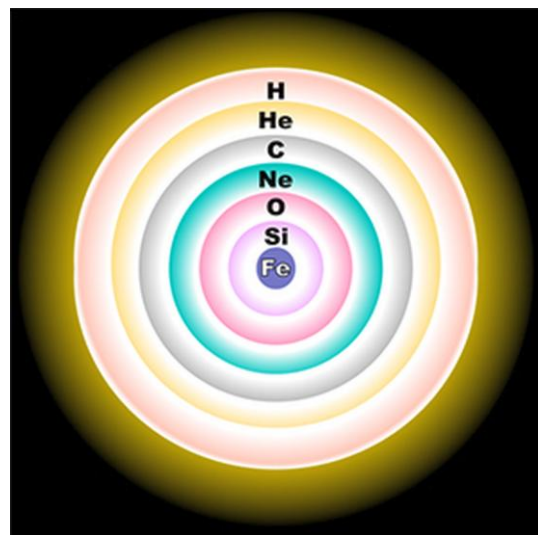
But in the absence of any evidence, few modelers even bothered to discuss the condensation of silica in stellar atmospheres. "We didn't know which model was right and which was not, because the models had so many parameters," said Pierre Haenecour, a graduate student in Earth and Planetary Sciences, who is the first author on the paper.

The first silica grains are discovered

In 2009 Christine Floss, PhD, research professor of physics at Washington University in St. Louis, and Frank Stadermann, PhD, since deceased, found the first silica grain in a meteorite. Their find was followed within the next few years by the discovery of four more grains. All of these grains were enriched in oxygen-17 relative to solar. "This meant they had probably come from red giant or AGB stars" Floss said.

When Haenecour began his graduate study with Floss, she had him look at a primitive meteorite that had been picked up in Antarctica by a U.S. team. Antarctica is prime meteorite-hunting-territory because the dark rocks show up clearly against the white snow and ice. Haenecour found 138 presolar grains in the meteorite slice he examined and to his delight one of them was a silica grain. But this one was enriched in oxygen-18, which meant it came from a core-collapse supernova, not a red giant.

He knew that another graduate student in the lab had found a silica grain rich in oxygen-18. Xuchao Zhao, now a scientist at the Institute of Geology and Geophysics in Beijing, China, found his grain in a meteorite picked up in Antarctica by the Chinese Antarctic Research Expedition.



A massive star that will explode at the end of its life, a core-collapse supernova has a layered structure rather like that of an onion. Credit: Wikipedia

With two specks to go on, Haenecour tackled the difficult problem of calculating how a supernova might have produced silica grains. Before it explodes, a supernova is a giant onion, made up of concentric layers dominated by different elements.

Some theoretical models predicted that silica might be produced in massive oxygen-rich layers near the core of the supernova. But if silica grains could condense there, Haenecour and his colleagues thought, they should be enriched in oxygen-16, not oxygen-18.

They found they could reproduce the oxygen-18 enrichment of the two grains by mixing small amounts of material from the oxygen-rich inner zones and the oxygen-18-rich helium/carbon zone with large amounts of material from the hydrogen envelope of the supernova.

In fact, Haenecour said, the mixing needed to produce the composition of the two grains was so similar that the grains might well come from the same supernova. Could it have been the supernova whose explosion is thought to have kick-started the collapse of the molecular cloud out of which the planets of the solar system formed?

How strange to think that two tiny grains of sand could be the humble bearers of such momentous tidings from so long ago and so far away.

More information: AJL paper: iopscience.iop.org/2041-8205/768/1/L17/

<http://www.sciencedaily.com/releases/2013/04/130419121012.htm>

From Blank Round to a Potently Active Substance?

A long-forgotten candidate for antiviral therapy is undergoing a renaissance:

Since the 1970s, the small molecule CMA has been considered a potent agent against viral infections, yet it was never approved for clinical use. Scientists at the Bonn University Hospital have now deciphered how the molecule can actually stimulate the immune system to combat viruses.

The results are now being presented in the journal *EMBO* of the European Molecular Biology Organization. Finding an active substance to stimulate the immune system and thus better combat dangerous viruses has been the dream of medical researchers for some time. Common viral diseases include influenza, hepatitis and AIDS. "A number of products have promised to activate the immune system but, in reality, there still is no such agent yet," says Prof. Dr. Veit Hornung from the Institute for Clinical Chemistry and Clinical Pharmacology of the Bonn University Hospital.

The only substances that have been on the market to date prevent the proliferation of specific viruses, themselves. An active substance that could arm the immune system against a variety of viruses has not yet been discovered.

The compound CMA was only effective in mice and not in humans

At the end of the 1970s, scientists were nearing a breakthrough: 10-carboxymethyl-9-acridanone (CMA) appeared to be a suitable candidate for antiviral therapy. In the mouse model, CMA yielded unexpectedly potent activation of the immune system and a significant release of interferon resulting in an extremely strong antiviral effect. However, the result was unfortunately not reproducible in human cells.

Why CMA stimulates the antiviral response in mice while showing no effect in humans has remained unexplained for quite sometime. That is until Prof. Hornung coincidentally saw an old publication regarding CMA and decided it was worthwhile to reexplore the mechanism of action of this molecule.

The same receptor -- differing mechanism of action

Prof. Hornung believed that the lack of transferability between mice and humans might be associated with the specific target structures that CMA latches on to. The team working with Prof. Hornung was then able to identify the protein to which CMA attaches, its receptor, in mouse cells.

However, the human counterpart of this receptor did not respond to CMA. When CMA binds to the receptor in mice, a signal cascade is set into motion that leads to the release of interferons which in turn boost the immune system. However, in order for this to work, CMA and its receptor must fit together like a lock and key.

Together with the laboratory of Prof. Dr. Karl-Peter Hopfner from the Gene Center at the Ludwig Maximilian University in Munich, the team from the Bonn University Hospital investigated the receptor variants of mice and humans in cell cultures and as purified proteins.

Animal models cannot easily be transferred to humans

"A few small differences in the receptor make the active substance completely ineffective in humans," reports lead author Taner Cavlar, postgraduate in Prof. Hornung's team. In humans, this prevents CMA from being able to latch its crucial receptor and release interferon, even though immune stimulation occurs in mice.

"This is an example of the fact that results from animal models cannot always be easily transferred to humans," says Prof. Hornung. "Comparative investigations on human cells should take place at an early stage of active substance development."

Findings inspire the search for an antiviral drug

Since the scientists were able to figure out the exact structure of the mouse and human receptors, they now have an approach to see if there are conditions under which CMA could also arm the human immune system to fight viruses. This is now the next step which the researchers want to address with their colleagues.

However, it will likely take many years until an effective drug to combat viruses becomes available.

"Nevertheless, when we are able to develop such a potent substance, only very small amounts would be enough to fight a variety of viral infections early on," says Prof. Hornung.

Journal Reference:

1. Taner Cavlar, Tobias Deimling, Andrea Ablasser, Karl-Peter Hopfner, Veit Hornung. *Species-specific detection of the antiviral small-molecule compound CMA by STING*. *The EMBO Journal*, 2013; DOI: [10.1038/emboj.2013.86](https://doi.org/10.1038/emboj.2013.86)

<http://www.sciencedaily.com/releases/2013/04/130420110651.htm>

Mathematical Models Out-Perform Doctors in Predicting Cancer Patients' Responses to Treatment

Mathematical prediction models are better than doctors at predicting the outcomes and responses of lung cancer patients to treatment

Mathematical prediction models are better than doctors at predicting the outcomes and responses of lung cancer patients to treatment, according to new research presented today (Saturday) at the 2nd Forum of the European Society for Radiotherapy and Oncology (ESTRO).

These differences apply even after the doctor has seen the patient, which can provide extra information, and knows what the treatment plan and radiation dose will be.

"The number of treatment options available for lung cancer patients are increasing, as well as the amount of information available to the individual patient. It is evident that this will complicate the task of the doctor in the future," said the presenter, Dr Cary Oberije, a postdoctoral researcher at the MAASTRO Clinic, Maastricht University Medical Center, Maastricht, The Netherlands. "If models based on patient, tumour and treatment characteristics already out-perform the doctors, then it is unethical to make treatment decisions based solely on the doctors' opinions. We believe models should be implemented in clinical practice to guide decisions."

Dr Oberije and her colleagues in The Netherlands used mathematical prediction models that had already been tested and published. The models use information from previous patients to create a statistical formula that can be used to predict the probability of outcome and responses to treatment using radiotherapy with or without chemotherapy for future patients.

Having obtained predictions from the mathematical models, the researchers asked experienced radiation oncologists to predict the likelihood of lung cancer patients surviving for two years, or suffering from shortness of breath (dyspnea) and difficulty swallowing (dysphagia) at two points in time:

- 1) after they had seen the patient for the first time, and
- 2) after the treatment plan was made. At the first time point, the doctors predicted two-year survival for 121 patients, dyspnea for 139 and dysphagia for 146 patients.

At the second time point, predictions were only available for 35, 39 and 41 patients respectively.

For all three predictions and at both time points, the mathematical models substantially outperformed the doctors' predictions, with the doctors' predictions being little better than those expected by chance.

The researchers plotted the results on a special graph [1] on which the area below the plotted line is used for measuring the accuracy of predictions; 1 represents a perfect prediction, while 0.5 represents predictions that were right in 50% of cases, i.e. the same as chance. They found that the model predictions at the first time point were 0.71 for two-year survival, 0.76 for dyspnea and 0.72 for dysphagia. In contrast, the doctors' predictions were 0.56, 0.59 and 0.52 respectively.

The models had a better positive predictive value (PPV) -- a measure of the proportion of patients who were correctly assessed as being at risk of dying within two years or suffering from dyspnea and dysphagia -- than the doctors. The negative predictive value (NPV) -- a measure of the proportion of patients that would not die within two years or suffer from dyspnea and dysphagia -- was comparable between the models and the doctors.

"This indicates that the models were better at identifying high risk patients that have a very low chance of surviving or a very high chance of developing severe dyspnea or dysphagia," said Dr Oberije.

The researchers say that it is important that further research is carried out into how prediction models can be integrated into standard clinical care. In addition, further improvement of the models by incorporating all the latest advances in areas such as genetics, imaging and other factors, is important. This will make it possible to tailor treatment to the individual patient's biological make-up and tumour type

"In our opinion, individualised treatment can only succeed if prediction models are used in clinical practice. We have shown that current models already outperform doctors. Therefore, this study can be used as a strong argument in favour of using prediction models and changing current clinical practice," said Dr Oberije.

"Correct prediction of outcomes is important for several reasons," she continued. "First, it offers the possibility to discuss treatment options with patients. If survival chances are very low, some patients might opt for a less aggressive treatment with fewer side-effects and better quality of life. Second, it could be used to assess which patients are eligible for a specific clinical trial. Third, correct predictions make it possible to improve and optimise the treatment. Currently, treatment guidelines are applied to the whole lung cancer population, but we know that some patients are cured while others are not and some patients suffer from severe side-effects while others don't. We know that there are many factors that play a role in the prognosis of patients and prediction models can combine them all."

At present, prediction models are not used as widely as they could be by doctors. Dr Oberije says there are a number of reasons: some models lack clinical credibility; others have not yet been tested; the models need to be available and easy to use by doctors; and many doctors still think that seeing a patient gives them information that cannot be captured in a model. "Our study shows that it is very unlikely that a doctor can outperform a model," she concluded.

President of ESTRO, Professor Vincenzo Valentini, a radiation oncologist at the Policlinico Universitario A. Gemelli, Rome, Italy, commented: "The booming growth of biological, imaging and clinical information will challenge the decision capacity of every oncologist. The understanding of the knowledge management sciences is becoming a priority for radiation oncologists in order for them to tailor their choices to cure and care for individual patients."

[1] For the mathematicians among you, the graph is known as an Area Under the Curve (AUC) of the Receiver Operating Characteristic (ROC).

[2] This work was partially funded by grants from the Dutch Cancer Society (KWF), the European Fund for Regional Development (INTERREG/EFRO), and the Center for Translational Molecular Medicine (CTMM).

<http://www.nytimes.com/2013/04/21/magazine/antibiotic-resistance.html?partner=rss&emc=rss&r=0>

Raiding Grandma's Medicine Cabinet

A renewed interest in treatments from a world before penicillin

By MAGGIE KOERTH-BAKER

Last month, the chief medical officer of Britain called antibiotic resistance a "ticking time bomb" and a threat as dangerous as global warming. In Europe alone, 25,000 people die every year from antibiotic-resistant bacteria — and that's only counting the infections that were picked up in supposedly sterile hospitals. For more than 80 years, antibiotics have been nothing short of miraculous. Capable of killing bacteria without killing people, they've turned grave illnesses into mere annoyances, providing doctors with license to shoot first and ask questions later, and do so safely — or so we thought. Broad-spectrum antibiotics are powerful fighters with one flaw: unable to smite every bacterium, those immune to their wrath thrive. With every ear infection we treat, and every healthy cow prophylactically dosed with antibiotics (which also helps fatten the animals), we make these drugs less useful for future generations.

Scientists all over the globe are in a race with evolution, scrambling to understand the underlying mechanisms of antibiotic resistance and to discover new ways to fight bacteria. We must diversify our methods for treating bacterial infections and simultaneously reduce the amount of antibiotics we use, says Brad Spellberg, an infectious-disease specialist at U.C.L.A. This has led to a renewed interest in treatments from a world before penicillin.

Ruth Greenwood, a friend's grandmother, knows the cruelty and desperation of this world well. In 1934, at age 9, she came up with a clever but shortsighted plan to get out of school: roll around in a patch of poison ivy. Greenwood succeeded in getting an itchy rash (and skipping class), but as the days went by, the rash became something much worse. Her legs swelled and broke out in a mass of tender, crimson sores that wept blood and pus. At night, the fluids soaked through her sheets and dried, fusing the bedding to her skin. Greenwood remembers being scooped up in the morning, sheets and all, and put in the bath to soak until the cloth could be peeled away from her flesh.

As she was scratching her rash, Greenwood made tiny cuts in her skin, allowing bacteria to get inside her body. The cells multiplied and infected her legs, most likely causing a disease that doctors now call cellulitis. Today she'd have been prescribed an oral antibiotic. Instead, her parents had to rely on the mess of medical hopes and snake oils that filled the shelves of the pre-antibiotic pharmacy.

First they had her sit in the sun for hours on end, hoping the cell-damaging rays would also destroy the bacteria — doctors would try the same with UV lamps, according to Spellberg. The infection was finally cured when her doctor prescribed a white cream spiked with ammoniated mercury to spread on the affected area. The metallic compound killed the bacteria somehow, possibly by stimulating inflammation that kicked Greenwood's own immune system into high gear. She was lucky: back then the death rate for skin infections was about 11 percent. With antibiotics, we've lowered that figure 100-fold.

That some pre-antibiotic medicines are poised to make a comeback, however, need not be a mortifying prospect. Two treatments — serum therapy and bacteriophages — are having an exciting late career, as scientists find ways to make them safer and more effective than their early-20th-century incarnations.

Serum therapy works like an all-points bulletin for your immune system. Made up of antibodies, the proteins that identify and attack invasive cells, serums essentially create a bodywide dragnet for bacterial fugitives. To procure them, doctors used to infect horses and other animals with bacteria and dose humans with the antibodies culled from the animals' blood. Invented in the 1890s, serum therapy earned one of its discoverers,

Emil von Behring, a Nobel Prize. In Central Park, there is a statue commemorating Balto, the Siberian husky that helped bring lifesaving diphtheria serum to Nome, Alaska, in 1925.

Bacteriophages, viruses that attack bacteria, were especially popular in Eastern Europe. Administered just like antibiotics, internally or directly on the skin, this technique continued to be researched in the postwar Eastern bloc, which couldn't depend on imported drugs from the United States and Western Europe.

Compared with the scorched-earth policy of broad-spectrum antibiotics, serums and phages are downright surgical. Antibodies are incredibly selective about which bacteria they'll attack and which they'll ignore.

Bacteriophages are only slightly less choosy. Those traits can be a liability. Doctors must determine which bacteria is causing an infection before treating it, leading to potentially deadly delays.

Antibiotics made a doctor's job easier, and this led to our current predicament, says Dr. Arturo Casadevall, an infectious-disease expert at Albert Einstein College of Medicine at Yeshiva University in New York. He and his colleagues are hoping for a return to alternative treatments for bacterial infections in the near future. By combining old ideas with modern technology, they and other scientists have helped renew interest in phages. In recent years, for example, federal regulators have approved the use of a variety of antibacterial phages in our food supply. Meanwhile, serum therapy now employs cloned antibodies (no horse blood required), and it's used to treat cancer and arthritis. Clinical trials are under way for modernized antibacterial serums.

The medicine cabinet of the future might contain treatments from an age when we would have tried anything to kill bacteria, but they'll be there only in a supporting role: to preserve the efficacy of the drugs that freed us from that madness.

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