http://www.sciencedaily.com/releases/2012/02/120219143003.htm

Which Anti-HIV Drug Combinations Work Best and Why?

Using a mathematical formula AIDS experts have calculated precisely how well dozens of such anti-HIV drugs work, alone or in any of 857 likely combinations, in suppressing the virus.

ScienceDaily - Using a mathematical formula that carefully measures the degree to which HIV infection of immune system cells is stalled by antiretroviral therapy, AIDS experts at Johns Hopkins have calculated precisely how well dozens of such anti-HIV drugs work, alone or in any of 857 likely combinations, in suppressing the virus. Results of the team's latest research reveal how some combinations work better than others at impeding viral replication, and keeping the disease in check.

"Our study results should help researchers and clinicians develop simpler treatments, using either existing or new drugs, for people who are just starting therapy or people who have already tried and developed resistance to another combination," says senior study investigator and infectious disease specialist Robert Siliciano, M.D., Ph.D.

Siliciano, a professor at the Johns Hopkins University School of Medicine and a Howard Hughes Medical Institute investigator, and colleagues constructed the measurement tool, called the instantaneous inhibitory potential, or IIP, in the laboratory several years ago by analyzing the shape of drug dose-response curves in human immune system cells infected with HIV. They found that the curves' steepness reflects the extent to which small increases in the amount of drugs can further suppress attempts by the virus to bounce back, reproduce and spread.

Researchers say their latest study findings, to be published in the journal Nature Medicine online Feb. 19, along with other recent studies, provide valuable information to physicians about the potential strength of different combination drug therapies, and can help in streamlining and tailoring so-called highly active antiretroviral therapy, or HAART, to as few possible drugs as needed. Several hundred thousand of the more than 1 million Americans living with HIV disease are currently using HAART to fight the disease.

Among the latest study's key findings was that the most potent drug combos included the drugs efavirenz (a non-nucleoside reverse transcriptase inhibitor) and darunavir (a protease inhibitor.) According to the Hopkins team's calculations, the drug mix suppressed viral replication by ***more than a trillion times***, enough to prevent infection of every single lymphocyte, or immune system cell, of which there are a trillion in the body.

The least-powerful drug was found to be one of the oldest anti-HIV medications, d4T, or stavudine (a nucleoside analogue reverse transcriptase inhibitor), which had the power to suppress viral replication by less than 10 times if used on its own (although, Siliciano points out, it works much better when taken in combination with other drugs.)

Siliciano says the most widely used combination, a single pill known as Atripla, consisting of tenofovir disoproxil fumarate (a nucleotide analogue reverse transcriptase inhibitor), emtricitabine (a nucleoside analogue reverse transcriptase inhibitor), and efavirenz, was able to reduce viral replication to as few as one in a billion.

Siliciano points out, however, that any drug combination which suppresses viral replication to the degree that out of every 100,000 lymphocytes exposed to the drugs, only one lymphocyte is likely to be infected (for five tenfold reductions) - is sufficient to keep the disease in check, so long as people take their medication as prescribed.

"This means that overall access to anti-HIV medications could also improve as we develop simpler combinations of fewer drugs to achieve near total suppression," says Siliciano. Less than 7 million of the 34 million people worldwide infected with HIV are taking antiretroviral therapy, he notes.

The Johns Hopkins team based its new calculations on five years of analyzing just how antiretroviral drugs hinder key steps in HIV's life cycle, preventing it from replicating and infecting other immune system cells.

Scientists have for decades focused on multiple drugs targeting different enzymes that are key to the viral life cycle, thinking that multiple barriers along the chain could best halt replication.

Although the strategy worked, scientists had, until now, no theory to explain why some drug combinations worked well and others did not. Indeed, they point out, one of the newest classes of anti-HIV medications, so-called integrase inhibitors, did not work well as single drug treatments in laboratory experiments, but were highly effective in people when combined with other drugs.

Siliciano says that as a result of the Hopkins team's latest research and another of their recent findings, published in Science Translational Medicine in July, experts can finally demonstrate how different drug combinations disrupt and halt viral replication.

Researchers found that the steepest curves occurred when the drug targeted a stage in HIV's life cycle, in which many copies of viral enzymes, were needed. Citing protease inhibitors as an example, Siliciano says

several copies of protease enzyme are needed to cleave the virus into hundreds of working parts before HIV can infect a new immune system cell. He goes on to say that "a level of inter-enzyme cooperation" is happening, specific to each stage of HIV replication.

"Our research shows that drugs like protease inhibitors really work like an on-off switch," says Siliciano. "Above a certain concentration, these drugs completely turn off viral replication. When you have only one copy of a viral enzyme needed in any key part of HIV's life cycle, a little more drug won't give you a lot more suppression; but, when you have more than one copy of enzyme needed for viral replication, then the dose-response curve for the drug will be a lot steeper, and a little more drug will completely shut off viral replication, which is what we want.

"It's gratifying to finally have a consistent metric for evaluating HAART medications that offers reliable information on how well they work in stopping HIV replication, and which also gives us a baseline target for suppression at less than one in 100,000 immune cells becoming infected in the presence of any drug combination," he adds.

The Johns Hopkins inhibition index was first developed to compare the level of viral inhibition from different drugs in different classes and to show how they could be graded.

Having measured the different potencies of many drugs, Siliciano conducted his next set of lab experiments to focus on the explanation behind different strengths of viral inhibition. The scientists measured the changes in the dose-response curves, plotting the results on graphs and comparing the sloping curves for each drug or combination of drugs.

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Currently, there are more than 34 million people in the world living with HIV, including an estimated 1,178,000 in the United States.

Funding for this study, conducted solely at Johns Hopkins, was provided by the Howard Hughes Medical Institute and the National Institute of Allergy and Infectious Diseases, a member of the National Institutes of Health (NIH).

Besides Siliciano, other Hopkins researchers who took part in this study were lead investigator Benjamin Jilek, Ph.D.; Melissa Zarr, B.Sc.; Maame Sampah, B.Sc.; Alireza Rabi, B.Sc.; Cynthia Bullen, B.Sc.; Jun Lai, B.Sc.; and Lin Shen, M.D., Ph.D.

Journal Reference: *Benjamin L Jilek, Melissa Zarr, Maame E Sampah, S Alireza Rabi, Cynthia K Bullen, Jun Lai, Lin Shen, Robert F Siliciano. A quantitative basis for antiretroviral therapy for HIV-1 infection. Nature Medicine, 2012; DOI: 10.1038/nm.2649*

http://medicalxpress.com/news/2012-02-microbiologist-hospitals-windows-bacterial-infections.html

Microbiologist suggests hospitals open windows to reduce bacterial infections

A microbiologist suggested hospital administrators take note of what nurse Florence Nightingale preached; open the windows to let in fresh air when tending to the sick, and they will heal better.

Medical Xpress - Doctor Jack Gilbert, a microbiologist with Argonne National Laboratory, spoke at the recent meeting of the American Association for the Advancement of Science (AAAS) in Vancouver, Canada, and among other things, suggested that hospital administrators take note of what famed nurse Florence Nightingale preached over a hundred and fifty years ago; namely, open the windows to let in fresh air when tending to the sick, and they will heal better.

Gilbert is a member of the team at Argonne that is attempting to identify and categorize every virus and bacteria that exists in nature. In his talk, he cited the work of the University of Oregon's Doctor Jessica Green, who conducted experiments that showed that sampled bacteria were more diverse when exposed to freely flowing air from the outdoors, than were those in highly sterilized environments. But that the bacteria in the sealed and sterilized areas had more of the kinds of bacteria that are considered to be harmful.

Gilbert says that when microbes are allowed to mix with others, they wind up having to compete for resources, which causes a diluting effect. When hospitals are overly sanitized however, there is far less competition, which allows "bad" bugs free rein. He suggests this may account for the high number of infections that occur in hospitals despite serious attempts to completely sterilize them. He compares it to antibacterial drugs given to patients to kill bad bugs in the gut, which in killing off all the good bugs, tend to leave an environment conducive to the bad. He also referenced a 2009 study by Andreas Voss that found that less than half of hospital staff washed their hands after using the rest room. His point is that no matter what hospital workers do, they are not going to be able to kill every virus and bacteria in any given environment, which

means that the bad ones that manage to evade such efforts will thrive without any competition and go on to infect people.

Gilbert also told of a colleague of his working in a South American environment where it wasn't possible to sterilize equipment before working on patients. Implements were simply scrubbed using soap and water. His colleague reported lower infection rates than he'd experienced when working in highly sterile hospital environments. When looked at from this point of view, he says, it all leads to the same common-sense conclusion. To reduce hospital infections, follow Ms. Nightingale's simple advice: open the windows.

Others are not so quick to accept Gilbert's ideas however, suggesting that even so-called good bugs can cause problems if allowed to creep into open wounds.

More information: bio.anl … gilbert.html

http://www.physorg.com/news/2012-02-cold-spellbinding-alignment-planets-sunset.html

Cold and spellbinding: An alignment of planets in the sunset sky

Note to sky watchers: Put on your winter coats. What you're about to read might make you feel an uncontrollable urge to dash outside.

The brightest planets in the solar system are lining up in the evening sky, and you can see the formation - some of it at least - tonight. Go out at sunset and look west. Venus and Jupiter pop out of the twilight even before the sky fades completely black. The two brilliant planets surrounded by evening blue is a beautiful sight.

If you go out at the same time tomorrow, the view improves, because Venus and Jupiter are converging. In mid-February they are about 20 degrees apart. By the end of the month, the angle narrows to only 10 degrees - so close that you can hide them together behind your outstretched palm. Their combined beauty grows each night as the distance between them shrinks.

A special night to look is Saturday, Feb. 25th, when the crescent Moon moves in to form a slender heavenly triangle with Venus, Jupiter and the Moon as vertices. One night later, on Sunday, Feb. 26th, it happens again. This arrangement will be visible all around the world, from city and countryside alike. The Moon, Venus and Jupiter are the brightest objects in the night sky; together they can shine through urban lights, fog, and even some clouds.

After hopping from Venus to Jupiter in late February, the Moon exits stage left, but the show is far from over.

In March, Venus and Jupiter continue their relentless convergence until, on March 12th and 13th, the duo lie only three degrees apart - a spectacular double beacon in the sunset sky (sky map). Now you'll be able to hide them together behind a pair of outstretched fingertips.

There's something mesmerizing about stars and planets bunched together in this way - and, no, you're not imagining things when it happens to you. The phenomenon is based on the anatomy of the human eye.

"Your eye is a bit like a digital camera," explains optometrist Dr. Stuart Hiroyasu of Bishop, California. "There's a lens in front to focus the light, and a photo-array behind the lens to capture the image. The photo-array in your eye is called the retina. It's made of rods and cones, the organic equivalent of electronic pixels."

There's a tiny patch of tissue near the center of the retina where cones are extra-densely packed. This is called "the fovea." "Whatever you see with the fovea, you see in high-definition," Hiroyasu says. The fovea is critical to reading, driving, watching television. The fovea has the brain's attention.

The field of view of the fovea is only about five degrees wide. Most nights in March, Venus and Jupiter will fit within that narrow cone. And when they do - presto! It's spellbinding astronomy.

Standing outdoors, mesmerized by planets aligned in a late winter sunset, you might just forget how cold you feel. Bring a coat anyway... *Provided by Science@NASA*

http://bit.ly/xfVulB

Polarized Display Sheds Light on Octopus and Cuttlefish Vision - and Camouflage

Octopuses are purportedly colorblind, but they can discern one thing that we can't: polarized light. This extra visual realm might give them a leg (er, arm) up on some of the competition.

By Katherine Harmon | February 20, 2012

And a team of researchers has created a new way to test just how sensitive cephalopods are to this type of light. Their results were published online Monday in Current Biology.

"We now know that polarization is tuned much more finely than we thought it was," says Shelby Temple, of the Ecology of Vision Laboratory at the University of Bristol in the U.K., who led the study.

But testing polarized light is tricky, especially since we humans aren't tuned to see it. As Temple and his co-authors wrote in their paper: "For animals that can see it, the polarization of light adds another dimension to vision, analogous to adding color to a black and white image." Polarized light is different from what we see in that it comes from a single angle, and animals that can detect it seem to see it in different resolutions based on

changes in its angle. (The closest we can get to using it is putting on a pair of polarized lenses to cut down on glare.)

Polarized light perception in the best-tuned animals was assumed to be limited to differences of about 10 to 20 degrees. But in the group's new experiments, the mourning cuttlefish (Sepia plangon) responded to just 1.05-degrees change of polarized light orientation.

For the experiments, the team used computer screens that had had the polarizing light filter removed (without these front filters on our liquid crystal displays - LCDs - our monitors would project polarized light images that we wouldn't be able to see). These modified displays played digital movie versions of "looming stimuli" such as an expanding circle, which would suggest a potential predator approaching. But instead of a color or intensity-based image, the one they created was based on changing polarized light orientation only.

Octopus don't yet seem to be quite as sensitive as cuttlefish to the fine gradients in polarized light, responding only after about 10 degrees shift. But, says Temple, "it may be the way that we're testing." As he points out, cuttlefish's knee-jerk response to an approaching predator is a quick change of color, which the researchers could use as an indication that they had seen even fine shifts in the polarized light angle.

"Cuttlefish, they wear their emotions on their sleeve, quite literally," Temple says. "They're showing everything that they're doing as a neural response." In fact, the cuttlefish responded so well, that he and his colleagues thought they were doing something wrong. They were afraid that in the digital renderings they might have accidentally included a non-polarized light clue, such as brightness or intensity. But they went back and checked and found that it was, indeed, just the slight change in polarized light that was frightening the animals.

With octopus, "there's no comparison," he says. But, he concedes that it is possible that the octopuses might have seen finer resolutions of polarized light shift but just didn't have the same simple, speedy reaction as the cuttlefish. And says Temple, "it could be that some species could do it better than others." So far, he has found that the blue ringed octopus looks to me more sensitive than the day octopus. He has plans to test different species of octopus soon.

Researchers are still working to get to the bottom of cephalopod vision, which is turning out to be highly complex. And this new work supports the idea that such sensitivity to polarized light emerged precisely because these animals don't see color well - if at all.

And if octopuses, cuttlefish and squid - and some of their predators and prey - can see polarized light so keenly, are they also using it, as they use color and luminosity, to actively create camouflage?

Other researchers are working on that very question. And Temple and his colleagues have observed that, at least in some cuttlefish, they can create a polarized light-based pattern on their skin. This play in light might "be used as part of a covert communication channel, invisible to animals lacking polarized vision," they wrote.

But the patterns remain tricky for us to pick up on. For that, Temple and his colleagues have developed a way for us to get a peak into the invisible world of polarized light and dark by modifying a digital single-reflex lens (SLR) camera and creating a computer program to feed false-color into varying degrees of polarized light. These mysterious rainbow-colored ecosystem images make it clear that, "We're not done with the story yet, for sure," Temple says.

http://www.physorg.com/news/2012-02-mars-quakes-volcanism-red-planet.html

Mars rocks indicate relatively recent quakes, volcanism, on Red Planet

Images of a martian landscape offer evidence that the Red Planet's surface not only can shake like the surface of Earth, but has done so relatively recently.

PhysOrg.com - If marsquakes do indeed take place, said the scientists who analyzed the high-resolution images, our nearest planetary neighbor may still have active volcanism, which could help create conditions for liquid water.

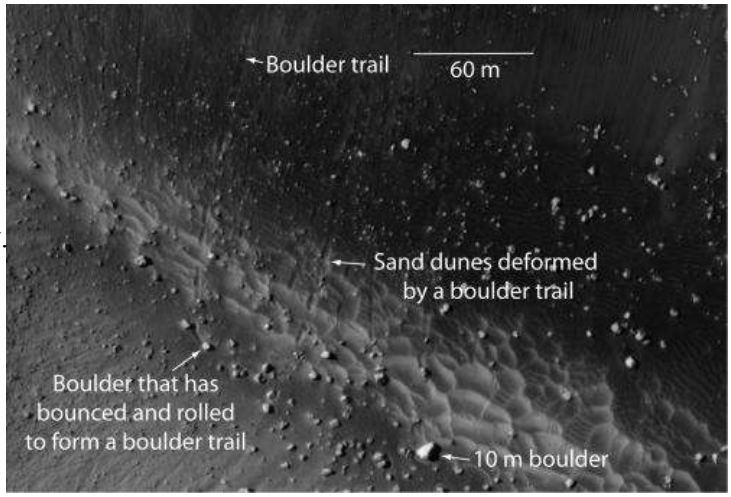
With High Resolution Imaging Science Experiment (HiRISE) imagery, the research team examined boulders along a fault system known as Cerberus Fossae, which cuts across a very young (few million years old) lava surface on Mars. By analyzing boulders that toppled from a martian cliff, some of which left trails in the coarse-grained soils, and comparing the patterns of dislodged rocks to such patterns caused by quakes on Earth, the scientists determined the rocks fell because of seismic activity. The martian patterns were not consistent with how boulders would scatter if they were deposited as ice melted, another means by which rocks are dispersed on Mars.

Gerald Roberts, an earthquake geologist with Birkbeck, an institution of the University of London, who led the study, said that the images of Mars included boulders that ranged from two to 20 meters (6.5 to 65 feet) in diameter, which had fallen in avalanches from cliffs. The size and number of boulders decreased over a radius of 100 kilometers (62 miles) centered at a point along the Cerberus Fossae faults.

"This is consistent with the hypothesis that boulders had been mobilized by ground-shaking, and that the severity of the ground-shaking decreased away from the epicenters of marsquakes," Roberts said.

The study, by Roberts and his colleagues, will be published Thursday in the Journal of Geophysical Research-Planets, a publication of the American Geophysical Union (AGU).

The team compared the pattern of boulder falls, and faulting of the martian surface, with those seen after a 2009 earthquake near L'Aquila, in central Italy. In that event, boulder falls occurred up to approximately 50 km (31 miles) from the epicenter. Because the area of displaced boulders in the marsscape stretched across an area approximately 200 km 124-miles) long, the quakes were likely to have had a magnitude greater than 7, the researchers estimated.



Scientists have found evidence of relatively recent quakes on the surface of Mars by studying boulders that fell off cliffs, leaving tracks behind. **(HiRISE image)**

By looking at the tracks that the falling boulders had left on the dust-covered martian surface, the team determined that the marsquakes were relatively recent - and certainly within the last few percent of the planet's history - because martian winds had not yet erased the boulder tracks. Trails on Mars can quickly disappear - for instance, tracks left by NASA robotic rovers are erased within a few years by martian winds, whereas other, sheltered tracks stick around longer. It is possible, the scientists concluded, that large-magnitude quake activity is still occurring on Mars.

The existence of marsquakes could be significant in the ongoing search for life on Mars, the researchers stated. If the faults along the Cerberus Fossae region are active, and the quakes are driven by movements of magma related to the nearby volcano, Elysium Mons, the energy provided in the form of heat from the volcanic activity under the surface of Mars could be able to melt ice. The resulting liquid water, they noted, could provide habitats friendly to life.

More information: *"Possible evidence of palaeomarsquakes from fallen boulder populations, Cerberus Fossae, Mars" Journal of Geophysical Research-Planets.*

http://bit.ly/wbTXCn

Bipolar drug fixes damaged nerves to restore movement

Sometimes salt is the good guy, in some forms anyway.

20:00 20 February 2012 by Jessica Hamzelou

Lithium chloride - a salt used as a mood stabiliser in bipolar disorder - appears to enhance the recovery of damaged neurons in mice. The drug may also help people with damaged nerves regain movement.

Charbel Massaad at Paris Descartes University in France and his colleagues recreated in mice the nerve damage that sports injuries and diabetes can cause in humans. When such damage occurs, neurons lose their myelin sheath - a coating that insulates the nerve, accelerating electrical impulses. People tend to lose the ability to move limbs as a result. After the mice's facial nerves were damaged, their whiskers became paralysed.

The team put lithium chloride in the rodents' drinking water. These mice completely recovered whisker movement within eight days, compared with mice who drank plain water, who had little movement at 20 days.

A closer inspection of the nerves revealed that myelin sheaths were much thicker in the treated mice.

Massaad hopes the drug will work as well in people: "Lithium could provide a novel, cheap therapy that stimulates myelination," he says.

Journal reference: *Proceedings of the National Academy of Sciences, DOI: 10.1073/pnas.1121367109*

http://nyti.ms/A2JceX

There's More to Nothing Than We Knew

Why is there something, rather than nothing at all?

By DENNIS OVERBYE

It is, perhaps, the mystery of last resort. Scientists may be at least theoretically able to trace every last galaxy back to a bump in the Big Bang, to complete the entire quantum roll call of particles and forces. But the question of why there was a Big Bang or any quantum particles at all was presumed to lie safely out of scientific bounds, in the realms of philosophy or religion.

Now even that assumption is no longer safe, as exemplified by a new book by the cosmologist Lawrence M. Krauss. In it he joins a chorus of physicists and cosmologists who have been pushing into sacred ground, proclaiming more and more loudly in the last few years that science can explain how something - namely our star-spangled cosmos - could be born from, if not nothing, something very close to it. God, they argue, is not part of the equation. The book, "A Universe From Nothing," is a best seller and follows recent popular tomes like "God Is Not Great," by the late Christopher Hitchens; "The God Delusion," by Richard Dawkins; and "The Grand Design," by the British cosmologist Stephen Hawking (with Leonard Mlodinow), which generated headlines two years ago with its assertion that physicists do not need God to account for the universe.

Dr. Krauss is a pint-size spark plug of erudition and ambition, who often seems to be jetting off in several directions at once on more missions than can be listed on a business card. Among other things he is Foundation Professor and director of the Origins Project at Arizona State University.

And he knows his universe. In 1995, he and Michael S. Turner of the University of Chicago made waves by arguing that many of the paradoxes regarding cosmology could be resolved if a large portion of the cosmos resided in the form of a hitherto-undiscovered energy, known then as the cosmological constant. Three years later astronomers discovered that the expansion of the universe was being accelerated by some "dark energy" that behaves exactly like the cosmological constant.

Dr. Krauss is also a prolific author of popular science books, including "The Physics of Star Trek." And he has been an outspoken critic of attempts to introduce creationist ideas and to censor the teaching of evolution in schools and textbooks.

The new book grew out of a talk he gave in 2009 that got more than a million hits on YouTube.

The point of the book, Dr. Krauss, a self-described nonbeliever, writes at the outset, is not to try to make people lose their faith, but to illuminate how modern science has changed the meaning of nothingness from a vague philosophical concept to something we can almost put under a lab microscope.

How well you think he succeeds might depend on how far you yourself want to go down the rabbit hole of nonbeing. Why, for example, should we assume that nothingness is more natural than somethingness? Indeed, you might ask why it is that we think there is something here at all. The total energy of the universe might actually be zero, according to the strange bookkeeping of Einstein's general theory of relativity, as Dr. Krauss points out. "The universe," Alan H. Guth, a physicist at M.I.T., likes to say, "might be the ultimate free lunch." Even space and time themselves might be a kind of holographic illusion, string theorists say.

You might think to dispute this by kicking a rock, but remember that both the rock and your foot are mostly empty space, prevented from intermingling by electric fields.

Dr. Krauss delineates three different kinds of nothingness. First is what may have passed muster as nothing with the ancient Greeks: empty space. But we now know that even empty space is filled with energy, vibrating with electromagnetic fields and so-called virtual particles dancing in and out of existence on borrowed energy courtesy of the randomness that characterizes reality on the smallest scales, according to the rules of quantum theory.

Second is nothing, without even space and time. Following a similar quantum logic, theorists have proposed that whole universes, little bubbles of space-time, could pop into existence, like bubbles in boiling water, out of this nothing.

There is a deeper nothing in which even the laws of physics are absent. Where do the laws come from? Are they born with the universe, or is the universe born in accordance with them? Here Dr. Krauss, unhappily in my view, resorts to the newest and most controversial toy in the cosmologist's toolbox: the multiverse, a nearly infinite assemblage of universes, each with its own randomly determined rules, particles and forces, that represent solutions to the basic equations of string theory - the alleged theory of everything, or perhaps, as wags say, anything.

Within this landscape of possibilities, almost anything goes.

But even the multiverse is not totally lawless, as Dr. Krauss acknowledged. We are not quite there yet. At the very least, there would still be the string equations and those quantum principles that undergird them. Is quantum randomness the secret of existence?

"Maybe in the true eternal multiverse there are truly no laws," Dr. Krauss said in an e-mail. "Maybe indeed randomness is all there is and everything that can happen happens somewhere."

It would be silly to think that we won't have better answers and better questions 50 or 100 years from now, but for the moment this is the story science can tell. If you find it bleak, that is your problem. "The universe is the way it is, whether we like it or not," Dr. Krauss writes.

It gets worse.

If nothing is our past, it could also be our future. As the universe, driven by dark energy - that is to say, the negative pressure of nothing - expands faster and faster, the galaxies will become invisible, and all the energy and information will be sucked out of the cosmos. The universe will revert to nothingness.

Nothing to nothing.

One day it's all going to seem like a dream.

But who is or was the dreamer?

http://bit.ly/AksmlJ

Hepatitis C Now Killing More Americans Than HIV

Now a different infectious disease is quietly killing even more people than HIV is: Hepatitis C

By Katherine Harmon | February 20, 2012

The number of people who die from HIV-related causes each year in the U.S. is now down to about 12,700 - from a peak of more than 50,000 in the mid-1990s - thanks to condom education and distribution campaigns, increased testing and improved treatments. But now a different infectious disease is quietly killing even more people than HIV is: Hepatitis C.

The majority of the 3.2 million people who are estimated to have chronic hepatitis C virus (HCV) in the U.S. are baby boomer adults.

And most of those infected with the virus do not know that they have it, which means they could easily be spreading it to others via exposure to blood - or, occasionally, sexual contact.

Although long-term intravenous drug users are at particular risk, so are "those who experimented with [such] drugs for a limited time in their youth," Harvey Alter and T. Jake Liang, both of the National Institutes of Health, wrote in an essay published online Monday in Annals of Internal Medicine. "These bygone experiences do not often connote risk to the affected persons nor serve as a reason to seek testing," they noted, making this slow-developing disease difficult to catch before it develops into cirrhosis or liver cancer (hepatocellular carcinoma). Their essay was part of a four-paper special series on hepatitis C.

More than 15,000 people died from hepatitis C-related issues in the U.S. in 2007 - about three quarters of whom were people aged 45 to 64, according to Alter and Liang. And that number is expected to double as the bulk of the population with the disease get older. The cost of treating all of these people is likely to top $6.7 billion in the decade of 2010 to 2019.

Much of that growth is anticipated because those infected with hepatitis C often don't seek treatment until the disease has caused serious damage, according to another paper published Monday in the same issue of Annals of Internal Medicine. "Hepatitis C virus infection is often asymptomatic or causes nonspecific symptoms (depression, arthralgia and fatigue) for decades," Kathleen Ly, of the U.S. Centers for Disease Control and Prevention (CDC), and her colleagues wrote in their paper.

The good news for those who do get diagnosed is that new hepatitis C drugs are coming onto the market. But they are not cheap. One new promising one, a protease inhibitor called boceprevir, runs about $1,100 per week, which when added to the double-drug cocktail of interferon and the antiviral ribavirin, makes for especially expensive treatment. Some researchers have proposed that testing patients for a genotype that has a cure rate of less than 40 percent with previous treatment might help make treatment the more cost effective.

A new analysis in the same issue of Annals of Internal Medicine, led by Shan Liu of the Center for Health Policy at Stanford University, found that giving HCV patients of all genotypes a triple-drug cocktail is, indeed, cost-effective for allowing patients to live longer, healthier lives. And as Alter and Liang pointed out, as opposed to HIV or even hepatitis B, HCV can often be effectively cured after six months to a year of antiviral treatment. "Every effectively treated high-risk individual diminishes the infectious pool and the likelihood of secondary transmission."

With treatment options expanding, many researchers are turning their attention back to the question of locating patients. "As innovative treatments for hepatitis C follow their now-destined progression, the most burning question will not be whether to treat, but rather how to identify the many chronic HCV carriers who are unaware of their infection and are at risk for cirrhosis, end-stage liver disease, or hepatocellular carcinoma," Alter and Liang wrote.

Knowing that those born between 1945 and 1964 are at the highest risk for HCV infection could help guide screening, according to another study published in the same issue of the journal, led by David Rein, of the CDC. "Because HCV progresses slowly, the risk for serious complications is increasing among infected Americans as time passes," he and his colleagues wrote. "Without changes in current case identification and treatment, deaths from HCV are forecasted to increase to 35,000 annually by 2030."

http://www.eurekalert.org/pub_releases/2012-02/sri-srs021612.php

Scripps research scientists unlock evolutionary secret of blood vessels

The ability to form closed systems of blood vessels is one of the hallmarks of vertebrate development.

LA JOLLA, CA - Without it, humans would be closer to invertebrates (think mollusks) in design, where blood simply washes through an open system to nourish internal organs. But vertebrates evolved closed circulation systems designed to more effectively carry blood to organs and tissues.

Precisely how that happened has remained a clouded issue. But now, a team of scientists from the California and Florida campuses of The Scripps Research Institute have shed light on the topic in a study published February 21, 2012, in the journal Nature Communications.

The process of building a closed circulation system is complicated biologically and, from an evolutionary perspective, time-consuming - involving billions of years. During this lengthy process, new domains (parts of a protein that can evolve and function independently of each other) have been added progressively to key molecules.

The scientists focused on one specific domain known as UNE-S. UNE-S is part of SerRS, a type of tRNA synthetase in species with closed circulatory systems; tRNA synthesases are enzymes that help charge tRNA with the right amino acid to correctly translate genetic information from DNA to proteins.

The scientists found that UNE-S is essential for proper development of an embryo, containing a specific sequence or "nuclear localization signal" that directs SerRS to the cell nucleus. There, it affects the expression of a key regulator of new blood vessel growth.

"I think a lot happened during this evolutionary transition to a closed system and the appearance of this domain on this specific synthetase is one of them," said Xiang-Lei Yang, a Scripps Research associate professor who led the collaborative study. "Because this synthetase plays such an essential role in vascular development, it must have had a role in the transition to a closed system."

To help elucidate the role of UNE-S, the researchers turned to zebrafish as a model organism. Shuji Kishi, an assistant professor on the Scripps Florida campus who worked on the new study, noted that zebrafish have emerged over the past decade as a powerful system to study both aging and development. "Zebrafish offer a number of advantages for study because embryonic development is external to the mother and the embryos are transparent, making them an ideal model for developmental biology," he said.

To find clues to SerRS function, the team examined SerRS mutants, which are linked to abnormal blood vessel formation and defective blood circulation. In their experiments, the scientists used a variety of techniques, including crystal structure, biochemical analysis, and cell biology experiments.

Interestingly, the findings show that SerRS mutants often delete the nuclear signal or keep it hidden in an alternative conformation - like locking someone in a closet under an assumed name - rendering it ineffective. "We were astonished by what we found," said Yang. "Sequestering is a very interesting property."

The scientists were able to design a second mutation to release the sequestered nuclear signal and to restored normal blood vessel development.

In addition to suggesting that acquisition of UNE-S has a role in the establishment of the closed circulatory systems of vertebrates, these results are the first to show an essential role for a tRNA synthetase-associated appended domain for an organism.

The first authors of the study, "Unique Domain Appended to Vertebrate Trna Synthetase is Essential For Vascular Development," are Xiaoling Xu and Yi Shi of Scripps Research. Other authors include Hui-Min Zhang of Florida State University, Eric C. Swindell of The University of Texas Medical School at Houston, Alan G. Marshall of Florida State University, and Min Guo of Scripps Research.

The study was supported by grants from the National Institutes of Health, the Skaggs Foundation, the State of Florida, and the National Foundation for Cancer Research.

http://www.eurekalert.org/pub_releases/2012-02/du-ded022112.php

Drexel engineers develop cement with 97 percent smaller CO2 and energy footprint

Drexel engineers have found a way to improve upon ordinary Portland cement (OPC), the glue that's bonded much of the world's construction since the late 1800s.

PHILADELPHIA - In research recently published in Cement and Concrete Composites the group served up a recipe for cement that is more energy efficient and cost effective to produce than masonry's most prevalent bonding compound. Drexel's "green" variety is a form of alkali-activated cement that utilizes an industrial byproduct, called slag, and a common mineral, limestone, and does not require heating to produce. According to Dr. Michel W. Barsoum, A.W. Grosvenor professor in the Department of Materials Science and Engineering,

this alternative production method and the ubiquity of the mix ingredients, lessens the cost of materials for Drexel's cement by about 40 percent versus Portland cement and reduces energy consumption and carbon dioxide production by 97 percent.

"Cement consumption is rapidly rising, especially in newly industrialized countries, and it's already responsible for 5 percent of human-made carbon dioxide. This is a unique way to limit the environmental consequences of meeting demand," Dr. Alex Moseson, one of the lead researchers on the project, said.

While forms of alkali-activated cement have been used as far back as the 1950s and 1960s in several buildings in the former Soviet Union, much of the inspiration for this research came from the Pyramids in Egypt, as well as buildings in ancient Rome. "Our cement is more like ancient Roman cement than like modern Portland," Moseson said. "Although we won't know for 2,000 years if ours has the longevity of Roman buildings, it gives us an idea of the staying power of this material."

In contrast to ordinary Portland cement, Drexel's cement is made of up to 68 percent unfired limestone, a plentiful, cheap, and low-carbon dioxide resource; American Society for Testing and Materials' standards for Portland cement limit the amount to 5 percent. To this base, a small amount of commercial alkali chemical is added along with the iron slag byproduct. In Portland cement the substitute for this mixture, called clinker, is produced by firing a number of ingredients in a kiln, thus requiring more energy and generating more carbon dioxide.

During Moseson's work in India to commercialize the technology, he developed products that meet local standards, using entirely local materials and techniques. He also investigated how the availability of green cement could help make quality building materials more affordable and accessible to marginalized populations living in slums, and create jobs by jump starting small-scale cement manufacturing in the country.

"Our results and the literature confirm that it performs as well or better than OPC," Barsoum said. "We are very close to having the cement pass an important commercialization milestone, ASTM C1157, a standard that judges cement-like products on performance, such as strength and setting-time, regardless of composition"

The next step for the cement is getting it to the market, which the group is working toward via a start-up company called Greenstone Technologies, Inc.

http://www.eurekalert.org/pub_releases/2012-02/cmaj-ivo021512.php

Influenza vaccination of pregnant women helps their babies

Randomized controlled trial

Vaccinating pregnant women against the influenza virus appears to have a significant positive effect on birth weight in babies, according to a study published in CMAJ (Canadian Medical Association Journal).

The study, a randomized controlled trial involving 340 healthy pregnant women in Bangladesh in the third trimester, looked at the effect of immunization with the influenza vaccine on babies born to vaccinated mothers. It was part of the Mother'sGift project looking at the safety and efficacy of pneumococcal and influenza vaccines in pregnant women in Bangladesh. The participants were divided into two groups, one with 170 women who received the influenza vaccine, and the second who received the pneumococcal vaccine as a control. Researchers compared the weight of babies born in two periods, one in which there was circulation of an influenza virus and one with limited circulation.

Babies that are small for their gestational age are at increased risk of health and other issues over their lives.

The researchers found that there were fewer babies who were small for their gestational age born to mothers in the influenza vaccine group when the virus was circulating, with 25.9% who were small compared with 44.8% in the control group. When the virus was dormant, the proportion of small-for-gestational-age births was similar in both groups. During the period with circulating influenza virus, the mean birth weight was 3178 g in the influenza vaccine group and 7% higher than 2978 g in the control group. The rate of premature births was lower in the influenza vaccine group as well.

"We found that immunization against influenza during pregnancy had a substantial effect on mean birth weight and the proportion of infants who were small for gestational age," writes Dr. Mark Steinhoff, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio, with coauthors. "Our data suggest that the prevention of infection with seasonal influenza in pregnant women by vaccination can influence fetal growth," state the authors.

The researchers calculate that 10 maternal influenza vaccinations given year-round prevented one small-for-gestational-age birth, dropping to 6 vaccinations during the period in which the influenza virus was circulating.

The study was conducted by a team of US and Bangladeshi researchers from the Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio; Johns Hopkins University, Baltimore, Maryland; Emory University,

Atlanta, Georgia; the International Centre for Diarrheal Disease Research, Dhaka, Bangladesh; and the Centers for Disease Control and Prevention, Atlanta, Georgia.

The authors suggest that if further research supports their findings, adding an influenza vaccine to routine vaccination programs during pregnancy could help children have a better start in life.

http://blogs.scientificamerican.com/guest-blog/2012/02/21/how-did-human-brains-get-to-be-so-big/

How Did Human Brains Get to Be so Big?

New research points to an ancient energy tradeoff that meant more fuel for brains, and less fuel for muscles.

By Robin Anne Smith | February 21, 2012

Recently while visiting the National Museum of Natural History in Washington, D.C., I found myself pondering the noggins of some very, very, old apes. Along one wall of the Hall of Human Origins - an exhibit on human evolution that opened in 2010 - were 76 fossil skulls from 15 species of early humans. Looking at these skulls, one thing was clear: millions of years of evolution have given us much bigger brains.

In the 8 to 6 million years since the ancestors of humans and chimps went their separate ways, the human brain more than tripled in size. If the earliest humans had brains the size of oranges, today's human brains are more akin to cantaloupes. As for our closest primate relatives, the chimps? Their brains haven't budged.

With our big brains we compose symphonies, write plays, carve sculptures and do math. But our big brains came at a cost, some scientists say.

In two recent studies, researchers from Duke University suggest the human brain boost may have been powered by a metabolic shift that meant more fuel for brains, and less fuel for muscles.

Our big, hungry brains

Co-author Olivier Fedrigo told me the full story one morning over coffee near his home in Durham, North Carolina. The human brain isn't just big, he explained. It's also hungry. While the brain makes up only 2% of our body mass, it consumes more than 20% of our oxygen supply and blood flow. Compare that to only 7-8% in other primate species, Fedrigo said. The human brain uses more energy, pound for pound, than any other tissue. Yet our body burns the same number of calories as other primates our size.

In 1995, two researchers in the U.K. published a landmark study arguing that if our overall energy budget didn't go up, our bodies must have compensated by diverting energy from somewhere else. The theory is called the expensive tissue hypothesis, first proposed by anthropologist Leslie Aiello, then of University College London, and physiologist Peter Wheeler of Liverpool John Moores University in England.

In the years after Aiello and Wheeler published their paper, the expensive tissue hypothesis started to gain support, though scientists had different ideas about which tissues paid the price for bigger brains. "There's been a lot of debate about how this tradeoff might have been accomplished," said Duke evolutionary biologist Greg Wray.

Brains versus brawn, paleo style

In 2003, an anthropologist at Northwestern University named William Leonard published a study arguing that the price we paid for a bigger brain may have been punier muscles. "[The thinking was that] even if you're totally buff, you're nothing compared to a chimp," Wray said.

Subsequent studies have raised questions about whether humans are really the scrawny members of the primate clan. Rather than having less muscle than would be expected for an ape of our size, it may be that our muscle is just distributed differently, said Duke anthropologist Christine Wall. Compared with other primates "humans are scrawny up top but bulky below," she said.

"But the hypothesis still holds," Fedrigo added. To build a bigger brain at the expense of muscle, "our muscles could have evolved to be smaller, or more efficient, or the metabolic cost of walking could have decreased, or it could have been some combination of these things," he said. "The possibilities aren't mutually exclusive."

In a study published last October, Fedrigo, Wray, Wall and colleagues tested the tradeoff hypothesis and pinpointed changes in two groups of molecules that may have shuttled more energy to our brains, and less to our muscles. "This is the first time the hypothesis has been tested at the molecular level," Wray told attendees at the 2011 meeting of the American Association for the Advancement of Science.

Brain food

The primary source of energy for the brain is glucose, which is pumped into cells where it is needed most with the help of proteins called glucose transporters. Glucose transporters are encoded by a family of about a dozen genes. The researchers zeroed in on two glucose transporter genes, one of which, called SLC2A1, is turned on mostly in brains, and the other, called SLC2A4, is turned on mostly in muscles.

Mutations in SLC2A1 lead to insufficient glucose getting across the blood-brain barrier, which can cause seizures, learning disabilities, or a condition called microcephaly, which turns a normal brain into a tiny one. "The brain basically starves," Wray said.

To get a better picture of how these genes evolved after humans and other primates went their separate ways, the researchers compared the human versions of the genes with the same genes in chimps and two more distantly related primates, orangutans and macaques. When they compared the DNA sequences of the genes from each species, they found a number of changes in the human version of each gene but not the other three species.

To find out if those changes may have helped to ferry more glucose to brains, and less to muscles, they measured the amount of mRNA copies of each gene - a measure of how much protein the gene is likely to make - in brain, muscle, and liver samples from each species. Compared with chimps, humans make three times more of the glucose transporter found in brains, but only 60% of that found in muscles.

"The tradeoff is exactly what one might predict," Wray said.

These probably weren't the only tradeoffs that led to our enlarged brains, the researchers say. In another study published last year, they pinpointed another set of genes that may have funneled more energy to brains, and less to muscles - this time in the form of a metabolite called creatine. Glucose is the brain's primary fuel, but creatine provides a backup source of quick-burn energy when glucose runs low.

Creatine is ferried in and out of cells with the help of several genes. When the researchers measured the expression levels of these genes in tissue samples from humans, chimps and macaques, they found that human brains had twice the levels of SLC6A8 and CKB, two genes that regulate how creatine is used by cells. But in contrast to brains, the levels in human muscles were no different from chimps.

Back at the Hall of Human Origins, I turned away from the wall of skulls and made my way to another part of the exhibit, where lifelike busts of eight early humans, outfitted with muscles, flesh and hair, stare out from their cases. "Meet your ancestors," a sign on the wall read.

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http://www.physorg.com/news/2012-02-recipe-success-recycled-glass-cement.html

Recipe for success: Recycled glass and cement

MSU researchers have found that concrete is more durable when crushed glass is added to the cement used to make the concrete.

PhysOrg.com - Michigan State University researchers have found that by mixing ground waste glass into the cement that is used to make concrete, the concrete is stronger, more durable and more resistant to water.

In addition, the use of glass helps reduce the amount of glass that ends up in landfills and helps to reduce carbon dioxide emissions which are common due to the high temperatures needed to create cement.

The concrete, in which about 20 percent of the cement that is used to produce the concrete is replaced by milled, or finely ground, glass, is being tested at a number of sites on the MSU campus. And, so far, the results have been pretty positive. "Milled glass enters a beneficial reaction with cement hydrates, so basically the chemistry of the cement improves with the glass," said Parviz Soroushian, a professor of civil and environmental engineering who has been studying the glass-concrete mix. "It makes it stronger and more durable and doesn't absorb water as fast as regular cement."

The test sites, which have been in existence for about three years, are located on sidewalks outside of the MSU Surplus Store and Recycling Center, south of the Breslin Student Events Center and near Fee and Hubbard halls on the east side of the campus.

"It's satisfying to see research done in MSU laboratories have very beneficial applications right here on our campus," said Lynda Boomer, energy and environmental engineer with the MSU Physical Plant. The concrete doesn't look too much different than standard concrete, Boomer said. "It's a little lighter in color, but, for the most part, pretty indistinguishable."

Soroushian and colleagues recently had two papers published on the durability of the mixture, including in the Journal of Solid Waste Technology and Management, and the Journal of Construction and Building Materials.

"Cement is processed at a very high temperature," Soroushian said. "Using milled glass significantly reduces the amount of energy used, as well as CO2 emissions."

"We anticipate that this novel practice of partially replacing cement in concrete with mixed-color waste glass, which is based on sound chemical principles and the pioneering laboratory work conducted at MSU, will yield significant environmental, energy and cost benefits," said Roz Ud-Din Nassar, a doctoral student in civil and environmental engineering who also worked on the project.

Provided by Michigan State University

http://nyti.ms/zXv4Gu

Research: Aspirin Shows Promise in Limiting Cancer for Women Who Have H.I.V., Scientists Say

Aspirin should be evaluated for its potential to prevent cervical cancer in women infected with H.I.V., say scientists who recently reported a connection between the virus and inflammation of cervical tissue.

By DONALD G. McNEIL Jr.

Their study, published last month in the journal Cancer Prevention Research, found that the virus that causes AIDS also drives up production of a prostaglandin called PGE2 in cervical tissue. PGE2 is linked to inflammation and the development of tumors.

Aspirin is a powerful blocker of a chemical called COX-2 that allows prostaglandins to be formed. Therefore, the authors suggested that a large study be carried out to see if low-dose aspirin could prevent cervical cancer in women at high risk of getting it.

Cervical cancer is caused by the human papillomavirus, and some scientists believe women co-infected with HIV are up to five times as likely to see cervical papilloma lesions progress to cancer.

Cervical cancer kills few women in rich countries, but it is a leading killer in poor ones where Pap smears are too expensive and vaccines against papillomaviruses are not yet available.

The study was small - it compared tissue samples from 48 women, some of whom had only H.I.V., some of whom had both HIV and papilloma infections and some of whom had neither. But the researchers, from NewYork-Presbyterian/Weill Cornell Medical Center and institutions in Haiti and Qatar, found levels of PGE2 high enough to suggest that a larger study is needed to test whether giving low-dose aspirin to thousands of women would save lives.

http://medicalxpress.com/news/2012-02-women-heart-dont-chest-pain.html

Many women having a heart attack don't have chest pain

Two out of five women having a heart attack do not experience chest pain, according to a new study.

HealthDay - Instead, they may have harder-to-recognize symptoms, such as pain in the jaw, neck, shoulders or back; stomach discomfort; or sudden trouble breathing, researchers said.

That may be one reason why women also have a higher risk of dying from a heart attack when they're in the hospital compared to men, the study found.

"The hallmark symptoms of a heart attack are chest pain and discomfort. But, women are more likely to have a different attack presentation," said study lead author Dr. John Canto, director of cardiovascular prevention, research and education at the Watson Clinic and director of the Chest Pain Center at Lakeland Regional Medical Center in Fla. The study is in the Feb. 22/29 issue of the Journal of the American Medical Association.

Men and women who have risk factors for heart disease, such as obesity, diabetes, high blood pressure, high cholesterol or a family history of heart disease, should be particularly concerned if they experience these symptoms. "The reality is that most people who have chest pain and discomfort aren't having a heart attack. But, you can't wait to find out. Time is heart muscle. If you delay seeking treatment, you may be outside the window where you can get the most effective treatment," he said.

Researchers analyzed data on more than 1.1 million patients seen at U.S. hospitals for heart attacks from 1994 to 2006. About 42 percent were women, who were also on average older than men when they had their heart attack.

Among both men and women, just over 35 percent - or about one in three - did not have chest pain.

However, women were more likely to experience an attack without chest pain compared to men, at 42 percent and 31 percent, respectively.

In-hospital deaths from heart attack were also more common among women: 14.6 percent of women died while still in the hospital, compared to just over 10 percent of men.

Dr. Suzanne Steinbaum, director of women and heart disease at Lenox Hill Hospital in New York City and a spokeswoman for the American Heart Association, said other heart attack symptoms women may experience include sweating, nausea and flu-like symptoms.

Though it can be hard to connect those symptoms to a heart attack, if "all of a sudden your daily activities become daunting, and you feel like you just can't function, you have to get checked out. If it's not your heart, so what? It's better to be safe than sorry," she said. She also advised women to be assertive about their worries with doctors. Say, "I think I'm having a heart attack," she recommended. Men may need to heed this advice as well, because they too may not have classic chest pain symptoms, she added.

The study found that for men and women - but particularly for young women - heart attacks without chest pain were associated with a greater risk of death. One of the main reasons, said Canto, is that people may delay going to the ER, and once they do call for help or go to the hospital, they may downplay their symptoms, leading to less urgent action from health care providers.

In the case of women, said Canto, the higher mortality rates may also be linked to biological differences in heart disease between men and women. When the researchers compared women without chest pain and men without chest pain, they still found a higher risk of death for women.

http://www.physorg.com/news/2012-02-superbugs-space-source-power.html

Superbugs from space offer new source of power

Bacteria normally found 30km above the earth have been identified as highly efficient generators of electricity.

Bacillus stratosphericus - a microbe commonly found in high concentrations in the stratosphere orbiting the earth with the satellites - is a key component of a new 'super' biofilm that has been engineered by a team of scientists from Newcastle University.

Isolating 75 different species of bacteria from the Wear Estuary, Country Durham, UK, the team tested the power-generation of each one using a Microbial Fuel Cell (MFC). By selecting the best species of bacteria, a kind of microbial "pick and mix" they were able to create an artificial biofilm, doubling the electrical output of the MFC from 105 Watts per cubic metre to 200 Watts per cubic metre. While still relatively low, this would be enough power to run an electric light and could provide a much needed power source in parts of the world without electricity.

Among the 'super' bugs was B. stratosphericus, a microbe normally found in the atmosphere but brought down to earth as a result of atmospheric cycling processes and isolated by the team from the bed of the River Wear.

Publishing their findings today in the American Chemical Society's Journal of Environmental Science and Technology, Grant Burgess, Professor of Marine Biotechnology at Newcastle University, said the research demonstrated the "potential power of the technique."

"What we have done is deliberately manipulate the microbial mix to engineer a biofilm that is more efficient at generating electricity," he explains. "This is the first time individual microbes have been studied and selected in this way. Finding B. altitudinis was quite a surprise but what it demonstrates is the potential of this technique for the future - there are billions of microbes out there with the potential to generate power."

The use of microbes to generate electricity is not a new concept and has been used in the treatment of waste water and sewage plants. Microbial Fuel Cells, which work in a similar way to a battery, use bacteria to convert organic compounds directly into electricity by a process known as bio-catalytic oxidation.

A biofilm - or 'slime' - coats the carbon electrodes of the MFC and as the bacteria feed, they produce electrons which pass into the electrodes and generate electricity.

Until now, the biofilm has been allowed to grow un-checked but this new study shows for the first time that by manipulating the biofilm you can significantly increase the electrical output of the fuel cell.

As well as B. stratosphericus, other electricity-generating bugs in the mix were Bacillus altitudinis - another bug from the upper atmosphere - and a new member of the phylum Bacteroidetes.

Newcastle University is recognised as a world-leader in fuel cell technology. Led by Professor Keith Scott, in the University's School of Chemical Engineering and Advanced Materials, the team played a key role in the development of a new lithium/air powered battery two years ago.

Professor Scott says this latest fuel cell research can take the development of MFC's to a new level.

More information: Enhanced electricity production by use of reconstituted artificial consortia of estuarine bacteria grown as biofilms. Jinwei Zhang, Enren Zhang, Keith Scott and Grant Burgess. ACS Journal of Environmental Science & Technology 2012. DOI:10.1021/es2020007

http://www.physorg.com/news/2012-02-road-users-gps.html

Study confirms that road users are jamming GPS signals

The first direct evidence of GPS jammers in use on British roads will be presented today alongside predictions of a major incident involving ships in the English Channel over the next decade caused by disruption to navigation signals.

GNSS Vulnerability 2012: Present Danger, Future Threats is organised by the ICT Knowledge Transfer Network and brings together the world's experts on location and timing systems to understand their susceptibility to attack.

Bob Cockshott, Director of Position, Navigation and Timing at the ICT Knowledge Transfer Network and organiser of the conference says: "Today's evidence from roadside monitoring shows that we have moved on from a potentially threatening situation to a real danger that we must address now. With the reliance on GPS systems in the maritime environment, highlighted by the General Lighthouse Authority, our vulnerability on land and at sea should not be underestimated. As well as immediate concerns, this conference has laid out the next generation of threats, in the form of spoofing and time sabotage - deliberately misleading users for criminal purposes rather than simply denying service. We must ensure that alongside dealing with the threat posed by jamming, we also stay ahead of advances in the criminal world."

The evidence of illegal jamming in the UK comes from roadside monitoring carried out by the SENTINEL project which looks at whether satellite navigation systems including GPS can be trusted by their users.

Jamming monitors have so far been placed at around 20 locations in the UK. At one particular location that has been monitored continuously for the past 6 months over 60 individual jamming incidents were recorded and the results at another have already led to the recovery of a device. The next step is to update the monitoring equipment to be able to differentiate between different jammers, giving researchers a better idea of how many individuals at a particular location are jamming GPS signals.

The projects consortium is led by Chronos Technology, the Forest of Dean based supplier of timing and GPS solutions, whose founder Charles Curry presented its findings. He says: "SENTINEL was set up to tackle the threat of GPS Jamming in three stages - identification, detection and mitigation. Whilst the identification of the threat is well established, and through roadside monitoring we are making great strides in the detection and location of these devices, the final stage, mitigation, is still some way off depending on the application and industry sector. The question for the authorities is what we are going to do once the owners of these jammers are identified and how can we prevent others using them."

The results from SENTINEL will be accompanied by a presentation from the General Lighthouse Authorities highlighting how overly reliant ships are on GPS. In 2010 researchers produced low level jamming from the coast and reviewed its effect on various systems onboard ships in the English Channel. The impacts included:

Ships veering off course without crew knowledge
Ships give out false information to other ships about their position - significantly increasing the likelihood of a collision
Communications channels failing, preventing crew talking to the coastguard
The failure of the emergency service system which sends out alarms and guide rescuers
Alarms from ship's radar and compass

Consultant and Location and Timing system expert, Prof David Last says: "Whilst we expected some disturbance to the ship's chart display, this research revealed four or five other systems, all reliant on GPS which failed. The spread of the jamming technology used in these trials, with devices available online for only £50, makes a major incident at sea, whether accidental or intentional, a real danger. In the English Channel, the world's busiest seaway, I personally believe we will see such an incident in the next decade."

Alongside GPS Jamming, speakers will look at the next major threat to navigation systems. Spoofing generates false GPS signals to alter user's perceptions of time and location. With the right technology it can be done without the victim ever knowing and is virtually untraceable.

Todd Humpheys from the University of Texas owns the world's most powerful civil GPS spoofer. At GNSS 2012 he reports on tests carried out by his team on GPS-based timing devices used in mobile phone transmitters in the US. Such attacks are capable of breaking up the network, preventing towers from handing over calls.

"So far no credible high profile attack has been recorded but we are seeing evidence of basic spoofing, likely carried out by rogue individuals or small groups. Whilst the leap to more advanced, untraceable spoofing is large, so are the rewards. It's therefore guaranteed that criminals are looking at this. All it takes is one person to put one together and publish it online and we have a major problem".

One sector at risk is high-frequency financial trading. At GNSS vulnerability 2012 Todd will warn that criminals could throw off the GPS timing systems that time-stamp financial trades, a process known as 'Time Sabotage". Even a few milliseconds discrepancy could create confusion and enable unscrupulous traders to leverage their knowledge of the timing discrepancy for financial gain via inter-market arbitrage.
Provided by National Physical Laboratory

http://www.bbc.co.uk/news/magazine-16964783

The myth of the eight-hour sleep

We often worry about lying awake in the middle of the night - but it could be good for you. A growing body of evidence from both science and history suggests that the eight-hour sleep may be unnatural.

By Stephanie Hegarty BBC World Service

In the early 1990s, psychiatrist Thomas Wehr conducted an experiment in which a group of people were plunged into darkness for 14 hours every day for a month. It took some time for their sleep to regulate but by the fourth week the subjects had settled into a very distinct sleeping pattern. They slept first for four hours, then woke for one or two hours before falling into a second four-hour sleep. Though sleep scientists were impressed by the study, among the general public the idea that we must sleep for eight consecutive hours persists.

In 2001, historian Roger Ekirch of Virginia Tech published a seminal paper, drawn from 16 years of research, revealing a wealth of historical evidence that humans used to sleep in two distinct chunks.

His book At Day's Close: Night in Times Past, published four years later, unearths more than 500 references to a segmented sleeping pattern - in diaries, court records, medical books and literature, from Homer's Odyssey to an anthropological account of modern tribes in Nigeria.

Much like the experience of Wehr's subjects, these references describe a first sleep which began about two hours after dusk, followed by waking period of one or two hours and then a second sleep. "It's not just the number of references - it is the way they refer to it, as if it was common knowledge," Ekirch says.

During this waking period people were quite active. They often got up, went to the toilet or smoked tobacco and some even visited neighbours. Most people stayed in bed, read, wrote and often prayed. Countless prayer manuals from the late 15th Century offered special prayers for the hours in between sleeps.

And these hours weren't entirely solitary - people often chatted to bed-fellows or had sex.

A doctor's manual from 16th Century France even advised couples that the best time to conceive was not at the end of a long day's labour but "after the first sleep", when "they have more enjoyment" and "do it better".

Ekirch found that references to the first and second sleep started to disappear during the late 17th Century. This started among the urban upper classes in northern Europe and over the course of the next 200 years filtered down to the rest of Western society. By the 1920s the idea of a first and second sleep had receded entirely from our social consciousness.

He attributes the initial shift to improvements in street lighting, domestic lighting and a surge in coffee houses - which were sometimes open all night. As the night became a place for legitimate activity and as that activity increased, the length of time people could dedicate to rest dwindled.

In his new book, Evening's Empire, historian Craig Koslofsky puts forward an account of how this happened.

"Associations with night before the 17th Century were not good," he says. The night was a place populated by people of disrepute - criminals, prostitutes and drunks.

"Even the wealthy, who could afford candlelight, had better things to spend their money on. There was no prestige or social value associated with staying up all night."

That changed in the wake of the Reformation and the counter-Reformation. Protestants and Catholics became accustomed to holding secret services at night, during periods of persecution. If earlier the night had belonged to reprobates, now respectable people became accustomed to exploiting the hours of darkness.

This trend migrated to the social sphere too, but only for those who could afford to live by candlelight. With the advent of street lighting, however, socialising at night began to filter down through the classes.

In 1667, Paris became the first city in the world to light its streets, using wax candles in glass lamps. It was followed by Lille in the same year and Amsterdam two years later, where a much more efficient oil-powered lamp was developed. London didn't join their ranks until 1684 but by the end of the century, more than 50 of Europe's major towns and cities were lit at night. Night became fashionable and spending hours lying in bed was considered a waste of time.

"People were becoming increasingly time-conscious and sensitive to efficiency, certainly before the 19th Century," says Roger Ekirch. "But the industrial revolution intensified that attitude by leaps and bounds."

Strong evidence of this shifting attitude is contained in a medical journal from 1829 which urged parents to force their children out of a pattern of first and second sleep.

"If no disease or accident there intervene, they will need no further repose than that obtained in their first sleep, which custom will have caused to terminate by itself just at the usual hour. "And then, if they turn upon their ear to take a second nap, they will be taught to look upon it as an intemperance not at all redounding to their credit."

Today, most people seem to have adapted quite well to the eight-hour sleep, but Ekirch believes many sleeping problems may have roots in the human body's natural preference for segmented sleep as well as the ubiquity of artificial light. This could be the root of a condition called sleep maintenance insomnia, where people wake during the night and have trouble getting back to sleep, he suggests. The condition first appears in literature at the end of the 19th Century, at the same time as accounts of segmented sleep disappear.

"For most of evolution we slept a certain way," says sleep psychologist Gregg Jacobs. "Waking up during the night is part of normal human physiology."

The idea that we must sleep in a consolidated block could be damaging, he says, if it makes people who wake up at night anxious, as this anxiety can itself prohibit sleeps and is likely to seep into waking life too.

Russell Foster, a professor of circadian [body clock] neuroscience at Oxford, shares this point of view.

"Many people wake up at night and panic," he says. "I tell them that what they are experiencing is a throwback to the bi-modal sleep pattern."

But the majority of doctors still fail to acknowledge that a consolidated eight-hour sleep may be unnatural.

"Over 30% of the medical problems that doctors are faced with stem directly or indirectly from sleep. But sleep has been ignored in medical training and there are very few centres where sleep is studied," he says.

Jacobs suggests that the waking period between sleeps, when people were forced into periods of rest and relaxation, could have played an important part in the human capacity to regulate stress naturally.

In many historic accounts, Ekirch found that people used the time to meditate on their dreams.

"Today we spend less time doing those things," says Dr Jacobs. "It's not a coincidence that, in modern life, the number of people who report anxiety, stress, depression, alcoholism and drug abuse has gone up."

So the next time you wake up in the middle of the night, think of your pre-industrial ancestors and relax. Lying awake could be good for you.

http://www.scientificamerican.com/article.cfm?id=the-truth-about-pot

Experts Tell the Truth about Pot

Marijuana use can be problematic but only rarely leads to addiction

By Hal Arkowitz and Scott O. Lilienfeld | Wednesday, February 22, 2012 | 34

In the classic 1936 cult film Reefer Madness, well-adjusted high school students who try marijuana suddenly sink into a life of addiction, promiscuity, aggression, academic failure, homicide and mental illness. The movie concludes with the ominous warning that "The dread marijuana may be reaching forth next for your son or daughter ... or yours ... or YOURS!" Newspaper headlines of the day often reflected a similar sentiment. On February 10, 1938, a headline in the Beloit (Wisc.) Daily News read, "Authorities Warn against Spread of Marijuana Habit - Insanity, Degeneracy and Violence Follow Use of Weed."

Such a position on pot seems extreme. Yet just as people have since cast aside the notion that marijuana use inevitably culminates in the destruction of the mind, so have they also begun to question the concept that it is benign. In particular, some evidence suggests that marijuana can, in some cases, be addictive and that it may present other health problems as well, particularly in heavy users. That said, most people suffer no ill effects from a single or occasional use of the drug.

How Many Get Hooked?

Marijuana, which is also known as cannabis, is the most widely used illicit substance in the world, according to a United Nations report from 2002. Recreational use is widespread in the U.S., and medical use is on the rise. In a 2007 study psychologist Louisa Degenhardt of Michigan State University and her colleagues found that 43 percent of U.S. adults aged 18 or older have tried marijuana at least once. Many adolescents are drawn to the drug as well. In the large, ongoing Monitoring the Future study, researchers at the University of Michigan found that 14 percent of eighth graders had used marijuana at least once in the previous year with the number increasing to 35 percent for 12th graders. Marijuana use will undoubtedly grow in the near future because 16 states have already legalized it for medical use, and many more are considering legislation that would make it legal.

Given the drug's growing popularity, many people have long been concerned about its potential dangers and, in particular, whether it can be addictive. People tend to use "addiction" and "dependence" interchangeably,

although drug experts now favor the term "dependence." In the current version of the mental health profession's "bible," the Diagnostic and Statistical Manual of Mental Disorders, a diagnosis of cannabis dependence (a type of substance dependence) requires a person to meet at least three of seven criteria.

A number of investigators have addressed this issue and found that only a relatively small percentage of those who try marijuana will become addicted. For example, in a large-scale survey published in 1994 epidemiologist James Anthony, then at the National Institute on Drug Abuse, and his colleagues asked more than 8,000 people between the ages of 15 and 64 about their use of marijuana and other drugs. The researchers found that of those who had tried marijuana at least once, about 9 percent eventually fit a diagnosis of cannabis dependence. The corresponding figure for alcohol was 15 percent; for cocaine, 17 percent; for heroin, 23 percent; and for nicotine, 32 percent. So although marijuana may be addictive for some, 91 percent of those who try it do not get hooked. Further, marijuana is less addictive than many other legal and illegal drugs.

Possible Perils

A hotly debated issue is whether marijuana is a "gateway" drug, leading to the use of more dangerous substances. Many studies have found that most people who used other illicit drugs had, in fact, used marijuana first. Although results such as these are consistent with the gateway hypothesis, they do not prove that using marijuana causes the use of other drugs. Those who are drawn to marijuana may simply be predisposed to drug use in general, regardless of their exposure to pot. In addition, individuals often smoke cigarettes or drink alcohol before they latch on to marijuana. Should we also be asking whether nicotine and alcohol are gateway drugs?

Researchers have also demonstrated that heavy marijuana use can lead to increased tolerance and withdrawal symptoms when trying to stop. In addition, heavy use can contribute to respiratory and cardiovascular problems as well as impairments in short-term memory. Marijuana may also trigger certain disorders, such as schizophrenia, in vulnerable persons [see "A Mind in Danger," by Victoria Costello], although researchers continue to debate the evidence on this issue. Finally, because marijuana is still illegal in most states and under federal law, people who possess or sell marijuana may face legal consequences.

On the other hand, marijuana has significant upsides for individuals with certain illnesses. In glaucoma patients, it can reduce the dangerously high eye pressure that can lead to vision loss. In addition, pot can provide relief from chronic pain, reduce nausea and vomiting from cancer chemotherapy, and limit the severe weight loss that results from AIDS and other diseases.

When a person does become addicted, several types of psychotherapy can help him or her kick the habit. One of the more effective types is a form of cognitive-behavior therapy (CBT) tailored to the addictive mind-set. Using CBT, therapists teach patients practical coping skills that lead to a change in behavior. They also try to modify the thoughts that contribute to a person's addiction. Two faster treatments are motivational interviewing and the closely related motivational-enhancement therapy. The goal of these methods is to boost a person's drive to stop or reduce their use of pot.

Unfortunately, relapse rates remain high for all addiction psychotherapies. In a study published in 2003 psychologist Brent A. Moore, now at Yale University, and his colleagues found that 41 percent of successfully treated marijuana addicts had relapsed within six months. Scientists are searching for ways to bring about long-term abstinence more consistently.

The public needs to be aware of the facts about marijuana so that it can dismiss fictions about the drug's effects. Only by knowing when marijuana pre-sents a real threat and when the risk is minimal can people properly weigh its dangers and benefits in specific situations. Both our health and sound social policy depend on it.

http://www.physorg.com/news/2012-02-links-uplifting-continents-biodiversity-earth.html

Research links uplifting continents to crashes in biodiversity on Earth

A mysterious cycle of booms and busts in marine biodiversity over the past 500 million years could be tied to a periodic uplifting of the world's continents, scientists report in the latest issue of The Journal of Geology.

PhysOrg.com - The researchers discovered periodic increases in the amount of the isotope strontium-87 found in marine fossils. The timing of these increases corresponds to previously discovered low points in marine biodiversity that occur in the fossil record roughly every 60 million years. Adrian Melott, professor of physics and astronomy at the University of Kansas and lead author, thinks these periodic extinctions and the increased amounts of strontium-87 are linked.

"Strontium-87 is produced by radioactive decay of another element, rubidium, which is common in igneous rocks in continental crust," Melott said. "So, when a lot of this type of rock erodes, a lot more Sr-87 is dumped into the ocean, and its fraction rises compared with another strontium isotope, Sr-86."

`An uplifting of the continents, Melott explains, is the most likely explanation for this type of massive erosion event.

"Continental uplift increases erosion in several ways," he said. "First, it pushes the continental basement rocks containing rubidium up to where they are exposed to erosive forces. Uplift also creates highlands and mountains where glaciers and freeze-thaw cycles erode rock. The steep slopes cause faster water flow in streams and sheet-wash from rains, which strips off the soil and exposes bedrock. Uplift also elevates the deeper-seated igneous rocks where the Sr-87 is sequestered, permitting it to be exposed, eroded and put into the ocean."

The massive continental uplift suggested by the strontium data would also reduce sea depth along the continental shelf where most sea animals live. That loss of habitat due to shallow water, Melott and collaborators say, could be the reason for the periodic mass extinctions and periodic decline in diversity found in the marine fossil record.

"What we're seeing could be evidence of a 'pulse of the earth' phenomenon," Melott said. "There are some theoretical works which suggest that convection of mantle plumes, rather like a lava lamp, should be coordinated in periodic waves." The result of this convection deep inside the earth could be a rhythmic throbbing - almost like a cartoon thumb smacked with a hammer - that pushes the continents up and down.

Melott's data suggest that such pulses likely affected the North American continent. The same phenomenon may have affected other continents as well, but more research would be needed to show that, he says.

The co-authors on the study were Richard Bambach of the National Museum of Natural History, Kenni Petersen of Aarhus University, Denmark, and John McArthur of University College London.

More information: *Adrian L. Melott, Richard K. Bambach, Kenni D. Petersen, and John M. McArthur, "A ~60 Myr periodicity is common to marine-87Sr/86Sr, fossil biodiversity, and large-scale sedimentation: what does the periodicity reflect?" The Journal of Geology 120:2 (March 2012, forthcoming). Provided by University of Kansas*

http://medicalxpress.com/news/2012-02-drug-combination-domino-effect-pancreatic.html

Drug combination domino effect destroys pancreatic cancer cells

Scientists have revealed how a combination of two very different drugs amplifies the destruction of pancreatic cancer cells

Medical Xpress - Cancer Research UK scientists have revealed how a combination of two very different drugs - currently being tested in clinical trials - amplifies the destruction of pancreatic cancer cells, according to research published in the Journal of Experimental Medicine, today.

The team at Cancer Research UK's Cambridge Research Institute showed in mice that combining a chemotherapy drug called gemcitabine with an experimental drug called MRK003 sets off a chain of events that ultimately kills cancer cells - multiplying the effect of each drug on its own.

This drug combination is being tested in a clinical trial managed by Cancer Research UK's Drug Development Office in partnership with Cambridge University Hospitals Foundation Trust.

The research showed that MRK003, a gamma secretase inhibitor, blocks an important cell signalling pathway called Notch in both pancreatic cancer cells and the endothelial cells that line the blood vessels supplying tumors with essential nutrients. The addition of MRK003 to gemcitabine - a drug used commonly in patients with pancreatic cancer - increased the ability of gemcitabine to destroy tumors.

Study author, Professor David Tuveson, group leader at Cancer Research UK's Cambridge Research Institute, said: "This research is a real example of how research taking place in the lab directly influences decisions made in the clinic to improve treatment for patients. "We've discovered why these two drugs together set off a domino effect of molecular activity to switch off cell survival processes and destroy pancreatic cancer cells."

The Cancer Research UK clinical trial is led by Duncan Jodrell, Professor of Cancer Therapeutics at the University of Cambridge.

Professor Jodrell, said: "We're delighted that the results of this important research are now being evaluated in a clinical trial, to test whether this might be a new treatment approach for patients with pancreatic cancer, although it will be some time before we're able to say how successful this will be in patients."

Father-of-two Richard Griffiths, 41, from Coventry, has been on the trial since being diagnosed with pancreatic cancer in May 2011. "Being told that I had cancer was devastating and it immediately made me worry about the future," he said. "I have a close group of family and friends and I have had great support from this network, and my work have been very supportive too.

"After I was diagnosed, I was told about the trial and came to Cambridge to meet the team. I was given a lot of information and agreed to take part in this trial. It was mentioned that it was funded by Cancer Research UK and, as I go through the treatment, I have really come to appreciate how important that money is.

"After six cycles of treatment, a scan showed the tumors had reduced and so I have continued with the treatment. The trial gives you hope - I really feel I can do this with the science behind me."

Around 8,000 people in the UK are diagnosed with pancreatic cancer each year and the disease is the fifth most common cause of cancer death in the UK Although the one-year survival rate for pancreatic cancer has more than doubled since the 1970s, the rate is still low with fewer than one in five patients surviving their disease for more than a year after diagnosis.

Dr. Julie Sharp, senior science information manager at Cancer Research UK, said: "This discovery shows how investigating the cell pathways involved in cancer can reveal new approaches to tackle the disease.

"There's an urgent need for new drugs for pancreatic cancer. The disease is often not diagnosed until it has spread, making it very difficult to treat. "Cancer Research UK previously funded the largest ever trial for people with operable pancreatic cancer, which led to a worldwide change in the way the disease is treated, helping to improve survival. But there is much more to be done. "We're prioritising research into pancreatic cancer, and other cancers where survival still remains low, aiming to save more lives in the future."

More information: *Journal of Experimental Medicine. Gamma Secretase inhibition promotes hypoxic necrosis in murine pancreatic ductal adenocarcinoma. Cook et al. Provided by Cancer Research UK*

http://www.eurekalert.org/pub_releases/2012-02/ind-ita022212.php

Is there a general motivation center in the depths of the brain?

A team have identified the part of the brain driving motivation during actions that combine physical and mental effort: the ventral striatum.

A team coordinated by Mathias Pessiglione, Inserm researcher at the "Centre de recherche en neurosciences de la Pitié Salpêtrière" (Inserm/UPMC-Université Pierre and Marie Curie/CNRS) have identified the part of the brain driving motivation during actions that combine physical and mental effort: the ventral striatum. The results of their study were published in PLoS Biology on 21 February 2012.

The results of an activity (physical or mental) partly depend on the efforts devoted to it, which may be incentive-motivated. For example, a sportsperson is likely to train with "increased intensity" if the result will bring social prestige or financial gain. The same can be said for students who study for their exams with the objective of succeeding in their professional career. What happens when physical and mental efforts are required to reach an objective?

Mathias Pessiglione and his team from Inserm unit 975 "Centre de recherche en neurosciences de la Pitié-Salpêtrière" examined whether mental and physical efforts are driven by a motivation 'centre' or whether they are conducted by different parts of the brain. The researchers studied the neural mechanisms resulting from activities that combine both action and cognition.

To this end, a series of 360 tests, combining mental and physical effort, were performed whilst being monitored by a scanner. The 20 voluntary participants were placed in the supine position, with their heads in a functional MRI scanner. They then had to complete a series of tasks through which they could accumulate winnings. However, in each series the winnings were limited to the first incorrect response. The tasks combined cognitive and motor actions. The participants had to find the highest number from among different-sized numbers and then select it by squeezing a handle located by their left or right hand (depending on the number's location). At the end of the test, a winnings summary was displayed to motivate the participant.

Using images obtained from the MRI scans taken during the test, Mathias Pessiglione and his team identified a general motivational system in the depths of the brain, i.e. a structure capable of activating any effort type, both mental (concentrating on the task in hand) or physical (lifting a load). The researchers observed that the ventral striatum was activated in proportion to the amount of money involved: the higher the degree of motivation, the higher the activation level. Furthermore, the ventral striatum is connected to the median part of the striatum (the caudate nucleus) when the task to be performed is cognitively difficult (when the physical size and the numerical value of the numbers did not correspond). This ventral region solicits the lateral part of the striatum (the putamen) when the difficulty is motor-related (when the handle had to be squeezed very tightly).

The researchers suggest that the expectation of a reward is encoded in the ventral striatum, which can then drive either the motor or cognitive part of the striatum, depending on the task, in order to boost performance. "The ventral striatum may commute connections in accordance with the request, i.e. enhance the neuronal activity in the caudate nucleus for a cognitive operation and in the putamen for a physical action" explains Mathias Pessiglione.

Sources *Neural Mechanisms Underlying Motivation of Mental Versus Physical Effort*
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http://www.eurekalert.org/pub_releases/2012-02/wifb-tot022112.php

Theory of the 'rotting' Y chromosome dealt a fatal blow

If you were to discover that a fundamental component of human biology has survived virtually intact for the past 25 million years, you'd be quite confident in saying that it is here to stay.

Written by Matt Fearer

CAMBRIDGE, Mass. - Such is the case for a team of Whitehead Institute scientists, whose latest research on the evolution of the human Y chromosome confirms that the Y - despite arguments to the contrary - has a long, healthy future ahead of it.

Proponents of the so-called rotting Y theory have been predicting the eventual extinction of the Y chromosome since it was first discovered that the Y has lost hundreds of genes over the past 300 million years. The rotting Y theorists have assumed this trend is ongoing, concluding that inevitably, the Y will one day be utterly devoid of its genetic content.

Over the past decade, Whitehead Institute Director David Page and his lab have steadily been churning out research that should have permanently debunked the rotting Y theory, but to no avail.

"For the past 10 years, the one dominant storyline in public discourse about the Y is that it is disappearing," says Page. "Putting aside the question of whether this ever had a sound scientific basis, the story went viral - fast - and has stayed viral. I can't give a talk without being asked about the disappearing Y. This idea has been so pervasive that it has kept us from moving on to address the really important questions about the Y."

To Page, this latest research represents checkmate in the chess match he's been drawn into against the "rotting Y" theorists. Members of his lab have dealt their fatal blow by sequencing the Y chromosome of the rhesus macaque - an Old World monkey whose evolutionary path diverged from that of humans some 25 million years ago - and comparing it with the sequences of the human and chimpanzee Y chromosomes. The comparison, published this week in the online edition of the journal Nature, reveals remarkable genetic stability on the rhesus and human Ys in the years since their evolutionary split.

Grasping the full impact of this finding requires a bit of historical context. Before they became specialized sex chromosomes, the X and Y were once an ordinary, identical pair of autosomes like the other 22 pairs of chromosomes humans carry. To maintain genetic diversity and eliminate potentially harmful mutations, autosome pairs swap genes with each other in a process referred to as "crossing over." Roughly 300 million years ago, a segment of the X stopped crossing over with the Y, causing rapid genetic decay on the Y. Over the next hundreds of millions of years, four more segments, or strata, of the X ceased crossing over with the Y. The resulting gene loss on the Y was so extensive that today, the human Y retains only 19 of the more than 600 genes it once shared with its ancestral autosomal partner.

"The Y was in free fall early on, and genes were lost at an incredibly rapid rate," says Page. "But then it leveled off, and it's been doing just fine since."

How fine? Well, the sequence of the rhesus Y, which was completed with the help of collaborators at the sequencing centers at Washington University School of Medicine and Baylor College of Medicine, shows the chromosome hasn't lost a single ancestral gene in the past 25 million years. By comparison, the human Y has lost just one ancestral gene in that period, and that loss occurred in a segment that comprises just 3% of the entire chromosome. The finding allows researchers to describe the Y's evolution as one marked by periods of swift decay followed by strict conservation.

"We've been carefully developing this clearcut way of demystifying the evolution of the Y chromosome," says Page lab researcher Jennifer Hughes, whose earlier work comparing the human and chimpanzee Ys revealed a stable human Y for at least six million years. "Now our empirical data fly in the face of the other theories out there. With no loss of genes on the rhesus Y and one gene lost on the human Y, it's clear the Y isn't going anywhere."

"This paper simply destroys the idea of the disappearing Y chromosome," adds Page. "I challenge anyone to argue when confronted with this data."

This work was supported by the National Institutes of Health, the Howard Hughes Medical Institute, and the Charles A. King Trust. David Page's primary affiliation is with Whitehead Institute for Biomedical Research, where his laboratory is located and all his research is conducted. He is also a Howard Hughes Medical Institute investigator and a professor of biology at Massachusetts Institute of Technology.

Full Citation: *"Strict evolutionary conservation followed rapid gene loss on human and rhesus Y chromosomes" Nature, online February 22, 2012*

Jennifer F. Hughes (1), Helen Skaletsky (1), Laura G. Brown (1), Tatyana Pyntikova (1), Tina Graves (2), Robert S. Fulton (2), Shannon Dugan (3), Yan Ding (3), Christian J. Buhay (3), Colin Kremitzki (2), Qiaoyan Wang (3), Hua Shen (3), Michael Holder (3), Donna Villasana (3), Lynne V. Nazareth (3), Andrew Cree (3), Laura Courtney (2), Joelle Veizer (2), Holland Kotkiewicz (2), Ting-Jan Cho (1), Natalia Koutseva (1), Steve Rozen (1), Donna M. Muzny (3), Wesley C. Warren (2), Richard A. Gibbs (3), Richard K. Wilson (2), David C. Page (1).
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http://www.eurekalert.org/pub_releases/2012-02/bcom-thb022112.php

The heart beats to the rhythm of a circadian clock

Sudden cardiac death - catastrophic and unexpected fatal heart stoppage - is more likely to occur shortly after waking in the morning and in the late night.

HOUSTON - In a report in the journal Nature (http://www.nature.com/nature/index.html), an international consortium of researchers that includes Case Western Reserve University School of Medicine (http://casemed.case.edu/) in Cleveland and Baylor College of Medicine (www.bcm.edu) explains the molecular linkage between the circadian clock and the deadly heart rhythms that lead to sudden death.

The answer begins with a controller of the circadian clock - krüppel-like factor 15 (Klf15), which has been a long-time target of the laboratory of Dr. Mukesh Jain of Case Western, said Dr. Xander Wehrens(http://www.bcm.edu/physio/wehrens/?pmid=6659), professor of molecular physiology and biophysics and cardiology at BCM, also an author. (Jain is corresponding author of the report.)

Klf15, in turn, controls the level of a potassium channel-interacting protein (KChIP2), which affects how potassium flows out of heart muscle cells called cardiac myocytes.

Because the level of this KChIP2 protein fluctuates during the circadian or daily cycle, it can change the size of the potassium current in cardiac myocytes. Changes in this subunit or Klf15 can affect the potassium current that governs repolarization of the cardiac myocyte. Overall, this can shorten or lengthen the time the heart muscle has to empty the heart's pumping chamber (ventricle) of blood. This time interval for repolarization is critical. Too much or too little can result in abnormal heart rhythms called arrhythmias. As the heart loses the regularity of the beat, it cannot pump blood efficiently.

Studies of mice that lacked Klf15 and mice with a genetic change that caused them to make more Klf15 than normal increased the risk of deadly arrhythmias. This was a proof of principle, said Wehrens. It is the first example of a molecular mechanism for the circadian change in susceptibility to cardiac arrhythmias," he said. "If there was too much Klf15 or none, the mice were at risk for developing the arrhythmias," he said.

Because Klf15 is regulated by the circadian "clock," the rate of flow through the potassium channel goes up and down and if disrupted, can lead to a change that results in one of two known heart problems linked to sudden death - long QT or short QT syndrome. (QT refers to an interval measured from an electrocardiogram or ECG, which corresponds to the electrical recovery time of heart.)

Wehrens credits Jain's laboratory with accomplishing much of the work. His laboratory performed the electrophysiology experiments with the mice that lacked Klf15 and those who produced too much, he said.
Much of the BCM work was done by Dr. Mark McCauley, a cardiology fellow who was a post-doctoral fellow in the laboratory at the time, said Wehrens.
Others who took part in this work include first author Darwin Jeyaraj, Saptarsi Haldar, Xiapoing Wan, Yuan Lu, Betty Eapen, Nikunj Sharma, Eckhard Ficker, Michael Cutler, and David Rosenbaum, all of Case Western; Jurgen A. Ripperger and Urs Albrecht of University of Fribourg in Switzerland; Kun Hu and Steven A. Shea of Brigham and Women's Hospital and Harvard Medical School in Boston; James Gulick, Atusushi Sanbe, and Jeffrey Robbins of Cincinnati Children's Hospital Medical Center; Sophie Demolombe of Universite de Nice Sophia Antipolis in Valbonne, France; and Roman Kondratov of Cleveland State University in Ohio.
Funding for this work came from the National Institutes of Health, the Heart Rhythm Society, the American Heart Association, the Swiss National Science Foundation, the Centre National de la Recherche Scientifique, and the Leducq Foundation.

http://bit.ly/w1oet3

Elsevier Boycott Not a Petition, But "A Declaration of Independence"

So says computer programmer and sauropod fan Mike Taylor in a particularly rich rallying cry at Discover's "The Crux" blog.

By David Dobbs

The ongoing boycott of academic-publishing giant Elsevier - almost 7000 researchers and counting - writes Bristol, [has] sometimes been described as a petition, but isn't trying to persuade Elsevier to do something. It's a declaration of independence.

It's a particularly sharp rundown of the forces in play in the growing open-science revolt, with due attention to both the changes that have created this revolt and to the changes still needed from researchers if it's to succeed in making open-access publication of scientific results the norm instead of the exception.

At this point, it seems clear that the old publishers aren't going to change; their support for the RWA is proof enough of this. To fix the academic publishing mess, researchers need to stop sending their work to barrier-based journals. And for that to happen, we need funding bodies and job-search committees to judge candidates on the quality of their work, not on which brand name it's associated with.

Happily, there are signs of movement in this direction: for example, The Wellcome Trust says "it is the intrinsic merit of the work, and not the title of the journal in which an author's work is published, that should be considered in making funding decisions." We need more funding and hiring bodies to make such declarations. Only then will researchers will be free of the need (real or apparent) to prop up parasitic publishers by sending their best work to big-name, barrier-based journals.

The move by Wellcome, among the biggest funders of scientific research in the UK, is particularly significant, since funder support of open-science principles can greatly speed change. There's a long way to go yet. But at this point, the pressure continues to grow on both Elsevier and hesitant researchers virtually by the day, and declarations of independence like the one voiced here by Taylor reveal the growing confidence of open-science advocates.

From: It's Not Academic: How Publishers Are Squelching Science Communication | The Crux | Discover Magazine.
Corrections: Initial post had Mike Taylor, the author of the post in question, as Mike Bristol. Taylor is at University of Bristol, and my mind was apparently elsewhere when I typed his last name. H/t to Stephen Curry for correction.

http://www.sciencenews.org/view/generic/id/338631/title/Old-fashioned_fish_regrow_fins

Old-fashioned fish regrow fins

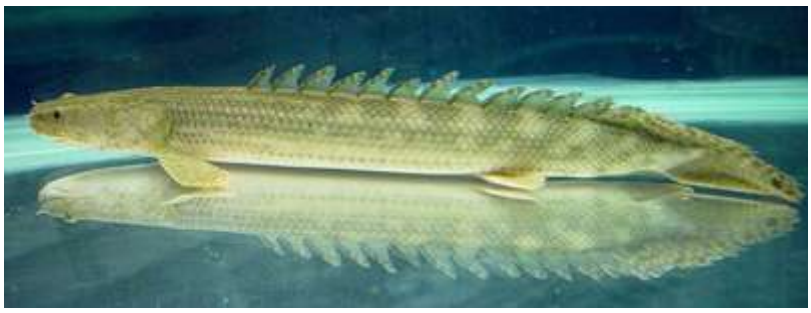
Fish from an ancient line can regenerate lost limbs with newt-like flair

By Susan Milius

The discovery that a long, skinny fish that can regrow its fin in a matter of weeks suggests that ancient vertebrates had considerable regenerative powers.

Two species of bichir from Africa can regrow amputated bony fins with remarkable accuracy, says developmental biologist Luis Covarrubias of the National Autonomous University of Mexico in Cuernavaca. Among the most ancient of the living lineages of ray-finned fishes, a group that includes most fresh- and saltwater species, the Polypterus bichirs share traits such as paired lungs with both modern amphibians and very early four-limbed vertebrates.

The venerable fishes' powers suggest that early vertebrates shared substantial limb regeneration capability during the ancient evolutionary transition from fins to feet, Covarrubias and his colleagues contend in a paper published online February 21 in the Proceedings of the National Academy of Sciences. Those first steps toward life on land took place at least 375 million years ago.



Polypterus bichir lapradei

Coauthor Rodrigo Cuervo, now at Veracruz University in Mexico, discovered the bichirs' powers while following his curiosity about regeneration. The fish can go from zero to a full-size new side fin within a month. Many vertebrates, including mammals, can't regenerate limbs at all. Biologists would love to understand why such a handy trait appears to have faded away in the course of evolution, or how it arose in the first place. "The real question is not why regeneration was lost but why it was 'won,' " Covarrubias says.

Among animals without backbones, limb regeneration isn't so startling. But only select groups of vertebrates living today can manage. Axolotls and other amphibians in the group of newts and salamanders can to varying degrees replace a lost limb, as can some other fish.

"Zebrafish are great at fin regeneration," says Ken Poss of Duke University, who studies them. But their fins, as do fins of many other fish, contain mostly bones related to the fishes' specialized, hardened skin. Bichir fins grow considerable fleshy tissue as well as bones of the type in the internal skeleton. Their comeback fins may prove useful for comparing regeneration systems, Poss says.

http://medicalxpress.com/news/2012-02-men-legs-source-hair-transplants.html

Men's legs may be new source for hair transplants

Hairlines require finer strands and for some patients legs offer a good supply, report shows.

HealthDay - Doctors may have a leg up on baldness: Transplanting hair from a patient's legs to his head for what may be a more natural look. In the February issue of the Archives of Dermatology, Dr. Sanusi Umar explained that the finer, softer hair found on the leg is an ideal candidate for hair grafts that aim to recreate the hairline.

"The whole idea is to take hair transplantation to the next level," said Umar, a private practitioner in Redondo Beach, Calif., and clinical instructor in dermatology at the University of California, Los Angeles.

There are "several problems" with traditional methods for hairline transplant, he believes.

"First, the traditional transplant takes hair from the middle of the back of the head, and that hair happens to be the thickest hair on the head," he said. That means that, "if you take it from there and put it in the hairline, despite your best efforts, it will end up slightly harsh[-looking] and unnatural in the hairline. It's problematic to say the least," Umar explained. "The other issue is that people bald or thin to varying degrees," he noted. "You can have mild baldness or it can be very severe." This means that the standard method of hair transplant is of little use to a man who has lost most of his head hair and therefore has no source for the transplant.

"You're fighting a losing battle because there's just not enough to work with. Most ethical practices will therefore tell a very bald person that they cannot do it because it will not look natural," Umar said.

"In addition to that, over the years there are a lot of patients that have had hair transplantation that is antiquated," he added. "They have a 'pluggy' look. They have scars. And they no longer have any donor supply left on the back of the head to deal with that issue, because it's already been used up."

Looking for a solution, about seven years ago Umar began exploring "advanced body hair transplantation" or the "U-graft method." Essentially, the technique involves scouting for hair from all over the body, keeping in mind that not all patients are equally hirsute. "With this approach I can combine beard hair, chest hair and leg hair, depending on the person's hair distribution," Umar noted. "Mixing that with some thicker head hair as well, I can come up with about 20,000 to 30,000 hairs, which means I'm then able to tackle some very severely bald individuals."

However, recreating a natural hairline at the forehead requires especially fine hair. Umar believes that leg hair "works the best in terms of simulating nature [in this spot]. Sometimes we can also take hair from the nape of the neck, which is also very fine. And then for behind the hairlines we can use some of the thicker head hair."

In his case report, Umar published the results of two such transplant efforts. One involved the exclusive use of leg hair follicles to recreate the front of the patient's original hairline/temple area, while the other involved mixing transplanted leg and head hair to soften and bring forward a custom-designed "widow's peak" hairline for a patient. In both cases, the transplant procedure gave rise to what Umar described as a "fully grown and soft-looking hairline" within nine months. Between 75 to 80 percent of the fine transplanted leg hair flourished in its new home on the head, and three to four years later both patients had experienced minimal hair loss in the transplant area.

However, Umar noted that men seeking such procedures should be both patient and prepared for a hefty bill. The procedures are typically spaced over two sessions (each involving three to five days) that are spread over the course of a year. And at $7 to $10 per hair follicle graft (with each follicle containing anywhere from one to four strands of hair), the bill will ultimately total in the thousands, Umar said, with so-called "slick bald" patients facing the highest expense. Opinions from other experts in hair transplantation were mixed.

Dr. Malcolm Roth is president of the American Society of Plastic Surgeons and chief of the division of plastic surgery at Albany Medical Center in Albany, N.Y. He hailed the innovation as "yet another example of how new techniques continue to refine and improve outcomes in cosmetic procedures to give patients more natural results."

However, Dr. Barry DiBernardo, who has a private practice in Montclair, N.J., said the procedure does raise a few questions and concerns. "Finding hair from other parts of the body is not new at all," he noted. "We've long considered that option, because clearly when you're designing a hairline . . . the more we can make it look like what was there in the first place, the better," DiBernardo explained.

"But when you use body hair it can be a different thickness," DiBernardo said. "It can have more curl to it than the original hair. So these reports sound fine. But the approach does raise the issue of a hair mismatch, which of course will depend on the person. Everybody varies," he said.

"The other thing is the question of the potential for scarring, or leaving pinpoint scars, following harvesting of hair," DiBernardo pointed out. "Because while you're not going to see the back of the head and it's a very good area for healing to begin with, you will see the leg. And the leg certainly doesn't heal as well as the scalp."

More information: *Find out more about hair transplants at the U.S. National Library of Medicine.*

http://medicalxpress.com/news/2012-02-aspirin-good-plavix-poor-leg.html

Aspirin as good as Plavix for poor leg circulation: study

Both work equally well in condition that causes pain while walking.

HealthDay - Aspirin works as well as Plavix in patients with blocked leg arteries, a new European study finds.

People with the condition, called peripheral artery disease, often suffer from intermittent claudication, which is pain while walking because of decreased blood supply to the legs. Animal experiments had suggested that aspirin might block the growth of blood vessels that bypass blockages and help get more blood to leg tissue, the Swiss and German researchers said. "Once again, we have shown that what happens in animals doesn't translate to humans," said Dr. Juan Zambrano, an assistant professor of cardiovascular medicine, coronary/endovascular and stem cell therapies at the University of Miami Miller School of Medicine.

Patients suffering from peripheral artery disease are also at increased risk of heart attack and stroke from blood clots traveling from the legs to the heart or brain, which is why these patients are given blood thinners such as Plavix (clopidogrel) or aspirin, explained Zambrano. "Either aspirin or Plavix is acceptable as a good preventive measure to avoid heart attack or stroke in these patients," he said. "A lot of people favor aspirin because it's cheaper."

However, the most interesting part of this study to Zambrano was the role of exercise in improving walking distance and time. "Something as simple as exercise can help improve claudication," he said. "Exercise is key and it doesn't matter how you treat the underlying condition, exercise is always going to help."

The report was published online Feb. 21 in the journal Cardiovascular and Cerebrovascular Disease.

For the study, a team led by Dr. Kurt Jaeger from University Hospital Basel in Switzerland, looked at the effectiveness of aspirin and Plavix in helping peripheral artery disease patients improve pain-free walking distance, which is a vital part of rehabilitation.

The researchers randomly assigned 229 patients to receive low-dose aspirin or Plavix, to see how they did during one hour walks. Jaeger's group found that, after 12 weeks, people taking aspirin improved pain-free walking distance almost 40 percent and could walk 35 percent longer before pain made it too hard to continue.

For patients taking Plavix, there was a 33 percent improvement in walking distance and an almost 35 improvement in pain-free walking time, the researchers noted. Walking is an important part of rehabilitation for peripheral artery disease patients. Walking can help increase blood flow to the legs and promote the growth of tiny blood vessels that help supply the leg with blood and oxygen.

It had been thought that aspirin wouldn't work because its anti-inflammatory properties could block the development of these tiny blood vessels that grow to get blood around the blockage. "It seems that the anti-inflammatory properties of low-dose aspirin and its inhibiting effects on [the growth of new blood vessels] are not of clinical relevance for rehabilitation programs in intermittent claudication," the researchers concluded.

More information: *For more on peripheral artery disease, visit the American Heart Association.*

http://www.eurekalert.org/pub_releases/2012-02/asfm-ohf022312.php

Opinion: H5N1 flu is just as dangerous as feared, now requires action

Scientists present their case that H5N1 is a very dangerous virus based on analysis of published studies of the seroepidemiology of H5N1 in humans

The debate about the potential severity of an outbreak of airborne H5N1 influenza in humans needs to move on from speculation and focus instead on how we can safely continue H5N1 research and share the results among researchers, according to a commentary to be published in mBio®, the online open-access journal of the American Society for Microbiology, on Friday, February 24.

H5N1 influenza has been at the center of heated discussions in science and policy circles since the U.S. National Science Advisory Board for Biosecurity (NSABB) asked the authors of two recent H5N1 investigations and the scientific journals that planned to publish the studies to withhold crucial details of the research in the interest of biosecurity.

In the mBio® commentary, Michael Osterholm* and Nicholas Kelley, of the Center for Infectious Disease Research and Policy at the University of Minnesota, present their case that H5N1 is a very dangerous virus, based on their analysis of published studies of the seroepidemiology of H5N1 in humans. H5N1 flu infections have exceedingly high mortality, they say, and current vaccines and antiviral drugs will not pull us out of a global H5N1 pandemic. "We believe that the assertion that the case-fatality rate of H5N1 influenza in humans may be overestimated is based on a flawed data analysis," Osterholm said.

Analysis of reports of H5N1 seroprevalence that include data from the 1997 Hong Kong outbreak as well as data from 2004 to date will give a misleading impression because the 1997 outbreak was a very different

"biologic event" that is recognized as such by the WHO, because the 1997 H5N1 virus has a significantly different genotype from that of later H5N1 viruses. This is why the WHO does not include the Hong Kong H5N1 virus data in any analysis of H5N1 transmission, and the 1997 Hong Kong virus is not recommended for inclusion in H5N1 vaccines, Osterholm explained.

Seroepidemiologic studies that have examined the exposure of various groups of people to H5N1 viruses only from 2004 onward indicate that only a small segment of the population has ever been exposed to H5N1, and that among those that have been exposed, many become seriously ill or die.

"The available seroepidemiologic data for human H5N1 infection support the current WHO reported case-fatality rates of 30% to 80%," Osterholm says. In the event of an H5N1 pandemic, they point out, if the virus is even one tenth or one twentieth as virulent as has been documented in these smaller outbreaks, the resulting fatality rate would be worse than in the 1918 pandemic, in which 2% of infected individuals died.

Vaccines will not head off an H5N1 pandemic either, the authors say, since the time required to develop and manufacture an influenza vaccine specific to new outbreak strain has resulted in "too little, too late" vaccine responses for the 1957, 1968, and 2009 influenza pandemics, and not much in the process has changed since 2009.

"The technology behind our current influenza vaccines is simply not sufficient to address the complex challenges associated with an influenza pandemic in the 21st century," Osterholm and Kelley say.

This is the heart of the matter, they say: there has been enough discussion about how severe an H5N1 pandemic might be. Moving forward, the current controversy has provided a valuable opportunity for scientists and public policy experts to discuss influenza research and preparedness and create "a roadmap for the future." The discussion among scientists and policy makers needs to move on from whether H5N1 poses a serious international threat - as it clearly does - and begin discussing how we can prevent these viruses from escaping labs and how scientists can share their flu-related results with those who have a need to know.

There are critical questions that need to be answered, the authors say. For instance, how can scientists conduct virus-transmission studies in mammals safely and how can scientists share research methods and results with those who have a need to know? We also need to come to agreement on how to ensure that strains of H5N1 viruses created in the lab don't escape those controlled environments, the authors say. And new, more effective vaccine technologies are needed that can enable substantially faster production. Resolving these issues could allow H5N1 research and preparedness to serve as a springboard for solving similar problems with existing or emerging pathogens. **Michael Osterholm is a member of the National Science Advisory Board for Biosecurity.*

http://www.eurekalert.org/pub_releases/2012-02/uov-bms022312.php

Blood mystery solved

2 new blood types decoded

You probably know your blood type: A, B, AB or O. You may even know if you're Rhesus positive or negative. But how about the Langereis blood type? Or the Junior blood type? Positive or negative? Most people have never even heard of these. Yet this knowledge could be "a matter of life and death," says University of Vermont biologist Bryan Ballif.

While blood transfusion problems due to Langereis and Junior blood types are rare worldwide, several ethnic populations are at risk, Ballif notes. "More than 50,000 Japanese are thought to be Junior negative and may encounter blood transfusion problems or mother-fetus incompatibility," he writes.

But the molecular basis of these two blood types has remained a mystery - until now.

In the February issue of Nature Genetics, Ballif and his colleagues report on their discovery of two proteins on red blood cells responsible for these lesser-known blood types. Ballif identified the two molecules as specialized transport proteins named ABCB6 and ABCG2."Only 30 proteins have previously been identified as responsible for a basic blood type," Ballif notes, "but the count now reaches 32." The last new blood group proteins to be discovered were nearly a decade ago, Ballif says, "so it's pretty remarkable to have two identified this year."

Both of the newly identified proteins are also associated with anticancer drug resistance, so the findings may also have implications for improved treatment of breast and other cancers.

As part of the international effort, Ballif, assistant professor in UVM's biology department, used a mass spectrometer funded by the Vermont Genetics Network. With this machine, he analyzed proteins purified by his longtime collaborator, Lionel Arnaud at the French National Institute for Blood Transfusion in Paris, France.

Ballif and Arnaud, in turn, relied on antibodies to Langereis and Junior blood antigens developed by Yoshihiko Tani at the Japanese Red Cross Osaka Blood Center and Toru Miyasaki at the Japanese Red Cross Hokkaido Blood Center.

After the protein identification in Vermont, the work returned to France. There Arnaud and his team conducted cellular and genetic tests confirming that these proteins were responsible for the Langereis and Junior blood types. "He was able to test the gene sequence," Ballif says, "and, sure enough, we found mutations in this particular gene for all the people in our sample who have these problems."

Beyond the ABO blood type and the Rhesus (Rh) blood type, the International Blood Transfusion Society recognizes twenty-eight additional blood types with names like Duffy, Kidd, Diego and Lutheran. But Langereis and Junior have not been on this list. Although the antigens for the Junior and Langereis (or Lan) blood types were identified decades ago in pregnant women having difficulties carrying babies with incompatible blood types, the genetic basis of these antigens has been unknown until now.

Therefore, "very few people learn if they are Langereis or Junior positive or negative," Ballif says.

"Transfusion support of individuals with an anti-Lan antibody is highly challenging," the research team wrote in Nature Genetics, "partly because of the scarcity of compatible blood donors but mainly because of the lack of reliable reagents for blood screening." And Junior-negative blood donors are extremely rare too. That may soon change.

With the findings from this new research, health care professionals will now be able to more rapidly and confidently screen for these novel blood group proteins, Ballif wrote in a recent news article. "This will leave them better prepared to have blood ready when blood transfusions or other tissue donations are required," he notes. "Now that we know these proteins, it will become a routine test," he says.

This science may be especially important to organ transplant patients. "As we get better and better at transplants, we do everything we can to make a good match," Ballif says. But sometimes a tissue or organ transplant, that looked like a good match, doesn't work - and the donated tissue is rejected, which can lead to many problems or death.

"We don't always know why there is rejection," Ballif says, "but it may have to do with these proteins."

The rejection of donated tissue or blood is caused by the way the immune system distinguishes self from not-self. "If our own blood cells don't have these proteins, they're not familiar to our immune system," Ballif says, so the new blood doesn't "look like self" to the complex cellular defenses of the immune system. "They'll develop antibodies against it," Ballif says, and try to kill off the perceived invaders. In short, the body starts to attack itself.

"Then you may be out of luck," says Ballif, who notes that in addition to certain Japanese populations, European Gypsies are also at higher risk for not carrying the Langereis and Junior blood type proteins.

"There are people in the United States who have these challenges too," he says, "but it's more rare."

Ballif and his international colleagues are not done with their search. "We're following up on more unknown blood types," he says. "There are probably on the order of 10 to 15 more of these unknown blood type systems - where we know there is a problem but we don't know what the protein is that is causing the problem."

Although these other blood systems are very rare, "if you're that one individual, and you need a transfusion," Ballif says, "there's nothing more important for you to know."

http://www.physorg.com/news/2012-02-plate-tectonics-realistically.html

Plate tectonics modelled realistically

Swiss scientists have for the first time succeeded in realistically simulating how an oceanic plate sinks of its own accord under an adjacent plate.

At the same time they showed why only one of the plates rather than both subducts into the Earth's mantle, and how this process affects the dynamics of the Earth's interior.

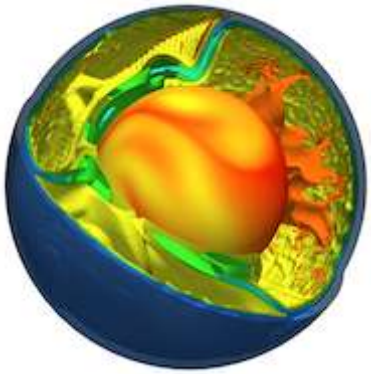
The Earth is probably the only planet in our solar system with active plate tectonics: the continental and oceanic plates move atop the Earth's mantle. New plate forms continuously at a mid-oceanic ridge, allowing an ocean basin to grow until the plate is old and heavy enough to sink under the adjacent continental margins. The oceanic plate pushes itself under the continental crust at active continental margins known as subduction zones, and older oceanic plate does so under younger oceanic plate at island arcs. If the plates become snagged together and then abruptly slide forward again, there is an earthquake. Like the mid-oceanic ridges and volcanoes, subduction zones result from processes mainly occurring deep in the Earth's interior. In the past four decades, computer simulations have contributed considerably to an understanding of these processes.

The models did not correspond to reality

Based on observation data, models are only an approximation to reality. Until now, scientists were unsuccessful in realistically simulating plates subducting into the Earth's mantle in global models. In previous simulations, both plates sank vertically down into the Earth's mantle together instead of one plate sliding obliquely under the adjacent plate.

ETH Zurich scientists have now succeeded for the first time in using global computer models to model an asymmetrical subduction of only one plate under the adjacent plate. The modelling was calculated on the "Monte Rosa" supercomputer belonging to the CSCS, Switzerland's National Supercomputing Centre, and the "Brutus" cluster at ETH Zurich. Thanks to the simulation, the researchers were able to gain new insights into the Earth's interior.

The boundary conditions of previous simulation models specify that the plates can move horizontally but not vertically, and thus there is no topography at all along the overthrust. However, the reality looks different: deep oceanic trenches up to more than 11 kilometres deep form along subduction zones. Thus the topography of the subducting oceanic plate is anything but flat. In his doctoral thesis with ETH Zurich Professor Paul Tackley and in collaboration with his colleagues, Fabio Crameri has now developed a simulation model in which the plates can move not only horizontally but also vertically - as in reality. The trick: Crameri used a viscous "layer of air" which he positioned over the surface of the crust in the simulation. He says "This layer of air is soft and has almost no density." It must be viscous like the Earth's mantle so it does not simply flow away during a time increment of several thousand years in the simulation of a plate overthrust.



Computer simulation of plate tectonics and the circulation of hot rock material in the Earth's mantle. The visible features include cold plates (blue/green) subducting down unilaterally from the surface of the Earth into the Earth's mantle and hot rock material (red) rising up from deeper regions of the mantle. **Tackley Research Group / ETH Zurich**

The scientists started runs of the global model with and without this layer of air. After a period of about 10 million years, which is short on a geological timescale, an asymmetrical unilateral subduction had already developed in the model with the layer of air. The model realistically replicates the deformation experienced by the subducting plate in this process, and the formation of the deep oceanic trench.

Soft crust as lubricant

These simulations show conclusively for the first time why always just one plate sinks into the Earth's mantle during subduction instead of both. When plates slide over one another, the rock is severely stressed by friction, pressure and temperature, but water carried by oceanic crust may reduce this. When the scientists superimposed a soft, water-rich layer of rock on the surface of the crust in addition to the air layer in their models, the simulation generated an even more stable unilateral subduction. This layer of rock is a kind of lubricant between the two plates. It ensures that the plates remain stable and slide over one another continuously without the subducting plate breaking off in the process.

In a three-dimensional simulation, the researchers were also able to show how the viscous Earth's mantle circulates around the obliquely subducting plate. According to this, the plate rests on top of the mantle and forces the viscous mantle rock under the plate at the front edge. Crameri says "The mantle moves around the subducting plates and deforms them."

Subducting crustal plates affect the dynamics of the Earth's mantle. This is why models of this kind are very important in understanding the processes in the Earth's interior to the beginning of plate tectonics on the Earth. However, they help towards a better understanding not only of plate tectonic processes but also of the associated earthquakes or volcanic activity. This is why such simulations are essential for hazard and risk assessment.

More information: Crameri F, et al: A free plate surface and weak oceanic crust produce single-sided subduction on Earth, Geoph. Res. Letters (2012), 39, L03306, doi:10.1029/2011GL050046 Provided by ETH Zurich

http://bit.ly/yRdTo6

Blame dark matter underdog for mystery missing lithium

AN UNDERDOG dark-matter particle could explain why the universe seems strangely low on lithium.

23 February 2012 by David Shiga

If the idea holds up, it will be a boon in the hunt for dark matter, the stuff needed to account for 80 per cent of the universe's matter.

In the universe's first few fiery minutes, nuclear reactions forged a host of light elements, including helium, deuterium and lithium, in a process called big bang nucleosynthesis. The amounts of these elements present in the early universe, gleaned from ancient stars and primordial gas clouds, match theory, except in one respect:

they contain much less of the dominant form of lithium, lithium-7, than expected. There has never been a satisfactory explanation for this.

Now help comes in the shape of hypothetical dark-matter particles called axions. These light particles were dreamed up in the 1970s as part of a theory to explain why the strong nuclear force, unlike the other forces, does not change if a particle is swapped for the antimatter counterpart of its mirror image. Axions are not the dominant theory for dark matter. That accolade goes to weakly interacting massive particles, or WIMPs. But as neither WIMPs nor axions have ever been observed, the jury is still out.

In the latest research, the underdog axions score a point. The rates of nuclear reactions that produced lithium-7 depend partly on the amount of energy that was present in the form of light. As we cannot tell how much light was there directly, we infer it from the cosmic microwave background (CMB), the echo of the big bang that emerged 380,000 years later. This is used to estimate how much lithium should be present: more light skews reaction rates and lowers expected levels of lithium.

Ozgur Erken of the University of Florida in Gainesville and colleagues suggest that something cooled photons between the synthesis of lithium and the emergence of the CMB, causing the photon energy to be underestimated, and inflating the expected amounts of lithium.

Born with very little kinetic energy, axions are a prime suspect. When their cooling power is accounted for, the predicted lithium abundance drops by half, the team calculate (Physical Review Letters, DOI: 10.1103/PhysRevLett.108.061304). "We're excited that it gives about the right correction," says Pierre Sikivie, Erken's colleague.

Adding in axions also creates a problem, however. Without them, CMB measurements are consistent with about four types of neutrino, close to the three types glimpsed in experiments. But if axions are present, they would skew this measurement and imply about seven neutrino types, Erken's team calculate. This makes Gary Steigman of Ohio State University in Columbus, who was not involved in the study, sceptical of the axion explanation for the lithium-7 anomaly.

An answer should come in 2013 when much better measurements of the CMB are expected from the Planck satellite. Our best chance of glimpsing axions, meanwhile, lies in an upgraded version of an experiment called ADMX, due to start up towards the end of this year. It may also be possible to infer their existence from data from the Large Hadron Collider at CERN near Geneva in Switzerland, where they should boost the production of Higgs bosons.

http://www.xconomy.com/new-york/2012/02/23/transparency-launches-as-linux-of-drug-development/

Transparency Launches as Linux of Drug Development

If computer coders can do open source, so can drug developers

Arlene Weintraub

When Tomasz Sablinski was working in pharmaceutical R&D, he was often frustrated by the demand for secrecy in the clinical trials process - a misdirected effort, he says, to keep competitors in the dark about what drug companies were up to. “The price you pay when you hide what you’re doing is you only get feedback from a precious few people,” he says. “There is very little new blood in the ideation process.”

Then Sablinski read an article about the open-source operating system Linux and he had an epiphany. “If said, ‘If computer coders can do open source, so can drug developers,’” he recalls. “You have to add patients to the mix, because they’re really the reason you’re doing drug development.”

So in late January, Sablinski and his company, Transparency Life Sciences, rolled out the beta version of a virtual community of physicians, scientists, and patients whose input is helping the company develop three drugs. The site (transparencyls.com), which is being managed by a handful of staff members in New York City and Boston, has only been live for a few weeks. But it has already attracted about 30 patients, who have been actively trading notes about their experiences and making suggestions for clinical trials, Sablinski says.

Sablinski hopes the population of registered users will balloon in the coming weeks, when Transparency begins reaching out to patient advocacy groups in the disease areas it’s working in: multiple sclerosis, peripheral vascular disease, and inflammatory bowel disease. “What we’re trying to do is channel this tremendous Web energy into helping us create experiments that will answer the right questions,” Sablinski says.

Here’s how it works: After people register as users on the site, they pick the drug development program that interests them, and then answer a series of questions about it. For example, users who enter the MS area identify themselves as either patients or researchers. Researchers are asked questions such as “Which patient population should be studied initially?” and then given choices such as “relapsing remitting” and “secondary progressive.” Patients, on the other hand, are asked to recount their experiences, as such: “Please think about medications you have tried for MS. Were you likely to need a lower or higher than usual dose?”

Sablinski says he plans to close out the question-and-answer period on the MS drug in the next two months or so, after which he will choose his principal investigators - possibly from the community of physicians that sign on to the site. From there, he and his team will design a clinical trial and go to the FDA for permission to run it, he says.

Transparency also has a strong social-media component. The site includes a forum where patients can ask questions about diseases and treatments. The forum is moderated by Lisa Abrams, who also answers private letters from patients and is creating a newsletter for patients and families. Abrams, a former drug-development consultant, received a business degree from MIT, where she specialized in studying how technologychanges the nature of work. But she also has a personal connection to Transparency's mission, having struggled with an intestinal disease for many years. "Patients are what's missing from the equation," she says. "I always wanted to do something like this." Transparency also maintains a growing presence on Facebook and Twitter.

Sablinski admits Transparency's first three drugs are not likely to be huge moneymakers. That's because they're all repurposed versions of generic drugs that are already on the market to treat other diseases. The MS treatment, for example, is lisinopril, an anti-hypertensive drug that has shown promise in animal studies as an immune system modulator. "We needed to prove the concept works, and a generic strategy reduces the financial risk," he says.

Part of what Sablinski needs to prove is that his virtual, crowd-sourcing model can be used to develop drugs at a fraction of the usual cost. In the typical clinical trial, patients must frequently visit the trial sites for physical exams and the like. Sablinski believes a lot of that follow-up can be done with telemedicine - by phone and Internet. "We want the first and last visits to be actual visits, but everything in between will be happening in patients' homes," he says. Sablinski and his staff are out searching for "gizmos," he says, that will allow patients to monitor their own vital signs, for example, or consult with study investigators via Skype videoconferencing.

Sablinski estimates that embracing telemedicine will allow Transparency to complete a clinical trial for about $700,000 - half of what it would cost if it were farmed out to a contract research organization. "CROs make money by introducing inefficiencies into the model," he says. "It's mind boggling. The savings are not going to be possible across all indications, but most trials can be done with a huge complement of telemedicine."

Transparency isn't the only pharma company dabbling in telemedicine. Last June, Pfizer announced a virtual trial of its marketed product tolterodine tartrate (Detrol LA) for overactive bladder. The company said the goal of the trial is to prove that patients in remote locales could participate in clinical trials by using their mobile phones and the Internet to provide data to trial investigators.

When Sablinski went to the FDA for preliminary discussions, he says, the agency was already inspired by Pfizer's lead. "The FDA wants trials to be patient-centric and they have guidelines for telemedicine," he says. "I don't expect much pushback from the FDA."

Sablinski, who once led clinical development and medical affairs for Novartis, is self-funding Transparency and running it when he's not at his day job as head of clinical development at Celtic Therapeutics, a life sciences private equity firm in New York. He says he wants to prove out his model before approaching venture capitalists.

At first, he struggled to persuade folks in pharma that his idea had legs, he says, but he quickly recruited some pretty impressive co-founders: Marc Foster, who commercialized a technology from MIT for FoldRx Pharmaceuticals and then sold the company to Pfizer; Martin Streeter, an e-health entrepreneur; and Lawrence Steinman, an MS specialist who is professor of neurology and neurological sciences, pediatrics, and genetics at Stanford School of Medicine.

Ultimately, Sablinski says, his goal is to use his open-source development model to rescue experimental drugs that have been shelved by cash-strapped pharmaceutical companies. "The real target is to get all these disparate assets from pharma - compounds that can't move because they require budgets that are too high," he says. "We will try to develop them with beautiful ideas from the crowd."

Transparency is a long way from proving that its transparent approach to drug development will actually work, but Sablinski's confidence is unwavering. On January 31, he announced the launch of the company during a speech he made at a conference in Philadelphia called Patient Centricity in Clinical Trials. Sablinski joked to the crowd that the pharma industry needing an official get-together to talk about how best to serve patients was akin to Detroit automakers having a meeting about driver-friendly car design. "Think about the state of the industry," he says. "You have to have a separate meeting to talk about patient-centric clinical trials? Pharma should be driven by what patients need."

http://www.eurekalert.org/pub_releases/2012-02/cwru-hha022412.php

How heavy and light isotopes separate in magma

Mass wins the race toward cool -- and leaves a clue to igneous rock formation

In the crash-car derby between heavy and light isotopes vying for the coolest spots as magma turns to solid rock, weightier isotopes have an edge, research led by Case Western Reserve University shows.

This tiny detail may offer clues to how igneous rocks form.

As molten rock cools along a gradient, atoms want to move towards the cool end.

This happens because hotter atoms move faster than cooler atoms and, therefore, hotter atoms move to the cool region faster than the cooler atoms move to the hot region.

Although all isotopes of the same element want to move towards the cool end, the big boys have more mass and, therefore, momentum, enabling them to keep moving on when they collide along the way.

"It's as if you have a crowded, sealed room of sumo wrestlers and geologists and a fire breaks out at one side of the room," said Daniel Lacks, chemical engineering professor and lead author of the paper.

"All will try to move to the cooler side of the room, but the sumo wrestlers are able to push their way through and take up space on the cool side, leaving the geologists on the hot side of the room."

Lacks worked with former postdoctoral researcher Gaurav Goel and geology professor James A.

Van Orman at Case Western Reserve; Charles J. Bopp IV and Craig C. Lundstrum, of University of Illinois, Urbana; and Charles E. Lesher of the University of California at Davis.

They described their theory and confirming mathematics, computer modeling, and experiments in the current issue of Physical Review Letters.

Lacks, Van Orman and Lesher also published a short piece in the current issue of Nature, showing how their findings overturn an explanation based on quantum mechanics, published in that journal last year.

"The theoretical understanding of thermal isotope separation in gases was developed almost exactly 100 years ago by David Enskog, but there is as yet not a similar full understanding of this process in liquids," said Frank Richter, who is the Sewell Avery Distinguished Professor at the University of Chicago and a member of the National Academy of Sciences. He was not involved in the research.

"This work by Lacks et al. is an important step towards remedying this situation."

This separation among isotopes of the same element is called fractionation.

Scientists have been able to see fractionation of heavy elements in igneous rocks only since the 1990s, Van Orman said.

More sensitive mass spectrometers showed that instead of a homogenous distribution, the concentration ratio of heavy isotopes to light isotopes in some igneous rocks was up to 0.1 percent higher than in other rocks.

One way of producing this fractionation is by temperature.

To understand how this happens, the team of researchers created a series of samples made of molten magnesium silicate infused with elements of different mass, from oxygen on up to heavy uranium.

The samples, called silicate melts, were heated at one end in a standard lab furnace, creating temperature gradients in each. The melts were then allowed to cool and solidify.

The scientists then sliced the samples along gradient lines and dissolved the slices in acid.

Analysis showed that no matter the element, the heavier isotopes slightly outnumbered the lighter at the cool end of the gradient.

Computer simulations of the atoms, using classical mechanics, agreed with the experimental results.

"The process depends on temperature differences and can be seen whether the temperature change across the sample is rapid or gradual," Lacks said.

Thermal diffusion through gases was one of the first methods used to separate isotopes, during the Manhattan Project.

It turns out that isotope fractionation through silicate liquids is even more efficient than through gases.

"Fractionation can occur inside the Earth wherever a sustained temperature gradient exists," Van Orman said. "One place this might happen is at the margin of a magma chamber, where hot magma rests against cold rock.

Another is nearly 1,800 miles inside the Earth, at the boundary of the liquid core and the silicate mantle."

The researchers are now adding pressure to the variables as they investigate further.

This work was done at atmospheric pressure but where the Earth's core and mantle meet, the pressure is nearly 1.4 million atmospheres.

Lacks and Van Orman are unsure whether high pressure will result in greater or lesser fractionation.

They can see arguments in favor of either.

http://www.eurekalert.org/pub_releases/2012-02/sp-crs022012.php

Could rosemary scent boost brain performance?

Hailed since ancient times for its medicinal properties, we still have a lot to learn about the effects of rosemary.

Now researchers writing in Therapeutic Advances in Psychopharmacology, published by SAGE, have shown for the first time that blood levels of a rosemary oil component correlate with improved cognitive performance.

Rosemary (Rosmarinus officinalis) is one of many traditional medicinal plants that yield essential oils. But exactly how such plants affect human behaviour is still unclear. Mark Moss and Lorraine Oliver, working at the Brain, Performance and Nutrition Research Centre at Northumbria University, UK designed an experiment to investigate the pharmacology of 1,8-cineole (1,3,3-trimethyl-2-oxabicyclo[2,2,2]octane), one of rosemary's main chemical components.

The investigators tested cognitive performance and mood in a cohort of 20 subjects, who were exposed to varying levels of the rosemary aroma. Using blood samples to detect the amount of 1,8-cineole participants had absorbed, the researchers applied speed and accuracy tests, and mood assessments, to judge the rosemary oil's affects.

Results indicate for the first time in human subjects that concentration of 1,8-cineole in the blood is related to an individual's cognitive performance - with higher concentrations resulting in improved performance. Both speed and accuracy were improved, suggesting that the relationship is not describing a speed - accuracy trade off.

Meanwhile, although less pronounced, the chemical also had an effect on mood. However, this was a negative correlation between changes in contentment levels and blood levels of 1,8-cineole, which is particularly interesting because it suggests that compounds given off by the rosemary essential oil affect subjective state and cognitive performance through different neurochemical pathways. The oil did not appear to improve attention or alertness, however.

Terpenes like 1,8-cineole can enter the blood stream via the nasal or lung mucosa. As small, fat-soluble organic molecules, terpenes can easily cross the blood - brain barrier. Volatile 1,8-cineole is found in many aromatic plants, including eucalyptus, bay, wormwood and sage in addition to rosemary, and has already been the subject of a number of studies, including research that suggests it inhibits acetylcholinesterase (AChE) and butyrylcholinesterase enzymes, important in brain and central nervous system neurochemistry: rosemary components may prevent the breakdown of the neurotransmitter acetylcholine.

"Only contentedness possessed a significant relationship with 1,8-cineole levels, and interestingly to some of the cognitive performance outcomes, leading to the intriguing proposal that positive mood can improve performance whereas aroused mood cannot," said Moss.

Typically comprising 35-45% by volume of rosemary essential oil, 1,8-cineole may possess direct pharmacological properties. However, it is also possible that detected blood levels simply serve as a marker for relative levels of other active compounds present in rosemary oil, such as rosmarinic acid and ursolic acid, which are present at much lower concentrations.

For an embargoed copy of the article please contact: jayne.fairley@sagepub.co.uk

Plasma 1,8-cineole correlates with cognitive performance following exposure to rosemary essential oil aroma by Mark Moss and Lorraine Oliver is published today, 24th February in Therapeutic Advances in Psychopharmacology.

http://www.sciencedaily.com/releases/2012/02/120225110942.htm

European Neanderthals Were On the Verge of Extinction Even Before the Arrival of Modern Humans

New findings from an international team of researchers show that most Neanderthals in Europe died off around 50,000 years ago.

ScienceDaily - The previously held view of a Europe populated by a stable Neanderthal population for hundreds of thousands of years up until modern humans arrived must therefore be revised. This new perspective on the Neanderthals comes from a study of ancient DNA published February 25 in Molecular Biology and Evolution.

The results indicate that most Neanderthals in Europe died off as early as 50,000 years ago. After that, a small group of Neanderthals recolonised central and western Europe, where they survived for another 10,000 years before modern humans entered the picture. The study is the result of an international project led by Swedish and Spanish researchers in Uppsala, Stockholm and Madrid.

“The fact that Neanderthals in Europe were nearly extinct, but then recovered, and that all this took place long before they came into contact with modern humans came as a complete surprise to us. This indicates that the Neanderthals may have been more sensitive to the dramatic climate changes that took place in the last Ice

Age than was previously thought", says Love Dalén, associate professor at the Swedish Museum of Natural History in Stockholm.

In connection with work on DNA from Neanderthal fossils in Northern Spain, the researchers noted that the genetic variation among European Neanderthals was extremely limited during the last ten thousand years before the Neanderthals disappeared.

Older European Neanderthal fossils, as well as fossils from Asia, had much greater genetic variation, on par with the amount of variation that might be expected from a species that had been abundant in an area for a long period of time. "The amount of genetic variation in geologically older Neanderthals as well as in Asian Neanderthals was just as great as in modern humans as a species, whereas the variation among later European Neanderthals was not even as high as that of modern humans in Iceland", says Anders Götherström, associate professor at Uppsala University.

The results presented in the study are based entirely on severely degraded DNA, and the analyses have therefore required both advanced laboratory and computational methods. The research team has involved experts from a number of countries, including statisticians, experts on modern DNA sequencing and paleoanthropologists from Denmark, Spain and the US.

Only when all members of the international research team had reviewed the findings could they feel certain that the available genetic data actually reveals an important and previously unknown part of Neanderthal history. "This type of interdisciplinary study is extremely valuable in advancing research about our evolutionary history. DNA from prehistoric people has led to a number of unexpected findings in recent years, and it will be really exciting to see what further discoveries are made in the coming years", says Juan Luis Arsuaga, professor of human paleontology at the Universidad Complutense of Madrid.

http://www.eurekalert.org/pub_releases/2012-02/mgh-mgr022112.php

Mass. General researchers isolate egg-producing stem cells from adult human ovaries

Findings support continued egg-cell production throughout reproductive life

For the first time, Massachusetts General Hospital (MGH) researchers have isolated egg-producing stem cells from the ovaries of reproductive age women and shown these cells can produce what appear to be normal egg cells or oocytes. In the March issue of Nature Medicine, the team from the Vincent Center for Reproductive Biology at MGH reports the latest follow-up study to their now-landmark 2004 Nature paper that first suggested female mammals continue producing egg cells into adulthood.

"The primary objective of the current study was to prove that oocyte-producing stem cells do in fact exist in the ovaries of women during reproductive life, which we feel this study demonstrates very clearly," says Jonathan Tilly, PhD, director of the Vincent Center for Reproductive Biology in the MGH Vincent Department of Obstetrics and Gynecology, who led the study. "The discovery of oocyte precursor cells in adult human ovaries, coupled with the fact that these cells share the same characteristic features of their mouse counterparts that produce fully functional eggs, opens the door for development of unprecedented technologies to overcome infertility in women and perhaps even delay the timing of ovarian failure."

The 2004 report from Tilly's team challenged the fundamental belief, held since the 1950s, that female mammals are born with a finite supply of eggs that is depleted throughout life and exhausted at menopause. That paper and a 2005 follow-up published in Cell showing that bone marrow or blood cell transplants could restore oocyte production in adult female mice after fertility-destroying chemotherapy were controversial; but in the intervening years, several studies from the MGH-Vincent group and other researchers around the world have supported Tilly's work and conclusions.

These supporting studies include a 2007 Journal of Clinical Oncology report from the MGH-Vincent team that showed female mice receiving bone marrow transplants after oocyte-destroying chemotherapy were able to have successful pregnancies, delivering pups that were their genetic offspring and not of the marrow donors. A 2009 study from a team at Shanghai Jiao Tong University in China, published in Nature Cell Biology, not only isolated and cultured oocyte-producing stem cells (OSCs) from adult mice but also showed that those OSCs, after transplantation into the ovaries of chemotherapy-treated female mice, gave rise to mature oocytes that were ovulated, fertilized and developed into healthy offspring.

"That study singlehandedly deflated many of the arguments from critics of our earlier Nature paper by showing that oocyte-producing stem cells exist in mice and could develop into fully functional eggs," says Tilly. Another paper from a west-coast biotechnology company, published in Differentiation in 2010, provided further independent confirmation of Tilly's earlier conclusions regarding the presence of oocyte-producing stem cells in ovaries of adult mice.

Tilly is quick to point out, however, "These follow-up studies, while providing definitive evidence that oocyte-producing stem cells exist in ovaries of adult female mammals, were not without their limitations, leaving the question open in some scientific circles of whether the adult oocyte pool can be renewed. For example, the protocol used to isolate OSCs in the 2009 Nature Cell Biology study is a relatively crude approach that often results in the contamination of desired cells by other cell types." To address this, the MGH-Vincent team developed and validated a much more precise cell-sorting technique to isolate OSCs without contamination from other cells.

The 2009 study from China also had isolated OSCs based on cell-surface expression of a marker protein called Ddx4 or Mvh, which previously had been found only in the cytoplasm of oocytes. This apparent contradiction with earlier studies raised concerns over the validity of the protocol. Using their state-of-the-art fluorescence-activated cell sorting techniques, the MGH-Vincent team verified that, while the marker protein Ddx4 was indeed located inside oocytes, it was expressed on the surface of a rare and distinct population of ovarian cells identified by numerous genetic markers and functional tests as OSCs.

To examine the functional capabilities of the cells isolated with their new protocol, the investigators injected green fluorescent protein (GFP)-labeled mouse OSCs into the ovaries of normal adult mice. Several months later, examination of the recipient mouse ovaries revealed follicles containing oocytes with and without the marker protein. GFP-labeled and unlabeled oocytes also were found in cell clusters flushed from the animals' oviducts after induced ovulation. The GFP-labeled mouse eggs retrieved from the oviducts were successfully fertilized in vitro and produced embryos that progressed to the hatching blastocyst stage, a sign of normal developmental potential. Additionally, although the Chinese team had transplanted OSCs into ovaries of mice previously treated with chemotherapy, the MGH-Vincent team showed that it was not necessary to damage the recipient mouse ovaries with toxic drugs before introducing OSCs.

In their last two experiments, which Tilly considers to be the most groundbreaking, the MGH-Vincent team used their new cell-sorting techniques to isolate potential OSCs from adult human ovaries. The cells obtained shared all of the genetic and growth properties of the equivalent cells isolated from adult mouse ovaries, and like mouse OSCs, were able to spontaneously form cells with characteristic features of oocytes. Not only did these oocytes formed in culture dishes have the physical appearance and gene expression patterns of oocytes seen in human ovaries – as was the case in parallel mouse experiments – but some of these in-vitro-formed cells had only half of the genetic material normally found in all other cells of the body. That observation indicates that these oocytes had progressed through meiosis, a cell-division process unique to the formation of mature eggs and sperm.

The researchers next injected GFP-labeled human OSCs into biopsied human ovarian tissue that was then grafted beneath the skin of immune-system-deficient mice. Examination of the human tissue grafts 7 to 14 days later revealed immature human follicles with GFP-negative oocytes, probably present in the human tissue before OSC injection and grafting, as well as numerous immature human follicles with GFP-positive oocytes that would have originated from the injected human OSCs.

"These experiments provide pivotal proof-of-concept that human OSCs reintroduced into adult human ovarian tissue performed their expected function of generating new oocytes that become enclosed by host cells to form new follicles," says Tilly, a professor of Obstetrics, Gynecology and Reproductive Biology at Harvard Medical School and chief of Research at the MGH Vincent Department of Obstetrics and Gynecology. "These outcomes are exactly what we see if we perform the same experiments using GFP-expressing mouse OSCs, and GFP-expressing mouse oocytes formed that way go on to develop into fully functional eggs.

"In this paper we provide the three key pieces of evidence requested by those who have been skeptical of our previous work," he adds. "We developed and extensively validated a cell-sorting protocol to reliably purify OSCs from adult mammalian ovaries, proving once again that these very special cells exist. We tested the function of mouse oocytes produced by these OSCs and showed that they can be fertilized to produce healthy embryos. And we identified and characterized an equivalent population of oocyte-producing stem cells isolated from adult human ovaries."

Among the many potential clinical applications for these findings that Tilly's team is currently exploring are the establishment of human OSC banks – since these cells, unlike human oocytes, can be frozen and thawed without damage – the identification of hormones and factors that accelerate the formation of oocytes from human OSCs, the development of mature human oocytes from OSCs for in vitro fertilization, and other approaches to improve the outcomes of IVF and other infertility treatments.

Tilly notes that an essential part of his group's accomplishment was collaboration with study co-author Yasushi Takai, MD, PhD, a former MGH research fellow on Tilly's team and now a faculty member at Saitama Medical University in Japan.

Working with his clinical colleagues at Saitama, Takai was able to provide healthy ovarian tissue from consenting patients undergoing sex reassignment surgery, many in their 20s and early 30s. Co-lead authors of the Nature Medicine report are Yvonne White, PhD, and Dori Woods, PhD, of the Vincent Center for Reproductive Biology at MGH. Additional co-authors are Osamu Ishihara, MD, PhD, and Hiroyuki Seki, MD, PhD, of Saitama Medical University.
The study was supported by a 10-year MERIT Award to Tilly from the National Institute on Aging, a Ruth L. Kirschstein National Research Service Award from the National Institutes of Health, the Henry and Vivian Rosenberg Philanthropic Fund, the Sea Breeze Foundation, and Vincent Memorial Hospital Research Funds. Tilly is a co-founder of OvaScience, Inc. (www.ovascience.com), which has licensed the commercial potential of these and other patent-protected findings of the MGH-Vincent team for development of new fertility-enhancing procedures.

http://news.discovery.com/human/apology-obama-koran-tiger-120226.html

Apologies: Do They Make It All Better?

At their best, public apologies restore relationships or even improve them. At their worst...

By Sheila Eldred Sun Feb 26, 2012 11:09 AM ET

In the past seven days, President Barack Obama has apologized to Afghanistan for NATO troops burning Qurans; German Chancellor Angela Merkel apologized to the relatives of 10 people believed to have been killed by a neo-Nazi group; the Mormon Church said it would discipline members who may have posthumously baptized Anne Frank; and a rising PGA golfer apologized for spitting on the course.

At their best, public apologies restore relationships or even improve them. At their worst, the perpetrator ends up needing to apologize for the botched attempt and the initial offense, said attorney and business ethics expert Lauren Bloom, author of "The Art of the Apology." Even a lousy attempt, however, is better than nothing.

"In many situations, an awkward initial apology can be remedied with a follow-up effort, especially if the person receiving the apology believes that the person making the apology was sincere," she said. "When something goes wrong, people often need to talk about it more than once. Even a clumsy apology can open the door to a healing dialogue."

Whether public or private, sincerity is the most essential element of an apology, experts agree. That adds a layer of complexity to public apologies: there's no lack of public opinion to suggest ulterior motives, said Ryan Fehr, assistant professor of management at the University of Washington, whose PhD is in psychology.

"For example, when (NFL star) Michael Vick tried to show he was apologetic for animal abuse, there were plenty of people to suggest that he was just trying to get back in the good graces of the sports league so he could play again," Fehr said.

Or take the case of golf's rising star Keegan Bradley, who apologized on Twitter this week for his habit of spitting. "It's like a reflex; I don't even know I'm doing it," he tweeted.

The incident became so public "even the golfer couldn't believe how many people cared," said Jennifer Thomas, co-author of "The Five Languages of Apology," who has a PhD in clinical psychology. "He said he didn't know why people were so interested in him."

Since the whole world is watching, Bloom said, public figures often work so hard scripting their speeches that the apology doesn't seem sincere.

"The longer you put it off and the more you polish it, you'll deliver something so perfect people don't believe it," Bloom said. "A lot of actors do this because they're performers anyway."

When done well, the effects of an apology are overwhelmingly positive.

"What an apology does is split the action and the person," said Fehr, who has published papers on apologies that work. "It says, the action was bad, but I'm not actually a bad person; I mean well. They can regain their status in the community. For the victim, it allows the process of forgiveness to get started."

So, what's the perfect apology? Experts have their own multi-faceted definitions, but they share common elements:

Timing: *The person making the apology needs to wait long enough to determine exactly what the apology is for, but no longer, Bloom says.*

Genuine repentance

Expression of regret: *"We all have our own scripts from childhood, what we were taught to say," Thomas said. The language, therefore, may vary and is most effective when it matches the language of the victim.*

Making amends: *Future actions are important, too. If the perpetrator shows the victim he or she will do better next time, forgiveness is easier.*

Taking responsibility

Emotional connection: *Recognizing that the pain you've caused also causes you pain helps the victim and perpetrator connect*

Willingness to listen to the victim

What perfect apologies don't do: Get defensive, deny, or use the conditional. Politicians often make this mistake, Bloom said, with lines like, “I apologize if I offended anyone.” “Their sincerity immediately comes into question,” Bloom said. “You know you have to apologize or you wouldn’t be doing it.”

Whether an apology works depends in large part on the person or people being apologized to. Reactions to apologies vary widely.

“When we surveyed 500 people about what they're looking to hear in an apology, their answers fell into five areas,” Thomas said. “I had thought that one of the five categories would get that most votes, and I thought it would be saying, ‘I'm sorry.’ But none of the five got more than 28 percent.”

How did this week’s apologies rate?

Obama hit many of the essential elements, experts said, in his apology to Afghanistan.

“President Obama generally does really well,” Bloom said. “He doesn’t delay. If he makes a mistake he admits it immediately and apologizes. He’s got the vernacular down: he talks like a real person, which makes him much more credible. He made one mistake in this apology: he said it was an accident. It wasn’t an accident; it was a mistake. But I give him more points for doing it immediately than not having the language perfect.”

Merkel’s apology was exceptionally spot-on, Bloom said. Americans often have a hard time admitting weakness, Bloom said. Merkel’s statement backs up her theory that Europeans are more comfortable apologizing.

The Mormon Church didn’t fare as well with its reaction to the Anne Frank baptism, experts agreed, appearing somewhat disingenuous.

“If more baptisms of Holocaust victims and survivors slip through the cracks, the church's statements of concern and remorse could be increasingly perceived as insincere,” Fehr said. “To demonstrate the sincerity of their concern and remorse, the church must devote sufficient resources to ensure that new names submitted for baptism are properly researched and checked.”

A hefty donation to the Holocaust Museum wouldn’t hurt, Bloom added.