http://www.eurekalert.org/pub_releases/2012-03/cumc-ana030912.php

A new approach to treating type I diabetes? Gut cells transformed into insulin factories

Study suggests a new approach could give patients the ability to make their own insulin-producing cells without a stem cell transplant

NEW YORK, NY -- A study by Columbia researchers suggests that cells in the patient's intestine could be coaxed into making insulin, circumventing the need for a stem cell transplant. Until now, stem cell transplants have been seen by many researchers as the ideal way to replace cells lost in type I diabetes and to free patients from insulin injections.

The research—conducted in mice—was published 11 March 2012 in the journal Nature Genetics.

Type I diabetes is an autoimmune disease that destroys insulin-producing cells in the pancreas. The pancreas cannot replace these cells, so once they are lost, people with type I diabetes must inject themselves with insulin to control their blood glucose. Blood glucose that is too high or too low can be life threatening, and patients must monitor their glucose several times a day.

A longstanding goal of type I diabetes research is to replace lost cells with new cells that release insulin into the bloodstream as needed. Though researchers can make insulin-producing cells in the laboratory from embryonic stem cells, such cells are not yet appropriate for transplant because they do not release insulin appropriately in response to glucose levels. If these cells were introduced into a patient, insulin would be secreted when not needed, potentially causing fatal hypoglycemia.

The study, conducted by Chutima Talchai, PhD, and Domenico Accili, MD, professor of medicine at Columbia University Medical Center, shows that certain progenitor cells in the intestine of mice have the surprising ability to make insulin-producing cells. Dr. Talchai, who works in Dr. Accili's lab, is a New York Stem Cell Foundation-Druckenmiller Fellow.

The gastrointestinal progenitor cells are normally responsible for producing a wide range of cells, including cells that produce serotonin, gastric inhibitory peptide, and other hormones secreted into the GI tract and bloodstream.

Drs. Talchai and Accili found that when they turned off a gene known to play a role in cell fate decisions—Foxo1—the progenitor cells also generated insulin-producing cells. More cells were generated when Foxo1 was turned off early in development, but insulin-producing cells were also generated when the gene was turned off after the mice had reached adulthood.

"Our results show that it could be possible to regrow insulin-producing cells in the GI tracts of our pediatric and adult patients," Dr. Accili says.

"Nobody would have predicted this result," Dr. Accili adds. "Many things could have happened after we knocked out Foxo1. In the pancreas, when we knock out Foxo1, nothing happens. So why does something happen in the gut? Why don't we get a cell that produces some other hormone? We don't yet know."

Insulin-producing cells in the gut would be hazardous if they did not release insulin in response to blood glucose levels. But the researchers say that the new intestinal cells have glucose-sensing receptors and do exactly that.

The insulin made by the gut cells also was released into the bloodstream, worked as well as normal insulin, and was made in sufficient quantity to nearly normalize blood glucose levels in otherwise diabetic mice.

"All these findings make us think that coaxing a patient's gut to make insulin-producing cells would be a better way to treat diabetes than therapies based on embryonic or iPS stem cells," Dr. Accili says. The location of the cells in the gut may also prevent the diabetes from destroying the new insulin-producing cells, since the gastrointestinal tract is partly protected from attack by the immune system.

The key to turning the finding into a viable therapy, Dr. Accili says, will be to find a drug that has the same effect on the gastrointestinal progenitor cells in people as knocking out the Foxo1 gene does in mice. That should be possible, he says, since the researchers found that they could also create insulin-producing cells from progenitor cells by inhibiting Foxo1 with a chemical.

"It's important to realize that a new treatment for type I diabetes needs to be just as safe as, and more effective than, insulin," Dr. Accili says. "We can't test treatments that are risky just to remove the burden of daily injections. Insulin is not simple or perfect, but it works and it is safe."

Additional contributors are Shouhong Xuan (CUMC), Tadahiro Kitamura (Gunma University, Maebashi, Japan), and Ronald A DePinho (Harvard Medical School).

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The authors report no financial or other conflict of interest.

http://www.eurekalert.org/pub_releases/2012-03/w-cmh030712.php

Circumcision may help protect against prostate cancer

A new analysis led by researchers at Fred Hutchinson Cancer Research Center has found that circumcision before a male's first sexual intercourse may help protect against prostate cancer.

Published early online in Cancer, a peer-reviewed journal of the American Cancer Society, the study suggests that circumcision can hinder infection and inflammation that may lead to this malignancy.

Infections are known to cause cancer, and research suggests that sexually transmitted infections may contribute to the development of prostate cancer. Also, certain sexually transmitted infections can be prevented by circumcision. Therefore, it stands to reason that circumcision should protect against the development of some cases of prostate cancer. This is what lead author Jonathan L. Wright, MD, an affiliate investigator in the Hutchinson Center's Public Health Sciences Division, and his colleagues set out to test.

For their study, the investigators analyzed information from 3,399 men (1,754 with prostate cancer and 1,645 without). Men who had been circumcised before their first sexual intercourse were 15 percent less likely to develop prostate cancer than uncircumcised men. This reduced risk applied for both less aggressive and more aggressive cancers. (Specifically, men circumcised before their first sexual intercourse had a 12 percent reduced risk for developing less aggressive prostate cancer and an 18 percent reduced risk for developing more aggressive prostate cancer.)

Sexually transmitted infections may lead to prostate cancer by causing chronic inflammation that creates a hospitable environment for cancer cells. Other mechanisms may also be involved. Circumcision may protect against sexually transmitted infections, and therefore prostate cancer, by toughening the inner foreskin and by getting rid of the moist space under the foreskin that may help pathogens survive.

"These data are in line with an infectious/inflammatory pathway which may be involved in the risk of prostate cancer in some men," said Dr. Wright, who is also an assistant professor of urology at the University of Washington School of Medicine. "Although observational only, these data suggest a biologically plausible mechanism through which circumcision may decrease the risk of prostate cancer. Future research of this relationship is warranted," he added.

http://www.eurekalert.org/pub_releases/2012-03/uob-ant031212.php

A new theory on the formation of the oldest continents

Geologists at the Universities of Bonn and Cologne have come up with a new idea as to how the earliest continents were formed

The earth's structure can be compared to an orange: its crust is the peel supported by the earth's heavy mantle. That peel is made up of a continental crust 30 to 40 kilometers thick. It is much lighter than the thinner oceanic crust and protrudes from the earth's mantle because of its lower density, like an iceberg in the sea. "According to the current theory, the first continental crusts were formed when tectonic plates would collide, submerging oceanic crusts into the earth's mantle, where they would partially melt at a depth of approximately 100 kilometers. That molten rock then ascended to the earth's surface and formed the first continents," says adjunct professor Dr. Thorsten Nagel of the Steinmann Institute of Geosciences at the University of Bonn, lead author of the study. The theory has been supported by the oldest known continental rocks – approximately 3.8 billion years old – found in western Greenland.

Following trace elements

The composition of the continental crust corresponds to a semiliquid version of the oceanic crust melted by 10 to 30 percent of its original state. Unfortunately, the concentrations of the main chemical components in the re-solidified rock do not provide much information about what depth the fusion occurred at. "In order to find that out, you have to know what minerals the remaining 70 to 90 percent of the oceanic crust consisted of," explains Prof. Dr. Carsten Münker of the Institute of Geology and Mineralogy at the University of Cologne. Researchers from Bonn and Cologne have now analyzed the Greenlandic rocks for different elements occurring at various high concentrations, also know as trace elements. "Trace elements provide geologists with a window to the origin of continental crust," says Prof. Münker. "With their help, we can identify minerals in the residual rock that were deposited in the depths by the molten rock."

Before the magma separated from the bedrock, the semifluid rock and the leftover solid minerals actively exchanged trace elements. "Different minerals have characteristic ways of separating when trace elements are smelted. In other words, the concentration of trace elements in the molten rock provide a fingerprint of the residual bedrock," explains Dr. Elis Hoffmann from Bonn, coauthor of the study. The concentration of trace elements in the oldest continental rock allows geoscientists to reconstruct possible bedrock based on their minerals and thus determine at what depth the continental crust originated.

The oceanic crust did not have to descend

Using computers, the scientists simulated the composition of bedrock and molten rock that would emerge from partially melting the oceanic crust at various depths and temperatures. They then compared the data calculated for the molten rock with the actual concentration of trace elements in the oldest continental rocks. "Our results paint a surprising picture," Dr. Nagel reports. "The oceanic crust did not have to descend to a depth of 100 kilometers to create the molten rock that makes up the rocks of the first continents." According to the calculations, a depth of 30 to 40 kilometers is much more probable.

The primeval oceanic crust could have 'oozed' continents

…it could definitely have had the power to do so in the Archean eon. Four billion years ago, the gradually cooling earth was still significantly warmer than it is today. The oceanic crust could have simply 'oozed' continents at the same time that other geological processes were occurring, like volcanism, orogeny, and the influx of water. "We think it is unlikely that the contents were formed into subduction zones. Whether or not tectonic plates of the primordial earth had such zones of subsidence is still a matter of debate," says the geologist from Bonn.

Publication: Generation of Eoarchean tonalite-trondhjemite-granodiorite series from thickened mafic arc crust, Geology, DOI: 10.1130/G32729.1

http://www.eurekalert.org/pub_releases/2012-03/uocd-mss030712.php

Major study stops bladder cancer from metastasizing to lungs

The diagnosis of localized bladder cancer carries an 80 percent five-year survival rate, but once the cancer spreads, the survival rate at even three years is only 20 percent.

A major study published today in the Journal of Clinical Investigation not only shows how bladder cancer metastasizes to the lungs but pinpoints a method for stopping this spread.

Specifically, the study shows that versican, a protein involved in cancer cell migration, is a driver of lung metastasis and that high levels of versican are associated with poor prognosis in bladder cancer patients. The study is the first to show how that when a cancer cell makes the protein RhoGDI2, it reduces the cell's production of versican, thus blocking the ability of the cancer cell to grow in the lungs.

"For a decade, we've known that the major challenge of treating bladder cancer is treating or preventing the metastatic form of the disease. This study represents an advance in the latter – by preventing the spread of bladder cancer to the lungs, we could improve patient survival," says Dan Theodorescu, MD, PhD, director of the University of Colorado Cancer Center, the paper's senior author.

When a cancer metastasizes from its birth location to another, it's not necessarily that cells suddenly become mobile and thus able to float through the blood or lymph to new homes. In fact, these cancer cells may have been floating through a patient's blood for quite some time, and metastasis occurs only when one of these intrepid cells is finally able to grow in the place where it is attached, such as the lungs.

When the first cancer cells to attach to, say, the lung, they have a tough time – they become distressed. Cancer cells express this distress in the form of versican. And the more versican they express, the more help they get, which arrives in the form of macrophages, a part of the body's immune response that eat pathogens and other debris.

In most cases, the fact that macrophages benefit distressed cells is good, but in addition to helping healthy cells survive, these arriving macrophages also promote the growth of cancer cells that have landed in distant sites such as the lung, thus promoting metastasis of the disease.

More versican made by the cancer cells calls more macrophages, which aid cancer cells' survival and increase the likelihood that a cancer cell's toehold will develop into a clinically significant tumor in the lung.

Theodorescu and colleagues showed that the protein RhoGDI2 reduces the expression of versican. Cancer cells that make more RhoDI2 produce less versican and thus call fewer macrophages, making it difficult for these high-RhoGDI2 cancer cells to survive.

Sure enough, when Theodorescu and colleagues added RhoGDI2 to tumors, versican went down and with it so did metastasis.

"We believe this study provides an important contribution to the scientific literature by delineating for the first time a new mechanism of metastasis suppression, namely that suppression of metastasis is possible by altering the tumor microenvironment, including reducing the presence macrophages," Theodorescu says.

In fact, this paper also shows for the first time one more step: versican's ability to attract macrophages to the tumor depends on a protein called CCL2. This step is important because drugs that inhibit CCL2 are already in clinical trials for other conditions.

If the effect in humans is the same as the effect in the laboratory – namely that inhibiting CCL2 reduces versican's ability to attract the macrophages that promote tumor growth at distant sites – one of these CCL2 inhibitors could soon become part of the treatment regimen for bladder cancer patients with tumors that make low levels of RhoGDI2 and high versican. This approach has the potential to lower the chance of bladder cancer metastasis and thus a significantly improved outcome for patients with high risk bladder cancer.

http://www.eurekalert.org/pub_releases/2012-03/jaaj-mrm030812.php

More red meat consumption appears to be associated with increased risk of death

Eating more red meat appears to be associated with an increased risk of all-cause mortality and death from cardiovascular disease and cancer

CHICAGO – Eating more red meat appears to be associated with an increased risk of all-cause mortality and death from cardiovascular disease and cancer, but substituting other foods including fish and poultry for red meat is associated with a lower mortality risk, according to a study published Online First by Archives of Internal Medicine, one of the JAMA/Archives journals.

Meat is a major source of protein and fat in many diets and previous studies suggest that eating meat is associated with increased risk for diabetes, cardiovascular disease (CVD) and certain cancers, the authors write in their study background.

An Pan, Ph.D., of the Harvard School of Public Health, Boston, and colleagues analyzed data from two prospective cohort studies with repeated measures of diet and up to 28 years of follow-up. Data from 37,698 men and 83,644 women were used. Researchers documented 23,926 deaths, including 5,910 from CVD and 9,464 from cancer.

"We found that a higher intake of red meat was associated with a significantly elevated risk of total, CVD and cancer mortality, and this association was observed for unprocessed and processed red meat, with a relatively greater risk for processed red meat," the authors comment. "Substitution of fish, poultry, nuts, legumes, low-fat dairy products and whole grains for red meat was associated with a significantly lower risk of mortality."

The elevated risk of total mortality in the pooled analysis for a one-serving-per-day increase was 12 percent for total red meat, 13 percent for unprocessed red meat and 20 percent for processed red meat, the results indicate.

In their substitution analyses, the authors estimated that replacing one serving of total red meat with one serving of fish, poultry, nuts, legumes, low-fat dairy products or whole grains daily was associated with a lower risk of total mortality: 7 percent for fish, 14 percent for poultry, 19 percent for nuts, 10 percent for legumes, 10 percent for low-fat dairy products and 14 percent for whole grains.

"We estimated that 9.3 percent in men and 7.6 percent in women of total deaths during follow-up could be prevented if all the participants consumed fewer than 0.5 servings per day of total red meat in these cohorts," they comment.

Commentary: What is Good for Patients is Good for the Planet

In an invited commentary, Dean Ornish, M.D., of the University of California, San Francisco, writes: "In addition to their health benefits, the food choices we make each day affect other important areas as well. What is personally sustainable is globally sustainable. What is good for you is good for our planet."

"More than 75 percent of the $2.6 trillion in annual U.S. health care costs are from chronic disease. Eating less red meat is likely to reduce morbidity from these illnesses, thereby reducing health care costs," he comments.

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http://www.eurekalert.org/pub_releases/2012-03/uom-bcm031312.php

Body clocks may hold key for treatment of bipolar disorder

Scientists have gained insight into why lithium salts are effective at treating bipolar disorder in what could lead to more targeted therapies with fewer side-effects.

Bipolar disorder is characterised by alternating states of elevated mood, or mania, and depression. It affects between 1% and 3% of the general population. The extreme 'mood swings' in bipolar disorder have been strongly associated with disruptions in circadian rhythms – the 24-hourly rhythms controlled by our body clocks that govern our day and night activity.

For the last 60 years, lithium salt (lithium chloride) has been the mainstay treatment for bipolar disorder but little research has been carried out to find out whether and how lithium impacts on the brain and peripheral body clockwork.

"Our study has shown a new and potent effect of lithium in increasing the amplitude, or strength, of the clock rhythms, revealing a novel link between the classic mood-stabiliser, bipolar disorder and body clocks," said lead researcher Dr Qing-Jun Meng, in the University's Faculty of Life Sciences.

"By tracking the dynamics of a key clock protein, we discovered that lithium increased the strength of the clockwork in cells up to three-fold by blocking the actions of an enzyme called glycogen synthase kinase or GSK3.

"Our findings are important for two reasons: firstly, they offer a novel explanation as to how lithium may be able to stabilise mood swings in bipolar patients; secondly, they open up opportunities to develop new drugs for bipolar disorder that mimic and even enhance the effect lithium has on GSK3 without the side-effects lithium salts can cause."

These side-effects include nausea, acne, thirstiness, muscle weakness, tremor, sedation and/or confusion. Promisingly, GSK3 inhibiting drugs are already in development, as they have been shown to be important in other diseases, including diabetes and Alzheimer's disease.

Dr Meng added: "Lithium salt has a wide spectrum of targets within cells, in addition to GSK3; drugs which only block the actions of GSK3 would therefore have the major advantage of reduced 'off-target' effects of lithium. "Our study has identified the robust rhythm-enhancing effect of GSK3 inhibition, which has potential to be developed as a new pharmacological approach to regulate body clocks. The implications of our study are that there may also be beneficial effects leading to new treatments for bipolar disorder, and this now needs to be tested."

The research, funded by the Medical Research Council and the Biotechnology and Biological Sciences Research Council (BBSRC), is published in the journal PLoS One.

A copy of the PLoS One paper, 'Lithium Impacts on the Amplitude and Period of the Molecular Circadian Clockwork,' is available on request.

http://www.physorg.com/news/2012-03-skorean-russian-scientists-clone-mammoth.html

S.Korean, Russian scientists bid to clone mammoth

Stem cell scientists are now setting their sights on the extinct woolly mammoth

Russian and South Korean scientists have signed a deal on joint research intended to recreate a woolly mammoth, an animal which last walked the earth some 10,000 years ago.

The deal was signed by Vasily Vasiliev, vice rector of North-Eastern Federal University of the Sakha Republic, and controversial cloning pioneer Hwang Woo-Suk of South Korea's Sooam Biotech Research Foundation, on Tuesday.

Hwang was a national hero until some of his research into creating human stem cells was found in 2006 to have been faked. But his work in creating Snuppy, the world's first cloned dog, in 2005, has been verified by experts.

Stem cell scientists are now setting their sights on the extinct woolly mammoth, after global warming thawed Siberia's permafrost and uncovered remains of the animal.

Hwang was a national hero until some of his research on human stem cells was found to have been faked

Sooam said it would launch research this year if the Russian university can ship the remains. The Beijing Genomics Institute will also take part in the project.

The South Korean foundation said it would transfer technology to the Russian university, which has already been involved in joint research with Japanese scientists to bring a mammoth back to life.

"The first and hardest mission is to restore mammoth cells," another Sooam researcher, Hwang In-Sung, told AFP. His colleagues would join Russian scientists in trying to find well-preserved tissue with an undamaged gene.

By replacing the nuclei of egg cells from an elephant with those taken from the mammoth's somatic cells, embryos with mammoth DNA could be produced and planted into elephant wombs for delivery, he said.

Sooam will use an Indian elephant for its somatic cell nucleus transfer. The somatic cells are body cells, such as those of internal organs, skin, bones and blood.

"This will be a really tough job, but we believe it is possible because our institute is good at cloning animals," Hwang In-Sung said.

South Korean experts have previously cloned animals including a cow, a cat, dogs, a pig and a wolf.

Last October Hwang Woo-Suk unveiled eight cloned coyotes in a project sponsored by a provincial government.

http://www.eurekalert.org/pub_releases/2012-03/cuor-irf031312.php

Italian researchers found how to stop low back pain

Discovered the molecular mechanism responsible for vertebral column degeneration

Italian researchers at the Catholic University of Sacred Heart in Rome found an important molecular mechanism responsible for low back pain and other acute vertebral problems like cervical axial pain, all due to aging and degeneration of the vertebral column.

The team led by Dr. Luigi Aurelio Nasto and Enrico Pola also developed an experimental drug to inhibit this degenerative mechanism, by blocking its principal culprit, the molecule, "NF-kB" and tested it successfully in mice. The study was carried out in collaboration with the University of Pittsburgh research team led by Paul Robbins, James Kang and Nam Vo (e-mail: von@upmc.edu).

Researchers reported their findings in the February 16 online edition of the journal Spine.

Nasto and Pola found that high concentration of NF-kB causes the degeneration of intervertebral discs (the structures that separate and damp the vertebrae), a degenerative process that could affect also young adults (30 year old), especially if they adopt a sedentary lifestyle. In other words when NF-kB becomes overactive, it triggers a series of deleterious reactions that ultimately affect the physiological structure of the vertebral column.

Due to aging, obesity and sedentary lifestyle, intervertebral discs degenerate, leading to the progressive stiffening of the column. The intervertebral disc degeneration is responsible for syndromes such as chronic low back pain or neck pain that affects a large proportion of the adult population.

Back pain and neck pain are ranked among the leading causes of lost working hours and disability in adults Italian scientists found the mechanism behind the degenerative processes of the column. They studied mice that are genetically programmed to age rapidly (progeroid mice). The average lifespan of normal mice is 2 years. The progeroid mice age more quickly and have a lifespan of 8 months. The progeroid mice perfectly mimic the process of spine degeneration that occur in old people and young adults who suffer from low back pain.

The researchers found that NF-kB plays a role in the degeneration of the spine. NF-kB is a transcription factor, it modulates the activation of specific target genes. Researchers found that NF-kB activates many genes related to inflammation and turn off anti-inflammatory protective genes. Moreover in many studies NF-kB was found hyperactive in both the spines of old mice and old people.

The results of the Italian research suggest that NF-kB induces the onset of deleterious inflammatory processes and inhibit anti-inflammatory mechanisms. Moreover "our study shows that by inhibiting NF-kB, we can stop spine degeneration", Dr. Nasto says. "Drugs that turn off or even only partially inactivate NF-kB could be used to prevent the degeneration of intervertebral discs in patients."

"In our study, we developed a specific drug, called NBD peptide, able to specifically inhibit the deleterious action of NF-kB – dr Pola explains. NBD has been already successfully tested by a US team in Pittsburgh to slow the course of muscular dystrophy in an animal model (NF-kB is also involved in this disease). This peptide will be soon tested in a clinical trial (phase I) to study its therapeutic effects on Duchenne muscular dystrophy".

According to Nasto and Pola, NBD may also be used to counteract the aging of the vertebral column. "We hope to develop other selective inhibitors of NF-kB to slow the degeneration of intervertebral discs" and cure low back pain, Pola concludes.

http://www.sciencedaily.com/releases/2012/03/120313190054.htm

Cool Hands May Be the Key to Increasing Exercise Capacity

Cooling the palms of the hands while working out could help you stick with a physical activity program

ScienceDaily - Cooling the palms of the hands while working out could help you stick with a physical activity program, according to a small study presented at the American Heart Association's Epidemiology and Prevention/Nutrition, Physical Activity and Metabolism 2012 Scientific Sessions.

In the study, obese women who exercised while using the AvaCore Rapid Thermal Exchange (RTX palm cooling device) improved their exercise tolerance and cardiovascular fitness.

"Obese women often complain about sweating and getting tired because they're walking around with extra insulation," said Stacy T. Sims, Ph.D., the study's lead researcher and exercise physiologist and nutrition scientist at Stanford University in California. "If you can slow the rate internal temperature rises and cool someone who is obese, they don't store as much heat and don't feel as uncomfortable. They can do more work."

The cooling devices cooled the palms of the hand and circulating blood, thus pulling heat off the body.

Sims suggested that holding a bottle of cold water may also cool palms and help exercisers feel cooler, less sweaty and less fatigued -- allowing them to work out longer and make them more likely to stick with their exercise regimen.

For 12 weeks, researchers studied 24 women, 30-45 years old, who had a body mass index between 30 and 34.9, which is considered obese. Half worked out with their hands in a cylinder containing water at 60.8 degrees Fahrenheit. The other half used the same device with water at 98.6 degrees Fahrenheit. Participants didn't know the difference in their devices and did the same fitness activities, starting with push-ups, lunges and then progressing to using the treadmill, which contained the device. The goal was to increase exercise duration up to 45-minute stretches at 80 percent of their maximum heart rates.

"The control group dropped out quite early," Sims said. "The women who had the cooling device continued to participate and didn't have an issue with attrition because they finally didn't feel uncomfortable exercising."

During the three-month study, the control group's data remained almost the same while the cooling group:

* Shaved an average five minutes off the time to walk 1.5 miles.
* Dropped almost three inches off their waists.
* Had lower resting blood pressure and greater exercise heart rate.

The device used in the study is costly and is typically found in professional sports training facilities, clinics and hospitals, not general fitness centers, Sims said.

Co-authors are Sandra Tsai, M.D., and Marcia L. Stefanick, Ph.D. Author disclosures are on the abstract. The Cardiovascular Institute, Women's Health, at Stanford University funded the study.

http://www.sciencedaily.com/releases/2012/03/120313230314.htm

Losing Belly Fat, Whether from a Low-Carb or a Low-Fat Diet, Helps Improve Blood Vessel Function

Overweight people who shed pounds, especially belly fat, can improve the function of their blood vessels no matter whether they are on a low-carb or a low-fat diet

ScienceDaily - Overweight people who shed pounds, especially belly fat, can improve the function of their blood vessels no matter whether they are on a low-carb or a low-fat diet, according to a study being presented by Johns Hopkins researchers at an American Heart Association scientific meeting in San Diego on March 13 that is focused on cardiovascular disease prevention.

In the six-month weight-loss study, Hopkins researchers found that the more belly fat the participants lost, the better their arteries were able to expand when needed, allowing more blood to flow more freely. The researchers also found that participants in the study who were on a low-carb diet lost about ten pounds more, on average, than those who were on a low-fat diet. Being overweight increases the risk of cardiovascular disease, especially if the fat is accumulated in the belly above the waist.

"After six months, those who were on the low-carb diet lost an average of 28.9 pounds versus 18.7 pounds among those on the low-fat diet," says lead investigator Kerry J. Stewart, Ed.D., a professor of medicine at the Johns Hopkins University School of Medicine and director of clinical and research exercise physiology at the Johns Hopkins Heart and Vascular Institute.

Stewart and his colleagues studied 60 men and women who weighed an average of 215 pounds at the start of the program. Half of the participants went on a low-carb diet while the others followed a low-fat diet. All took part in moderate exercise and their diets provided a similar amount of calories each day.

In order to evaluate the health of the participants' blood vessels before and after the weight loss program, the researchers conducted a blood flow test by constricting circulation in the upper arm for five minutes with a blood pressure cuff. With this type of test, when the cuff is released, a healthier artery will expand more, allowing more blood to flow through the artery. The researchers measured how much blood reached the fingertips before, during, and after the constriction of the artery. Stewart says this test can give an indication of the overall health of the vascular system throughout the body. The researchers found that the more belly fat a person had lost, the greater the blood flow to the finger, signaling better the function of the artery.

"Our study demonstrated that the amount of improvement in the vessels was directly linked to how much central, or belly fat, the individuals lost, regardless of which diet they were on," says Stewart. "This is important since there have been concerns that a low-carb diet, which means eating more fat, may have a harmful effect on cardiovascular health. These results showed no harmful effects from the low-carb diet."

In the low-carb diet used in the study, up to 30 percent of calories came from carbs such as bread, pasta and certain fruits, while 40 percent was from fat consumed from meat, dairy products and nuts. In contrast, the low-fat diet consisted of no more than 30 percent of calories from fat and 55 percent from carbs.

Stewart notes that participants on the low-carb diet lost more weight and at a faster pace, on average, which has also been seen in several other studies. He says eating higher amounts of carbohydrates can slow down the rate of body fat loss while on a weight reduction diet.

The findings were consistent with early results presented by Stewart in June 2011 at the annual meeting of the American College of Sports Medicine in Denver. That initial report was based on results after participants in the study had lost their first 10 pounds. These longer-term results show that weight loss, along with exercise, is important for improving vascular health, and suggests following a low-carb diet rather than the conventionally recommended low-fat diet for weight loss is not a concern in terms of vascular health.

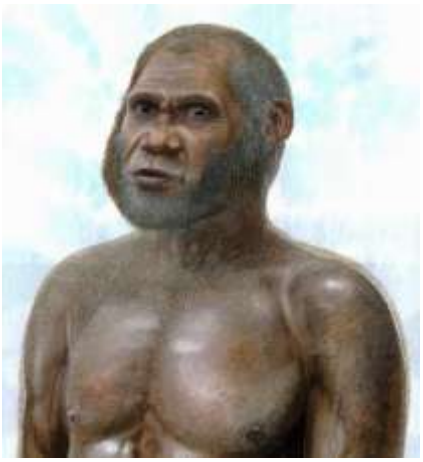
http://www.eurekalert.org/pub_releases/2012-03/uons-mhf031112.php

Mystery human fossils put spotlight on China

Youngest of their kind ever found in mainland East Asia

Fossils from two caves in south-west China have revealed a previously unknown Stone Age people and give a rare glimpse of a recent stage of human evolution with startling implications for the early peopling of Asia. The fossils are of a people with a highly unusual mix of archaic and modern anatomical features and are the youngest of their kind ever found in mainland East Asia.

Dated to just 14,500 to 11,500 years old, these people would have shared the landscape with modern-looking people at a time when China's earliest farming cultures were beginning, says an international team of scientists led by Associate Professor Darren Curnoe, of the University of New South Wales, and Professor Ji Xueping of the Yunnan Institute of Cultural Relics and Archeology. Details of the discovery are published in the journal PLoS One. The team has been cautious about classifying the fossils because of their unusual mosaic of features.



"These new fossils might be of a previously unknown species, one that survived until the very end of the Ice Age around 11,000 years ago," says Professor Curnoe. "Alternatively, they might represent a very early and previously unknown migration of modern humans out of Africa, a population who may not have contributed genetically to living people."

An artist's reconstruction of fossils from two caves in southwest China have revealed a previously unknown Stone Age people and give a rare glimpse of a recent stage of human evolution with startling implications for the early peopling of Asia. **Art copyright by Peter Schouten**

The remains of at least three individuals were found by Chinese archaeologists at Maludong (or Red Deer Cave), near the city of Mengzi in Yunnan Province during 1989. They remained unstudied until research began in 2008, involving scientists from six Chinese and five Australian institutions.

A Chinese geologist found a fourth partial skeleton in 1979 in a cave near the village of Longlin, in neighbouring Guangxi Zhuang Autonomous Region. It stayed encased in a block of rock until 2009 when the international team removed and reconstructed the fossils. The skulls and teeth from Maludong and Longlin are very similar to each other and show an unusual mixture of archaic and modern anatomical features, as well as some previously unseen characters.

While Asia today contains more than half of the world's population, scientists still know little about how modern humans evolved there after our ancestors settled Eurasia some 70,000 years ago, notes Professor Curnoe. The scientists are calling them the "red-deer people" because they hunted extinct red deer and cooked them in the cave at Maludong. The Asian landmass is vast and scientific attention on human origins has focussed largely on Europe and Africa: research efforts have been hampered by a lack of fossils in Asia and a poor understanding of the age of those already found.

Until now, no fossils younger than 100,000 years old have been found in mainland East Asia resembling any species other than our own (Homo sapiens). This indicated the region had been empty of our evolutionary cousins when the first modern humans appeared. The new discovery suggests this might not have been the case after all and throws the spotlight once more on Asia. "Because of the geographical diversity caused by the Qinghai-Tibet plateau, south-west China is well known as a biodiversity hotspot and for its great cultural diversity. That diversity extends well back in time" says Professor Ji.

In the last decade, Asia has produced the 17,000-year-old and highly enigmatic Indonesian Homo floresiensis ("The Hobbit") and evidence for modern human interbreeding with the ancient Denisovans from Siberia.

"The discovery of the red-deer people opens the next chapter in the human evolutionary story – the Asian chapter – and it's a story that's just beginning to be told," says Professor Curnoe.

http://www.eurekalert.org/pub_releases/2012-03/idso-ssl031212.php

Study suggests link between H. pylori bacteria and adult Type 2 diabetes

A recent study shows that the presence of H. pylori bacteria is associated with elevated levels of glycosylated hemoglobin (HbA1c), an important biomarker for blood glucose levels and diabetes.

This association was stronger in obese individuals with a higher Body Mass Index (BMI). The results, which suggest the bacteria may play a role in the development of diabetes in adults, are published in The Journal of Infectious Diseases and are now available online.

H. pylori infection of the stomach may be acquired in early childhood, become persistent, and can lead to gastric and duodenal ulcers; these bacteria have also been associated with an increased risk of gastric cancer. Treatment and eradication of these bacteria with antibiotics have cured many patients with ulcers, revolutionizing treatment of this disorder.

Type II diabetes causes an estimated 3.8 million adult deaths globally. There have been conflicting reports about the association between H. pylori infection and type II diabetes. To better understand the relationship between H. pylori and the disease, Yu Chen, PhD, and Martin Blaser, MD, at NYU School of Medicine, part of NYU Langone Medical Center, cross-analyzed data from participants in two National Health and Nutrition Surveys (NHANES III and NHANES 1999-2000) to assess the association between H. pylori and levels of HbA1c. According to the study authors, "H. pylori was consistently positively related to HbA1c level in adults, a valid and reliable biomarker for long-term blood glucose levels."

In addition, this association was stronger in individuals with a high BMI compared to those with a lower value. The researchers hypothesized that H. pylori may affect the levels of two stomach hormones that help regulate blood glucose, and they suggest that eradicating H. pylori using antibiotics in some older obese individuals could be beneficial. More research will be needed to evaluate the health effects of H. pylori and its eradication among different age groups and in relation to obesity status, the authors noted.

An accompanying editorial points out that while previous studies have addressed the association between type II diabetes and H. pylori in small samples, this study analyzed two independent large national samples of the general population. The editorial authors agreed with the study investigators, suggesting that adults infected with H. pylori with higher BMI levels, even if asymptomatic, may need anti-H. pylori therapy to control or prevent type II diabetes. If the study findings are confirmed, lead editorial author Dani Cohen, PhD, of Tel Aviv University in Israel, noted, they "could have important clinical and public health implications."

Fast Facts: Type II diabetes causes an estimated 3.8 million adult deaths globally. H. pylori was consistently positively related to levels of glycosylated hemoglobin (HbA1c), an important biomarker for blood glucose levels and diabetes. The association between H. pylori and HbA1c was stronger in individuals with a higher Body Mass Index (BMI).

The study and the accompanying editorial are available online. They are embargoed until 12:01 a.m. EDT on Wednesday, March 14, 2014:

Association between gastric Helicobacter pylori colonization and glycated hemoglobin levels
Association between Helicobacter pylori colonization and glycated hemoglobin levels: Is this another reason to eradicate Helicobacter pylori in adulthood?

http://www.eurekalert.org/pub_releases/2012-03/vcu-ncd031312.php

New compound discovered that rapidly kills liver cancer

Scientists have identified a new compound that rapidly kills hepatocellular carcinoma (HCC) cells, the most common form of liver cancer and fifth most common cancer worldwide, while sparing healthy tissue.

Richmond, Va. – The compound, Factor Qunolinone Inhibitor 1 (FQI1), works by inhibiting an oncogene originally discovered by a team of researchers led by Devanand Sarkar, M.B.B.S., Ph.D., Harrison Scholar at Virginia Commonwealth University (VCU) Massey Cancer Center, Blick Scholar and assistant professor in the Department of Human and Molecular Genetics and member of the VCU Institute of Molecular Medicine at the VCU School of Medicine.

Recently published in the journal Proceedings of the National Academy of Sciences, the study demonstrates that HCC cells have what is known as an "oncogene addiction" to the transcription factor Late SV40 Factor (LSF). Oncogene addiction is a term used when a cancer cell is found to be dependent on a single gene to survive. Using the compound Factor Quinolinone Inhibitor 1 (FQI1), the scientists prevented LSF from binding to HCC DNA during the transcription process, which is the first step in a series of actions that lead to cell

division and duplication. This action caused rapid HCC cell death in laboratory experiments and a dramatic reduction in tumor growth in mouse models with no observable toxicity to normal liver cells.

"We may be on the verge of developing a new, effective drug for liver cancer," said Sarkar. "In the last 2 to 3 years, we demonstrated the role of LSF in liver cancer and have been screening over 110,000 compounds to identify the ones that inhibit LSF function. We identified FQI1 as one of a class of effective compounds, but we never anticipated it would work this well."

Sarkar discovered LSF's role in liver cancer in 2010 when he demonstrated significantly higher LSF levels in HCC patients in comparison to healthy individuals, and showed that inhibition of LSF reduced the progression of HCC in laboratory experiments. This finding led to the collaboration between VCU and Boston University that resulted in the discovery of FQI1.

Now that FQI1 has been identified, pharmacokinetic studies are being conducted to determine how the drug behaves in the human body. Once the scientists have determined how the drug is absorbed, distributed, metabolized and eliminated from the body, they will work with clinicians to translate their findings into phase I clinical trials in patients with liver cancer.

"We have proven this compound is effective and nontoxic in living animals," said Sarkar. "While we won't know how FQI1 reacts in humans until the first clinical trial, we are very excited by our findings and hope they lead to a new drug for a disease that is currently very difficult to treat."

The lead investigators on this study were Trevor J. Grant and Joshua Bishop, Ph.D., from Boston University. In addition to Grant and Bishop, Sarkar collaborated with Ayesha Siddiq, Ph.D., Rachel Gredler and Xue-Ning Shen, M.D., from VCU School of Medicine; Jennifer Sherman and Kevin Fitzgerald, Ph.D., from Alnylam Pharmaceuticals, Inc.; Sriharsa Pradhan, Ph.D., from New England Biolabs, Inc.; Laura A. Briggs, Ph.D., and William H. Andrews, Ph.D., from Sierra Sciences, LLC; and Lisa Christadore, Girish Barot, Ph.D., Hang Gyeong Chin, Sarah Woodson, John Kavouris, Tracy Meehan, Scott E. Schaus, Ph.D., and Ulla Hansen, Ph.D., from Boston University.

The full manuscript is available online at: http://www.pnas.org/content/early/2012/03/02/1121601109.full.pdf+html

http://www.eurekalert.org/pub_releases/2012-03/mbl-aes031412.php

An evolutionary surprise

In a brainless marine worm, MBL researchers find the developmental 'scaffold' for the vertebrate brain

This is an adult acorn worm with its proboscis on the bottom right and tail on the top left. **A. Pani**

WOODS HOLE, MA - The origin of the exquisitely complex vertebrate brain is somewhat mysterious. "In terms of evolution, it basically pops up out of nowhere. You don't see anything anatomically like it in other animals," says Ariel Pani, an investigator at the Marine Biological Laboratory (MBL) in Woods Hole and a graduate student at the University of Chicago.

But this week in the journal Nature, Pani and colleagues report finding some of the genetic processes that regulate vertebrate brain development in (of all places) the acorn worm, a brainless, burrowing marine invertebrate that they collected from Waquoit Bay in Falmouth, Mass.

The scientists were searching for ancestral evidence of three "signaling centers" in the vertebrate embryo that are major components of an "invisible scaffold that sets up the foundation of how the brain develops," Pani says. Diagnostic molecular features of these signaling centers are mostly missing in the sea squirts and the lancelets, the invertebrate chordates that are the closest evolutionary relatives of the vertebrates. This had suggested that these signaling centers are key innovations that arose de novo in the vertebrate lineage.

Yet, surprisingly, the scientists found highly similar signaling centers in the more distantly related acorn worm (Saccoglossus kowalevskii), a hemichordate. Acorn worm embryos lack nervous system structures comparable to vertebrate brains, and their lineages diverged from vertebrates more than 500 million years ago. Pani and colleagues found that, in the acorn worm, the signaling centers direct the formation of the embryonic body plan.

"What this means is the last (common) ancestor of the hemichordates and the vertebrates, even though it presumably did not have a vertebrate-like nervous system, had some very complex and vertebrate-like mechanisms for establishing its body plan," Pani says. "And one of the broad implications is that weird, squishy marine animals can be very informative in terms of understanding the evolution of vertebrate development and genetics in a way that you wouldn't expect."

But the sea squirt shouldn't worry: it has not been usurped by the acorn worm. "The lancelet and ascidians (sea squirts) will still be the first animals we will look at if we want to understand vertebrate evolution. But if

we find differences, we now know it is important to look at anatomically divergent animals, where you wouldn't have previously expected to find compelling similarities," Pani says. "I think this principle applies broadly to understanding animal evolution."

The MBL, where more than 200 different types of marine animals are collected and maintained, has long been a center for comparative studies of evolution and development. "It is a valuable perspective that scientists can now implement in a pretty straightforward way," Pani says. "Because of the advances in gene sequencing and developmental techniques, a lot of researchers are now free to pick an animal in an interesting place (in the evolutionary tree) and pursue research on it at a speed that wasn't possible before. I think that is going to have a really big impact."

Christopher Lowe, Pani's Ph.D. advisor, has been working on hemichordates at MBL since 2002, in collaboration with the labs of John Gerhart, Marc Kirschner, Elena Casey, and Mark Terasaki. "The MBL has been a great place for us to work," Pani says. "There is a lot of expertise on the rearing and spawning of the animals, and we have had a ton of help from staff. Zeiss and Nikon have loaned us equipment at the MBL for years. It's just been a really unique and collaborative environment combining organismal knowledge with high-end technical facilities."

http://www.eurekalert.org/pub_releases/2012-03/tmsh-ndn031412.php

New drug now available for actinic keratosis

A new topical gel now available by prescription significantly decreases the amount of time needed to treat actinic keratosis, a skin condition that is a common precursor to skin cancer

A new topical gel now available by prescription significantly decreases the amount of time needed to treat actinic keratosis, a skin condition that is a common precursor to skin cancer, according to a multi-center trial led by researchers at Mount Sinai School of Medicine. The gel, called ingenol mebutate, is applied to the skin for just a few days, making it quicker and even more effective as current therapies require weeks to months to apply. The Phase III study results of the trial are published in the March 15, 2012 issue of the The New England Journal of Medicine.

Actinic keratoses are premalignant skin lesions very common in fair-skinned individuals who always burn and rarely tan. It is the most common precursor to sun-related squamous-cell carcinoma, the second most common type of skin cancer. Current topical medications to treat actinic keratosis often causes skin irritation and result in many patients not completing the full treatment regimen. Topical gels are used as an alternative treatment to cryosurgery, a method of freezing lesions using liquid nitrogen as the cooling solution, to destroy the precancerous skin lesions. Cryosurgery is the most common form of treatment, but is only practical in treating areas with single lesions, not multiple lesions.

"The shorter application period is what makes ingenol mebutate a breakthrough in the treatment of actinic keratosis," said Mark Lebwohl, MD, lead study author and Professor and Chair of the Department of Dermatology at Mount Sinai School of Medicine. "Many patients find it difficult to stick with the current regimen. The shorter period is a more effective option for patients who don't want a treatment that interferes with their everyday lives for weeks or even months."

Euphorbia peplus

Ingenol mebutate is derived from the active ingredient in the sap of the plant Euphorbia peplus, which has long been used as a traditional remedy for common skin lesions. The study found patients require just two to three days of application with results comparable or improved to rates of current actinic keratosis clearance. The shorter treatment period also results in 98 percent of patients completing the full treatment regimen.

Researchers studied two cohorts; 547 patients with actinic keratoses on the face or scalp and 458 patients with actinic keratoses on the trunk or extremities. About half of each group received ingenol mebutate with the other half receiving a placebo. The first group applied treatment at a .015 percent concentration for three days and the second at a .05 percent concentration for two days. At the end of the evaluation period, 42 percent of the first group that received ingenol mebutate and 34 percent of the second group showed complete clearance of actinic keratosis, compared to about 4 and 5 percent, respectively, of the placebo groups.

The approval of ingenol mebutate was announced at the 2012 The American Academy of Dermatology's Annual Meeting and is currently available for prescription under the name Picato®.

Funding for this research was provided LEO Pharma. Dr. Lebwohl is currently a paid consultant for LEO Pharmaceuticals (LEO) but did not have any financial interests in LEO during the period this study was active.

http://bit.ly/xAULxx

Fish that swallowed a pterosaur that swallowed a fish

Dining can be a dangerous business.

Colin Barras, environment news editor

About 150 million years ago, a winged pterosaur called Rhamphorhynchus swooped down to pluck an unsuspecting fish out of the Jurassic ocean. Before the reptile could enjoy its meal, though, a much larger fish - Aspidorhynchus - grabbed the pterosaur and pulled it beneath the waves.

We're not done yet, though: before the predatory fish could tuck into its flying snack, it too somehow managed to die - perhaps choking on what was clearly an awkward meal. All three unfortunate beasts then sank to settle on the sea floor, where they fossilised.

The impressive find was unearthed in 2009 in Eichstätt, a town in southern Germany, and has now been described by Eberhard Frey and Helmut Tischlinger of the State Museum of Natural History Karlsruhe. It comes from the Solnhofen limestone, already famous as the final resting place of every specimen of early bird Archaeopteryx yet found.

Image: Eberhard Frey, Helmut Tischlinger/PLoS One

http://nyti.ms/xUFKZv

Bumps on Teeth Tell Of Mammals' Earlier Rise

It was long believed that mammals began to diversify and flourish only after dinosaurs died out in the mass extinction at the end of the Cretaceous period, about 66 million years ago.

By SINDYA N. BHANOO

But a new study in the journal Nature suggests that some mammals diversified well before that. "The story appears more complex," said an author of the study, Gregory Wilson, a vertebrate paleontologist at the University of Washington.

Using 3-D imaging and CT scanning, he and his colleagues studied the teeth of multituberculates, a group of rodentlike mammals that lived from 165 million years ago to about 35 million years ago. Some of the teeth were tiny: as small as four-hundredths of an inch across.

The researchers found that over time, the mammals' teeth evolved to have more patches, or bumps.

"In modern mammals, the greater number of patches you have, the more likely you are to have a diet composed of high-fiber or plant materials," Dr. Wilson said.

From that, the researchers inferred that the multituberculates diversified at least 20 million years before dinosaurs disappeared. "They were able to expand their range pretty dramatically, and the teeth complexity implies they ate plants," Dr. Wilson said.

The multituberculates started out the size of mice, he added, but "by the time they started to get more complex teeth, they started to increase in body size such that they were up to the size of porcupines and beavers."

http://news.bbc.co.uk/today/hi/today/newsid_9705000/9705853.stm

Herbal dental remedy a 'potent anaesthetic'

A herbal remedy for toothache, used for centuries by a remote Incan tribe in the Amazon is being turned into a commercial treatment for dental pain.

Francoise Barbira-Freedman, a medical anthropologist at Cambridge University, described how she discovered the remedy, which is derived from the rare Acmella oleracea plant, while visiting the tribe in the rainforest. She told the Today programme's Justin Webb that while she was collecting data in the area, she began to have "excruciating pain" with her wisdom teeth and without access to a dentist.

The local people gave her this "very effective" plant. She went on to say that despite being very grateful for the treatment she forgot about it until 20 years later and then got permission to bring the plant here.

A Cambridge researcher is hoping to bring a natural remedy to the market as an alternative to synthetic painkillers. Acmella oleracea, commonly known as spilantes, is used to treat ailments like toothache.

Dr Barbira-Freedman described how they have created a very effective gel which can be used as a "potent anaesthetic" saving people from having to get injections like those used in periodontal treatment.

When asked about how the tribe will benefit from the product, she said that there is a very careful model of redistribution for the local people which will invest the royalties into education and conservation.

http://www.nature.com/news/drug-data-reveal-sneaky-side-effects-1.10220

Drug data reveal sneaky side effects

Mining of surveillance data highlights thousands of previously unknown consequences when drugs are taken together.

Heidi Ledford

An algorithm designed by US scientists to trawl through a plethora of drug interactions has yielded thousands of previously unknown side effects caused by taking drugs in combination.

The work, published today in Science Translational Medicine1, provides a way to sort through the hundreds of thousands of 'adverse events' reported to the US Food and Drug Administration (FDA) each year. "It's a step in the direction of a complete catalogue of drug–drug interactions," says the study's lead author, Russ Altman, a bioengineer at Stanford University in California.

Although clinical trials are often designed to assess the safety of a drug in addition to how well it works, the size of the trials needed to detect the full range of drug interactions would surpass even the large, late-stage clinical trials sometimes required for drug approval. Furthermore, clinical trials are often done in controlled settings, using carefully defined criteria to determine which patients are eligible for enrolment — including other conditions they might have and which medicines they can take alongside the trial drug.

Once a drug hits the market, however, things can get messy as unknown side-effects pop up. And that's where Altman's algorithm comes in.

"Even if you show a drug is safe in a clinical trial, that doesn't mean it's going to be safe in the real world," says Paul Watkins, director of the Hamner–University of North Carolina Institute for Drug Safety Sciences in Research Triangle Park, North Carolina, who was not involved in the work. "This approach is addressing a better way to rapidly assess a drug's safety in the real world once it is approved."

Bias cut

Altman and his colleagues have been studying drug–drug interactions as a way to understand how a person's genes influence their response to pharmaceuticals. To do that, he says, you must first have a good picture of the molecular mechanisms that underlie drug responses.

"Adverse events are incredibly valuable clues to what these drugs are doing in the body," Altman says. "They can tell you the other pathways in the cell that are being tickled by these drugs."

But reports of adverse drug events are notoriously prone to bias. For example, cholesterol-lowering treatments are more often taken by older patients, and so conditions associated with ageing, such as heart attack, could be wrongly linked to a drug as a side effect.

Altman and his colleagues reduced this bias by adopting an approach sometimes used in observational clinical trials. They developed an algorithm that would match data from each drug-exposed patient to a nonexposed control patient with the same condition. The approach automatically corrected for several known sources of bias, including those linked to gender, age and disease1.

The team then used this method to compile a database of 1,332 drugs and possible side effects that were not listed on the labels for those drugs. The algorithm came up with an average of 329 previously unknown adverse events for each drug — far surpassing the average of 69 side effects listed on most drug labels.

Double trouble

The team also compiled a similar database looking at interactions between pairs of drugs, which yielded many more possible side effects than could be attributed to either drug alone. When the data were broken down by drug class, the most striking effect was seen when diuretics called thiazides, often prescribed to treat high blood pressure and oedema, were used in combination with a class of drugs called selective serotonin reuptake inhibitors, used to treat depression. Compared with people who used either drug alone, patients who used both drugs were significantly more likely to experience a heart condition known as prolonged QT, which is associated with an increased risk of irregular heartbeats and sudden death.

A search of electronic medical records from Stanford University Hospital confirmed the relationship between these two drug classes, revealing a roughly 1.5-fold increase in the likelihood of prolonged QT when the drugs were combined, compared to when either drug was taken alone. Altman says that the next step will be to test this finding further, possibly by conducting a clinical trial in which patients are given both drugs and then monitored for prolonged QT.

What should the drug regulators do with the thousands of possible side effects Altman and his team uncovered? That is a complex problem, says Watkins, who adds that regulators will have to factor in the

availability of alternative treatments and the magnitude and seriousness of the side effect, among other considerations.

Altman, who serves as an adviser on the FDA's Science Board, says that he plans to present his results to the agency. He suggests that the algorithm could be used with the FDA's existing drug-surveillance programs to remove bias. However, he points out the enormity of the task: "We've just released a database with 10,000 or more adverse events," he says. "I do not expect the FDA to uncritically take these results and add them to every drug label."

Nature doi:10.1038/nature.2012.10220

ReferencesTatonetti, N. P., Ye, P. P., Daneshjou, R. and Altman, R. B. Sci. Transl. Med. 4, 125ra31 (2012).

http://www.eurekalert.org/pub_releases/2012-03/uow-awm031512.php

A wandering mind reveals mental processes and priorities

Odds are, you're not going to make it all the way through this article without thinking about something else.

MADISON – In fact, studies have found that our minds are wandering half the time, drifting off to thoughts unrelated to what we're doing – did I remember to turn off the light? What should I have for dinner?

A new study investigating the mental processes underlying a wandering mind reports a role for working memory, a sort of a mental workspace that allows you to juggle multiple thoughts simultaneously.

Imagine you see your neighbor upon arriving home one day and schedule a lunch date. On your way to add it to your calendar, you stop to turn off the drippy faucet, feed the cat, and add milk to your grocery list. The capacity that allows you to retain the lunch information through those unrelated tasks is working memory.

The new study, published online March 14 in the journal Psychological Science by Daniel Levinson and Richard Davidson at the University of Wisconsin–Madison and Jonathan Smallwood at the Max Planck Institute for Human Cognitive and Brain Science, reports that a person's working memory capacity relates to the tendency of their mind to wander during a routine assignment. Lead author Levinson is a graduate student with Davidson, a professor of psychology and psychiatry, in the Center for Investigating Healthy Minds at the UW–Madison Waisman Center.

The researchers asked volunteers to perform one of two simple tasks – either pressing a button in response to the appearance of a certain letter on a screen, or simply tapping in time with one's breath – and compared people's propensity to drift off. "We intentionally use tasks that will never use all of their attention," Smallwood explains, "and then we ask, how do people use their idle resources?"

Throughout the tasks, the researchers checked in periodically with the participants to ask if their minds were on task or wandering. At the end, they measured each participant's working memory capacity, scored by their ability to remember a series of letters given to them interspersed with easy math questions.

In both tasks, there was a clear correlation. "People with higher working memory capacity reported more mind wandering during these simple tasks," says Levinson, though their performance on the test was not compromised. The result is the first positive correlation found between working memory and mind wandering and suggests that working memory may actually enable off-topic thoughts.

"What this study seems to suggest is that, when circumstances for the task aren't very difficult, people who have additional working memory resources deploy them to think about things other than what they're doing," Smallwood says.

Interestingly, when people were given a comparably simple task but filled with sensory distractors (such as lots of other similarly shaped letters), the link between working memory and mind wandering disappeared.

"Giving your full attention to your perceptual experience actually equalized people, as though it cut off mind wandering at the pass," Levinson says.

Working memory capacity has previously been correlated with general measures of intelligence, such as reading comprehension and IQ score. The current study underscores how important it is in everyday situations and offers a window into the ubiquitous – but not well-understood – realm of internally driven thoughts.

"Our results suggest that the sorts of planning that people do quite often in daily life – when they're on the bus, when they're cycling to work, when they're in the shower – are probably supported by working memory," says Smallwood. "Their brains are trying to allocate resources to the most pressing problems."

In essence, working memory can help you stay focused, but if your mind starts to wander those resources get misdirected and you can lose track of your goal. Many people have had the experience of arriving at home with no recollection of the actual trip to get there, or of suddenly realizing that they've turned several pages in a book without comprehending any of the words. "It's almost like your attention was so absorbed in the mind wandering that there wasn't any left over to remember your goal to read," Levinson says.

Where your mind wanders may be an indication of underlying priorities being held in your working memory, whether conscious or not, he says. But it doesn't mean that people with high working memory capacity are doomed to a straying mind. The bottom line is that working memory is a resource and it's all about how you use it, he says. "If your priority is to keep attention on task, you can use working memory to do that, too."

Levinson is now studying how attentional training to increase working memory will affect wandering thoughts, to better understand the connection and how people can control it. "Mind wandering isn't free – it takes resources," he says. "You get to decide how you want to use your resources."

The work was supported by the Fetzer Institute, the National Institutes of Health, and the Roke Foundation.

http://www.eurekalert.org/pub_releases/2012-03/tju-cps031412.php

Cancer paradigm shift: Biomarker links clinical outcome with new model of lethal tumor metabolism

A powerful new strategy for personalized anti-cancer therapy

PHILADELPHIA— Researchers at the Kimmel Cancer Center at Jefferson have demonstrated for the first time that the metabolic biomarker MCT4 directly links clinical outcomes with a new model of tumor metabolism that has patients "feeding" their cancer cells. Their findings were published online March 15 in Cell Cycle.

To validate the prognostic value of the biomarker, a research team led by Agnieszka K. Witkiewicz, M.D., Associate Professor of Pathology, Anatomy and Cell Biology at Thomas Jefferson University, and Michael P. Lisanti, M.D., Ph.D., Professor and Chair of Stem Cell Biology and Regenerative Medicine at Jefferson, analyzed samples of patients with triple negative breast cancer, one of the most deadly of breast cancers, with fast-growing tumors that often affect younger women.

A retrospective analysis of over 180 women revealed that high levels of the biomarker MCT4, or monocarboxylate transporter 4, were strictly correlated with a loss of caveolin-1 (Cav-1), a known marker of early tumor recurrence and metastasis in several cancers, including prostate and breast.

"The whole idea is that MCT4 is a metabolic marker for a new model of tumor metabolism and that patients with this type of metabolism are feeding their cancer cells. It is lethal and resistant to current therapy," Dr. Lisanti said. "The importance of this discovery is that MCT4, for the first time, directly links clinical outcome with tumor metabolism, allowing us to develop new more effective anti-cancer drugs."

Analyzing the human breast cancer samples, the team found that women with high levels of stromal MCT4 and a loss of stromal Cav-1 had poorer overall survival, consistent with a higher risk for recurrence and metastasis, and treatment failure.

Applying to a Triple Threat

Today, no such markers are applied in care of triple negative breast cancer, and as a result, patients are all treated the same. Identifying patients who are at high risk of failing standard chemotherapy and poorer outcomes could help direct them sooner to clinical trials exploring new treatments, which could ultimately improve survival. "The idea is to combine these two biomarkers, and stratify this patient population to provide better personalized cancer care," said Dr. Witkiewicz.

The findings suggest that when used in conjunction with the stromal Cav-1 biomarker, which the authors point out has been independently validated by six other groups worldwide, MCT4 can further stratify the intermediate-risk group into high and low risk.

Since MCT4 is a new druggable target, researchers also suggest that MCT4 inhibitors should be developed for treatment of aggressive breast cancers, and possibly other types. Targeting patients with an MCT4 inhibitor, or even simple antioxidants, may help treat high-risk patients, who otherwise may not respond positively to conventional treatment, the researchers suggest.

Paradigm Shift

But the work stems beyond triple negative breast cancer, challenging an 85-year-old theory about cancer growth and progression.

This paper is the missing clinical proof for the paradigm shift from the "old cancer theory" to the "new cancer theory," known as the "Reverse Warburg Effect," said Dr. Lisanti. The new theory being that aerobic glycolysis actually takes place in tumor associated fibroblasts, and not in cancer cells, as the old theory posits.

"The results by Witkiewicz et al. have prominent conceptual and therapeutic implications," wrote Lorenzo Galluzzi, Ph.D., Oliver Kepp, Ph.D., and Guido Kroemer, M.D., Ph.D. of the French National Institute of Health and Medical Research and Institut Gustave Roussy, in an accompanying editorial. "First, they strengthen the notion that cancer is not a cell-autonomous disease, as they unravel that alterations of the tumor stroma may constitute clinically useful biomarkers. Second, they provide deep insights into a metabolic crosstalk between tumor cells and their stroma that may be targeted by a new class of anticancer agents."

Dr. Kroemer entitled his commentary "Reverse Warburg: Straight to Cancer" to emphasize that the connective tissue cells (fibroblasts) are directly "feeding" cancer cells, giving them a clear growth and survival advantage. New personalized therapies would cut off the "fuel supply" to cancer cells, halting tumor growth and metastasis.

http://www.sciencedaily.com/releases/2012/03/120315225751.htm

White Rice Increases Risk of Type 2 Diabetes, Study Claims

The risk of type 2 diabetes is significantly increased if white rice is eaten regularly, claims a study published today on bmj.com.

ScienceDaily - The authors from the Harvard School of Public Health look at previous studies and evidence of the association between eating white rice and the risk of type 2 diabetes. Their study seeks to determine whether this risk is dependent on the amount of rice consumed and if the association is stronger for the Asian population, who tend to eat more white rice than the Western world.

The authors analysed the results of four studies: two in Asian countries (China and Japan) and two in Western countries (USA and Australia). All participants were diabetes free at study baseline.

White rice is the predominant type of rice eaten worldwide and has high GI values. High GI diets are associated with an increased risk of developing type 2 diabetes. The average amount of rice eaten varies widely between Western and Asian countries, with the Chinese population eating an average of four portions a day while those in the Western world eat less than five portions a week.

A significant trend was found in both Asian and Western countries with a stronger association found amongst women than men. The results also show that the more white rice eaten, the higher the risk of type 2 diabetes: the authors estimate that the risk of type 2 diabetes is increased by 10% with each increased serving of white rice (assuming 158g per serving).

White rice has a lower content of nutrients than brown rice including fibre, magnesium and vitamins, some of which are associated with a lower risk of type 2 diabetes. The authors report, therefore, that a high consumption of white rice may lead to increased risk because of the low intake of these nutrients.

In conclusion, the authors state that "higher white rice intake is associated with a significantly elevated risk of type 2 diabetes." This applies for both Asian and Western cultures, although due to findings suggesting that the more rice eaten the higher the risk, it is thought that Asian countries are at a higher risk. The authors recommend eating whole grains instead of refined carbohydrates such as white rice, which they hope will help slow down the global diabetes epidemic.

In an accompanying editorial, Dr Bruce Neal from the University of Sydney suggests that more, bigger studies are needed to substantiate the research hypothesis that white rice increases the chances of getting type 2 diabetes.

Journal References: *E. A. Hu, A. Pan, V. Malik, Q. Sun. White rice consumption and risk of type 2 diabetes: meta-analysis and systematic review. BMJ, 2012; 344 (mar15 3): e1454 DOI: 10.1136/bmj.e1454*

B. Neal. White rice and risk of type 2 diabetes. BMJ, 2012; 344 (mar15 3): e2021 DOI: 10.1136/bmj.e2021

http://www.eurekalert.org/pub_releases/2012-03/esoc-ais031412.php

Art improves stroke survivors' quality of life

Stroke survivors who like art have a significantly higher quality of life than those who do not, according to new research.

Copenhagen, - Patients who appreciated music, painting and theatre recovered better from their stroke than patients who did not. The research was presented at the 12th Annual Spring Meeting on Cardiovascular Nursing, 16-17 March, in Copenhagen, Denmark.

Stroke is the third cause of death in the western world and the first cause of disability in adults. More and more older people are having strokes and undergoing recovery. "We know that every six seconds there is a person affected by stroke in the world," says lead author Dr Ercole Vellone, assistant professor in nursing science at the School of Nursing, University Tor Vergata, Rome, Italy. "Identifying strategies to improve stroke recovery and patients' quality of life represent a priority for the health care system and art exposure seems to be promising."

For the research (FPN 38), 192 stroke survivors (average age 70 years) were asked if they liked or did not like art (music, painting, theatre). Quality of life was compared for patients interested in art (105) and patients not interested in art (87).

Patients interested in art had better general health, found it easier to walk, and had more energy. They were also happier, less anxious or depressed, and felt calmer. They had better memory and were superior communicators (speaking with other people, understanding what people said, naming people and objects correctly).

Dr Vellone says: "Stroke survivors who saw art as an integrated part of their former lifestyle, by expressing appreciation towards music, painting and theatre, showed better recovery skills than those who did not."

"In our study the 'art' group of patients showed a comparable clinical picture to the 'no art' group," he adds. "This is important because it means that patients belonging to the 'art' group had a better quality of life independently from the gravity of stroke. The results suggest that art may make long term changes to the brain which help it recover when things go wrong."

Other researchers have shown that listening to our favourite music directly stimulates a feeling a pleasure by releasing dopamine in the brain. Dopamine is the starting point of the so-called gratification circuit that activates oxytocin (the hormone of love) and finally endorphins (the molecules of pleasurable emotions). "Dopamine improves quality of life each time it is released in the brain," says Dr Vellone. "Further research is needed to see if other art forms stimulate dopamine release."

He adds: "These results shed light on the importance of lifelong exposure to art for improving the recovery process after a stroke. Introducing art into nursing care after stroke could help improve stroke survivors' quality of life."

http://www.npr.org/blogs/health/2012/03/14/148612711/get-to-know-number-needed-to-treat

Get To Know 'Number Needed To Treat'

A single number can help show how beneficial, or not, a treatment is.

by Scott Hensley

While reading over an analysis of decades-old studies of LSD as a treatment for alcoholism last week, I found that the so-called number needed to treat was 6 to prevent alcohol misuse. In other words, treat six people and one would benefit.

That may not sound great, but in medicine a single-digit NNT is actually quite an achievement. For comparison, consider that an aspirin taken regularly to prevent cardiovascular disease in people already known to have heart disease or to have survived as stroke has an NNT of 50.

The best NNT is 1: everybody treated benefits.

In the post I eventually wrote about the LSD study, I didn't mention the NNT, choosing to focus on the question of why scientists think hallucinogens might make sense as treatments for addiction. But knowing that the NNT was so low helped me decide looking at the study would be worth the time.

The LSD study sparked quite a bit of chatter about NNT that got me thinking it might be worth organizing in one place. Here goes.

Decoding the number needed to treat

Storified by Scott Hensley

Meet 'NNT': A Health Statistic That's Simple

The number needed to treat, or NNT, is a statistic that can help you cut through the gobbledygook of clinical studies. Read on to learn why.

1. Here's the post that got me thinking about NNT. LSD Gets Another Look As Alcoholism Treatment : NPR

You might be tempted to chuckle about some Norwegian researchers peering back at experiments done during the '60s and '70s with LSD as a ...NPR

2. I tweeted when I found the NNT of 6. My version of thinking out loud.

That led to a Twitter conversation with a bunch of journalists. There's a video that walks you through how NNT is calculated. And, finally, if you stick with this, you'll find a link to a post by William Heisel about how health journalists can make use of NNT. Or skip right to it.

Looking over the LSD for alcoholism meta-analysis. NNT for benefit: 6. Let me repeat: 6! bit.ly/zijahe Scott Hensley

@scotthensley What's NNT? (Forgive my ignorance.) alexismadrigal

@alexismadrigal Sorry. Number Needed to Treat. It's the study geek's trump card. Explained here: bit.ly/zjQVmR Scott Hensley

3. Here's a video that explains how NNT is calculated, too. The NNT Tutorial ubergraham

@scotthensley And NNT of 6, I take it, is actually a pretty good number. alexismadrigal

@alexismadrigal Yes. NNT = 1 is the best. Everyone treated benefits. But anything with single digits is pretty good. Scott Hensley

.@scotthensley That's not so unusual. For naltrexone NNT=5, acamprosate NNT=7, in terms of preventing relapse. bit.ly/wOdbFU

joe rojas-burke

@rojasburke Good points. But 1 dose of LSD and NNT = 6 gets my attention. Lotsa caveats, of course. But I didn't expect that. Scott Hensley

@scotthensley Are there NNT rankings of different treatments for things? That'd be sweet. alexismadrigal

@alexismadrigal Yep. See "by ratings" at thennt.com/. Coded by color. Green is good! Click through for numbers. Scott Hensley

I second Scott's endorsement, thennt.com is great RT @scotthensley: @alexismadrigal Yep. See "by ratings" at thennt.com/ Ivan Oransky
how did i not know about this? fantastic. RT @ivanoransky thennt.com @scotthensley Maryn McKenna
Fantastic indeed @marynmck RT @ivanoransky thennt.com @scotthensley" Tom Clarke
@scotthensley @alexismadrigal OMG I never knew there were NNT analyses online. My mind has just been blown. THX Melinda Wenner Moyer
Valuable medical tools/resources Thx @scotthensley! vsb.li/6LhzbW and vsb.li/C6fQjS @grahamwalker Judy Stone
Keep NNT on the tip of your tongue. bit.ly/zCgeSa insp. by @scotthensley @rojasburke @KristinaMPT William Heisel
William Heisel did a brilliant job of boiling it all down and sharing the info with other journalists.
Complete Health Reporting: Keep NNT on the Tip of Your Tongue | Reporting on Health
This is part of my ongoing Complete Health Reporting series explaining the 10 essential elements to writing a complete story about a trea... Reportingonhealth

http://arstechnica.com/science/news/2012/03/new-fossil-finds-filling-in-history-of-tetrapods.ars

New fossil finds filling in history of tetrapods

An amphibious tetrapod from the Carboniferous period

By Scott K. Johnson | Published 2 days ago

An amphibious tetrapod from the Carboniferous period

Back in 2004, a fossil tetrapod from the Canadian Arctic achieved near-celebrity status, at least for mineralized skulls. The newly discovered specimen, named Tiktaalik roseae, made appearances on the Colbert Report and PBS NewsHour. (The scientists involved got to share a bit of the spotlight, as well.) The find was noteworthy because it supplied a long sought-after link between fish and their four-legged descendants. We had plenty of fossil fish that fill the bill as ancestor and a number of early tetrapods, but we were missing some of the details about how our ancestors lost their "fishiness."

The old joke about finding a new fossil is that it simply creates two new gaps in the record, one on either side. But a bit after Tiktaalik, there was an actual gap: Romer's Gap, named for the scarcity of fossils that covered the first appearance of four-limbed animals on land. Several new finds in Scotland are now filling in Romer's gap.

In the 1950s, paleontologist A.S. Romer pointed out a 30 million year long break in the tetrapod fossil record, a blank space that picked up his name. Later work whittled the gap down to 15 million years, but the transition was still pretty stark.

Prior to the gap, tetrapods were amphibious, using their four limbs to navigate shallow water and riverine environments. On the other side of the gap, many were already fully terrestrial. The early, amphibious tetrapods still had fish-like tail fin structures and appendages with more than five digits. Their terrestrial descendants had fewer digits and their skulls were smaller and less flattened.

Romer's Gap begins with an extinction event at the end of the Devonian, about 359 million years ago. Geologists have found evidence that the extinction was caused by an abrupt glacial period accompanied by large swings in sea level. Tetrapods weren't the only group to come out of the catastrophe looking a bit different than they did on the way in, but it's not entirely clear how the glacial period drove so many terrestrial and marine animals to extinction.

In a new study published in the Proceedings of the National Academy of Sciences, researchers from Cambridge and the University of Southampton describe the discovery of a number of new fossils that will help fill in Romer's Gap and allow us to test some ideas about that extinction event.

The fossils come from four sites in Scotland, just east of Edinburgh. All the fossils were found in the same layer of mudstone, which was deposited towards the end of the 15 million year gap. The mudstone yielded a number of tetrapods as well as a host of other organisms; the tetrapods represented include both terrestrial and aquatic species.

The finds suggest that Romer's Gap is mainly a gap in collection. Rocks of the right age simply haven't been sought out and worked thoroughly enough. Rather than a scenario where tetrapods changed dramatically, either right after the end-Devonian extinction or at the end of Romer's Gap, the researchers see evidence of a gradual transition.

Other hypotheses about this time period will also be testable at these new sites. In 2006, a group of paleontologists proposed that atmospheric oxygen may have dropped sharply, stressing the early tetrapods' newly-adapted respiratory systems and sending them back to the water. Such a change would also impact

terrestrial arthropods, which were also uncovered at the new sites in Scotland. A close look at those arthropods may allow researchers to rule out the effect of atmospheric oxygen.

Gaps like Romer's are exciting for paleontologists, because where there's an unknown, there's something fascinating waiting to be discovered. These finds in Scotland promise to supply plenty of material for paleontologists to learn about what was going on during Romer's Gap, which may soon be a misnomer.

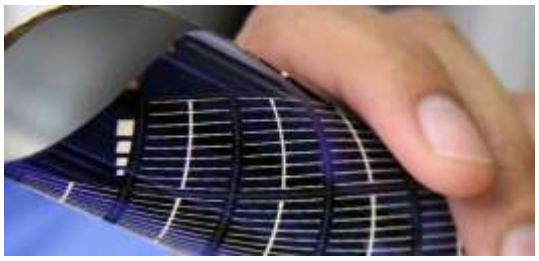
This should also be a lesson for young scientists—don't be too flattered if your name becomes attached to an unexplained phenomenon. It won't last. *PNAS, 2012. DOI: 10.1073/pnas.1117332109 (About DOIs).*

http://bit.ly/Aq3f07

Ion-beam manufacturing halves production cost of PV panels

A small Mississippi solar panel factory claims that its unique manufacturing process allows photovoltaic panels to be produced at almost half the cost of conventional methods.

By James Holloway | Published a day ago



A small Mississippi solar panel factory that, until this week, had been working in semi-secrecy, claims that its unique manufacturing process allows photovoltaic panels to be produced at almost half the cost of conventional methods. The key, according to Twin Creeks Technologies, is in the thinness of its monocrystalline wafers, dramatically reducing the material required.

A 20-micrometer thick solar wafer created with Twin Creeks' "Hyperion" manufacturing system

Where conventional solar wafers can be sliced down to about 180 micrometers in thickness, Twin Creeks is able to produce laminas only 20 micrometers wide using what it calls its "Hyperion" manufacturing system.

This system employs a technique Twin Creeks calls Proton Induced Exfoliation. During this process, hydrogen ions are embedded into layers within standard silicon monocrystalline wafers without altering the wafer's inherent characteristics. The ions are embedded using a high-voltage, high-current ion accelerator which Twin Creeks CEO Siva Sivaram told Technology Review is "10 times more powerful" than any accelerator commercially available. The embedded depth is precisely controlled via the voltage of the accelerator beam.

When the ion layer is heated inside a furnace, a thin lamina of the host wafter is separated from the rest. The process can be repeated with the same wafer to extract up to 10 usable layers. A metal-coating is applied to each layer to add strength.

Twin Creeks claims that only 10 percent of a standard wafer performs useful work. Though the company has not announced specific performance figures for panels created with its technology, it says that solar cells, LEDs and other devices made with its skinny laminae have "similar or better levels of performance" than those made using conventional wafers.

Though conventional solar wafer thickness has come down over the years, the 20-micrometer wafer available now is a disruptive breakthrough. But rather than position itself as usurper, Twin Creeks seems to be pitching its manufacturing technology to established solar panel manufacturers rather than selling solar cells itself. The company claims that a factory equipped with its technology can manufacture solar cells for 40 cents per Watt. By comparison First Solar, which positions itself as the "premier provider of comprehensive PV solar systems", announced only last month that it had cut costs to 73 cents per Watt.

Research technologies (thin-wafers included) that threaten to multiply the efficiency of photovoltaic panels emerge with clockwork regularity, but generally such developments are far from proven at the commercial level. By contrast, Twin Creeks claims its Hyperion 3 systems are available for shipment immediately, and can individually produce 1.5 million skinny wafers—sufficient for over 6MW of solar cells—per year.

The exfoliation method is also applicable to germanium, silicon carbide, gallium nitride and other III-V compounds. Though Twin Creeks' initial focus is on solar cells, it claims its process is suitable in the manufacture of LEDs, power electronics equipment, image sensors and 3D packaging.

http://bit.ly/ylbqRF

Stem cell brain injections ease Parkinson's

MONKEYS with Parkinson's disease-like symptoms have had their suffering eased by an injection of human embryonic stem cells (hESCs) into their brain.

Jun Takahashi of Kyoto University in Japan and colleagues injected these cells into monkeys whose brains had been damaged by a chemical that destroys dopamine-producing neurons and so causes Parkinson's symptoms.

Two monkeys received hESCs that had been matured into an early form of neural cell. Six months later, the monkeys had recovered 20 to 45 per cent of the movement they had lost before treatment. Post-mortems a year

after treatment showed that the cells had developed into fully functioning dopamine-secreting neurons. Another monkey that received less-mature neural cells also showed improvements (Stem Cells, DOI: 10.1002/stem.1060).

"Monkeys starting with tremors and rigidity [began] to move smoothly, and animals originally confined to sitting down were able to walk around," says Takahashi.

The team says it will probably be four to six years before clinical trials in humans begin.

http://www.eurekalert.org/pub_releases/2012-03/bc-tjt031612.php

The Japanese traditional therapy, honokiol, blocks key protein in inflammatory brain damage

Microglia are the first line defence of the brain and are constantly looking for infections to fight off.

Overactive microglia can cause uncontrolled inflammation within the brain, which can in turn lead to neuronal damage. New research published in BioMed Central's open access journal Journal of Neuroinflammation shows that, honokiol (HNK) is able to down-regulate the production of pro-inflammatory cytokines and inflammatory enzymes in activated microglia via Klf4, a protein known to regulate DNA.

Scientists from the National Brain Research Centre, Manesar, India, used lipopolysaccharide (LPS), a molecule present on the surface of bacteria, to stimulate an immune response from microglia cells. LPS mimics the effect of a bacterial infection and the microglia cells spring into action, releasing proinflammatory cytokines, such as TNFa.

Activation of microglia also stimulates the production of nitric oxide (NO) and Cox-2, which co-ordinate the immune response, leading to inflammation. However uncontrolled inflammation can lead to neuronal death and permanent brain damage. Microglial inflammation is also observed in several neurodegenerative diseases including Alzheimer's disease, Parkinson's disease, and multiple sclerosis.

The team led by Dr Anirban Basu found that the inflammatory response was mediated by Klf4, a 'transcription' factor which binds directly to DNA to enhance or impede gene expression. Treating microglia with HNK reduced their activation and HNK treated cells secreted less cytokines in response to LPS. HNK also down regulated the activity of Klf4 (and pNF-kb - another regulator of inflammation).

Dr Basu suggested that HNK down regulates Klf4 which in turn down regulates NO and Cox-2 production. He said, "HNK can easily move across the blood brain barrier and we found that HNK reduced levels of pNF-kb and Klf4 as well as the number of activated microglia in the brains of LPS treated mice."

He continued, "Our work with HNK has found that Klf4 is an important regulator of inflammation. Both HNK and Klf4 may be important not only in regulating inflammation due to infection, but may also have applications in other diseases which affect the brain and nervous system."

1. ***Therapeutic targeting of Kruppel-like factor 4 abrogates microglial activation*** *Deepak K Kaushik, Rupanjan Mukhopadhyay, Kanhaiya L Kumawat, Malvika Gupta and Anirban Basu Journal of Neuroinflammation (in press)*

http://www.eurekalert.org/pub_releases/2012-03/nu-hso031612.php

Hazy shades of life on early Earth

A 'see-sawing' atmosphere over 2.5 billion years ago preceded the oxygenation of our planet and the development of complex life on Earth, a new study has shown.

Research, led by experts at Newcastle University, UK, and published today in the journal Nature Geoscience, reveals that the Earth's early atmosphere periodically flipped from a hydrocarbon-free state into a hydrocarbon-rich state similar to that of Saturn's moon, Titan.

This switch between "organic haze" and a "haze-free" environment was the result of intense microbial activity and would have had a profound effect on the climate of the Earth system.

Similar to the way scientists believe our climate behaves today, the team say their findings provide us with an insight into the Earth's surface environment prior to oxygenation of the planet.

Study lead Dr Aubrey Zerkle, based in the School of Civil Engineering and Geosciences at Newcastle University, explains: "Models have previously suggested that the Earth's early atmosphere could have been warmed by a layer of organic haze. "Our geochemical analyses of marine sediments from this time period provide the first evidence for such an atmosphere. "However, instead of evidence for a continuously 'hazy' period we found the signal flipped on and off, in response to microbial activity.

"This provides us with insight into Earth's surface environment prior to oxygenation of the planet and confirms the importance of methane gas in regulating the early atmosphere."

Dr Zerkle, working along with Dr James Farquhar at the University of Maryland, USA, and Dr Simon Poulton at Newcastle University, UK, analysed the geochemistry of marine sediments deposited between 2.65 and 2.5

billion years ago in what is now South Africa. They found evidence of local production of oxygen by microbes in the oceans, but carbon and sulphur isotopes indicate that little of that oxygen entered the atmosphere.

Instead, the authors suggest that the atmosphere transitioned repeatedly between two states: one with a thin, hydrocarbon haze and the other haze-free. These geochemical records were supported by models of the ancient atmosphere performed by colleagues at the NASA Astrobiology Institute, led by Dr Mark Claire (currently at the University of East Anglia, UK) and Dr Shawn Domagal-Goldman, which demonstrated how the transitions could be caused by changes in the rate of methane production by microbes.

The conditions which enabled the bi-stable organic haze to form permanently ended when the atmosphere became oxygenated some 100 million years after the sediments were laid down.

"What is most surprising about this study is that our data seems to indicate the atmospheric events were discrete in nature, flip-flopping between one stable state into another," explains co-author Dr Farquhar.

"This type of response is not all that different from the way scientists think climate operates today, and reminds us how delicate the balance between states can be."

Professor Mark Thiemens, Dean of Physical Sciences at the University of California San Diego, adds: "Another important facet of the work is that it provides insight into the formation of atmospheric aerosols, particularly organic ones. "Besides the obvious importance for the evolution of the atmosphere, the role of aerosol formation is one of the most poorly understood components in the present day climate models. This provides a new look into this process that is quite new and valuable."

http://www.bbc.co.uk/nature/17404059

Hibernating bears' wounds heal without scars

Black bears have a surprising capacity to heal as they hibernate, say researchers in the US.

By Victoria Gill Science reporter, BBC Nature

Medical researchers and zoologists worked together to find that the bears' wounds healed with almost no scarring, and were infection-free.

The scientists hope, eventually, to find out exactly how the bears' bodies heal while their body temperature, heart rate and metabolism are reduced.

This could aid studies of human wound-healing.

The findings, ***published in the journal Integrative Zoology***, are of particular relevance to medical researchers hoping to improve slow-healing and infection-prone wounds in elderly, malnourished or diabetic patients.

This study part of a project by scientsts from the universities of Minnesota, Wyoming and the Minnesota Department of Natural Resources, who have tracked 1,000 black bears, in order to monitor their health and behaviour, for 25 years.

Whilst tracking the bears - using radio collars - the researchers noticed some early evidence of their surprising healing abilities.

They wrote in their paper: "We identified a few animals each year with injuries resulting from gunshots or arrows from hunters; bite marks from other bears or predators...

"These wounds were considered to have been incurred some time before the bears denned, and were often infected or inflamed... in early winter.

"Yet typically, when we revisited bears in their dens a few months later, most wounds had completely resolved whether or not we [cleaned them], sutured the areas or administered antibiotics."

The big sleep
Black bears hibernate for five to seven months a year
During hibernation, they do not eat, drink, urinate, or defecate
The animals also suppress their metabolism to a quarter of its normal rates
The bears' heart rates are reduced from 55 beats per minute to as few as nine

To test the bear's healing abilities experimentally, the team carefully tracked the healing progess of small cuts on the skin of 14 of their radio-collared bears in northern Minnesota.

Between November (when the bears first settled down in their dens) and March (about a month before they emerged) the wounds healed with "minimal evidence of scarring".

Added to this, there were no signs of infection, the layers of damaged skin regrew and many of the bears even grew hair from newly formed follicles on the site of their injuries.

One of the researchers, Prof David Garshelis from the University of Minnesota, told BBC Nature: "It seems so surprising to us that their wounds would heal so well and so completely when they're hibernating and their metabolism is slowed down.

But, he added, the animals had many other "remarkable adaptations to hibernation".

"They sit in the den for six months and don't lose any appreciable muscle or bone mass, so I guess this healing is another adaptation," Prof Garshelis said.

During its winter hibernation, a black bear's core body temperature is reduced by as much as 7C and their heart rate lowers dramatically. In humans, a lowered body temperature, or conditions that hamper circulation can seriously complicate wound-healing.

For this reason, the team hope to find out the mechanism behind the bears' remarkable healing abilities.

He told BBC Nature: "We consider this to have implcations for medical research.

"If we can work out how the bears heal, we hope there'll be potential to translate this research to [studies of] human healing."

This could be especially important for the development of treatments for skin wounds in malnourished, hypothermic, diabetic and elderly patients.