http://www.nature.com/news/mutations-explain-poor-showing-of-2012-flu-vaccine-1.14940

Mutations explain poor showing of 2012 flu vaccine

Study raises questions over production of flu vaccines in chicken eggs.

Declan Butler

In November 2012, as an early and severe flu season bore down on North America, the news from the US Centers for Disease Control and Prevention (CDC) in Atlanta, Georgia, was reassuring. "So far, this season, most (90%) of the influenza viruses … are well-matched to the 2012–2013 influenza vaccine; this should mean that the vaccine will offer good protection," the agency stated.

Yet vaccine effectiveness against H3N2, the main flu strain circulating that season, proved to be only 46% in adults aged 18–49, 50% in those aged 50–64, and a dismal 9% in people aged over 65, a vulnerable group. Flu hospitalizations and deaths were the highest in almost a decade. What went wrong?

Research published on 25 March in PLoS ONE1 by Danuta Skowronski from the BC Centre for Disease Control in Vancouver, British Columbia, and colleagues at other Canadian public-health research centres, shows that the H3N2 vaccine strain selected by the World Health Organization (WHO) was indeed well matched to the wild viruses circulating at the time. But the strain sent to vaccine makers - which is first adapted to grow better in the hens' eggs used to produce the vaccine - was mismatched and poorly effective, they find. The likely cause, the scientists found, is three mutations in the egg-adapted strain that were not present in the WHO strain, resulting in changes at key sites of the haemagglutinin surface protein known to affect antibody responses.

Poor outlook

Moreover, the Canadian researchers found that the same problem probably arose with a revised H3N2 component of the 2013–14 flu vaccine (each season's vaccine is also designed to ward off H1N1 and influenza B type viruses) and the upcoming 2014–15 vaccine. This suggests that effectiveness against H3N2 may be poor in these seasons' vaccines, too.

Such mismatches are unlikely to be one-off incidents, says Michael Osterholm, who heads the University of Minnesota's Center for Infectious Disease Research and Policy in Minneapolis. "I'm sure this has had to have happened before," he says. "It's another reason why we need to accelerate efforts to come up with really game-changing flu vaccines."

Flu viruses are continually evolving, and so seasonal flu vaccine strains are changed from year to year to better match the circulating strains. Any reduction in effectiveness has previously been explained as 'antigenic drift' taking place in the circulating strains, a process in which mutations accumulate in the genes encoding the flu antigens seen by the immune system, producing strains that it no longer recognizes.

But the new findings show that it is important to ensure that the egg-adapted virus is well matched, and also to better understand how particular mutations affect vaccine effectiveness, says Skowronski.

Scrambled egg virus

H3N2 viruses do not grow well in eggs, so in preparing the vaccine, the WHO strain is 'reassorted' with other strains that do. These fast-growing 'seed strains' are used for manufacture (see 'The virus grower').

"There is always a concern about egg-adaptation mutations resulting in alteration of antigenicity of the vaccine seed strain," says Doris Bucher, a microbiologist at New York Medical College in Valhalla, New York, whose lab creates such seed strains. Efforts are made to monitor mutations and select for the least changes, she says.

Quality control of the seed strains is done by the WHO Collaborating Centres. "I'm surprised that the antigenic difference did not become obvious much earlier in the process of testing the high growth reassortant before it was provided to the manufacturers," says an official at one flu vaccine company who did not wish to be named.

The WHO briefly alluded to the problem of mismatch in February 2013 when it recommended that the H3N2 strain used in the 2012–13 season should not be used for the 2013–14 season but should be substituted with a different strain.

But the Canadian scientists found that the egg-adapted version of the new vaccine strain is similarly mismatched against 2012–13 wild virus, and data in a WHO report released last month suggest a similar mismatch for 2013–14 wild viruses. The finding, says Bucher, "is clearly of concern for the 2014–15 vaccine effectiveness of the H3N2 component". The WHO has recommended that the new strain be used in the 2014–15 season. The UN agency had not responded to Nature's questions by this article's deadline.

Skowronski says that the findings should prompt discussion of switching vaccine production from eggs, a 1930s technology, to modern production systems using cultured human cells.

Flu vaccination remains the best tool to protect against flu, says Osterholm, but its overall effectiveness is poor compared to vaccines for other diseases. "We need much improved vaccines than what we have now," he says.

Nature *doi:10.1038/nature.2014.14940*

References *Skowronski, D. M. et al. PLoS ONE http://dx.doi.org/10.1371/journal.pone.0092153 (2014).*

http://www.eurekalert.org/pub_releases/2014-03/acoc-nht033114.php#rssowlmlink

New human trial shows stem cells are effective for failing hearts

Injecting bone marrow-derived stem cells directly into heart muscle improves heart function

WASHINGTON - Patients with severe ischemic heart disease and heart failure can benefit from a new treatment in which stem cells found in bone marrow are injected directly into the heart muscle, according to research presented at the American College of Cardiology's 63rd Annual Scientific Session.

"Our results show that this stem cell treatment is safe and it improves heart function when compared to placebo," said Anders Bruun Mathiasen, M.D., research fellow in the Cardiac Catherization Lab at Rigshospitalet University Hospital Copenhagen, and lead investigator of the study. "This represents an exciting development that has the potential to benefit many people who suffer from this common and deadly disease."

Ischemic heart disease, also known as coronary artery disease, is the number one cause of death for both men and women in the United States. It results from a gradual buildup of plaque in the heart's coronary arteries and can lead to chest pain, heart attack and heart failure.

The study is the largest placebo-controlled double-blind randomized trial to treat patients with chronic ischemic heart failure by injecting a type of stem cell known as mesenchymal stromal cells directly into the heart muscle. Six months after treatment, patients who received stem cell injections had improved heart pump function compared to patients receiving a placebo. Treated patients showed an 8.2-milliliter decrease in the study's primary endpoint, end systolic volume, which indicates the lowest volume of blood in the heart during the pumping cycle and is a key measure of the heart's ability to pump effectively. The placebo group showed an increase of 6 milliliters in end systolic volume.

The study included 59 patients with chronic ischemic heart disease and severe heart failure. Each patient first underwent a procedure to extract a small amount of bone marrow. Researchers then isolated from the marrow a small number of mesenchymal stromal cells and induced the cells to self-replicate. Patients then received an injection of either saline placebo or their own cultured mesenchymal stromal cells into the heart muscle through a catheter inserted in the groin. "Isolating and culturing the stem cells is a relatively straightforward process, and the procedure to inject the stem cells into the heart requires only local anesthesia, so it appears to be all-in-all a promising treatment for patients who have no other options," Mathiasen said.

Although there are other therapies available for patients with ischemic heart disease, these therapies do not help all patients and many patients continue to face fatigue, shortness of breath and accumulation of fluid in the lungs and legs. Previous studies have shown mesenchymal stromal cells can stimulate repair and regeneration in a variety of tissues, including heart muscle. Mathiasen said in the case of ischemic heart failure, the treatment likely works by facilitating the growth of new blood vessels and new heart muscle.

The study also supports findings from previous, smaller studies, which showed reduced scar tissue in the hearts of patients who received the stem cell treatment, offering additional confirmation that the treatment stimulates the growth of new heart muscle cells. The researchers will continue to monitor the patients to assess their long-term outcomes.

"We hope that the improvements in heart pump function will not only improve the patients' symptoms but also will result in increased survival for these severely diseased patients," Mathiasen said. A larger, Phase III clinical trial will be needed to move toward approval of this treatment as a more widely used therapy for ischemic heart failure. "Our results should offer sufficient evidence that a larger trial is indeed warranted as a next step," Mathiasen said. *The study was funded by grants from several private foundations.*

http://www.eurekalert.org/pub_releases/2014-03/bmj-7dp032714.php#rssowlmlink

Seven+ daily portions of fruit and veg linked to lowest risk of death from all causes

Veg may be more protective than fruit; change in dietary recommendations may be warranted

Eating at least seven daily portions of fruit and vegetables may confer the best chance of staving off death from any cause, indicates research published online in the Journal of Epidemiology and Community Health.

And vegetables may pack more of a protective punch than fruit, the data suggest.

The UK government currently recommends eating five daily portions of fruit and vegetables, prompting the suggestion in an accompanying editorial that it may be time to review national dietary recommendations.

A diet rich in fruit and vegetables has been linked to good health, but many of the studies on which this association is based have largely been carried out on people who are already likely to be health conscious.

And while plenty of fruit and vegetables in the diet are recommended to boost cardiovascular health, the evidence for its impact on warding off cancer has been less clear-cut.

The authors therefore analysed lifestyle data for more than 65,000 randomly selected adults aged at least 35, derived from annual national health surveys for England between 2001 and 2008. And they tracked recorded deaths from among the sample for an average of 7.5 years.
On average, the survey respondents said they had eaten just under four portions of fruit and vegetables the previous day. During the monitoring period 4399 people died (6.7% of the sample).
The analysis revealed that eating fruit and vegetables was associated with a lower risk of death, overall, and deaths from heart disease/stroke and cancer. The higher the intake of fruit and vegetables, the greater the protective effects seemed to be. Eating at least seven daily portions was linked to a 42% lower risk of death from all causes and from cancer and heart disease/stroke of 25% and 31%, respectively, after excluding deaths within the first year of the monitoring period.
Vegetables may be more protective, the figures suggest: 2-3 daily portions were linked to a 19% lower risk of death, compared with a 10% lower risk for the equivalent amount of fruit. And each portion of salad or vegetables seemed to confer a 12-15% lower risk of death. But while fresh and dried fruit seemed to strongly curb the risk of death, a portion of frozen/tinned fruit seemed to increase it by 17%, which public health doctors from the University of Liverpool describe in an accompanying editorial as "intriguing."
Might added sugars in 'processed' fruit products explain this finding, they wonder.
They conclude that current dietary guidance, which includes consumption of dried or tinned fruit, smoothies, and fruit juice as legitimate ways of reaching the '5-a-day' goal, might need to be revised.
"150 ml of freshly squeezed orange juice (sugar 13 g); 30 g of dried figs (sugar 14 g); 200 ml of a smoothie made with fruit and fruit juice (sugar 23 g) and 80 g of tinned fruit salad in fruit juice (sugar 10 g)...contain a total of some 60 g of refined sugar," they point out. "This is more than the sugar in a 500 ml bottle of cola."
As only one in four adults in England gets their recommended '5 a day' the health benefits of getting everyone else to up their game are "huge," they suggest. But the study findings imply that even those who do get their recommended quota, need to eat more, they say. "Is it perhaps now time for the UK to update the '5 a day' message to '10 a day'? they ask.

[Fruit and vegetable consumption and all-cause, cancer and CVD mortality: analysis of Health Survey for England data Online First doi 10.1136/jech-2013-203500]

[Fruit and vegetable consumption and non-communicable disease: time to update the '5 a day' message? Online First doi 10.1136/jech-2014-203981]

http://www.eurekalert.org/pub_releases/2014-03/nrr-nri033114.php#rssowlmlink

NTS's role in the protection of pre-moxibustion on gastric mucosal lesions

Moxibustion may have protective effects on the stomach mucous membrane against stress gastric ulcer.

The potential mechanism of moxibustion may be mediated by transforming growth factor-α, gastric mucosa cell proliferation, inhibition of apoptosis, and the expression of heat shock protein-70. Previous studies have shown that somatic sensation by acupuncture and visceral nociceptive stimulation can converge in the nucleus tractus solitarii (NTS) where neurons integrate signals impacting on the function of organs. To explore the role of the NTS in the protective mechanism of pre-moxibustion on gastric mucosa, Dr. Liang Peng and co-workers from College of Acupuncture and Tuina, Hunan University of Chinese Medicine in China pointed out that moxibustion pretreatment at the Zusanli point is protective against acute gastric mucosa injury, and NTS damage inhibits these responses. Therefore, the NTS may be an important area for regulating the signal transduction of the protective effect of pre-moxibustion on gastric mucosa. The relevant paper has been published in the Neural Regeneration Research (Vol. 9, No. 2, 2014).

Article: " Role of the nucleus tractus solitarii in the protection of pre-moxibustion on gastric mucosal lesions," by Liang Peng, Mi Liu, Xiaorong Chang, Zhou Yang, Shouxiang Yi, Jie Yan, Yan Peng (College of Acupuncture and Tuina, Hunan University of Chinese Medicine, Changsha 410007, Hunan Province, China)

Peng L, Liu M, Chang XR, Yang Z, Yi SX, Yan J, Peng Y. Role of the nucleus tractus solitarii in the protection of pre-moxibustion on gastric mucosal lesions. Neural Regen Res. 2014;9(2):198-204.

http://www.eurekalert.org/pub_releases/2014-03/uoa-ati033114.php#rssowlmlink

Anesthetic technique important to prevent damage to brain

Researchers at the University of Adelaide have discovered that a commonly used anesthetic technique to reduce the blood pressure of patients undergoing surgery could increase the risk of starving the brain of oxygen.

Reducing blood pressure is important in a wide range of surgeries – such as sinus, shoulder, back and brain operations – and is especially useful for improving visibility for surgeons, by helping to remove excess blood from the site being operated on. There are many different techniques used to lower patients' blood pressure for surgery - one of them is known as hypotensive anesthesia, which slows the arterial blood pressure by up to 40%.

Professor PJ Wormald, a sinus, head and neck surgeon from the University's Discipline of Surgery, based at the Queen Elizabeth Hospital, led a world-first study looking at both the effectiveness of hypotensive anesthesia from the surgeon's point of view and its impact on the patients. The study followed 32 patients who underwent endoscopic sinus surgery. The results have now been published online in the journal The Laryngoscope.
"There is an important balance in anesthesia where the blood pressure is lowered so that the surgeon has good visibility and is able to perform surgery safely. There are numerous sensitive areas in sinus surgery – the brain, the eye and large vessels such as the carotid. However, if the blood pressure is lowered too far this may cause damage to the brain and other organs," says Professor Wormald.
"We know from previous research that a person's brain undergoing anesthesia has lower metabolic requirements than the awake brain, and therefore it can withstand greater reductions in blood flow.
"There is also a widely accepted concept that the brain has the ability to autoregulate – to adapt and maintain a constant blood flow as needed, despite a wide range of blood pressure conditions. Our studies challenge this; they show that the brain can only autoregulate up to a point, and cannot completely adapt to such low blood pressures. "This drop in blood pressure poses a risk of starving the brain of much-needed oxygen and nutrients, which could result in injury. There have been cases, for example, where patients have reported memory loss following surgery.
"Given that hypotensive anesthesia is a widely used technique, not just in sinus surgery but in many different types of surgery, we've made recommendations in our paper that suggest a safer approach to this technique. This would reduce risk to the patient while enabling the surgeon to carry out their work effectively," Professor Wormald says.

http://www.eurekalert.org/pub_releases/2014-03/miot-awm032714.php#rssowlmlink

Ancient whodunit may be solved: The microbes did it!

Methane-producing microbes may be responsible for the largest mass extinction in Earth's history

Evidence left at the crime scene is abundant and global: Fossil remains show that sometime around 252 million years ago, about 90 percent of all species on Earth were suddenly wiped out - by far the largest of this planet's five known mass extinctions. But pinpointing the culprit has been difficult, and controversial.
Now, a team of MIT researchers may have found enough evidence to convict the guilty parties - but you'll need a microscope to see the killers.
The perpetrators, this new work suggests, were not asteroids, volcanoes, or raging coal fires, all of which have been implicated previously. Rather, they were a form of microbes - specifically, methane-producing archaea called Methanosarcina - that suddenly bloomed explosively in the oceans, spewing prodigious amounts of methane into the atmosphere and dramatically changing the climate and the chemistry of the oceans.
Volcanoes are not entirely off the hook, according to this new scenario; they have simply been demoted to accessories to the crime. The reason for the sudden, explosive growth of the microbes, new evidence shows, may have been their novel ability to use a rich source of organic carbon, aided by a sudden influx of a nutrient required for their growth: the element nickel, emitted by massive volcanism at just that time.
The new solution to this mystery is published this week in the Proceedings of the National Academy of Sciences by MIT professor of geophysics Daniel Rothman, postdoc Gregory Fournier, and five other researchers at MIT and in China.
The researchers' case builds upon three independent sets of evidence. First, geochemical evidence shows an exponential (or even faster) increase of carbon dioxide in the oceans at the time of the so-called end-Permian extinction. Second, genetic evidence shows a change in Methanosarcina at that time, allowing it to become a major producer of methane from an accumulation of carbon dioxide in the water. Finally, sediments show a sudden increase in the amount of nickel deposited at exactly this time.
The carbon deposits show that something caused a significant uptick in the amount of carbon-containing gases - carbon dioxide or methane - produced at the time of the mass extinction. Some researchers have suggested that these gases might have been spewed out by the volcanic eruptions that produced the Siberian traps, a vast formation of volcanic rock produced by the most extensive eruptions in Earth's geological record. But calculations by the MIT team showed that these eruptions were not nearly sufficient to account for the carbon seen in the sediments. Even more significantly, the observed changes in the amount of carbon over time don't fit the volcanic model.
"A rapid initial injection of carbon dioxide from a volcano would be followed by a gradual decrease," Fournier says. "Instead, we see the opposite: a rapid, continuing increase."
"That suggests a microbial expansion," he adds: The growth of microbial populations is among the few phenomena capable of increasing carbon production exponentially, or even faster.

But if living organisms belched out all that methane, what organisms were they, and why did they choose to do so at that time?
That's where genomic analysis can help: It turns out that Methanosarcina had acquired a particularly fast means of making methane, through gene transfer from another microbe - and the team's detailed mapping of the organism's history now shows that this transfer happened at about the time of the end-Permian extinction. (Previous studies had only placed this event sometime in the last 400 million years.) Given the right conditions, this genetic acquisition set the stage for the microbe to undergo a dramatic growth spurt, rapidly consuming a vast reserve of organic carbon in the ocean sediments.
But there is one final piece to the puzzle: Those organisms wouldn't have been able to proliferate so prodigiously if they didn't have enough of the right mineral nutrients to support them. For this particular microbe, the limiting nutrient is nickel - which, new analysis of sediments in China showed, increased dramatically following the Siberian eruptions (which were already known to have produced some of the world's largest deposits of nickel). That provided the fuel for Methanosarcina's explosive growth.
The resulting outburst of methane produced effects similar to those predicted by current models of global climate change: a sudden, extreme rise in temperatures, combined with acidification of the oceans. In the case of the end-Permian extinction, virtually all shell-forming marine organisms were wiped out - consistent with the observation that such shells cannot form in acidic waters. "A lot of this rests on the carbon isotope analysis," Rothman says, which is exceptionally strong and clear in this part of the geological record. "If it wasn't such an unusual signal, it would be harder to eliminate other possibilities."
While no single line of evidence can prove exactly what happened in this ancient die-off, says Rothman, who is also director of MIT's Lorenz Center, "the cumulative impact of all these things is much more powerful than any one individually." While it doesn't conclusively prove that the microbes did it, it does rule out some alternative theories, and makes a strong and consistent case, he says.
The research was supported by NASA, the National Science Foundation, the Natural Science Foundation of China, and the National Basic Research Program of China.

http://blogs.scientificamerican.com/symbiartic/2014/03/31/pinch-of-pigment-mummy-brown/#rssowlmlink

Pinch of Pigment: Mummy Brown

Many of the early Pre-Raphaelite paintings may have paint made from dead Egyptians.

By Glendon Mellow | March 31, 2014

***Temperantia* by Edward Burne-Jones, 1872.**

Considered to be a highly variable pigment between raw umber (almost greenish brown) and burnt umber (a ruddier brown), Mummy Brown was a transparent brown good for mixing. And it was appalling. Made from ancient Egyptian human and feline mummies grave-robbed investigated as antiquities in Europe, there was a craze to use the bodies for everything from fertilizer to beauty creams to fine art paint pigment.
Edward Burne-Jones was reportedly, appropriately disturbed when informed of the pigment's true nature by fellow painter Alma-Tadema (and in the company of Burne-Jones' nephew, a young Rudyard Kipling) that he performed a ceremony for his paint tube there in the yard, and buried it.[1]

"…When assured that it was actually compounded of real mummy, he left us at once, hastened to the studio, and returning with the only tube he had, insisted on our giving it decent burial there and then. So a hole was bored in the green grass at our feet, and we all watched it put safely in, and the spot was marked by one of the girls planting a daisy root above it"

-from Philip McCouat, "The life and death of Mummy Brown", Art in Society

The pigment itself wasn't easily imitated. It wasn't just made regular long-dried out corpses. The mummification process involved asphaltum or bitumen, often in place of the removed organs. Whole mummies were then ground for commercial and just plain wrong use.[2] Mummy Brown was a fugitive colour, meaning it faded easily. While it was easy for 19th century painters to give up using it due to ick, gross it was still manufactured long after. That practice didn't end until the 1960s, when paint companies more or less ran out. Today, you can get a wholly mineral imitation of Mummy Brown made from hematite, calcium carbonate, iron oxide, kaolin and clay silica; similar in colour, but likely with many different properties.
Philip McCouat, "The life and death of Mummy Brown", Art in Society
Ray Smith, The Artist's Handbook. Alfred A Knopf, (7th printing). ISBN 0-394-55585-6;p14
Note: I do not know if Burne-Jones painting Temperantia contains Mummy Brown; that could only be determined by mass spectrometry or historical notes. It is however, one of his earlier paintings so it is possible.

http://bit.ly/1hzLhVZ

Smart Door Handles Sanitize Your Hands

Although door handles are one of the filthiest surfaces in a building, I can never bring myself to use a piece of paper towel to grab a handle after washing my hands in a restroom, for example.

Mar 31, 2014 11:13 AM ET // by Nic Halverson

It's just a tad more neurotic than I care to be.

However, I would totally use the PullClean. Designed by British design studio Agency of Design, it's a concept that customizes door handles to dispense hand sanitizer. Therefore, reluctant folks like myself and those who skip hand washing altogether have no excuse not to disinfect.

The PullClean's clever approach is designed to look like a nondescript handle, but a blue section at the bottom pumps out hand sanitizer. While the device could easily be ignored, it's equipped with Count Clean software that not only monitors how often people sanitize their hands, but also how much sanitizer is in the handle. That way, staff knows when more sanitizer is needed and how often people are using PullClean.

Agency of Design began trials of the device in U.S. hospitals and are already seeing rates of hand sanitizing jumping from 22 percent to 77 percent. That's pretty impressive, especially considering the Center For Disease Control estimates that 1 in 25 hospital patients get a staph infection during their stay.

PullClean could hit the market later this year and sell for $200. Until then, check out the following video of the device and for the sake of us all, wash your hands.

http://phys.org/news/2014-03-ancient-virus-dna-remnants-pluripotency.html#rssowlmlink

Researchers discover ancient virus DNA remnants necessary for pluripotency in humans

A team of Canadian and Singaporean researchers has discovered that remnants of ancient viral DNA in human DNA must be present for pluripotency to occur in human stem cells.

Phys.org - In their paper published in the journal Nature Structural and Molecular Biology, the team describes how they disabled a viral remnant in stem cell samples and discovered that doing so prevented the stem cell from being able to grow into all but one type of human cell.

All of the cells in the human body start out as stem cells - the ability of such cells to do so is known as pluripotency. Scientists don't really understand how individual stem cells know which type to become but are working hard to find out - it could lead to the development of cures for many diseases or the regeneration of lost limbs. In this new effort, the researchers wondered about the role of remnant viral DNA in stem cell DNA and pluripotency in general.

Scientists have known for some time that viral DNA exists in human DNA, the result of retrovirus infections millions of years ago. Retroviruses reproduce by injecting their own DNA into the DNA of a host - if it occurs in sperm or egg cells, the virus DNA can end up in the DNA of the host. Until now, scientists have thought that remnant viral DNA was simply "junk" DNA - meaning it didn't do anything at all. Now it appears clear that at least one type of such DNA - HERV-H - actually plays a very important role in pluripotency.

The researchers treated some human stem cells with a small amount of RNA designed to suppress HERV-H. Doing so, they found, removed the stem cell's ability to develop into any human cell - instead they would only grow into cells that resembled fibroblasts - cells normally found in connective tissue. A closer look revealed that suppressing HERV-H also suppressed the production of proteins necessary for pluripotency. Thus, at least in humans, the remnant viral DNA appears to be necessary for normal human development - without it, human life would be impossible.

Because of the role HERV-H plays in pluripotency, its possible other remnant viral DNA plays a role in human development as well, thus it's very likely that other research efforts will focus on testing each to see if they are more than just junk left over from infections over the course of human evolution.

Abstract

Human endogenous retrovirus subfamily H (HERVH) is a class of transposable elements expressed preferentially in human embryonic stem cells (hESCs). Here, we report that the long terminal repeats of HERVH function as enhancers and that HERVH is a nuclear long noncoding RNA required to maintain hESC identity. Furthermore, HERVH is associated with OCT4, coactivators and Mediator subunits. Together, these results uncover a new role of species-specific transposable elements in hESCs.

More information: The retrovirus HERVH is a long noncoding RNA required for human embryonic stem cell identity, Nature Structural & Molecular Biology (2014) DOI: 10.1038/nsmb.2799

http://nyti.ms/1i1ZOWI

What Really Killed William Henry Harrison?

Historians have long accepted the diagnosis of Harrison's doctor, Thomas Miller: "pneumonia of the lower lobe of the right lung, complicated by congestion of the liver."

By JANE McHUGH and PHILIP A. MACKOWIAK MARCH 31, 2014

William Henry Harrison, the ninth president of the United States, holds a distinction that with luck will never be equaled: He was our shortest-serving president, dying on April 4, 1841, after just a month in office.

What killed him? Historians have long accepted the diagnosis of Harrison's doctor, Thomas Miller: "pneumonia of the lower lobe of the right lung, complicated by congestion of the liver."

The pneumonia was thought to be a direct result of a cold the 68-year-old Harrison caught while delivering a numbingly long Inaugural Address (at 8,445 words, the longest in history) in wet, freezing weather without a hat, overcoat or gloves.

But a new look at the evidence through the lens of modern epidemiology makes it far more likely that the real killer lurked elsewhere - in a fetid marsh not far from the White House.

The first clue that the pneumonia diagnosis was wrong lies in Miller's own apparent uneasiness with it. "The disease," he wrote, "was not viewed as a case of pure pneumonia; but as this was the most palpable affection, the term pneumonia afforded a succinct and intelligible answer to the innumerable questions as to the nature of the attack."

Harrison - who had had some medical training as a young man - summoned Miller to the White House on March 26, complaining not of a lung ailment but of anxiety and fatigue. Miller did not bleed him, as was the standard treatment for pneumonia at the time. (More about what he did do in a moment.) But Miller may have overlooked a clue that was in front of his nose.

In those days the nation's capital had no sewer system. Until 1850, some sewage simply flowed onto public grounds a short distance from the White House, where it stagnated and formed a marsh; the White House water supply was just seven blocks downstream of a depository for "night soil," hauled there each day at government expense. That field of human excrement would have been a breeding ground for two deadly bacteria, Salmonella typhi and S. paratyphi, the causes of typhoid and paratyphoid fever - also known as enteric fever, for their devastating effect on the gastrointestinal system.

An 1846 map of Washington, top, shows the home (A) of William Henry Harrison, above, its water supply (B), and a field of "night soil" (C) that could have harbored deadly bacteria.

Two other antebellum presidents, James K. Polk and Zachary Taylor, developed severe gastroenteritis while living in the White House. Taylor died, while Polk recovered, only to be killed by what is thought to have been cholera a mere three months after leaving office.

A new exhibit at the American Museum of Natural History will feature great reptiles that soared over 60 million years ago; historians may be dead wrong about what killed the shortest-tenured American president; how safe are the medical devices in use in hospitals and doctors' offices?

Harrison had a history of dyspepsia, or indigestion, which potentially heightened his risk of infection by gastrointestinal pathogens that might have found their way into the White House water supply.

Although we have no record of how he managed his dyspepsia, the standard treatment in the 1840s was carbonated alkali, which would have neutralized the gastric acid that otherwise kills harmful bacteria. In the absence of the gastric acid barrier, gastroenteritis can be caused by as few as one ten-thousandth the number of bacteria usually needed. In 1841 there was no effective treatment for enteric fever. The most a doctor could do was adhere steadfastly to medicine's most sacred tenet, primum non nocere - first do no harm.

At least Miller did not bleed the president. But he gave him a host of toxic medications that were then considered the standard of care - including opium, which retards the intestine's ability to rid itself of microbial pathogens, facilitating their invasion into the bloodstream.

Enemas, which Miller repeatedly gave to Harrison, are also potentially dangerous in such patients. They can perforate ulcers produced by S. typhi and S. paratyphi in the ileum, the lower end of the small intestine, through which the bacteria would be able to escape from the intestine into the bloodstream, resulting in sepsis.

As he lay dying, Harrison had a sinking pulse and cold, blue extremities, two classic manifestations of septic shock. Given the character and course of his fatal illness, his untimely death is best explained by enteric fever. Pneumonia was a secondary diagnosis - as Harrison's hapless doctor perhaps suspected all along.

Jane McHugh is a writer in San Antonio. Dr. Philip A. Mackowiak, a scholar in residence at the University of Maryland, is the author of "Diagnosing Giants: Solving the Medical Mysteries of Thirteen Patients Who Changed the World."

http://www.eurekalert.org/pub_releases/2014-04/icl-ndg033114.php#rssowlmlink

New discovery gives hope that nerves could be repaired after spinal cord injury

A new discovery suggests it could one day be possible to chemically reprogram and repair damaged nerves after spinal cord injury or brain trauma.

Researchers from Imperial College London and the Hertie Institute, University of Tübingen have identified a possible mechanism for re-growing damaged nerve fibres in the central nervous system (CNS). This damage is currently irreparable, often leaving those who suffer spinal cord injury, stroke or brain trauma with serious impairments like loss of sensation and permanent paralysis.

Published in Nature Communications today, the research highlights the role of a protein called P300/CBP-associated factor (PCAF), which appears to be essential for the series of chemical and genetic events that allow nerves to regenerate. Regenerating nerve fibres is one of the best hopes for those suffering from CNS damage to recover.

When researchers injected PCAF into mice with damage to their central nervous system, this significantly increased the number of nerve fibres that grew back, indicating that it may be possible to chemically control the regeneration of nerves in the CNS.

"The results suggest that we may be able to target specific chemical changes to enhance the growth of nerves after injury to the central nervous system," said lead study author Professor Simone Di Giovanni, from Imperial College London's Department of Medicine. "The ultimate goal could be to develop a pharmaceutical method to trigger the nerves to grow and repair and to see some level of recovery in patients. We are excited about the potential of this work but the findings are preliminary.

"The next step is to see whether we can bring about some form of recovery of movement and function in mice after we have stimulated nerve growth through the mechanism we have identified. If this is successful, then there could be a move towards developing a drug and running clinical trials with people. We hope that our new work could one day help people to recover feeling and movement, but there are many hurdles to overcome first," he added.

The researchers were interested in understanding how axons in the peripheral nervous system (PNS) make a vigorous effort to grow back when they are damaged, whereas CNS axons mount little or no effort. If damage occurs in the peripheral nervous system, which controls areas outside of the brain and spinal cord, about 30% of the nerves grow back and there is often recovery of movement and function. The researchers wanted to explore whether it was possible to generate a similar response in the CNS.

Co-author Dr Radhika Puttagunta from the University of Tübingen said: "With this work we add another level of understanding into the specific mechanisms of how the body is able to regenerate in the PNS and have used this knowledge to drive regeneration where it is lacking in the CNS. We believe this will help further our understanding of mechanisms that could enhance regeneration and physical recovery after CNS injury."

To investigate the differences between how the two systems respond to damage, the researchers looked at mouse models and cells in culture. They compared the responses to PNS damage and CNS damage in a type of neuron called a dorsal root ganglion, which connects to both the CNS and the PNS.

They found that epigenetic mechanisms were at the core of this capacity to regenerate. Epigenetic mechanisms are processes that, without altering our DNA, manage to activate or deactivate genes in response to the environment. They normally take the form of chemical reactions and have been shown to control how genes influence diseases such as cancer and diabetes. However this is the first demonstration of a specific epigenetic mechanism responsible for nerve regeneration.

When nerves are damaged in the PNS, the damaged nerves send 'retrograde' signals back to the cell body to switch on an epigenetic program to initiate nerve growth. Very little was previously known about the mechanism which allows this 'switching on' to occur.

The researchers identified the sequence of chemical events that lead to the 'switching on' of the program to initiate nerve regrowth and pinpointed the protein PCAF as being central to the process. Furthermore when they injected PCAF into mice with damage to their central nervous system, there was a significant increase in the number of nerve fibres that grew back.

The research was funded by the Hertie Foundation, the Wings for Life Spinal Cord Research Foundation and the German Research Foundation (DFG).

1. Reference: R. Puttagunta et al. 'PCAF-dependent epigenetic changes promote axonal regeneration in the central nervous system', Nature Communications (2014), doi: 10.1038/n-comms4527.

http://www.eurekalert.org/pub_releases/2014-04/wuis-ans033114.php#rssowlmlink

Ancient nomads spread earliest domestic grains along Silk Road, study finds

Findings push back earliest known East-West interaction along Slik Road by 2,000 years

Charred grains of barley, millet and wheat deposited nearly 5,000 years ago at campsites in the high plains of Kazakhstan show that nomadic sheepherders played a surprisingly important role in the early spread of domesticated crops throughout a mountainous east-west corridor along the historic Silk Road, suggests new research from Washington University in St. Louis.

"Our findings indicate that ancient nomadic pastoralists were key players in an east-west network that linked innovations and commodities between present-day China and southwest Asia," said study co-author Michael Frachetti, PhD, an associate professor of archaeology in Arts & Sciences at Washington University and principal investigator on the research project.

"Ancient wheat and broomcorn millet, recovered in nomadic campsites in Kazakhstan, show that prehistoric herders in Central Eurasia had incorporated both regional crops into their economy and rituals nearly 5,000 years ago, pushing back the chronology of interaction along the territory of the 'Silk Road' more than 2,000 years," Frachetti said. The study, to be published April 2 in the Proceedings of the Royal Society B, establishes that several strains of ancient grains and peas had made their way across Eurasia thousands of years earlier than previously documented.

While these crops have been known to exist much earlier in ancient China and Southwest Asia, finding them intermingled in the Bronze Age burials and households of nomadic pastoralists provides some of the earliest concrete signs for east-west interaction in the vast expanse of Eurasian mountains and the first botanical evidence for farming among Bronze Age nomads.

Bread wheat, cultivated at least 6,000 years ago in Southwest Asia, was absent in China before 2500 B.C. while broomcorn millet, domesticated 8,000 years ago in China, is missing in southwest Asia before 2000 B.C. This study documents that ancient grains from eastern China and soutwest Asia had made their way to Kazakhstan in the center of the continent by 2700-2500 B.C. (nearly 5,000 years ago).

"This study starts to rewrite the model for economic change across Eurasia," said first author Robert Spengler, PhD, a paleoethnobotanist and research associate in Arts & Sciences at WUSTL. "It illustrates that nomads had diverse economic systems and were important for reshaping economic spheres more generally."

Findings are based on archaeobotanical data collected from four Bronze Age pastoralist campsites in Central Eurasian steppe/mountains: Tasbas and Begash in the highlands of Kazakhstan and Ojakly and Site 1211/1219 in Turkmenistan. "This is one of the first systematic applications of archaeobotany in the region, making the potential for further future discovery very exciting," Spengler said.

Frachetti and a team of WUSTL researchers led the on-site excavations, working closely with archaeologists based in Turkmenistan, Kazakhstan and Italy. Spengler conducted the paleoethnobotany laboratory work at WUSTL, under the directorship of Gayle J. Fritz, PhD, professor of archaeology and expert in human-plant relationships. "Finding this diverse crop assemblage at Tasbas and Begash illustrates first evidence for the westward spread of East Asian and Southwest Asian crops eastward, and the surprise is that it is nomads who are the agents of change," Frachetti said.

Washington University co-authors include three anthropology graduate students: Paula Doumani, Lynne Rouse and Elissa Bullion. Doumani led the excavations at Tasbas in Kazakhstan while Rouse co-led the excavations at Ojakly in Turkmenistan. Other co-authors are Barbara Cerasetti, of the Universita`degli Studi di Bologna, Italy, and Alexei Mar'yashev, of the Institute of Archaeology in Kazakhstan.

Funding was provided by National Science Foundation grant nos. 1010678, 0535341, 1132090 and 1036942, as well as Lambda Alpha National Honor Society, the Mary Morris-Stein Foundation, Wenner-Gren grant no. 8157, George F. Dales Foundation and International Research & Exchanges Board IARO.

http://nyti.ms/1gO60FO

Diet's Link to Longevity: After 2 Studies Diverge, a Search for Consensus

Wisconsin's study concluded that calorie restriction lengthened life, but a later study suggested the opposite.

By NICHOLAS WADE APRIL 1, 2014

Two rival research groups set out in 1987 to answer a tantalizing question: Could a diet kept meager in calories pay off in longevity?

Both teams, one at a National Institute on Aging laboratory in Baltimore and the other at the University of Wisconsin, studied colonies of rhesus monkeys, which can live past age 40, and it was 22 years before the first results were released. The restricted diet, the Wisconsin team reported in 2009, seemed to be working.

But three years later, the Baltimore team said that its monkeys on reduced-calorie diets were living no longer than those given a normal diet. The differing results puzzled the researchers.

Now, the Wisconsin team has struck back, asserting on Tuesday in the journal Nature Communications that the Baltimore study was effectively in error because its control monkeys were also fed a leaner than normal diet.
The studies are immensely expensive because the monkeys must be followed for their lifetimes and given almost the same standard of health care as human beings.
But these long-running experiments are also of great importance. In laboratory mice, reducing the calories in a normal diet increases longevity by up to 40 percent, and it does so by postponing the onset of age-related diseases. The monkey studies are the most direct way of determining whether the same would be true of people.
Though few people can stick to a diet with 30 percent fewer calories than normal, drugs designed to mimic caloric restriction are being developed and could in principle have far-reaching effects on a population's health and longevity.
In 2009, the Wisconsin team, led by Richard Weindruch, reported that caloric restriction had reduced diabetes, cancer, cardiovascular disease and brain atrophy in the monkey subjects. Mortality was also slightly lower than in the comparison group of monkeys, known as controls, which were allowed to eat as much as they wanted.
Round 2 came in 2012 when the National Institute on Aging team issued a much less enthusiastic report. In one group of its monkeys, which were already adults when caloric restriction was started, the diet did not improve health or longevity compared with control monkeys.
Monkeys that started the diet at an earlier age had fewer incidents of cancer, but they died at the same rate as the controls. Caloric restriction "has not improved survival outcomes," was the verdict of the team, led by Rafael de Cabo.
How could the two studies arrive at such different conclusions?
At the beginning of the Wisconsin experiment, its designers decided the control monkeys should eat like the American population at large - as much as they wanted of a not particularly healthy diet, loaded with sucrose, and in which all foods were laboratory purified. At the National Institute on Aging, by contrast, the control monkeys were fed whole foods and were given fixed portions, based on what they naturally ate before the study started.
The upshot is that even their control animals had a diet that was restricted in calories, at least to a moderate extent, Rozalyn M. Anderson and colleagues from Dr. Weindruch's team say in the new report. So no wonder the Baltimore test monkeys fared little better than the controls - both were benefiting from caloric restriction, Dr. Anderson says.
Moreover, the Baltimore study indicates that the minor restriction of calories may be just as effective as significant restriction. If so, "this would be an extremely important discovery," Dr. Anderson writes.
Continue reading the main story
Dr. de Cabo said in an interview that it was appropriate for the Weindruch team to write such a paper, but that it confused the issue. The two teams are working on a joint report that he hopes will better explain the differing results.
The best way to design a feeding study is to have healthy controls, Dr. de Cabo said, and his animals were much healthier than the Wisconsin control monkeys. Caloric restriction does not work all the time, in his view, but is context dependent, meaning it works with some individuals and some diets, so the task ahead is to find out who will benefit.
There is no doubt that with an overweight population, a 10 percent reduction in body weight would have tremendous health benefits. "But will that improve longevity?" Dr. de Cabo asked. "That's a question that remains to be seen."
The varying conclusions drawn by the two teams put emphasis on a difference in their studies' designs. Is it better to have healthy monkeys as controls, or ones that are allowed to get obese and prone to diabetes?
Dr. Anderson said that "in hindsight, it's great that the studies differed in design," because more can be learned from them.
But Steven Austad, an expert on aging at the University of Alabama at Birmingham, said it would have been better if both studies had used the same kind of controls, whether healthy monkeys or those allowed to feed until obesity.
"Science depends on replication, and if you don't have replication, there's always a question," he said.
The joint paper being worked on by the two groups can be seen as an effort to construct a unified and useful conclusion out of two multimillion-dollar experiments that so far are at loggerheads.
Dr. Anderson said that any disagreements would be resolved by consensus. And there is some chance the two competing teams will end up seeing eye to eye: Both use the same group of statisticians, based at the University of Alabama.

http://www.eurekalert.org/pub_releases/2014-04/wuso-lci032814.php#rssowlmlink

Likely culprit in spread of colon cancer identified

New research at Washington University School of Medicine in St. Louis and Vanderbilt University Medical Center in Nashville has implicated a poorly understood protein called PLAC8 in the spread of colon cancer.

While elevated PLAC8 levels were known to be associated with colon cancer, the researchers now have shown that the protein plays an active role in shifting normal cells lining the colon into a state that encourages metastasis. The work appears April 1 in the Journal of Clinical Investigation.

"We knew levels of this protein are elevated in colon cancer," said co-author Lilianna Solnica-Krezel, PhD, professor and head of the Department of Developmental Biology at Washington University. "Now we've shown what PLAC8 could be doing -- causing the cells to transition to a state that allows them to spread.

"This discovery developed from a collaboration between my group studying zebrafish and Robert Coffey's lab looking at human cells, both initially at Vanderbilt," she said. "Since 2010, my group has continued the zebrafish work at Washington University."

Senior author Robert Coffey, MD, the Ingram Professor of Cancer Research at Vanderbilt University, and his group have been developing new methods to grow colon cancer cells in three dimensions, rather than using typical procedures to grow cells in a flat dish.

Coffey's group observed that colon cancer cells growing in three dimensions formed either smooth hollow balls or spiky clumps with protrusions extending into the surroundings. Compared to the smooth balls, the spiky clumps were shown to form rapidly spreading tumors in mice. When the researchers compared gene expression between the cells forming smooth balls and those forming spiky clumps, PLAC8 stood out. It was expressed at extremely high levels in the spiky clumps that formed aggressive tumors.

To gain a better understanding of PLAC8, Haiting Ma, PhD, a former graduate student in the Solnica-Krezel and Coffey labs, used a zebrafish model system to investigate the roles of this protein.

"We looked at this protein in zebrafish and saw that it was also expressed in the gut," said Solnica-Krezel. "In normal zebrafish, PLAC8 is present on the inner lining of the gut. We also noticed PLAC8 is heavily expressed in the early embryos of zebrafish."

Ma and his colleagues looked further into the develop

ental roles of PLAC8 and found that when there is too much of this protein, the zebrafish embryo developed abnormally, with slower cell movements resulting in an abnormal body shape and other developmental defects.

"We realized that these defects were very similar to abnormalities we see when the protein E-cadherin is mutated," Solnica-Krezel said. "E-cadherin is a cell adhesion molecule present on the cell surface, which allows cells to stick to one another. The amount of E-cadherin on the surface is very important for cell movement, with too much or too little being detrimental to mobility."

E-cadherin is also important in maintaining the sheet-like tissue structure called epithelium, which forms the inner lining of many organs, including the gut. Loss of E-cadherin can indicate a process known as epithelial-to-mesenchymal transition, where the cells detach, and the tissue loses its sheet-like nature, making it easier for the cells to migrate.

During early development, these transitions are normal, as cells must migrate to different parts of the developing organism and form new tissues and organs. But in cancer, this transition to more mobile cells can be the tipping point that causes them to break away from a tumor and invade neighboring tissues.

"Scientists know a lot about E-cadherin," Solnica-Krezel said. "But this is the first link between PLAC8 and E-cadherin. Nobody knew that PLAC8 could regulate it. Too much PLAC8 causes E-cadherin levels to go down, and low E-cadherin is associated with abnormal cell movement."

Moving full circle, first with human cells, then with zebrafish, the researchers returned to human tissues to investigate PLAC8 and associated proteins in colorectal tumors. They demonstrated that many markers of the epithelial-to-mesenchymal transition observed in zebrafish embryos with too much PLAC8 were also present at the edge of a human colon tumor.

Solnica-Krezel speculates PLAC8 could be an interesting target for future work in developing new cancer therapies.

"One could think about finding chemicals that might inhibit PLAC8's activity," she said. "But at present, this finding may have prognostic value. Those tumors expressing PLAC8 at high levels will be the most invasive."

This work was supported by the National Institutes of Health (NIH). Grant numbers CA174377, CA46413, CA095103, CA119925, CA009582, CA68485 and GM55101.

Li C, Ma H, Wang Y, Cao Z, Graves-Deal R, Powell AE, Starchenko A, Ayers GD, Washington MK, Kamath V, Desai K, Gerdes MJ, Solnica-Krezel L, Coffey RJ. Excess PLAC8 promotes an unconventional ERK2-dependent EMT in colon cancer. Journal of Clinical Investigation. April 1, 2014.

http://www.eurekalert.org/pub_releases/2014-04/aps-apc040114.php#rssowlmlink

A protein could be a key weapon in the battle of the bulge

High levels of GDNF protein could help the body resist weight gain despite high-fat diet

Bethesda, MD - More than one-third of people in the US are obese. Obesity and its related health problems - including high blood pressure, high cholesterol, diabetes, insulin resistance, and belly fat - affect so many, yet effective treatments are very few. In a new study, Simon Musyoka Mwangi and colleagues tested whether higher levels of a certain protein help fight the weight gain and health problems caused by eating the wrong foods.

Glial cell line-derived neurotrophic factor - or GDNF for short - is a protein integral to keeping the body's systems in balance (homeostasis) and helping develop and maintain the nerve cells responsible for a host of bodily functions such as digestion and muscle control. Previous research has shown that elevated levels of GDNF can lead to weight loss in rodents and primates with age-related obesity and prevent weight gain in younger animals. In this study, researchers looked specifically at how the increased presence of GDNF might affect obesity caused by a high fat diet.

Researchers compared mice bred to have higher levels of GDNF protein with control mice. The mice were fed either a regular rodent diet (containing ~6% fat) or a high-fat diet (~34% fat).They found that the GDNF-mice fed a high-fat diet resisted diet-induced weight gain, visceral (around the organs) fat development, fatty liver, high lipid (fat) levels in the blood, and insulin resistance. The GDNF mice also experienced improved insulin sensitivity and increased calorie burn compared to control mice on a high-fat diet.

More research is needed into how GDNF works in the body, but the data presented by Mwangi et al. suggest that it may cause increased calorie burn in both brown and white fat cells and in muscle tissue. Their research also suggests that GDNF and its receptors may be unique and effective targets for obesity prevention and treatment therapies.

The article "Glial cell line-derived neurotrophic factor protects against high-fat diet-induced obesity" is published in the March 2014 issue of the American Journal of Physiology - Gastrointestinal and Liver Physiology.

This article is highlighted as one of this month's "best of the best" from the American Physiological Society's 10 peer-reviewed journals under the APSselect program. View the full study here: http://ajpgi.physiology.org/content/306/6/G515. Read all of this month's selected research articles at http://apsselect.physiology.org/.

http://www.eurekalert.org/pub_releases/2014-04/uoc--sst033114.php#rssowlmlink

Scientists solve the riddle of zebras' stripes

Why zebras have black and white stripes is a question that has intrigued scientists and spectators for centuries. A research team led by the University of California, Davis, has now examined this riddle systematically. Their answer is published April 1 in the online journal Nature Communications.

The scientists found that biting flies, including horseflies and tsetse flies, are the evolutionary driver for zebra's stripes. Experimental work had previously shown that such flies tend to avoid black-and-white striped surfaces, but many other hypotheses for zebra stripes have been proposed since Alfred Russel Wallace and Charles Darwin debated the problem 120 years ago. These include:

1. ***A form of camouflage***
2. ***Disrupting predatory attack by visually confusing carnivores***
3. ***A mechanism of heat management***
4. ***Having a social function***
5. ***Avoiding ectoparasite attack, such as from biting flies***

The team mapped the geographic distributions of the seven different species of zebras, horses and asses, and of their subspecies, noting the thickness, locations, and intensity of their stripes on several parts of their bodies. Their next step was to compare these animals' geographic ranges with different variables, including woodland areas, ranges of large predators, temperature, and the geographic distribution of glossinid (tsetse flies) and tabanid (horseflies) biting flies. They then examined where the striped animals and these variables overlapped. After analyzing the five hypotheses, the scientists ruled out all but one: avoiding blood-sucking flies.

"I was amazed by our results," said lead author Tim Caro, a UC Davis professor of wildlife biology. "Again and again, there was greater striping on areas of the body in those parts of the world where there was more annoyance from biting flies."

While the distribution of tsetse flies in Africa is well known, the researchers did not have maps of tabanids (horseflies, deer flies). Instead, they mapped locations of the best breeding conditions for tabanids, creating an environmental proxy for their distributions. They found that striping is highly associated with several consecutive months of ideal conditions for tabanid reproduction.

Why would zebras evolve to have stripes whereas other hooved mammals did not? The study found that, unlike other African hooved mammals living in the same areas as zebras, zebra hair is shorter than the mouthpart length of biting flies, so zebras may be particularly susceptible to annoyance by biting flies.
"No one knew why zebras have such striking coloration," Caro said. "But solving evolutionary conundrums increases our knowledge of the natural world and may spark greater commitment to conserving it."
Yet in science, one solved riddle begets another: Why do biting flies avoid striped surfaces? Caro said that now that his study has provided ecological validity to the biting fly hypothesis, the evolutionary debate can move from why zebras have stripes to what prevents biting flies from seeing striped surfaces as potential prey, and why zebras are so susceptible to biting fly annoyance.
Co-authors on the study include Amanda Izzo and Hannah Walker with the UC Davis Department of Wildlife, Fish and Conservation Biology; Robert C. Reiner Jr., of the UC Davis Department of Entomology and the Fogarty International Center, National Institutes of Health; and Theodore Stankowich with the Department of Biological Sciences at California State University.

http://www.medscape.com/viewarticle/822929?src=rss

Pay for Academic Leaders on Pharma Boards Tops $300K

Academic medical center (AMC) leaders frequently serve on the boards of directors for large pharmaceutical companies, and their dual roles have "potentially far-reaching consequences," researchers conclude in a new study.

Marcia Frellick

Timothy S. Anderson, MD, from the Department of Internal Medicine, University of Pittsburgh Medical Center in Pennsylvania, and colleagues found that 19 (40%) of the 47 major pharmaceutical companies studied had at least a single board member who also held a leadership position at an AMC in 2012. Those board members (excluding 6 industry executives) received a mean $312,564 in annual financial compensation for board membership. The researchers published their data in the April 2 issue of JAMA.
Of all the board members in the study, 18 (3%) held clinical or leadership positions, including 2 university presidents, 6 hospital or health system executive officers, 6 deans, and 7 clinical department chairs or center directors.
The findings are no surprise to Eric G. Campbell, PhD, professor of medicine at Harvard Medical School and research director for Mongan Institute for Health Policy, Boston, Massachusetts. He was lead author of a study published in October 2007 in JAMA that found similar results. His study found that 60% of all department chairs in medical schools had some sort of financial relationship with a drug company.
"Based on data from surveys of department chairmen, other medical school leaders, physicians, medical students, and so on, the data show there's not a single aspect of medical education, medical research, or the practice of medicine in which financial relationships with the pharmaceutical industry are not ubiquitous," he told Medscape Medical News.
Dr. Campbell said AMC leaders are an important commodity to drug companies because they tend to be the key opinion leaders in the practice of medicine in the United States. "They are often great researchers and good physicians, and they have risen to the top of their game."
He said he could not comment on whether the amount of the compensation mentioned in the Pittsburgh study might raise the potential for improper influence in academic decisions without knowing the breakdown of what work the medical center leaders performed for the money. However, he said, "I think it's fair to say that if these were faculty members having these kinds of relationships [and] making that much money, I think institutions would take a very hard look at it."
He noted that there are positive aspects as well when pharmaceutical companies link with medical school leaders. "Drug companies, I think, have a right to have access to the kind of knowledge and skills embodied in the people who run these institutions. The fact that these relationships exist is a decent way to transfer knowledge from the academic sector into the industrial sector," Dr. Campbell said.
Study authors agree that severing ties between companies and the AMC leaders would erase those benefits, but cutting just fiduciary ties by banning voting board members would still allow the leaders to serve as board consultants, they note.
Compensation figures include annual compensation, including cash, stock awards, dividends, and charitable contribution matching. Authors defined AMCs as US medical schools, health professional schools, teaching hospitals, and healthcare systems. Leadership positions included chief executive officers, clinical department chairs, division directors, medical school deans, hospital boards of directors, university presidents, and boards of directors.

The authors are careful to note that they do not draw any conclusions as to whether the relationships led to actual conflicts of interest, but they say the potential for them is real.
"[G]iven the magnitude of competing priorities between academic institutions and pharmaceutical companies, dual leadership roles cannot simply be managed by internal disclosure. These relationships present potentially far-reaching consequences beyond those created when individual physicians consult with industry or receive gifts," they write.
Dr. Anderson has received travel reimbursements from the American Medical Student Association for speaking on conflict-of-interest topics. One coauthor has reported receiving research funding through RAND from Express Scripts for work unrelated to this article and is supported by a VA Health Services Research and Development grant. Dr. Campbell has disclosed no relevant financial relationships.
JAMA. 2014;311:1353-1355.

http://www.eurekalert.org/pub_releases/2014-04/sfsu-cte032814.php#rssowlmlink

Contrary to expectations, life experiences better use of money than material items

Study shows shoppers might buy material items because of mistaken belief they provide more value

SAN FRANCISCO -- Despite knowing that buying life experiences will make them happier than buying material items, shoppers might continue to spend money on the latter because they mistakenly believe items are a better value, according to a San Francisco State University study published today. That belief, however, isn't accurate. Those surveyed after making a purchase rated life experiences both making them happier and as a better use of their money, indicating many are sacrificing their well-being for a sense of value that never materializes.
The study is one of the first to shed light on why people buy material items even though years of research has shown experiences provide a greater happiness boost. "People actually do know, and accurately predict, that life experiences will make them happier," said SF State Associate Professor of Psychology Ryan Howell, a co-author of the study who has extensively researched the link between spending and happiness.
"What they really underestimate is how much monetary value they will get out of a life experience. Even though they're told experiences will make them happier and they know experiences will make them happier, they still perceive material items as being a better value."
Part of the reason, Howell suggests, is that material items are a tangible reminder of what the item is worth. Life experiences produce only memories, which can be harder to put a price tag on. "We naturally associate economic value with stuff. I bought this car, it's worth $8,000," he said. "We have a hard time estimating the economic value we would place on our memories."
To conduct the study, Howell and lead author Paulina Pchelin, a student at SF State when the research took place, surveyed individuals both before and after making a purchase. Prior to the purchase, respondents said they believed a life experience would make them happier but a material item would be a better use of their money. After the purchase, however, respondents reported that life experiences not only made them happier but were also the better value.
"There were just huge underestimates in how much value people expected to get from their purchase," Howell said. "It's almost like people feel they will get no economic value from their life experiences and therefore they feel this tension in spending money on them." Adjusting an individual's priorities, the study showed, can change spending behavior. In an additional experiment, those asked to prioritize value when making a purchase gravitated toward material items, while those asked to prioritize happiness chose experiences.
Determining the best way to encourage the general public to prioritize happiness over value will require additional research, Howell said. The implications, however, extend far beyond the realm of psychology or even retail. "Happiness is not some fleeting, positive emotion we experience in the moment," he said. "There are tremendous benefits to happiness. Companies want their employers to be happier because they are more productive. Doctors want their patients to be happier because they will be healthier. We should try to figure out how to help people maximize their happiness because of all the benefits that come from it."
As next step, Howell is inviting people to forecast their happiness from consumer items by taking part in studies on his website BeyondThePurchase.Org.
"The Hidden Cost of Value-seeking: People do not Accurately Forecast the Economic Benefits of Experiential Purchases," by Paulina Pchelin and Ryan T. Howell was published online April 2 in the Journal of Positive Psychology.

http://phys.org/news/2014-04-phage-cocktail-percent-coli-meat.html#rssowlmlink

Phage 'cocktail' wipes out 99 percent of E. coli in meat, spinach

Treating food products with select bacteriophages - viruses that target and kill bacteria - could significantly reduce concentrations of E. coli, a Purdue University study shows.

Phys.org - An injection of bacteriophages - also known informally as "phages" - nearly eradicated a toxin-producing strain of E. coli in contaminated spinach and ground beef, in some cases decreasing E. coli concentrations by about 99 percent. The study suggests that bacteriophage treatment could be an effective tool to help ensure the safety of food products, said Paul Ebner, associate professor of animal sciences.

"Phage treatment is a way of harnessing the natural antibacterial properties of phages to limit E. coli and other important foodborne pathogens," Ebner said. "Applying this kind of therapy to contaminated foods will make them safer."
While most strains of E. coli are harmless, some can cause severe and potentially fatal illnesses. The strain used in Ebner's study - E. coli O157:H7 - caused more than 63,000 illnesses, 2,100 hospitalizations and 20 deaths in the U.S. in 2011. Ingesting as few as 10 colony-forming units of E. coli O157:H7 can result in serious illness. Most E. coli infections are caused by eating undercooked meat contaminated with the bacteria, but outbreaks associated with fresh produce such as spinach are on the rise.
Ebner and Purdue graduate students Yingying Hong and Yanying Pan infected fresh spinach leaves and ground beef with about 10 million cells of E. coli, a far greater amount than typically found in contaminated food products, Ebner said. The researchers then treated the food with a "phage cocktail," a liquid containing three kinds of phages selected for their ability to quickly and efficiently kill E. coli. Using a variety of phages also helps prevent the bacteria from developing resistance. After 24 hours, the treatment had reduced E. coli concentrations in the spinach, stored at room temperature, by more than 99.9 percent. E. coli dropped by more than 99.8 percent and about 99.8 percent in spinach after 48 and 72 hours, respectively.
In ground beef stored at room temperature, the phages cleaned up about 99 percent of E. coli bacteria within 24 hours. The number of E. coli in refrigerated and undercooked ground beef shrunk by about 68 percent and 73 percent, respectively. "Bacteria have viruses just like we do," Ebner said. "We're taking what already exists in nature and concentrating it to have an impact on these bacteria."
The search-and-destroy methods of phages sound like the stuff of science fiction: Spaceship-like phages dock onto the receptor sites of a host bacterium cell and deploy a syringe-like device that penetrates the cell wall. They inject their own DNA into the host cell, transforming it into a phage-making factory. The cell assembles phages until it contains so many it explodes, releasing the next generation of phages to find new hosts.
"Phages are the most abundant life forms on the planet - if you consider viruses to be alive," Ebner said. "You can eat thousands of phages just by licking your lips." Ingesting phages does not pose a threat to human health because phages are highly host-specific, only targeting certain types of bacteria, said Ebner.
"Phage therapy is a way of using microbes beneficially, similar to using probiotics in yoghurt," he said.
Interest in using phages as antibacterial treatments has increased with the rise of antibiotic-resistant bacteria. The host specificity of phages can be an advantage over broad-spectrum antibiotics, which can wipe out both pathogenic and beneficial bacteria, Ebner said. He said phage therapy is not a substitute for antibiotics, but "it can be very effective when used at specific time points and for shorter periods."
More information: "Development of bacteriophage treatments to reduce E. coli O157:H7 contamination of beef products and produce."
Y. Hong, Y. Pan, and P. D. Ebner. J ANIM SCI jas.2013-7272; published ahead of print. February 3, 2014. DOI: 10.2527/jas.2013-7272

http://www.eurekalert.org/pub_releases/2014-04/w-ccr040214.php#rssowlmlink

Coffee consumption reduces mortality risk from liver cirrhosis

Drinking tea, fruit juice or soft drinks not found to affect risk of cirrhosis death

New research reveals that consuming two or more cups of coffee each day reduces the risk of death from liver cirrhosis by 66%, specifically cirrhosis caused by non-viral hepatitis. Findings in Hepatology, a journal published by Wiley on behalf of the American Association for the Study of Liver Diseases, show that tea, fruit juice, and soft drink consumption are not linked to cirrhosis mortality risk. As with previous studies heavy alcohol use was found to increase risk of death from cirrhosis.
A 2004 report from The World Health Organization (WHO) estimates that each year 1.3% of total death worldwide is caused by liver cirrhosis. Previous research shows that 29 million Europeans have chronic liver disease, with 17,000 deaths annually attributed to cirrhosis. Further WHO reports state that liver cirrhosis is the 11th leading cause of death in the U.S.
"Prior evidence suggests that coffee may reduce liver damage in patients with chronic liver disease," said lead researcher, Dr. Woon-Puay Koh with Duke-NUS Graduate Medical School Singapore and the National University of Singapore. "Our study examined the effects of consuming coffee, alcohol, black tea, green tea, and soft drinks on risk of mortality from cirrhosis."
This prospective population-based study, known as The Singapore Chinese Health Study, recruited 63,275 Chinese subjects between the ages of 45 and 74 living in Singapore. Participants provided information on diet, lifestyle choices, and medical history during in-person interviews conducted between 1993 and 1998. Patients were followed for an average of nearly 15 years, during which time there were 14,928 deaths (24%); 114 of them died from liver cirrhosis. The mean age of death was 67 years.

Findings indicate that those who drank at least 20 g of ethanol daily had a greater risk of cirrhosis mortality compared to non-drinker. In contrast, coffee intake was associated with a lower risk of death from cirrhosis, specifically for non-viral hepatitis related cirrhosis. Non-alcoholic fatty liver disease (NAFLD), a chronic liver disease related to the metabolic syndrome and more sedentary affluent lifestyle, likely predominates among the non-viral hepatitis related cirrhosis group. In fact, subjects who drank two or more cups per day had a 66% reduction in mortality risk, compared to non-daily coffee drinkers. However, coffee intake was not associated with viral hepatitis B related cirrhosis mortality.

"Our study is the first to demonstrate a difference between the effects of coffee on non-viral and viral hepatitis related cirrhosis mortality," concludes Dr. Koh. "This finding resolves the seemingly conflicting results on the effect of coffee in Western and Asian-based studies of death from liver cirrhosis. Our finding suggests that while the benefit of coffee may be less apparent in the Asian population where chronic viral hepatitis B predominates currently, this is expected to change as the incidence of non-viral hepatitis related cirrhosis is expected to increase in these regions, accompanying the increasing affluence and westernizing lifestyles amongst their younger populations."

This study was funded by grants from the U.S. National Institutes of Health (NCI R01 CA55069, R35 CA53890, R01 CA80205 and R01 CA144034).

Full citation: "Coffee, Alcohol and Other Beverages in Relation to Cirrhosis Mortality: The Singapore Chinese Health Study." George Boon-Bee Goh, Wan-Cheng Chow, Renwei-Wang, Jian-Min Yuan and Woon-Puay Koh. Hepatology; (DOI: 10.1002/hep.27054) URL: http://doi.wiley.com/10.1002/hep.27054

http://www.eurekalert.org/pub_releases/2014-04/cfb-cbp040114.php

Cereal box psychology

Eyes in the aisles: Why is Cap'n Crunch looking down at my child?

Silly rabbit, Trix are for kids! In a study of 65 cereals in 10 different grocery stores, Cornell researchers found that cereals marketed to kids are placed half as high on supermarket shelves as adult cereals - the average height for children's cereal boxes is 23 inches versus 48 inches for adult cereal. A second key finding from the same study is that the average angle of the gaze of cereal spokes-characters on cereal boxes marketed to kids is downward at a 9.6 degree angle whereas spokes-characters on adult cereal look almost straight ahead.

To examine the influence of cereal box spokes-characters Cornell Food and Brand Lab Researchers Aner Tal and Brian Wansink, in collaboration with research assistant Aviva Musicus from the Yale Rudd Center for Food Policy and Obesity, asked two questions: 1. Do cereal characters make eye contact? 2. Does eye contact with cereal spokes-characters influence choice?

First, the researchers conducted a study to determine whether the angle of the gaze of spokes-characters on children cereal boxes was such that it would create eye contact with children. To test this, they evaluated 65 types of cereal and 86 different spokes-characters in 10 different grocery stores in New York and Connecticut.

"The eyes of spokes-characters on cereal boxes look directly in the eyes of their target market. For instance, the eyes on adult cereal boxes look straight ahead and on children's cereals the eyes look down at a 9.6 degree angle." -- Brian Wansink, PhD, Cornell Food and Brand Lab **Credit: Daniel Miller**

For each character the angle of the gaze was calculated four feet from the shelf - the standard distance from which shoppers view the boxes. Results show that characters on cereals marketed to children make incidental eye contact with children and cereals marketed to adults make incidental eye contact with adult shoppers. Of the 86 different spokes-characters evaluated, 57 were marketed to children with a downward gaze at an angle of 9.67 degrees. In contrast, the gazes of characters on adult marketed cereals were nearly straight ahead, at a .43 degree upward angle. In agreement with previous studies, the children's cereals were placed on the bottom 2 shelves while the adult cereals were placed on the top 2 shelves. Thus the average height of the spokes-characters gaze was 53.99 inches for adult cereals and 20.21 inches for children's cereals.

In a second study researchers examined the extent to which eye contact with cereal box spokes-characters influences feelings of trust and connection with a brand. 63 individuals from a private northeastern university participated. They were asked to view a Trix box and rate their feelings of trust and connection to the brand. Participants were randomly shown one of two versions of the box, in one version the rabbit was looking straight at the viewer and in the other the rabbit looked down.

Findings show that brand trust was 16% higher and the feeling of connection to the brand was 10% higher when the rabbit made eye contact. Furthermore, participants indicated liking Trix better, compared to another cereal, when the rabbit made eye contact. This finding shows that cereal box spokes-characters that make eye contact may increase positive feelings towards the product and encourage consumers to buy it.
Creating spokes-characters who make eye contact with a product's target audience (child or adult) is a package design that can be used as an advertising tool that influences people to buy and develop brand loyalty. Two key take-aways from this study are:
If you are a parent who does not want your kids to go "cuckoo for Cocoa Puffs" avoid taking them down the cereal aisle.
If you are a cereal company looking to market healthy cereals to kids, use spokes-characters that make eye contact with children to create brand loyalty!

http://www.eurekalert.org/pub_releases/2014-04/mu-nbs040214.php#rssowlmlink

Noisy brain signals: How the schizophrenic brain misinterprets the world

People with schizophrenia often misinterpret what they see and experience in the world. New research provides insight into the brain mechanisms that might be responsible for this misinterpretation.

The study from the Montreal Neurological Institute and Hospital – The Neuro - at McGill University and McGill University Health Centre, reveals that certain errors in visual perception in people with schizophrenia are consistent with interference or 'noise' in a brain signal known as a corollary discharge. Corollary discharges are found throughout the animal kingdom, from bugs to fish to humans, and they are thought to be crucial for monitoring one's own actions. The study, published in the April 2 issue of the Journal of Neuroscience, identifies a corollary discharge dysfunction in schizophrenia, which could aid with diagnosis and treatment of this difficult disorder. It was carried out in collaboration with researchers Veronica Whitford, Gillian O'Driscoll, and Debra Titone in the Department of Psychology, McGill University.
"A corollary discharge is a copy of a nervous system message that is sent to other parts of the brain, in order to make us aware that we are doing something," said Dr. Christopher Pack, neuroscientist at The Neuro and lead investigator on the study. "For example, if we want to move our arm, the motor area of the brain sends a signal to the muscles to produce a movement. A copy of this command, which is the corollary discharge, is sent to other regions of the brain, to inform them of the impending movement. If you were moving your arm, and you didn't have the corollary discharge signal, you might assume that someone else was moving your arm. Similarly, if you generated a thought, and you had an impaired corollary discharge, then you might assume that someone else placed the thought in your mind. Corollary discharges ensure that different areas of the brain are communicating with each other, so that we are aware that we are moving our own arm, talking, or thinking our own thoughts."
Schizophrenia is a disorder that interferes with the ability to think clearly and to manage emotions. People with schizophrenia often attribute their own thoughts and actions to external sources, as in the case of auditory hallucinations. Other common symptoms include delusions and disorganized thinking and speech.
Recent research has suggested that an impaired corollary discharge can account for some of these symptoms. However, the nature of the impairment was unknown. In their study, Dr. Pack and his colleagues (including Dr. Alby Richard, neurology resident at The Neuro) used a test called a perisaccadic localization task, to investigate corollary discharge activity. In this test, subjects are asked to make quick eye movements to follow a dot on a computer screen. At the same time they are also asked to localize visual stimuli that appear briefly on the screen from time to time. In order to perform this task accurately, subjects need to know where on the screen they are looking – in other words they use corollary discharges signals that arise from the brain structures that control the eye muscles.
The results showed that people with schizophrenia were less accurate in figuring out where they were looking. Consequently they made more mistakes in estimating the position of the stimuli that were flashed on the screen.
"What is interesting and potentially clinically important is that the pattern of mistakes made by the patients correlated with the extent of their symptoms," said Dr. Pack. ""This is particularly interesting because the circuits that control eye movements include the best-understood structures in the brain. So we are optimistic that we can work backward from the behavioral data to the biological basis of the corollary discharge effects. We have already started to do this with computational modeling. Mathematically we can convert the corollary discharge of a healthy control into the corollary discharge of a patient with schizophrenia by adding noise and randomness. It is not that people with schizophrenia have no corollary discharge, or a corollary discharge with delayed or weaker amplitude. Rather the patients appear primarily to have a noisy corollary discharge signal. This visual test is very easy thing to do and quite sensitive to individual differences. "

The study shows that patients with schizophrenia make larger errors in localizing visual stimuli compared to controls. These results could be explained by a corollary discharge signal, which also predicts patient symptom severity, suggesting a possible basis for some of the most common symptoms of schizophrenia.
This work was supported by The Natural Sciences and Engineering Research Council of Canada, The Brain & Behavior Research Foundation (NARSAD) and the EJLB Foundation.

http://www.eurekalert.org/pub_releases/2014-04/sri-tin040214.php#rssowlmlink

Team identifies novel biomarker for head and neck cancer, non-small cell lung cancer

A team led by a scientist from the Florida campus of The Scripps Research Institute (TSRI) has identified a new biomarker linked to better outcomes of patients with head and neck cancers and non-small cell lung cancer.

JUPITER, FL –The work could help scientists develop new diagnostics and therapies and help physicians determine the best long-term treatments for patients with these cancers. The findings, which were published this week online ahead of print by the journal Cancer, focus on a protein called Choline phosphate cytidylyltransferase-α CCT-α or CCTα, an "antigen" that prompts the immune system to produce antibodies against it.

"Based on what we found, a high CCTα expression appears to be indicative of survival, making CCTα a promising biomarker," said Laura Niedernhofer, a TSRI associate professor who led the study with Gerold Bepler of the Karmanos Cancer Institute. "Our findings suggest that CCTα may, in fact, be more important in determining outcomes in patients with both types of cancer than the already established ERCC1."

The new study, in fact, turns previous studies on ERCC1 on their heads. Dozens of large clinical trials are being conducted using expression of the ERCC1 DNA-repair protein as a determinant of whether patients with lung, pancreatic, gastric, colorectal, esophageal or ovarian cancer should be treated with platinum-based therapy, a very potent but toxic DNA-damaging agent.

However, the new research suggests that these positive results were not actually due to ERCC1, but to CCTαwhich also binds to the antibody most frequently used to measure ERCC1 expression. "Our results show CCTα may be a better predictor of patient outcomes than expression of ERCC1," said Niedernhofer.

While ERCC1 is associated with DNA repair, CCTα is involved in the synthesis of a major component of cell membranes, active in membrane-mediated signaling and embryo survival.

The new results were based on an examination of samples from 187 patients with non-small cell lung cancer and 60 patients with head and neck squamous cell carcinomas. CCTα expression was associated with longer survival rates, including for patients with non-small cell lung cancer who were treated with surgery alone - without the use of platinum-based chemotherapy drugs and associated toxic side effects.

The first author of the study, "Choline Phosphate Cytidylyltransferase-α is a Novel Antigen Detected by the Anti-ERCC1 Antibody 8F1 with Biomarker Value in Patients with Lung and Head and Neck Squamous Cell Carcinomas," is Alec Vaezi of the University of Pittsburgh.

In addition to Niedernhofer, Bepler and Vaezi, other authors include Agnes Malysa and Wei Chen of the Karmanos Cancer Institute; and Nikhil Bhagwat, Jennifer Rubatt, Brian Hood, Thomas Conrads, Lin Wang and Carolyn Kemp of the University of Pittsburgh. For more information, see http://onlinelibrary.wiley.com/doi/10.1002/cncr.28643/abstract

The study was supported by National Institute of Environmental Health Sciences (grant R01-ES016114), the National Cancer Institute (grants R01-CA129343 and P50-CA097190) and the American Head and Neck Society.

http://bit.ly/1ieOve8

Dating the collision that formed the Moon using late-arriving debris

The magma ocean that resulted acted like a reset button on the age of the Earth.

by John Timmer - Apr 3 2014, 2:36am TST

When did the Earth actually form? There are a number of ways to approach that question. We can use radioactive dating to look at material that has fallen to Earth after remaining largely undisturbed since the formation of our Solar System, or we can obtain a date for the oldest materials we've found on Earth. But those methods simply provide an upper and lower limit; the Earth formed some time after the smaller material in the Solar System, while the earliest materials on Earth would have been produced some time after its formation.

Now, researchers have provided a new date for the formation of the Earth, based on the last time the planet was entirely molten - an event that was triggered by a collision with a body that ultimately created the Moon. The data is calculated using what we know about the early Solar System combined with the debris that fell to Earth after the big collision.

The early Solar System was a violent place, as small particles aggregated into bodies that then grew larger by collisions. These collisions eventually produced planetesimals the size of large asteroids, which merged to form the current collection of planets. So there was no clear start to what would ultimately become the Earth, but there was a clear end to the primary process of its formation.

That end came when the proto-Earth was smacked by a Mars-sized body. The resulting collision would have left the Earth a magma ocean, blown away its atmosphere and any volatile liquids on its surface, and put enough debris in orbit to form the Moon. In effect, it acted like a reset button for the timing of the Earth's formation, remixing all its components so that the raw material for radioactive dating - the stable maintenance of isotope differences caused by radioactive decay - was eliminated. Everything started afresh.

Figuring out the timing of that collision is important if we want to understand the conditions on the early Earth and in the early Solar System in general. The new study uses a clever way of providing an estimate, based on the fact that the last major collision in the Earth's history didn't mean that the Earth escaped further bombardment from space.

The logic is pretty clever. In the wake of the Moon-forming collision, the entire Earth was molten, which allowed the iron to sink to the core. A number of heavy elements that have an affinity for iron sunk to the core with it. This would have left the surface of the Earth completely stripped of these metals. (These elements, which include gold and platinum, are generically referred to as siderophiles.) But it's possible to mine this material from the crust.

The elements are there because the Earth's supply was partly refreshed by the arrival of new material in collisions with other planetesimals and smaller asteroids. (The most famous asteroid, the one that killed the dinosaurs, was first identified through the presence of a layer of another siderophile, iridium, which it carried to Earth.) If we total how much of these elements are in the crust and compare that number to the composition of asteroids in our Solar System, we can get an estimate of how much mass must have struck the Earth after the Moon-forming collision.

How do you go from that mass to a date? The authors recognized that over time, these bodies were lost through collisions with Earth and the other planets. Thus, early in the Solar System's history, there was an ever-shrinking stock of planetesimals that could have delivered material to Earth. To find out the timing of when the stock was depleted, the researchers relied on models of Solar System formation.

In fact, they relied on two different types of models: one that keeps the giant outer planets in their current locations and a second class in which Jupiter and Saturn engage in what's called a "Grand Tack," moving inward early in the Solar System's history before receding back out to their current locations. The Grand Tack simulations were more likely to produce a set of rocky inner planets that look like our Solar System, but in both cases, the planetesimals got depleted pretty rapidly.

Their vanishing act sets limits on when the Moon-forming collision could have happened and, thus, when the Earth could have formed. Too early, and the Earth would have seen lots of additional collisions and had its crust loaded with the elements that are now rare. Too late, and there wouldn't be enough around to give us any significant quantities. Consequently, the authors calculate that there's only a 0.1 percent chance that the Moon-forming collision took place prior to 40 million years after material started condensing in our Solar System. Instead, they place the likely date at 95 million years, with a margin of error of 30 million years on either side.

The authors suggest that we might want to revisit some of the results that were generated using isotope data - a few of these put the collision at 30 million years, and understanding why they got the number wrong may provide some details of the mechanics of the collision itself.

They also think that the reloading of the Earth with rare metals tells us something about the distribution of mass during the formation of the Solar System, which can constrain our models of planet formation. Right now, those models don't do a very good job of creating many of the tightly packed systems that we're currently discovering, so any improvements to them would be a positive step. *Nature, 2014. DOI: 10.1038/nature13172*

http://www.bbc.com/news/health-26647738##rssowlmlink

Ketamine 'exciting' depression therapy

The illegal party drug ketamine is an "exciting" and "dramatic" new treatment for depression, say doctors who have conducted the first trial in the UK.

By James Gallagher Health and science reporter, BBC News

Some patients who have faced incurable depression for decades have had symptoms disappear within hours of taking low doses of the drug. The small trial on 28 people, reported in the Journal of Psychopharmacology, shows the benefits can last months. Experts said the findings opened up a whole new avenue of research.

Depression is common and affects one-in-10 people at some point in their lives. Antidepressants, such as prozac, and behavioural therapies help some patients, but a significant proportion remain resistant to any form of treatment.

A team at Oxford Health NHS Foundation Trust gave patients doses of ketamine over 40 minutes on up to six occasions. Eight showed improvements in reported levels of depression, with four of them improving so much they were no longer classed as depressed.

Some responded within six hours of the first infusion of ketamine. Lead researcher Dr Rupert McShane said: "It really is dramatic for some people, it's the sort of thing really that makes it worth doing psychiatry, it's a really wonderful thing to see. He added: "[The patients] say 'ah this is how I used to think' and the relatives say 'we've got x back'." Dr McShane said this included patients who had lived with depression for 20 years.
The duration of the effect is still a problem. Some relapse within days, while others have found they benefit for around three months and have since had additional doses of ketamine.
There are also some serious side-effects including one case of the supply of blood to the brain being interrupted. Doctors say people should not try to self-medicate because of the serious risk to health outside of a hospital setting. "It is exciting, but it's not about to be a routine treatment as where we need to be going is maintaining the response... it's not about to replace prozac." However, it does offer a new avenue of research into a field that has struggled to find new treatments for depression.

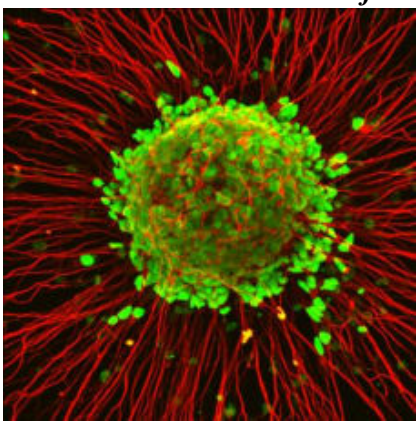
'Something chemical'

David Taylor, professor of psychopharmacology at the Maudsley Hospital, London, told the BBC: "In these kinds of patients, spontaneous remission almost never happens, people going to these clinics are at the end of the road. "It shows that depression is something chemical, that it can be reversed with chemicals, it dispenses for once and for all that you can just pull your socks up. "What restricts it is the potential for disturbing psychological adverse effects and the route by which is given - intravenous - does restrict it to a small number of people." He said in the future drug companies would develop a chemical that had the benefits, but without the side-effects, and that could be taken by something such as an inhaler.
The Home Office is reclassifying ketamine in the UK to be a class B drug, although it is already used in medicine for the treatment of back pain and as an anaesthetic.

http://www.eurekalert.org/pub_releases/2014-04/uow-shu040114.php#rssowlmlink

Study helps unravel the tangled origin of ALS

By studying nerve cells that originated in patients with a severe neurological disease, a University of Wisconsin-Madison researcher has pinpointed an error in protein formation that could be the root of amyotrophic lateral sclerosis.



MADISON, Wis. - Also called Lou Gehrig's disease, ALS causes paralysis and death. According to the ALS Association, as many as 30,000 Americans are living with ALS. After a genetic mutation was discovered in a small group of ALS patients, scientists transferred that gene to animals and began to search for drugs that might treat those animals. But that approach has yet to work, says Su-Chun Zhang, a neuroscientist at the Waisman Center at UW-Madison, who is senior author of the new report, published April 3 in the journal Cell Stem Cell.
Zhang has been using a different approach - studying diseased human cells in lab dishes. Those cells, called motor neurons, direct muscles to contract and are the site of failure in ALS.

In this microscope photo of motor neurons created in the laboratory of Su-Chun Zhang at the University of Wisconsin-Madison, green marks the nucleus, and red marks the nerve fibers. Zhang and co-workers at the Waisman Center have identified a misregulation of protein in the nucleus as the likely first step in the pathology of ALS, a fatal neurological disorder that blocks nerve signals to the muscles, and later causes motor neurons to die. **Hong Chen and Su-Chun Zhang, Waisman Center, University of Wisconsin-Madison**

About 10 years ago, Zhang was the first in the world to grow motor neurons from human embryonic stem cells. More recently, he updated that approach by transforming skin cells into iPS (induced pluripotent stem) cells that were transformed, in turn, into motor neurons.
IPS cells can be used as "disease models," as they carry many of the same traits as their donor. Zhang says the iPS approach offers a key advantage over the genetic approach, which "can only study the results of a known disease-causing gene. With iPS, you can take a cell from any patient, and grow up motor neurons that have ALS. That offers a new way to look at the basic disease pathology."
In the new report, Zhang, Waisman scientist Hong Chen, and colleagues have pointed a finger at proteins that build a transport structure inside the motor neurons. Called neurofilament, this structure moves chemicals and cellular subunits to the far reaches of the nerve cell. The cargo needing movement includes neurotransmitters, which signal the muscles, and mitochondria, which process energy.
Motor neurons that control foot muscles are about three feet long, so neurotransmitters must be moved a yard from their origin in the cell body to the location where they can signal the muscles, Zhang says. A patient lacking this connection becomes paralyzed; tellingly, the first sign of ALS is often paralysis in the feet and legs.

Scientists have known for some time that in ALS, "tangles" along the nerve's projections, formed of misshapen protein, block the passage along the nerve fibers, eventually causing the nerve fiber to malfunction and die. The core of the new discovery is the source of these tangles: a shortage of one of the three proteins in the neurofilament.

The neurofilament combines structural and functional roles, Zhang says. "Like the studs, joists and rafters of a house, the neurofilament is the backbone of the cell, but it's constantly changing. These proteins need to be shipped from the cell body, where they are produced, to the most distant part, and then be shipped back for recycling. If the proteins cannot form correctly and be transported easily, they form tangles that cause a cascade of problems."

Finding neurofilament tangles in an autopsy of an ALS patient "will not tell you how they happen, when or why they happen," Zhang says. But with millions of cells — all carrying the human disease — to work with, Zhang's research group discovered the source of the tangles in the protein subunits that compose the neurofilaments. "Our discovery here is that the disease ALS is caused by misregulation of one step in the production of the neurofilament," he says.

Beyond ALS, Zhang says "very similar tangles" appear in Alzheimer's and Parkinson's diseases. "We got really excited at the idea that when you study ALS, you may be looking at the root of many neurodegenerative disorders."

While working with motor neurons sourced in stem cells from patients, Zhang says he and his colleagues saw "quite an amazing thing. The motor neurons we reprogrammed from patient skin cells were relatively young, and we found that the misregulation happens very early, which means it is the most likely cause of this disease. Nobody knew this before, but we think if you can target this early step in pathology, you can potentially rescue the nerve cell."

In the experiment just reported, Zhang found a way to rescue the neural cells living in his lab dishes. When his group "edited" the gene that directs formation of the deficient protein, "suddenly the cells looked normal," Zhang says.

Already, he reports, scientists at the Small Molecule Screening and Synthesis Facility at UW-Madison are looking for a way to rescue diseased motor neurons. These neurons are made by the millions from stem cells using techniques that Zhang has perfected over the years.

Zhang says "libraries" of candidate drugs, each containing a thousand or more compounds, are being tested. "This is exciting. We can put this into action right away. The basic research is now starting to pay off. With a disease like this, there is no time to waste."

http://phys.org/news/2014-04-stench-resource-hydrogen-sulfide-solar.html#rssowlmlink

From stench to resource: Splitting hydrogen sulfide with solar energy

Splitting hydrogen sulfide with solar energy

Phys.org - No one who has cracked open a rotten egg will forget its infernal stench. Biofuel plants, sewage treatment plants, and petroleum refineries can generate substantial amounts of foul-smelling hydrogen sulfide gas, which is highly toxic at higher concentrations. In the journal Angewandte Chemie, a team of Australian and Chinese researchers has now introduced an innovative photoelectrochemical process in which solar energy is used to split this undesirable by-product into sulfur and hydrogen, converting it to a source of raw materials.

A variety of techniques have been used to remove hydrogen sulfide (H2S) from polluted exhaust gases and occasionally put it to further use. While sulfur can be extracted in some processes, the hydrogen cannot. This is unfortunate because hydrogen is actually an important energy source for future fuel-cell technology. Unfortunately, it isn't possible to split H2S to gain hydrogen and sulfur simultaneously. Approaches using photochemical splitting seem particularly attractive because solar energy could be used to meet the high energy demand of this reaction. However, no ecologically and economically feasible process has been found to date. This could now change thanks to a new approach developed by a team headed by Lianzhou Wang (University of Queensland, Australia) and Can Li (Chinese Academy of Sciences and Dalian Laboratory for Clean Energy, China).

Their success lies in a photochemical–chemical loop whose reactions are coupled through a redox pair. A redox pair is a combination of the reduced and oxidized form of the same element that can easily be interconverted. For their process, the researchers used either divalent and trivalent iron ions (Fe^{2+}/Fe^{3+}) or the iodide/triiodide (I^-/I_3^-) system.

The hydrogen sulfide gas is introduced into the electrolyte of the anodic compartment of an electrochemical cell. Here, a chemical reaction causes it to be bound to the oxidized form of the redox pair (which is thus reduced) and converted to sulfur, which precipitates out as a yellow solid, and hydrogen cations (protons). The protons

can pass through the semipermeable membrane that separates the anodic and cathodic compartments. The second reaction is photoelectrochemical: as protons are reduced at the cathode by taking up electrons, the reduced form of the redox pair is returned to its oxidized state by giving up electrons at the anode. The driving force for this is sunlight, which generates "electron–hole pairs" at the photoanode. These holes can then be filled by the absorbed electrons.

The redox pairs continuously cycle between the oxidized and reduced forms so that the overall reaction is the splitting of hydrogen sulfide into sulfur and hydrogen by sunlight.

More information: "An Integrated Photoelectrochemical–Chemical Loop for Solar-Driven Overall Splitting of Hydrogen Sulfide." Angewandte Chemie International Edition, Permalink to the article: dx.doi.org/10.1002/anie.201400571

http://www.eurekalert.org/pub_releases/2014-04/uow-cwh040314.php#rssowlmlink

Calcium waves help the roots tell the shoots

For Simon Gilroy, sometimes seeing is believing. In this case, it was seeing the wave of calcium sweep root-to-shoot in the plants the University of Wisconsin-Madison professor of botany is studying that made him a believer.

MADISON - Gilroy and colleagues, in a March 24, 2014 paper in the Proceedings of the National Academy of Sciences, showed what long had been suspected but long had eluded scientists: that calcium is involved in rapid plant cell communication. It's a finding that has implications for those interested in how plants adapt to and thrive in changing environments. For instance, it may help agricultural scientists understand how to make more salt- or drought-tolerant plants. "How do you think plants live?" Gilroy asks. "If I poke you, I see an instant response. You move away. Plants live in a slightly different world. They are rooted to the ground, literally, and they respond to the world either by growing or creating chemicals."

Calcium is involved in transmitting information in the cells of humans and other animals, contracting muscles, sending nerve signals and more. In plants, scientists believed it had to also play a role in processing information and sending rapid signals so that plants can respond quickly to their environments.

Imagine you are a plant being eaten by a caterpillar: "It's like a lion chewing your leg," says Gilroy. "If an insect is chewing your leaf, you're gone unless you determine something effective immediately." But no one had ever been able to see it before. Even Gilroy's team found it by accident.

The team was using a specific calcium sensor they thought wasn't going to work. They speculated it could serve as a control in their studies.

The sensor's brightness changes in the presence of calcium, displayed on screen as a change from green to red through a process known as fluorescence resonance energy transfer, or FRET. Typically, this particular sensor is so sensitive to calcium it is nearly always red.

But when researchers applied stress to the tip of a plant's roots — a high concentration of sodium chloride salt — it triggered a wave of red that traveled rapidly from the root to the top of the plant.

"We were kind of like, 'Why is it even working?' says Gilroy. "It was probably telling us we were looking in the wrong realm. It's like we could only hear the people shouting and we couldn't hear the talking."

The calcium wave, a flush of red on an otherwise green palette, traveled on a scale of milliseconds, traversing about eight plant cells per second — too quick to be explained by simple diffusion of salt. "It fit with a lot of our models," Gilroy says. "But the idea that it's a wave is one step beyond what our models would predict."

Within 10 minutes of applying a small amount of salt to the plants' roots, typical stress response genes were turned on in the plant.

Also turned on was the machinery to make more of a protein channel called two pore channel 1 (TPC1). Within one-to-two minutes, there was 10 times more of the building blocks needed to make the channel, which is thought to be involved in calcium signaling.

Gilroy and his team then looked at plants with a defect in TPC1. They had a much slower calcium wave — about 25 times slower — than plants with normal TPC1. When they studied plants expressing more of the TPC1 protein, the calcium wave moved 1.7 times faster. Plants with more channels also grew larger and contained more chlorophyll than plants with normal or mutated TPC1 when grown in salt water.

The protein channel is present in all land plants, says Gilroy, and it's found throughout the plant. This is one of the many reasons it surprised the team to learn the calcium wave moves only through specific cells in the plant, like electrical signals moving through nerve cells in humans and other animals.

"We weren't expecting that," Gilroy says. "It means specific cell types have specific functions … there must be something special about those cells. We're really at the beginning." The lab is now looking at the molecular machinery that makes up TPC1, to figure out how the parts of the channel work.

And now that the scientists know that calcium talks, the volume is turned up. The work is just getting started. "We can hear the screaming," says Gilroy. "Now we're trying to see what the vocal chords are doing."

http://www.eurekalert.org/pub_releases/2014-04/uoc-eoa040314.php#rssowlmlink

Examination of a cave-dwelling fish finds a possible genetic link to human disorders

A high-tech examination of a cave-dwelling fish finds a possible genetic link to human disorders.

Researchers have identified a genetic association with facial asymmetry in an ancient cavefish, a natural trait that may solve mysteries surrounding facial asymmetries in humans – conditions such as cleft palate or hemifacial microsomia. This exciting discovery by Joshua Gross, a University of Cincinnati assistant professor for the Department of Biological Sciences; and doctoral students Amanda Krutzler and Brian Carlson, is published in the research journal, Genetics.

The researchers are studying the craniofacial features of the eyeless, cave-dwelling fish, Astyanax mexicanus, which has lived in the pitch-black caves of the Sierra de El Abra region of Mexico for millions of years. They're comparing those features with closely related sighted surface-dwelling fish that are found in Mexico, Texas and New Mexico.

These cavefish have no eyes, although they are acutely sensitive to sound and vibration. Despite being eyeless, they have several similar bony features in their eye regions compared to their sighted, surface- dwelling counterparts. These similarities allowed the researchers to directly compare traits in the surface-dwelling fish with the cavefish. The cavefish, however, appear drastically different since they are albino and nearly translucent, compared with the darker pigmented surface-dwelling fish.

The researchers are screening the genomes of every individual fish from a hybrid pedigree housed in their lab – looking for genes that may lead to variations in eye size or pigmentation. In the cavefish, they discovered genetic markers on two separate chromosomes that are associated with extensive bone fragmentation on the right side of the skull. Although bone fragmentation also occurs on the left side of the skull, no genetic associations were detected when scoring on the left side of the cranium. The sighted surface-dwelling fish never demonstrated any of these craniofacial abnormalities. "By understanding how genes are behaving differently on the right versus the left sides, we hope to discover why many craniofacial alterations are more severe or present on only one side of the face in humans," says Gross.

Researchers are now narrowing in on the precise genes associated with these cranial abnormalities, with indications that two genes previously shown to be associated with cleft palate in humans, bone morphogenetic protein number four (BMP4) and transforming growth factor beta family member 3 (TGFB3), may similarly be involved in natural forms of bone asymmetry. Previous research discovered that the gene that causes red hair and pale skin in humans was the same gene that caused the albino-like cavefish to have less pigmentation than the surface-dwelling species. Funding for the research was supported by a federal grant from the National Institute of Dental and Craniofacial Research, National Institutes of Health.

Building a Family Pedigree

The researchers bred the cave fish with the surface-dwelling fish, and then intercrossed the hybrid offspring. Some members of this family pedigree resembled the albino qualities of the cave-dwelling fish but had a perfectly well-developed eye. Others demonstrated the dark pigmentation qualities of the surface-dwelling parent, but had a very small eye.

"We can make progress towards understanding the genetic origin of several analogous human disorders by expanding the repertoire of model systems represented by lab mice, zebrafish and so forth," explains Gross. "Many techniques and technologies have been developed in these powerful model systems, however they're extremely inbred. As a result, an inbred model system is not going to enable us to understand how and why craniofacial abnormalities evolve in nature. We can use the blind Pachón cave-dwelling fish to inform unresolved questions, such as how and why asymmetric craniofacial malformations occur in humans."

"Additional research, utilizing an increasing number of emerging cave-dwelling models, offers the exciting prospect of clarifying longstanding problems in contemporary evolutionary and vertebrate biology," says Gross.

High-Tech Imagery Used to Support Research

The UC researchers are using cutting-edge technology as they build a high-resolution, three-dimensional reconstructions of hybrids of the surface-dwelling and cave-dwelling fish, Astyanax mexicanus. The researchers turned to the Imaging Resource Center at Cincinnati Children's Hospital Medical Center to perform an imaging technique called micro-computed tomography, or micro-CT, on more than 200 related fish. The technology allowed the researchers to capture more than 1,000 X-ray images for each fish, which they combined and rendered into a high-resolution, 3-D skull, using the Amira software program.

Doctoral student and researcher Amanda Krutzler says the interactive program allows the researchers to rotate the fish skull in 3-D and take precise measurements for any traits of interest. In addition, micro-CT allows the researchers to visualize soft tissues, such as the brain or cardiovascular systems. "These scans will generate a

massive amount of data for our lab, which will provide projects for undergraduate students and graduate students like me," says Krutzler. The National Institute of Dental and Craniofacial Research grant provided the funding for the software.
In addition, doctoral student Brian Carlson used Circos software to visualize the connections between the cavefish genome and the zebrafish genome. "The more markers shared between a given cavefish linkage group and zebrafish chromosome, the thicker the ribbon that connects them. These representations are helpful in highlighting similarities between the cavefish and zebrafish genomes and may ultimately aid in identifying the genetic loci underlying the traits we examine by indicating which portions of the zebrafish genome may harbor genes that affect these traits," says Carlson.

http://phys.org/news/2014-04-homo-primate-tooth-size-decreases.html#rssowlmlink

'Homo' is the only primate whose tooth size decreases as its brain size increases

They are the only primates whose tooth size has decreased alongside the increase in their brain size throughout their 2.5-million year history.

Andalusian researchers, led by the University of Granada, have discovered a curious characteristic of the members of the human lineage, classed as the genus Homo: they are the only primates where, throughout their 2.5-million year history, the size of their teeth has decreased alongside the increase in their brain size.
The key to this phenomenon, which scientists call "evolutionary paradox", could be in how Homo's diet has evolved. Digestion starts first in the mouth and, so, teeth are essential in breaking food down into smaller pieces. Therefore, the normal scenario would be that, if the brain grows in size, and, hence, the body's metabolic needs, so should teeth.
However, in the case of Homo, this has not been the case, according to scientists in an article recently published in the journal BioMed Research International. The main author of the study, researcher Juan Manuel Jimenez Arenas, from the University of Granada's Department of Pre-History and Archaeology, points out that "This means that significant changes must have occurred in order to maintain this trend".
A change in diet, incorporating a higher amount of animal food, must have been one of the keys to this phenomenon. The quality leap in Homo's diet, through a greater intake in animal proteins, fats and certain olio-elements, is essential for a correct working and maintenance of the brain. On a similar note, a larger brain allows greater social and cultural development, which, at that time, led to the achievement of important technological innovations.
In order to validate this theory, the researchers evaluated the relationship between the size of post-canine teeth and the volume of the endocranium in a wide set of primates, among which were found the main representatives of Homo fossils. "Before we started the study, it was well known that, throughout the evolution of humans, tooth-size diminished and brain-size increased. We have established that they are two opposing evolutionary trends that have been linked for 2.5 million years, when our first ancestors within the Homo genus first appeared on the evolutionary stage".

Genetic Study

The study's authors also relate these changes to the inactivation of gene MYH16, linked to temporalis musculature, which fell in size approximately 2.4 million years ago. This would do away with an important barrier for encephalization (a hypertrophied temporalis musculature prevents the development of the cranial dome). Likewise, they analyzed their relationship with the inactivation of gene SRGAP2, which helps towards the evolution of the neo-cortex, playing a principal role in human brain development.

http://www.eurekalert.org/pub_releases/2014-04/twi-bgb040414.php#rssowlmlink

Bacterial gut biome may guide colon cancer progression

Wistar findings suggest link between colon microbiome and genome stability

PHILADELPHIA - Colorectal cancer develops in what is probably the most complex environment in the human body, a place where human cells cohabitate with a colony of approximately 10 trillion bacteria, most of which are unknown. At the 2014 American Association for Cancer Research Annual Meeting in San Diego, researchers from The Wistar Institute will present findings that suggest the colon "microbiome" of gut bacteria can change the tumor microenvironment in a way that promotes the growth and spread of tumors.
Their results suggest that bacterial virulence proteins may suppress DNA repair proteins within the epithelial cells that line the colon. The research opens the possibility of modifying colon cancer risk by altering the population makeup of bacteria in the intestines of people at risk due to genetics or environmental exposure.
"There is a drastic, unmet need to look at new ways to define exactly how colon cancer forms in the gut and what triggers its progression into a lethal form," said Frank Rauscher, III, Ph.D., a professor in The Wistar

Institute Cancer Center. "We suggest that some bacterial proteins can promote genetic changes that create conditions in the gut that would favor the progression of colon cancer."
While colorectal cancer incidence rates have declined, likely due to more widespread screening, survival rates have not. According to the American Cancer Society, about 50,000 Americans will die from colorectal cancer this year. "While our understanding of the gene mutations involved in colon cancer has improved, this has not lead to the promised increases in overall survival," Rauscher said.
Intestinal bacteria typically provide many benefits to their human hosts, aiding in digestion and crowding out more directly pathogenic bacteria. However, both "friendly" commensal bacteria and infective, pathogenic bacteria have been shown to actively reduce inflammation, an important tool used by the human innate immune system to promote healing and prevent the spread of infection.
In these studies, Rauscher and his colleagues injected anti-inflammatory proteins produced by EPEC (Enteropathogenic Escherichia coli) bacteria into colon epithelial cells. One of these proteins, NLEE, is an enzyme that targets TAB2, a human scaffolding protein involved in the transduction of chemical signals in the NF-κB pathway. Targeting TAB2 results in the inactivation of numerous inflammatory activities in the gut.
Rauscher and colleagues looked for other human proteins that could be targeted by NLEE. Remarkably, they found that NLEE also has the capability of shutting off a protein, ZRANB3 involved in DNA repair. If bacterially infected colon cells can no longer repair damage to their DNA, mutations will accumulate, which will promote cancer growth.
In addition, along with collaborators in the laboratory of Feng Shao, Ph.D., at the National Institute of Biological Sciences in Beijing, China, they demonstrated that NLEE proteins attack TAB2 and ZRANB3 by methlylating these proteins—essentially adding a single methyl molecule—which unfolds the target proteins. NLEE appear to specifically attack a structure on TAB2 and ZRANB3 known as a "zinc finger," which is a common structural motif used in many other proteins. When the researchers determined the structure of NLEE, they found a deep cleft on the protein specific to a certain zinc finger pattern. A survey of EPEC-infected colon cells showed that this zinc finger pattern was common to at least three DNA repair enzymes, suggesting that NLEE has the capability of having widespread influence on mechanisms in the colon that typically prevent cancer growth.
"Our results suggest that some infective intestinal bacteria, which normally can simply cause gastric distress, have the capability of inducing genetic changes (by limiting repair) in our intestinal cells which could lead to tumor development," Rauscher explained. "It is possible that limiting the amount of this bacteria in our gut may protect us from the genetic changes which accumulate in our intestinal cells over time and lead to cancer development."
According to Rauscher, this is a new way to look at the microenvironment in the gut as an incubator for colon cancer, depending upon which type and species of bacteria are resident and potentially infectious in our large intestines. Rauscher and his collaborators are currently embarking on a project to further test their hypothesis.
Collaborators on this project include Jayashree Karar, Ph.D., and Hongzhuang Peng, Ph.D., of the Rauscher laboratory at Wistar; Li Zhang, Ph.D., Qing Yao, Ph.D., and Feng Shao, Ph.D., of the National Institute of Biological Sciences, Beijing, China; and Ilan Rosenshine, Ph.D., of the Hebrew University of Jerusalem, Israel.
American Association for Cancer Research, 2014 Annual Meeting
Presentation Title: Control of DNA repair and genome stability by the colon microbiome: The EPEC bacterially encoded NLEE virulence effector protein methylates and inactivates the human ZRANB3 DNA repair helicase

http://www.wired.com/2014/04/enceladus-ocean-cassini/#rssowlmlink

Underground Ocean Makes This Saturn Moon a Top Bet for Extraterrestrial Life

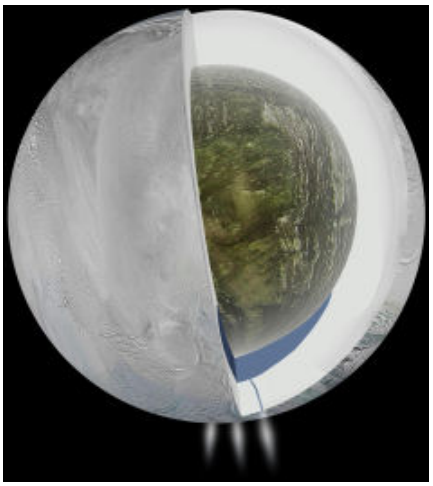
Scientists have determined that a hidden ocean of liquid water likely lies beneath the frozen crust of Saturn's moon Enceladus.

By Adam Mann

Because the tiny moon freely sends samples of this water into space via spectacular geysers, the finding could rocket Enceladus to the forefront of searches for life beyond our planet.
Enceladus has been known as an oddball in the outer solar system ever since the discovery in 2005 of its incredible water jets.
The finding, made by NASA's Cassini spacecraft, revealed that the tiny world – only one-seventh the size of our own moon – is geologically active. Cassini has been back to Enceladus many times since, exploring and photographing enormous cracks at the moon's south pole known as tiger stripes, and even flying through the geysers to sample their composition.
Scientists knew the water in Enceladus' jets must have been coming from somewhere. But exactly how much liquid water the moon kept on hand at any given time was something of a mystery. Perhaps subterranean ice

blocks were rubbing together, generating friction and heat that melted the ice and powered the geysers. The idea of an ocean has long been a more attractive explanation and, in this sense, the recent finding wasn't unanticipated.

"I was not surprised because we knew there was liquid water," said aerospace engineer Luciano Iess of Sapienza University of Rome, lead author of a paper appearing today in Science on the finding. "But quantifying the amount of water was a different story. It could have been rather shallow or a remarkable mass, like the one we have found."



The Cassini data suggests that the Enceladus ocean contains about the same mass as Lake Superior. But what it lacks in quantity, it makes up for in scale. The moon's ocean is on average six miles deep, comparable to some of the deepest spots on our world's oceans. Not bad for a tiny world dwarfed in size by our own.

Since arriving at Saturn in 2004, Cassini has made 19 flybys of Enceladus, including three that brought it within a very close 62 miles of the moon's surface. By precisely tracking the spacecraft's flight path during the close flybys, engineers could map out exactly how the icy world's gravity tugged on the spacecraft.

Cutaway showing what may be happening below Enceladus' frozen exterior. **Image: NASA/JPL-Caltech**

The pull that Cassini felt at Enceladus' south pole was a bit stronger than it would be if the mass there was made entirely of ice. This suggests that a large reservoir of water, which is denser than ice and would therefore contain more mass, exists under the frozen crust. The gravity mapping data indicated that the ice sheet at Enceladus' south pole is about 20 miles thick, followed by a watery ocean six miles deep, and then a rocky core. Because two of Cassini's three close flybys took the probe over only the south pole, that is the area of highest gravitational mapping. Enceladus' ocean could actually extend farther than 50 degrees south latitude.

"If anything that's a lower limit," said planetary scientist David Stevenson of Caltech, another co-author of the recent work. "It could even be global."

The presence of geysers at Enceladus' south pole creates many other odd features there. Cassini has measured hot spots at the tiger stripes that appear to be the source of the jets. And the surface is geologically young, possibly only a few million years old, based on the scarcity of impact craters that accumulate on all celestial bodies over time.

Because of there are so many things that an underground ocean could help explain, most planetary scientists will probably have an easy time accepting these latest results.

"You could think of crazy other explanations" to explain the gravity map data, said planetary scientist John Spencer of the Southwest Research Institute in Colorado, who was not involved in the study. "But this is the most reasonable. The ocean we suspected is really there."

This puts Enceladus in the same company as other outer solar system worlds with liquid oceans, such as its neighbor Titan and Jupiter's Europa.

NASA's philosophy on finding life beyond Earth is "Follow the water," so all these moons are potential places to explore. Given that it shoots free samples from the interior up into space, some scientists are now saying that Enceladus should get priority for future life-finding missions.

"Enceladus has the most accessible extraterrestrial habitable zone," said planetary scientist Carolyn Porco, leader of Cassini's imaging team and who was also not involved in the recent work. "This place is really where we should be going."

Along with several co-authors, Porco published an article on Mar. 31 in the journal Astrobiology making the case for an astrobiology probe to Enceladus. While Europa has long been the most attractive ocean-bearing moon, its thick icy crust is an impediment to sample collection. Though recent evidence suggests that Europa, too, may have spouts of water erupting from its south pole, the findings still need to be confirmed with future observations.

Cassini has already sampled Enceladus' interior water with its onboard mass spectrometer, finding carbon, nitrogen, simple organic compounds, and other elements commonly used in living organisms. A future spacecraft outfitted with a more powerful instrument could potentially detect complex organics such as amino acids or even conduct a sample return mission, though this presents problems protecting against interplanetary contamination. But given NASA's budget crunch in planetary science exploration, it seems like it might take some time before a mission to any outer moon will get funded.

http://www.bbc.com/news/health-26871259##rssowlmlink

Lung cancer survival stats reveal poor outlook

Half of people with lung cancer die within six months of diagnosis, says a report from Macmillan Cancer Support which looked at variations in cancer survival rates.

While breast cancer and prostate cancer have a five-year survival rate of more than 80%, lung cancer's is around 10%. Those who survive lung cancer for five years are then 10 times more likely to get another cancer. Macmillan said improving early diagnosis was key. In their report, the cancer charity carried out an analysis of almost 85,000 cancer patients' experiences of the NHS in England from 2004 to 2011. They looked in detail at what happened to people with one of four types of cancer - breast, prostate, lung or brain cancer - after they were diagnosed.

Good health?

The research showed that one in five (20%) women with breast cancer and one in four (25%) men with prostate cancer survived for at least seven years after diagnosis in good health. But the picture was significantly worse for people with lung cancer, or the most common form of brain cancer, of whom less than 1% survived long-term and in good health. The report suggests that one in five people with lung cancer die within one month of being diagnosed and 73% die within one year.

Although survival rates for some cancers "have soared" over the past 40 years in England, the report says other cancers are lagging behind and the figures make the case for improving cancer care across the UK more urgent. In its report, Cancer's unequal burden, Macmillan Cancer Support urges NHS leaders and GPs to plan cancer services better, improve early diagnosis and provide the best treatment available regardless of age or location.

'Biggest killer'

Ciaran Devane, chief executive of Macmillan Cancer Support, said the findings revealed "stark variations".

"Cancer is not just one disease, and therefore there is no one-size-fits-all approach to treatment and aftercare.

"The NHS needs to get much better at using robust data to understand the complex needs of people with different cancers so that services can be planned accordingly. It's no good papering over the cracks any longer, we need a complete system overhaul."

Dr Penny Woods, chief executive of the British Lung Foundation, said the report made an important call for improvements in early diagnosis. "Late presentation and diagnosis is one of the main reasons lung cancer survival rates in this country lag so far behind rates in Europe and the US, as well as rates for other cancers. As such, the report's revelation that over half of lung cancer patients die within just six months of diagnosis is sadly very telling."

Symptoms of lung cancer

a cough that won't go away, caused by irritation of the tubes that carry air in and out of your lungs
breathlessness - if the tumour is either large or blocks off an airway
wheezing from that side of the chest which may make it difficult to sleep on one side
blood in your phlegm
pain - usually only if the tumour reaches the edge of the lung
weight loss - because cancers use up energy to grow.

If you have these symptoms, you should see your doctor. But these symptoms are also very common in people with other lung diseases.

British Lung Foundation

Dr Woods said evidence suggested that public awareness campaigns were starting to increase early diagnosis rates. But she added: "It is no coincidence that survival rates are so much greater for the likes of breast cancer, given the amount of research funding allocated to such areas have long dwarfed the amount given to lung cancer. "Lung cancer is by far the biggest cancer killer in this country: it's time we stopped treating it like the poor relation."

Most cases of lung cancer are related to smoking, which is the biggest risk factor for the disease. Although rates of lung cancer are decreasing in men, they are rising in women because of the number of women who continued to smoke during the post-war period and into the 1970s.

http://bit.ly/1hwssOY

Coal fuelled China long before industrial revolution

CHINA now consumes nearly as much coal as the rest of the world combined. And perhaps it always did: it seems coal was routinely burned 3500 years ago in what is now China – the earliest evidence we have for the practice.

04 April 2014 by Colin Barras

John Dodson at the Australian Nuclear Science and Technology Organisation in Sydney, and his colleagues in China, were examining early evidence of bronze casting in northern China when they found chunks of burned coal in the ancient slag piles instead of the charcoal they expected. "We got one of the guys to take samples and he sieved out some seeds, which we radiocarbon dated in Sydney," says Dodson. The seeds were chosen

because they formed at the time the coal was burned, whereas the coal formed millions of years earlier. "You can't just radiocarbon date the coal because it is already ancient carbon," he says.
The results confirmed that coal had been burned in the area around 3500 years ago. The team also found coal at four more sites, dating back 3500 to 3700 years – with one of them dating back even further, to about 4600 years ago (The Holocene, doi.org/rw8).
"We have been looking at vegetation change in the landscape and it seems the coal appears in the archaeological sites just as the evidence for ancient forests in the region disappeared," says Dodson. He thinks the locals switched to coal once they had burned all the wood in the forests for fuel.
"With no other energy supply you would be forced to move on. But here, coal was lying around on the surface – you don't even have to mine it – and life could continue," says Dodson.
The finding is remarkable because it is practically the only evidence of coal burning in the archaeological record. One rare exception is a study from the 1990s, which reported limited evidence that lignite (brown coal) was used for fuel around 73,000 years ago in ice age Europe – but not on a routine basis as seems to be the case in Bronze-Age China.
Early coal use could imply that the climate change associated with burning fossil fuels may have begun long before the industrial revolution in the 18th century. "Maybe things were set in train thousands of years ago," says Dodson.
William Ruddiman at the University of Virginia in Charlottesville has long argued so. His "early Anthropocene" hypothesis suggests human-induced climate change may have begun 8000 years ago. Ruddiman thinks the latest study is consistent with his idea, "because people would have only turned to coal when wood became unavailable because deforestation was nearly complete", he says.
Jennifer Marlon at Yale University thinks it is unlikely that the coal combustion in China had much of a global climatic impact. "Emissions would have been way too small still," she says.

http://www.bbc.com/news/world-africa-26882013##rssowlmlink

Ebola outbreak: Mali on alert

Mali is on alert over the deadly Ebola virus after three suspected cases were reported near the border with Guinea, where 86 people have died.

A BBC correspondent says there are tight controls on people entering the capital, Bamako, from the border area.
He says thermal-imaging cameras are screening passengers at the airport in case they have a fever. The virus, which is spread by close contact and kills 25%- 90% of its victims, has already spread to Liberia.
Meanwhile, an Air France plane which landed in Paris from Guinea was quarantined for two hours on Friday morning after the crew suspected a passenger was infected with Ebola. "The test turned out negative," a spokesman for the airline said. Six people have died in Liberia, out of 12 suspected cases, according to the local health authorities.
Sierra Leone has also reported suspected cases, while Senegal has closed its normally busy border with Guinea.

Visas suspended

The BBC's Alou Diawara in Bamako says the three people feared to have Ebola have been moved to isolation wards on the edge of the city. Samples have been sent to the US for testing and the results are expected in a few days. Mali's government has advised its nationals against all non-essential travel to areas affected by Ebola.
WHO spokesperson Tarik Jasarevic in Conakry told the BBC the reports of cases in Mali were a "concern". "Everyone should be vigilant and aware of what is going on. But we need to wait for the results to confirm if it is Ebola," he said.
The virus was first spotted in Guinea's remote south-eastern region of Nzerekore, where most of the deaths have been recorded. But it was not confirmed as Ebola for six weeks. It has now spread to Guinea's capital, Conakry, where five deaths have been recorded out of 12 suspected cases. Saudi Arabia suspended visas for Muslim pilgrims from Guinea and Liberia on Tuesday, in a sign of the growing unease about the outbreak.
This is the first known outbreak in Guinea - most recent cases have been thousands of miles away in the Democratic Republic of Congo and Uganda.
There is no known cure or vaccine for Ebola. The tropical virus leads to haemorrhagic fever, causing muscle pain, weakness, vomiting, diarrhoea and, in severe cases, organ failure and unstoppable bleeding.

http://www.medscape.com/viewarticle/823110?src=rss

Paxil Manufacturer Recalls Drug After FDA Knuckle Rapping

GlaxoSmithKline recalled certain batches of the antidepressant to wholesalers

Caroline Cassels

Following a letter from the US Food and Drug Administration (FDA) citing potential contamination of paroxetine, the active ingredient in the antidepressants Paxil/Seroxat, during the manufacturing process, the drugs' maker, GlaxoSmithKline (GSK), recalled certain batches of the antidepressant to wholesalers.

The FDA's letter to GSK following its inspection of the company's manufacturing plant in Cork, Ireland, in October 2013 states that paroxetine was contaminated with material from the plant's pharmaceutical waste tank. The FDA letter states that until GSK corrects these manufacturing deviations, it "may withhold approval of any new applications or supplements listing your firm as an API [active pharmaceutical ingredient] manufacturer." According to the company, it is taking the FDA's statement "very seriously."

"GSK acknowledges the concerns raised by the FDA and we are recommending a Class 3 recall — that is a recall from wholesalers — of certain batches of Paxil/Seroxat containing the paroxetine API supplied by the Cork site that are implicated in the Warning Letter. Based on a medical assessment, GSK considers that there is no increased risk of harm to patients taking finished product manufactured from the implicated batches of paroxetine API," the company said in a statement.

The company added that it is currently "reviewing the content of the Warning Letter to assess the concerns raised, in order to develop appropriate Corrective and Preventative Actions. We will be able to comment further once we have prepared and submitted a comprehensive response to the Warning Letter to FDA by April 9."

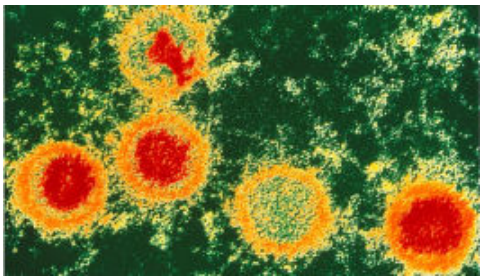
This recall marks the second time in as many weeks that the company has recalled a product. Last week, as reported by Medscape Medical News, the company's weight-loss drug orlistat (alli) was recalled because of potential tampering concerns.

http://www.bbc.com/news/health-26857610##rssowlmlink

Cancer virus discovery helped by delayed flight

Bad weather and a delayed flight might be a recipe for misery - but in one instance 50 years ago it led to a discovery that has saved countless thousands of lives.

By Paula McGrath Health Check, BBC World Service



Electron micrograph of the Epstein Barr virus, **Dr Gopal Murti/Science Photo Library**

The discovery of the Epstein Barr virus - named after British doctor Anthony Epstein - resulted from his specialist knowledge of viruses which caused tumours in chickens plus his skills gained using one of the first commercially-available electron microscopes. His hunch was assisted by a longer than expected journey of some tumour cells from Uganda, which were nearly thrown in the bin. But it would never have happened if Epstein's curiosity hadn't been fired up by a lecture by the Irish doctor turned "bush surgeon", Denis Burkitt.

In the lecture, billed as a staff meeting on "The Commonest Children's Cancer in Tropical Africa", Burkitt described how he had noticed a number of cases of debilitating tumours which grew around the jawbone of children in specific regions - particularly those with high temperatures and high rainfall.

We now know this as Burkitt lymphoma.

Sir Anthony Epstein, now 93, speaking to the BBC's Health Check programme, recalls: "I thought there must be some biological agent involved. I was working on chicken viruses which cause cancer. I had virus-inducing tumours at the front of my head. I thought... [it] was being carried by some insect vector, or some tic. That's why it was temperature-related."

The Epstein Barr virus belongs to the family of herpes viruses - and is linked to a number of different conditions, depending on where you live. Most people are infected with the Epstein Barr virus. It's best known in high-income countries for causing glandular fever which causes a sore throat, extreme fatigue and swollen glands in the neck.

According to Dorothy Crawford, emeritus professor of microbiology at Edinburgh University, up to 95% of all adults are infected with the virus. "The virus is spread in childhood at different rates - in the saliva, so through close contact. In African countries most children have it by the age of two because they share cups in their household. "The rate is lower in middle-class areas of England, so if you haven't already been exposed by your early teens it can cause glandular fever." This has given it the nickname the kissing disease because, she explained: "People kissing in the back row of the cinema exchange more saliva than young children sharing toys."

Epstein asked for samples of the tumours from Burkitt and they were sent back on overnight flights from Uganda. For almost three years Epstein's efforts to retrieve virus from the tumour cells failed, despite trying several culture methods used successfully for other viruses like influenza and measles. In the end bad weather came to the rescue.

Fog delayed one flight which was diverted to Manchester, 200 miles from London. So the sample taken from the upper jaw of a nine-year-old girl with Burkitt lymphoma didn't get to Epstein until late one Friday afternoon on 5 December 1963.

At that point it looked past its sell-by date. "The fluid was cloudy. This suggested it had been contaminated on the way," Epstein said. "Was it full of multiplying bacteria? Before we threw it away I looked at it under a wet preparation microscope and saw huge numbers of free-floating, healthy looking tumour cells which had been shed from the edge of the tumour."


***Sir Anthony Epstein and Dr Yvonne Barr,* courtesy of Anthony Epstein**

Traditionally, growing cells successfully in culture had involved sticking them to a glass surface for support, but the lymphoma cells seemed to favour growing in a suspension. Once all other conventional tests for identifying the virus from the cultured cells had failed, Epstein tried electron microscopy. The very first grid square he viewed included a cell filled with herpes virus.

Exhilarated by what he'd seen, Epstein went for a walk in the winter snow and came back feeling calmer.

"I was extremely frightened in case the electron beam [of the microscope] burned up the sample. I recognised at once the herpes virus - there were five then, now nine. Any of the then-known ones would have wiped the culture out when they were replicating but this wasn't happening. I had the feeling that this was something special."

Our understanding of this pervasive virus, named after Epstein and one of his PhD students Yvonne Barr who helped to prepare the samples, has increased over the years since Epstein confirmed his findings with American virologist colleagues. Burkitt's data helped to identify that the tumour named after him was seen in children with chronic malaria, which reduced their resistance to the Epstein Barr virus, allowing it to thrive. But most of us live quite happily with the virus.

"If you disturb the host-virus balance in any way then changes take place which lead to very unpleasant consequences," says Epstein. "Once the link between Epstein Barr virus and Burkitt lymphoma was established, other seemingly unrelated conditions followed. These include a cancer at the back of the nose which is the commonest cancer seen in men in southern China and the second commonest in women in the same region. There is also a link to Hodgkins lymphoma, a cancer of the white blood cells. "Each one came out of the blue," according to Epstein, "and we've just heard about another. About 20% of Japanese cancers of the stomach are associated with the virus."

Yet another connection was made by Professor Dorothy Crawford, while waiting for the lift at the Royal Free hospital in London. "It's such a tall building everyone meets outside the lifts. I was standing next to a renal [kidney] transplant surgeon and overheard him say they'd just had their first case of post-transplant lymphoma. So I went with him to the pathology department and asked for some sections of the tissue to look at under the microscope." Burkitt lymphoma can now often be treated successfully with chemotherapy.

At a recent meeting in Oxford of the Epstein Barr Virus Association future directions for research were explored. Attention is now focusing on a vaccine for the Epstein Barr virus - and some efficacy has already been demonstrated. Epstein hopes that a vaccine will lead to the kind of success seen in other cancers caused by viruses - such as Hepatitis B and the human papillomavirus, which cause liver and cervical cancer respectively.

http://www.eurekalert.org/pub_releases/2014-04/esfr-iro040414.php#rssowlmlink

Increased risk of developing lung cancer after radiotherapy for breast cancer

Women who have radiotherapy for breast cancer have a small but significantly increased risk of subsequently developing a primary lung tumour, and now research has shown that this risk increases with the amount of radiation absorbed by the tissue.

Vienna, Austria: Dr Trine Grantzau (MD) told the 33rd conference of the European Society for Radiotherapy and Oncology (ESTRO33) in Vienna: "We found that for each Gray [1] delivered to the lung as part of radiotherapy for a breast tumour, the relative risk of developing a subsequent primary lung cancer increased. This increased risk was similar to the reported increased risk of heart disease after radiotherapy for breast cancer.

"Our findings suggest that any reduction in the dose of radiation to the lung would result in a reduction in the risk of radiation-induced subsequent lung cancers. With the advances in breast cancer treatment and the

introduction of breast cancer screening, a growing number of women are becoming long-term survivors, and so we need to have an increased awareness of treatment-induced second cancers and take steps to reduce those risks by using radiotherapy techniques that spare normal tissue as much as possible."
Dr Grantzau, a doctor in the department of experimental clinical oncology at Aarhus University Hospital (Aarhus, Denmark), and her colleagues investigated the incidence of second primary lung cancers (i.e. a new lung cancer and not a secondary tumour that has spread from the original breast cancer) in a group of 23,627 women in Denmark who had been treated with post-operative radiotherapy for early breast cancer between 1982 and 2007.
Among this large group of women, 151 (0.6%) were diagnosed with a new lung cancer (the group of cases) and they were matched with 443 women who had not developed lung cancer (the control group).
In a previous study including the 23,627 irradiated women and, additionally, 22,549 unirradiated breast cancer patients, results showed that the risk of developing a radiation-induced second lung cancer was approximately one in every 200 women treated with postoperative radiotherapy.
"In the current study, we wanted to see if there was a dose-response correlation for second primary lung cancer after breast cancer irradiation. We further wished to estimate the excess relative risk per delivered Gray to the lung. As smoking is strongly correlated to lung cancer, we also looked into the effect of radiation and smoking," explained Dr Grantzau.
The researchers retrieved radiotherapy records of the previous breast cancer radiation treatment (including the delivered dose, field size and treatment technique) together with the smoking status for all cases and controls. For the cases they also obtained radiographic images of the lung cancers. With this information they were able to reconstruct the ways that the women had been treated for the original breast cancer and to estimate the amount of radiation that was delivered to the part of the lung where the subsequent tumour developed.
They tested the accuracy of their calculated radiation doses on a model, or "phantom", and made adjustments to take into account the higher doses that they found were actually delivered to areas outside the main field of radiation.
The median age of the women when they were diagnosed with breast cancer was 54 (with a range of 34-74) and the median age when a second primary lung cancer was diagnosed was 68 (range 46-90). Seventy percent of the lung cancers were diagnosed five or more years after radiotherapy for breast cancer, ranging from five to 26 years. The majority (91%) of the lung cancer cases were smokers, whereas 40% of the controls were smokers.
The mean average dose of radiotherapy during breast cancer treatment that had been delivered to the site of the lung tumour was 8.7 Gy, while it was 5.6 Gy to the comparable site in the women who had not developed lung cancer.
Although the absolute risk of developing a second lung cancer is small, the researchers showed that among women who had survived breast cancer for at least five years, the relative risk of subsequently developing a lung cancer increased by 8.5% per delivered Gy to the lung.
"These results show that the risk of second lung cancer after radiotherapy in early breast cancer patients is associated with the delivered dose to the lung," said Dr Grantzau.
"It is, however, important to place the risk of getting a radiation-induced second lung cancer in a perspective that is balanced with the known benefits of radiotherapy in the adjuvant treatment of breast cancer. Post-operative radiotherapy in breast cancer patients decreases the likelihood of breast cancer recurrence and improves overall survival. The challenge for radiation oncologists is to reduce the delivered dose of radiotherapy in a way that minimises the dose to the normal tissue to avoid radiation-induced malignancies, without compromising its efficacy in the cancerous breast tissue."
She added: "Furthermore, clinicians should be continually advising breast cancer patients to quit smoking in order to reduce their risk of developing lung cancer. It's important to emphasise that the risk of getting a tobacco-induced lung cancer is much higher than the risk of getting a radiation-induced second lung cancer.
Professor Vincenzo Valentini, president of ESTRO and a radiation oncologist at the Policlinico Universitario A. Gemelli, Rome, Italy, commented: "This research shows the importance of monitoring the safety of radiotherapy procedures so that we can use the information gained to achieve a good balance between the risks and benefits of a particular treatment. Reducing the radiation dose to normal tissue is always beneficial, and knowing the exact target and the best radiation dose will help to reduce any long-term side-effects of a therapy that research has long shown to be instrumental in helping to save the lives of women with breast cancer.
Dr Grantzau's research suggests there is a small increased risk of lung cancer in the years after radiotherapy for breast cancer, particularly in women who smoke. This underlines the importance to women of not smoking, as this increases the risk of a range of diseases. We, as radiation oncologists, will continue to work to monitor and improve the safety and efficacy of our therapies."

Abstract no: O-0489, Clinical breast cancer session, 10.30-11.30 hrs (CEST) on Monday, 7 April, Auditorium.
[1] A Gray (Gy) is the absorption of one joule of energy, in the form of ionizing radiation, per kilogram of (body) tissues.
[2] The study received funding from Aarhus University, Faculty of Health Sciences, CIRRO (Danish Centre for Interventional Research in Radiation Oncology), the Danish Cancer Society, and from the European Atomic Energy Community's Seventh Framework Programme.

http://bit.ly/1lKc0Ck

Flimsy rocks allowed Earth's plates to start moving

Fragile things can be useful. Earth's surface is a lively place, made up of shifting plates of rock. Now it seems the surface only moves because it is partly made of flimsy rocks that have been damaged in the planet's heart.

18:00 06 April 2014 by Samuel Osborne

Uniquely in the solar system, Earth's crust is divided into several sections. These tectonic plates move over millions of years, throwing up mountains and triggering earthquakes. Often, one plate gets forced under another and sinks into the mantle beneath, a process called subduction. Elsewhere, new material is brought to the surface. If the plates did not recycle themselves like this, our planet might not have such a stable climate, or be so rich in the chemicals vital for life.

So the beginning of plate tectonics is a critical event in our planet's history. But it is unclear how the plates first started to move, or when. The first subduction seems to have happened about 4 billion years ago, but clear evidence that all the plates were moving and subducting only appears 3 billion years ago.

To explain this delay, David Bercovici of Yale University and Yanick Ricard of the University of Lyon in France studied how rocks behave on a small scale, and then extrapolated to the planet as a whole.

Crumbling rocks

Bercovici and Ricard modelled what happens to rocks in the upper mantle, just below the plates. There, the strong currents shrink the grains that make up rocks, a bit like the way stirring foam makes smaller bubbles. As a result, weak zones form and grow. Over time, more and more of these damaged rocks build up in the upper mantle, and eventually are thrust back up to form new sections of plate. Because these new plates are partly made of fragile rocks, their edges are more breakable, making it easier for one plate to be forced under another.

Bercovici suggests that the first rocks underwent subduction 4 billion years ago, and over the next billion years were gradually damaged in the mantle and got reincorporated into the surface plates. By 3 billion years ago, the plates were fragile enough that subduction could get going in earnest.

Only on Earth

"Their model makes intuitive sense," says Catherine McCammon of the University of Bayreuth in Germany. "They take things one step further and show quantitatively that it can work." McCammon says that, although we will probably never know for sure how plate tectonics began, Bercovici and Ricard's model offers a plausible story.

The model could help to explain why Earth is the only planet known to have active plate tectonics. The key is that true plates can only evolve from weak zones in rocks. Venus's surface atmosphere, for example, is much hotter than Earth's, so its weak zones heal faster, stopping tectonic activity before it starts.

Journal reference: Nature, DOI: 10.1038/nature13072

http://www.eurekalert.org/pub_releases/2014-04/uom-ccp040414.php#rssowlmlink

Circumcision could prevent prostate cancer... if it's performed after the age of 35

Montreal study shows the effect is particularly strong amongst black men

Researchers at the University of Montreal and the INRS-Institut-Armand-Frappier have shown that men circumcised after the age of 35 were 45% less at risk of later developing prostate cancer than uncircumcised men. This is one of the findings that resulted from a study undertaken by Andrea Spence and her research directors Marie-Élise Parent and Marie-Claude Rousseau. The researchers interviewed 2114 men living on the Island of Montreal. Half of them had been diagnosed with prostate cancer between 2005 and 2009, while the others participated in the study as the control group. The questions covered their lifestyle and medical history, if they were circumcised, and if so, the age at which the operation had been performed.

Greater benefit for Black men

Across the board, the participants who were circumcised were 11% less likely to later develop a prostate cancer compared to those who weren't. The size of the reduction is not statistically significant. "This proportion reflects what has been shown in other studies," Parent explained. However, babies who were circumcised before the age of one were 14% less likely to develop prostate cancer. Moreover, the removal of the foreskin at a young age provides protection, over the long term, against the most aggressive forms of cancer.

Prostate cancer is rare amongst Jewish or Muslim men, the majority of whom are circumcised. While the specific causes of this cancer remain unknown, three risk factors have been identified: aging, a family history of this cancer, and Black African ethnic origins.

Amongst the 178 Blacks who took part in the study – of whom 78% were of Haitian origin – the risk of prostate cancer was 1.4 times higher than amongst Whites. 30% of the Black men were circumcised compared to 40% of the White men. Interestingly, the protective effect of the circumcision was limited to the Black men, whose risk of developing prostate cancer was decreased by 60%, with a very significant statistical effect.

Circumscribing the discovery

Researchers do not know what mechanism enables circumcision to protect men from prostate cancer. However, many studies have shown that this operation reduces the risk of acquiring a sexually transmitted infection (STI). "Unlike the skin that covers our bodies, the inner surface of the foreskin is composed of mostly non-keratinized mucosal epithelium, which is more easily penetrated by microbes that cause infections," Parent explained. Removing the foreskin could therefore reduce the risk of an infection that might be associated with prostate cancer. In any case, the protective effect of circumcision (in particular the effect observed in the Black population) must be confirmed by other studies, especially in consideration of the relatively few Black men who participated in research.