http://www.eurekalert.org/pub_releases/2013-07/ucl-eom072513.php

Evolution of monogamy in humans the result of infanticide risk

The threat of infants being killed by unrelated males is the key driver of monogamy in humans and other primates.

The study by academics from UCL, University of Manchester, University of Oxford and University of Auckland, is the first to reveal this evolutionary pathway for the emergence of pair living.

The team also found that following the emergence of monogamy males are more likely to care for their offspring. Where fathers care for young, not only can they protect infants from other males, but they can also share the burden of childcare.

Dr Kit Opie (UCL Anthropology), lead author of the study published in the journal PNAS, said: "This is the first time that the theories for the evolution of monogamy have been systematically tested, conclusively showing that infanticide is the driver of monogamy. This brings to a close the long running debate about the origin of monogamy in primates."

Infants are most vulnerable when they are fully dependent on their mother because females delay further conception while nursing slowly developing young. This leads to the threat from unrelated males, who can bring the next conception forward by killing the infant. Sharing the costs of raising young both shortens the period of infant dependency and can allow females to reproduce more quickly.

An additional benefit of sharing the burden of care is that females can then have more costly young. The considerable cognitive requirements of living in complex societies has resulted in many primate species having large, and costly, brains.

Growing a big brain is expensive and requires that offspring mature slowly. Caring fathers can help alleviate the burden of looking after young with long childhoods and may explain how large brains could evolve in humans. Humans, uniquely among primates, have both very long childhoods and mothers that can reproduce quickly relative to other great apes. Until now, a number of hypotheses have been proposed to explain the evolution of monogamy among mammals. These include:

Paternal care, when the cost of raising offspring is high
Guarding solitary females from rival males
Infanticide risk, where males can provide protection against rival males

To uncover the evolutionary pathway the team gathered data across 230 primate species. These were then plotted on a family tree of the relationships between those species. Bayesian methods were used to re-run evolution millions of times across the family tree to discover whether different behaviours evolved together across time, and if so, which behaviour evolved first.

This then allowed the team to determine the timing of trait evolution and show that male infanticide is the cause of the switch from a multi-male mating system to monogamy in primates, while bi-parental care and solitary ranging by females are a result of monogamy, not the cause.

Dr Susanne Shultz, from the University of Manchester, said: "What makes this study so exciting is that it allows us to peer back into our evolutionary past to understand the factors that were important in making us human. Once fathers decide to stick around and care for young, mothers can then change their reproductive decisions and have more, brainy offspring."

http://www.eurekalert.org/pub_releases/2013-07/uomh-sug072913.php

Study unravels genetics behind debilitating inflammatory disease Takayasu arteritis

International team of researchers identifies five genes that play major role in disease

ANN ARBOR, Mich. - Researchers have uncovered the genetics behind what makes some people susceptible to Takayasu arteritis, a debilitating disease that can lead to poor circulation, easy tiredness in the legs and arms, organ damage and stroke.

A study led by the University of Michigan has identified five genes tied to Takayasu arteritis, an inflammation that damages the aorta and can lead to narrowed arteries, aneurysms, high blood pressure, and heart failure. The findings appear in the August issue of The American Journal of Human Genetics.

"Discovering the genetic makeup of Takayasu arteritis is a pivotal step that will lead to fundamental understanding of the disease mechanisms and developing therapies to more effectively treat it," says senior author Amr Sawalha, M.D., associate professor of internal medicine in the division of rheumatology at the U-M Medical School. "This disease can be devastating but is understudied and poorly understood."

Takayasu arteritis mainly causes inflammation in the aorta – the large artery that carries blood from the heart to body– and other major blood vessels. This inflammation can also affect the heart valves, reduce blood flow to the legs and arms, and cause a stroke. Other symptoms include weight loss, fever, night sweats, fatigue and joint and muscle pain.

The disease is most common among women and typically occurs between the ages 20 and 40.
The new findings increase the number of genes linked to susceptibility to the disease to five risk areas both in the HLA (an inherited group of genes known as human leukocyte antigen) and outside the HLA. In addition to the previously established genetic association in HLA-B for Takayasu arteritis, researchers discovered and carefully localized novel genetic risk areas in HLA-DQB1/HLA-DRB1, FCGR2A/FCGR3A, and PSMG1.
"We have established and localized the genetic association with IL12B, which encodes the P40 subunit of the interleukin-12 (IL-12) and IL-23," says Güher Saruhan-Direskeneli, M.D., professor of physiology at Istanbul University and co-author of the study.
"Therapies to inhibit the IL12/IL23 pathway have been successful in other inflammatory diseases, and these recent findings support investigating this pathway closer in Takayasu arteritis as a potential therapeutic target," Sawalha adds.
Additional authors: Travis Hughes, Kenan Aksu, Gokhan Keser, Patrick Coit, Sibel Z. Aydin,Fatma Alibaz-Oner, Sevil Kamalı, Murat Inanc, Simon Carette, Gary S. Hoffman, Servet Akar, Fatos Onen, Nurullah Akkoc, Nader A. Khalidi, Curry Koening, Omer Karadag, Sedat Kiraz, Carol A. Langford, Carol A. McAlear, Zeynep Ozbalkan, Askin Ates,Yasar Karaaslan, Kathleen Maksimowicz-McKinnon, Paul A. Monach, Hu¨seyin T. Ozer, Emire Seyahi, Izzet Fresko, Ayse Cefle, Philip Seo, Kenneth J. Warrington, Mehmet A. Ozturk, Steven R. Ytterberg, Veli Cobankara, A. Mesut Onat, Joel M. Guthridge, Judith A. James, Ercan Tunc, Nursxen Duzgun, Muge Bıcakcıgil, Sibel P. Yentu¨r, Peter A. Merkel, Haner Direskeneli.
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Reference: "Identification of Multiple Genetic Susceptibility Loci in Takayasu Arteritis," American Journal of Human Genetics, August, 2013, http://dx.doi.org/10.1016/j.ajhg.2013.05.026.

http://www.sciencedaily.com/releases/2013/07/130729133002.htm

Therapeutic Fecal Transplant: Hope for Cure of Childhood Diarrhea Comes Straight from the Gut

Call it therapeutic poop, if you will, but the best hope yet for an effective treatment of childhood infections with the drug-resistant bacterium C. difficile.may come straight from the gut, according to recent research.

This is why pediatric gastroenterologists at the Johns Hopkins Children's Center are launching a fecal transplantation program for patients with recurrent diarrhea caused by what they say is a wily pathogen that is increasingly impervious to drugs and a rapidly growing problem among children and adults.
Over the last 20 years, cases of antibiotic-associated diarrhea have more than doubled, with nearly three million new infections each year, with up to a fourth of patients not responding to antibiotics, research shows. Most such cases, the researchers say, stemmed from infections with C. difficile.
Enter poop transplants. Studies in adults show that more than 90 percent of patients are cured following such therapy and, experts say, they have every reason to believe the numbers would be equally impressive in children. "Fecal transplantation -- or the transfer of 'good' bacteria from the colon of one person into the colon of another -- should be considered for all children with C. diff infections who don't respond to two standard courses of antibiotics," says Maria Oliva-Hemker, M.D., director of pediatric gastroenterology at Johns Hopkins Children's Center.
The rise in refractory C. difficile infections has been fueled by the growing use of antibiotics, experts say. "Antibiotics are lifesavers, but anytime we give them to a patient to eradicate one pathogen, there's collateral damage, in that along with the bad bacteria we wipe off some good organisms that help keep the complex workings of our gut in perfect balance," Oliva-Hemker says.
Such beneficial bacteria work by keeping rogue players in check, Oliva-Hemker explains, so any shifts in gut environment -- such as ones caused by antibiotics -- can have dire consequences. When good bacteria are killed off by antibiotics, the bad guys multiply causing an imbalance or "dysbiosis," Oliva-Hemker says. Typically, gut infections caused by one antibiotic are treated with another one to eradicate the overgrowth of harmful pathogens, but drugs often fail to do so fully or permanently because they only treat part of the problem.
"When we administer an antibiotic to treat the C. diff infection, we destroy some of the bad bacteria, but that does not address the other half of the problem -- the loss of good bacteria that might have led to the infection to begin with, so we never truly restore the balance in the gut and often the diarrhea returns with a vengeance in a matter of weeks," says Suchitra Hourigan, M.D., a pediatric gastroenterology fellow at Hopkins with a special interest in fecal transplantation.
The concept of treating poop woes with poop is hardly new. The method originated with ancient Chinese healers who gave their diarrhea-ravaged patients "yellow soup," a concoction of fecal matter and water.
Thousands of years later, the delivery approach has evolved. Nowadays, fecal transplants are often performed during a colonoscopy, and improvement can be seen in as short as two weeks, as beneficial bacteria start to repopulate the patient's gut, Hourigan says. Fecal donors, usually parents or relatives, are carefully screened for

risks much like any blood donor, Hourigan says. The donor's blood is tested for infectious pathogens, such as HIV and hepatitis C. People with autoimmune diseases or other chronic conditions, such diabetes or obesity, may not qualify as donors.
"The gut microbiome plays a major role in immunity and overall health, and right now we simply do not know whether fecal matter can somehow inadvertently also transfer the propensity toward such disorders from donor to recipient," Hourigan says.
The new pediatric protocol makes Johns Hopkins Children's Center one of a handful of pediatric hospitals in the country to offer this therapy for a condition that can cause dehydration, anemia and pain, and can seriously affect a child's quality of life, leading to absence from school. In its more extreme form, recurrent diarrhea can cause life-threatening colon inflammation, which is for some 14,000 deaths each year, according to the Centers for Disease Control and Prevention. Beyond the human toll, refractory diarrhea drains the health care system of more than $3 billion each year, research has shown.
Its great therapeutic success notwithstanding, some important questions remain: How precisely do donor bacteria change the recipient's gut microbiota and which bacteria make the best poop transplants? And because poop contains trillions of bacteria and hundreds of bacterial species, scientists have not quite figured out which ones are our best friends and worst foes and which ones are mere bystanders. These are some of the questions Oliva-Hemker and Hourigan's ongoing research is attempting to answer.
And with the growing understanding of gut dynamics, better therapies should emerge. In a decade or so, Oliva-Hemker predicts, scientists would be able to design the perfect fecal concoction in a lab, obviating the need for fecal transplants.
"In less than a decade, we'll have lab-cooked poop that we can administer to restore balance in the guts of people with a wide array of conditions caused by the imbalance between good and bad germs."

http://www.sciencedaily.com/releases/2013/07/130729133632.htm

Plant-Based Compound May Inhibit HIV

A compound found in soybeans may become an effective HIV treatment without the drug resistance issues faced by current therapies, according to new research by George Mason University researchers.

by Michele McDonald

It's in the early stages, but genistein, derived from soybeans and other plants, shows promise in inhibiting the HIV infection, says Yuntao Wu, a professor with the George Mason-based National Center for Biodefense and Infectious Diseases and the Department of Molecular and Microbiology.
Still, that doesn't mean people should begin eating large amounts of soy products. "Although genistein is rich in several plants such as soybeans, it is still uncertain whether the amount of genistein we consume from eating soy is sufficient to inhibit HIV," Wu says.
Genistein is a "tyrosine kinase inhibitor" that works by blocking the communication from a cell's surface sensors to its interior. Found on a cell's surface, these sensors tell the cell about its environment and also communicate with other cells. HIV uses some of these surface sensors to trick the cell to send signals inside. These signals change cell structure so that the virus can get inside and spread infection.
But genistein blocks the signal and stops HIV from finding a way inside the cell. It takes a different approach than the standard antiretroviral drug used to inhibit HIV.
"Instead of directly acting on the virus, genistein interferes with the cellular processes that are necessary for the virus to infect cells," Wu says. "Thus, it makes the virus more difficult to become resistant to the drug. Our study is currently it its early stage. If clinically proven effective, genistein may be used as a complement treatment for HIV infection."
Wu sees possibilities in this plant-based approach, which may address drug toxicity issues as well. Because genistein is plant-derived, it may be able to sidestep drug toxicity, a common byproduct of the daily and lifelong pharmaceutical regimen faced by patients with HIV to keep the disease at bay, Wu says. Typically, patients take a combination of multiple drugs to inhibit the virus. The frequency can lead to drug toxicity. Plus, HIV mutates and becomes drug-resistant.
Wu and his team are working at finding out how much genistein is needed to inhibit HIV. It's possible that plants may not have high enough levels, so drugs would need to be developed, Wu says.
Wu's research is feeling the financial squeeze these days due to sequestration and budget cuts within the National Institutes of Health, he says. His lab has turned to novel ways to fund the HIV research, including the genistein project. A bicycle ride dubbed NYC DC AIDS Research Ride raised money for Wu's lab a few years ago and has stepped up its efforts with a new fundraiser.

Other George Mason researchers on the genistein project include Jia Guo, Taban Rasheed, Alyson Yoder, Dongyang Yu, Huizhi Liang, Fei Yi and Todd Hawley.Xuehua Xu and Tian Jin from the National Institute of Allergy and Infectious Diseases in Rockville, Md., and Binhua Ling from Tulane University Health Sciences Center are also working on the research.

Jia Guo, Xuehua Xu, Taban K Rasheed, Alyson Yoder, Dongyang Yu, Huizhi Liang, Fei Yi, Todd Hawley, Tian Jin, Binhua Ling, Yuntao Wu. Genistein interferes with SDF-1- and HIV-mediated actin dynamics and inhibits HIV infection of resting CD4 T cells. Retrovirology, 2013; 10 (1): 62 DOI: 10.1186/1742-4690-10-62

http://www.sciencedaily.com/releases/2013/07/130729144622.htm

Make It Yourself With a 3-D Printer and Save Big Time

It may seem like a stretch to envision a 3D printer in every home. However, a Michigan Technological University researcher is predicting that personal manufacturing, like personal computing before it, is about to enter the mainstream in a big way.

"For the average American consumer, 3D printing is ready for showtime," said Associate Professor Joshua Pearce.

3D printers deposit multiple layers of plastic or other materials to make almost anything, from toys to tools to kitchen gadgets. Free designs that direct the printers are available by the tens of thousands on websites like Thingiverse. Visitors can download designs to make their own products using open-source 3D printers, like the RepRap, which you build yourself from printed parts, or those that come in a box ready to print, from companies like Type-A Machines.

3D printers have been the purview of a relative few aficionados, but that is changing fast, Pearce said. The reason is financial: the typical family can already save a great deal of money by making things with a 3D printer instead of buying them off the shelf. Pearce drew that conclusion after conducting a lifecycle economic analysis on 3D printing in an average American household.

In the study, Pearce and his team chose 20 common household items listed on Thingiverse. Then they used Google Shopping to determine the maximum and minimum cost of buying those 20 items online, shipping charges not included.

Next, they calculated the cost of making them with 3D printers. The conclusion: it would cost the typical consumer from $312 to $1,944 to buy those 20 things compared to $18 to make them in a weekend.

Open-source 3D printers for home use have price tags ranging from about $350 to $2,000. Making the very conservative assumption a family would only make 20 items a year, Pearce's group calculated that the printers would pay for themselves quickly, in a few months to a few years.

The group chose relatively inexpensive items for their study: cellphone accessories, a garlic press, a showerhead, a spoon holder, and the like. 3D printers can save consumers even more money on high-end items like customized orthotics and photographic equipment.

3D printing isn't quite as simple as 2D printing a document from your home computer -- yet. "But you don't need to be an engineer or a professional technician to set up a 3D printer," Pearce said. "Some can be set up in under half an hour, and even the RepRap can be built in a weekend by a reasonably handy do-it-yourselfer."

It's not just about the money. 3D printing may herald a new world that offers consumers many more choices as everything can be customized. "With the exponential growth of free designs and expansion of 3D printing, we are creating enormous potential wealth for everyone." explains Pearce.

Before 3D printers become as ubiquitous as cellphones, they could form the basis of small-scale manufacturing concerns and have huge potential both here and for developing countries, where access to many products is limited.

"Say you are in the camping supply business and you don't want to keep glow-in-the-dark tent stakes in stock," Pearce said. "Just keep glow-in-the-dark plastic on hand, and if somebody needs those tent stakes, you can print them." "It would be a different kind of capitalism, where you don't need a lot of money to create wealth for yourself or even start a business," Pearce said.

B.T. Wittbrodt, A.G. Glover, J. Laureto, G.C. Anzalone, D. Oppliger, J.L. Irwin, J.M. Pearce. Life-cycle economic analysis of distributed manufacturing with open-source 3-D printers. Mechatronics, 2013; DOI: 10.1016/j.mechatronics.2013.06.002

http://bit.ly/1c7xSTk

Oxygen boost aided carnivore evolution in Cambrian Explosion | Life

Atmospheric change and rise of predators caused burst in complexity of life

By Erin Wayman

A rise in oxygen more than half a billion years ago paved the way for the origin of the first carnivores. The meat eaters in turn triggered the Big Bang of animal evolution, researchers argue.

The major groups of modern animals — everything from insects to creatures with a backbone — popped up 540 million to 500 million years ago in a proliferation known as the Cambrian Explosion. Fossil and molecular

evidence hint that the most primitive animals appeared a couple hundred million years earlier, leading scientists to wonder about the cause of the lag. Now scientists have stitched together earlier theories to come to a comprehensive explanation. Erik Sperling, an earth scientist at Harvard University, and colleagues say an increase in oxygen in the geologic record at the onset of the Cambrian period allowed carnivores to evolve. The oxygen boost could have accommodated the high energy costs of pursuing and digesting prey, Sperling says.

ANIMAL REVOLUTION A rise in oxygen may have allowed carnivores to evolve, a new study of polychaete worms (one shown) suggests. The origin of predators may have then kicked off an arms race that triggered the Cambrian Explosion more than half a billion years ago. Christina Frieder

Once carnivores arrived, an evolutionary arms race broke out between predator and prey, the team suggests July 29 in the Proceedings of the National Academy of Sciences. As prey evolved new defenses and predators developed new weapons, new kinds of animals sprung up.

Support for the oxygen-carnivore theory comes from modern polychaetes, tiny earthworm relatives that live on the seafloor and vary in their feeding habits. Combing through data from previous studies on polychaetes, Sperling's team examined 962 worm species from 68 locations worldwide. The researchers found a clear association: The number of carnivorous species was lower in areas with the lowest oxygen levels. In some of these regions, predatory polychaetes were completely absent.

Seafloor-dwelling polychaetes (one shown) vary in their diet. Carnivorous species are rare and often absent in areas with little oxygen, researchers report. **Christina Frieder**

Previously, scientists either invoked an oxygen increase or an arms race to account for the Cambrian Explosion, says Guy Narbonne, a paleobiologist at Queen's University in Kingston, Ontario. Linking oxygen to carnivores provides strong evidence that the two explanations are "intimately interrelated," he says.

Paleobiologist Nicholas Butterfield of the University of Cambridge sees the data differently. He thinks the rise of oxygen was actually an effect of the animals on the environment. He contends that shallow marine areas, where early animals most likely lived, were probably well oxygenated and therefore a lack of the gas did not stifle their evolution. It just took a while for a burst of complex animals to arise from simpler ones, he says. "It takes a whole lot of tinkering and experimenting and false starts until you trip over something that works."

E. Sperling et al. Oxygen, ecology, and the Cambrian radiation of animals. Proceedings of the National Academy of Sciences. Published online the week of July 29, 2013. doi:10.1073/pnas.1312778110. ***[Go to]***

http://www.medscape.com/viewarticle/808589?src=rss

ACE Inhibitors May Slow Cognitive Decline

Centrally acting angiotensin-converting enzyme inhibitors (CACE-Is) reduce the rate of cognitive decline in patients with dementia, regardless of blood pressure levels at the time of their hypertension diagnosis, a new study has found.

Pauline Anderson

The study also shows that the rate of cognitive change was improved in the first 6 months after dementia patients started taking these drugs.

"There's a growing body of literature now showing that these drugs slow down the deterioration that people with Alzheimer's disease experience, probably by between 20% and 30% a year compared to another antihypertensive drug or no centrally acting ACE inhibitor," said study author D. William Molloy, professor, Center for Gerontology and Rehabilitation, University College Cork, Cork City, Ireland.

The results prompt the question of whether these CACE agents would actually delay or prevent the onset of Alzheimer's disease (AD) in people with normal blood pressure who are at risk for dementia, said Dr. Molloy. The study was published online July 22 in BMJ Open.

Significant Change

Researchers used the Geriatric Assessment Tool (GAT) database, which contains over 8000 physician assessments of 1749 people aged 41 to 104 years. The data, collected from 1999 to 2010, includes age, sex, education, medical diagnoses, blood pressure, laboratory findings, medications, and other measures from patients at 2 university hospitals in Hamilton, Ontario, Canada. It also includes the scores of 2 cognitive screening tests — the Standardized Mini-Mental State Examination (SMMSE) and the Quick Mild Cognitive

Impairment (Qmci) screen. The Qmci has 6 subtests covering 5 cognitive domains: orientation, working memory, semantic memory, visual spatial, and 2 tests of episodic memory.
The analysis included only patients with AD, vascular or mixed dementias (Alzheimer's/vascular). These patients were grouped into those not taking a CACE inhibitor (the NoCACE-I group; n = 276) and those prescribed a CACE inhibitor (the CACE-I group; n = 85). (CACE inhibitors include perindopril, ramipril, trandolapril, captopril, fosinopril, lisinopril, and prinivil.) The researchers also looked at a group of 30 patients who began receiving a CACE inhibitor within the previous 6 months (NewCACE-I group).
The rate of cognitive decline was defined as the baseline cognitive score minus the endpoint score times 6 divided by duration in months.
The study found that the median change in SMMSE scores between the baseline and endpoint was 0.69 point per 6 month. The median SMMSE score differences for the CACE-I, NoCACE-I, and New CACE-I groups were 0.8, 1.0, and -1.2, respectively, per 6 months. For the Qmci, the median change was 2 points per 6 months, with median Qmci score differences for the CACE-I and NoCACE-I groups of 1.8 and 2.1, respectively, per 6 months.
There was a borderline significant difference in the median 6-month rate of decline in Qmci scores between CACE-I (1.8 points) and NoCACE-I (2.1 points) (P = .049). There were similar but nonsignificant changes in SMMSE (P = .77).
Newly treated patients also showed improvements. The median decline in scores for the NewACE-I group on the SMMSE was -1.2 points during the first 6 months of taking the drug.
Unlike some studies that show significant change but aren't clinically significant, this study uncovered a more definitive effect from use of CACE-I drugs, said Dr. Molloy. "This was clearly clinically significant, I think; it's not just Mickey Mouse change; it's significant change."
Among the different CACE-I agents, perindopril appeared to outperform the others, according to Dr. Molloy. "From the data we looked at, my impression was that perindopril was better than ramipril. It has a longer half-life so it has a smoother action over 24 hours, and it might have better tissue penetration."
It didn't seem to matter how long patients had been taking a CACE-I. Researchers didn't have enough data on dosage to determine whether this affected the rate of cognitive decline, said Dr. Molloy.
What's clear from this study is that CACE-I drugs, which are lipid soluble, do not work by lowering blood pressure, said Dr. Molloy. "We show here that in the ACE inhibitor class, it's the ones that cross the blood-brain barrier that are having the effect, suggesting that it's not a blood pressure–lowering effect, that there's something about this penetration of the central nervous system."

Anti-inflammatory Effect

But it's not clear how CACE drugs actually slow down cognitive decline in patients with AD. Dr. Molloy believes, though, that AD is probably the result of chronic inflammation in the brain and that CACEs have an effect on that inflammation.
"By crossing over, they may penetrate the tissues and they may be having some kind of anti-inflammatory effect or somehow switch off the inflammation," he said.

Quite Exciting

Dr. Molloy found the study results "quite exciting," especially the finding that the drugs seem to have an effect even after patients have been taking them for many years. The study, he said, offers some new hope for patients with AD. "We don't have a handle on Alzheimer's disease at all; we don't have anything to prevent it, and we don't really have much to slow it down."
Tempering that excitement, however, is the concern that in some people, ACE inhibitors might interfere with degradation of amyloid-β, thereby contributing to increase amyloid burden. It could be, said Dr. Molloy, that AD isn't a homogenous disease, that in some people it's more an issue of accumulating amyloid-β than a problem with inflammation.
A limitation of the study was that many patients in the database did not have both SMMSE and Qmci results at baseline and at the end of the study, limiting the numbers that could be included in the analysis. As well, different effects may have become apparent had the analysis covered a longer period.
The study results are only observational, and Dr. Molloy wants to "toss the coin" and test the findings in a clinical trial. "I would love to do a proper randomized trial of a centrally acting ACE inhibitor versus a non–centrally acting ACE inhibitor and treat patients for a couple of years and see what happens."
In addition to ACE inhibitors, other antihypertensive drugs have been associated with a lower risk of developing dementia, including calcium channel blockers, diuretics, and angiotensin-receptor blockers.
According to background information in the paper, about 80 million people worldwide will be affected by dementia by the year 2040.

Support for Previous Findings

Medscape Medical News sought the opinion of Kaycee M. Sink, MD, associate professor of medicine, director of the Kulynych Memory Assessment Clinic, Wake Forest School of Medicine, Salem, North Carolina, who has done research in this area.

"The results of this study add support to previous findings, including our own, that centrally active ACE inhibitors may be beneficial to cognition," said Dr. Sink.

However, the impact of the study is lessened by limitations of the study, which include the small sample size, possible confounding by indication (not everyone had an indication for an ACE inhibitor or even a blood pressure medication), and a very small effect size (probably not clinically significant).

"I don't think clinicians should use this study to support starting patients with dementia on a centrally active ACE inhibitor for treatment of dementia," said Dr. Sink. "However, if a patient has an indication for an ACE inhibitor (for example, hypertension, congestive heart failure, chronic kidney disease), then choosing a centrally active ACE inhibitor rather than a non–centrally active one probably makes sense."

The Centre for Gerontology and Rehabilitation is funded by Atlantic Philanthropies, the Health Services Executive Ireland, the Irish Hospice Foundation, and the Canadian Institutes of health Research. The authors have disclosed no relevant financial relationships.

http://www.bbc.co.uk/news/health-23492425

New teeth grown from urine - study

Scientists have grown rudimentary teeth out of the most unlikely of sources, human urine.

By James Gallagher Health and science reporter, BBC News

The results, published in Cell Regeneration Journal, showed that urine could be used as a source of stem cells that in turn could be grown into tiny tooth-like structures. The team from China hopes the technique could be developed into a way of replacing lost teeth. Other stem cell researchers caution that that goal faces many challenges.

Teams of researchers around the world are looking for ways of growing new teeth to replace those lost with age and poor dental hygiene. Stem cells - the master cells which can grow into any type of tissue - are a popular area of research.

The group at the Guangzhou Institutes of Biomedicine and Health used urine as the starting point.

Cells which are normally passed from the body, such as those from the lining of the body's waterworks, are harvested in the laboratory. These collected cells are then coaxed into becoming stem cells. A mix of these cells and other material from a mouse was implanted into the animals. The researchers said that after three weeks the bundle of cells started to resemble a tooth: "The tooth-like structure contained dental pulp, dentin, enamel space and enamel organ." However, the "teeth" were not as hard as natural teeth.

This piece of research is not immediately going to lead to new options for the dentist, but the researchers say it could lead to further studies towards "the final dream of total regeneration of human teeth for clinical therapy".

'Worst source'

Prof Chris Mason, a stem cell scientist at University College London, said urine was a poor starting point.

"It is probably one of the worst sources, there are very few cells in the first place and the efficiency of turning them into stem cells is very low. "You just wouldn't do it in this way."

He also warned that the risk of contamination, such as through bacteria, was much higher than with other sources of cells. Prof Mason added: "The big challenge here is the teeth have got a pulp with nerve and blood vessels which have to make sure they integrate to get permanent teeth."

http://bit.ly/158TewF

Natural chemical boosts organ regeneration

Your body naturally contains a chemical that can boost organ regeneration and speed up wound healing.

12:44 30 July 2013 by Andy Coghlan

Epoxyeicosatrienoic acids (EETs) help new blood vessels to form, so Dipak Panigrahy at Harvard Medical School in Boston and colleagues wondered whether they might also accelerate other types of growth. To find out, they injected mice with EETs straight after the surgical removal of a lung or part of their liver.

Four days later, treated mice had 23 per cent more tissue growth in their remaining lung or 46 per cent more liver growth compared with mice that had received a placebo injection. Applying EETs to wounds in mice shortened healing time. The team also showed that EET concentrations in blood trebled in the week after human liver donors had undergone surgery.

"This looks promising," says Dan Weiss, who studies lung regeneration at the University of Vermont in Burlington. "EETs have been overlooked in regeneration schemes, so this might provide a window of opportunity." *Journal reference: PNAS, DOI: 10.1073/pnas.1311565110*

http://www.eurekalert.org/pub_releases/2013-07/bmj-ndo072613.php

New definition of chronic kidney disease labels 1 in 8 adults as sick

Risk of overdiagnosis warrants greater professional scrutiny and more public awareness, argue experts

A new definition of chronic kidney disease labels over 1 in 8 adults and around half of people over 70 years of age as having the disease. Yet low rates of kidney failure suggest many of those diagnosed will never progress to severe disease. On bmj.com today, Ray Moynihan and colleagues argue this is evidence of overdiagnosis. They call for a re-examination of the definition and urge clinicians to be cautious about labelling patients, particularly older people.

This article is the second of a series looking at the risks and harms of overdiagnosis in a range of common conditions. The series, together with the Preventing Overdiagnosis conference in September, are part of the BMJ's Too Much Medicine campaign to help tackle the threat to health and the waste of money caused by unnecessary care.

In 2002, a new framework for defining and classifying "chronic kidney disease" (CKD) was introduced. It defines chronic kidney disease as the presence of kidney damage or decreased kidney function for three months or more, irrespective of the cause, and is based largely on laboratory measures. The framework has been widely embraced by many countries because it was assumed that earlier detection and treatment would slow progression towards kidney failure, and was updated in 2012.

But some doctors have raised concerns because the adoption of this definition has resulted in more than 1 in 8 adults (almost 14%) in the US being labelled as having chronic kidney disease and as many as 1 in 6 adults in Australia. Before the 2002 framework, it was estimated that 4.2 million Americans (1.7%) had chronic kidney disease. In the UK, specialist referrals for chronic kidney disease are up 60% within a single NHS trust covering a population of 560,000 people, according to a University of Cardiff study, and up 40% at a hospital in Brisbane, Australia.

Advocates of the definition claim that "early detection can help prevent the progression of kidney disease." But despite the large numbers now labelled as having chronic kidney disease, low rates of kidney failure suggest many of those diagnosed will never progress to serious disease.

This say the authors, is evidence of overdiagnosis, and they point to the psychological effect of a disease label and the burden and costs of repeated assessment, testing, and potentially unnecessary treatment.

They argue that the benefits, harms, and costs of testing, monitoring, and treating the increased number of people being identified as having chronic kidney disease "need to be established by prospective studies."

They acknowledge that inferring overdiagnosis has limitations, but say the risk of overdiagnosis "warrants greater professional scrutiny and more public awareness" and they urge clinicians to be cautious about labelling patients, particularly older people. "It is in everyone's interest to find the best way to maximise prevention of kidney disease and its consequences while minimising the risks and costs of overdiagnosis," they conclude.

http://www.wired.com/wiredscience/2013/07/carbapenem-resistance-worse/

More on 'Nightmare Bacteria': Maybe Even Worse Than We Thought?

New research suggests the problem of carbapenem-resistant bacteria has been understated

By Maryn McKenna

In my last post I talked about the under-appreciated emergence of "nightmare bacteria" (those are the Centers for Disease Control and Prevention's words, not mine) that are widely distributed in hospitals and nursing homes around the world and do not respond to a last-ditch small family of antibiotics called carbapenems. That seemed dire enough, but new research suggests the problem, bad as it looks, has been understated.

There's an ahead-of-print article in Antimicrobial Agents and Chemotherapy whose authors include David Shlaes, a physician-researcher and former pharmaceutical executive, now consultant, and Brad Spellberg, an infectious disease physician on the UCLA medical faculty and author among other books of Rising Plague, about antibiotic resistance. In a commentary examining the Food and Drug Administration's promised "reboot" of antibiotic development rules, they analyze privately gathered data on resistance in the United States and conclude the incidence of highly resistant bacteria is greater than the CDC has estimated.

I'll let them tell it (I've reparagraphed for clarity). For non-medical readers, the organisms being discussed here are Klebsiella and Acinetobacter, common causes of ICU infections that have become resistant first to a class of drugs called the third-generation cephalosporins, and after that, to the carbapenems. After the carbapenems, there are literally one to two drugs left, neither of them very effective (and one of them quite toxic).

In the report from CDC in 2008, taken from ICU isolates, the resistance among E. coli to third generation cephalosporins was 5% while in our analysis (using different methods) it stands at 8-11%.

K. pneumoniae resistance to third generation cephalosporins was 15% in the CDC study. In our updated analysis it ranges from 20-27%. Resistance to carbapenems among these isolates is now between 7 and 11%.

For A. baumannii the resistance is even more drastic. In the CDC report 11% were carbapenem-resistant while our data show that number to be over 50%.
These data indicate that for Acinetobacter baumannii infections, the carbapenems are already obsolete. This holds true for both intensive care and non-intensive care patients and for urinary and non-urinary infections. The same can be said for our third-generation cephalosporins… in the treatment of K. pneumoniae infections. For these organisms, the carbapenems are also rapidly losing efficacy. Even among E. coli isolates, our third generation cephalosporins are no longer completely reliable although the carbapenems remain a solid backup.
…None of the …antibiotics (currently in the development pipeline) by themselves can address all these resistance problems. We will therefore continue to confront serious infections caused by pathogens for which are treatment options are either limited or non-existent.
The researchers made this dire analysis as part of an argument pressing the FDA to revise its rules of clinical-trial design in hopes of coaxing pharmaceutical manufacturers back into the antibiotic market. Their analysis is pretty granular, but these paragraphs sum it up:
…the FDA process of determining how antibacterial trials should be conducted has badly lost its way. As a result, 1) many companies do not invest in the trials; 2) those that do(,) enroll patients where it is possible to withhold therapy while the patients are enrolled in trials, with resulting ethical concerns; 3) the results become less meaningful and relevant to patients in the US because US patients are not enrolled. Pharmaceutical companies have voted with their feet. Twenty years ago, more than twenty large companies had active discovery and development programs for antibacterial agents; in 2013, only four have active discovery programs. Our approval rate for new antibiotics has fallen to dismally low levels.
The "reboot" of antibiotic programs at the FDA — promised a year ago, according to the paper — has not yet happened. It's clear, from the details of this analysis, that there are going to be controversial aspects to any reframing of trial design. It's hard to imagine that any new effort can be stood up quickly. About all we can say for sure is that the further emergence of resistance won't wait for us to catch up.
Cite: Shlaes DM et al. The FDA Reboot of Antibiotic Development. AAC Accepts, published online ahead of print on 29 July 2013. Antimicrob. Agents Chemother. doi:10.1128/AAC.01277-13
*Update: Almost exactly as I published this, Mike the Mad Biologist was posting about a possible new treatment for carbapenem-resistant bacteria. **Take a look**.*

http://www.sciencedaily.com/releases/2013/07/130730163138.htm

Evidence of Nerve Damage in About Half of Fibromyalgia Patients

About half of a small group of patients with fibromyalgia was found to have damage to nerve fibers in their skin

About half of a small group of patients with fibromyalgia -- a common syndrome that causes chronic pain and other symptoms -- was found to have damage to nerve fibers in their skin and other evidence of a disease called small-fiber polyneuropathy (SFPN). Unlike fibromyalgia, which has had no known causes and few effective treatments, SFPN has a clear pathology and is known to be caused by specific medical conditions, some of which can be treated and sometimes cured. The study from Massachusetts General Hospital (MGH) researchers will appear in the journal PAIN and has been released online.
"This provides some of the first objective evidence of a mechanism behind some cases of fibromyalgia, and identifying an underlying cause is the first step towards finding better treatments," says Anne Louise Oaklander, MD, PhD, director of the Nerve Injury Unit in the MGH Department of Neurology and corresponding author of the Pain paper.
The term fibromyalgia describes a set of symptoms -- including chronic widespread pain, increased sensitivity to pressure, and fatigue -- that is believed to affect 1 to 5 percent of individuals in Western countries, more frequently women. While a diagnosis of fibromyalgia has been recognized by the National Institutes of Health and the American College of Rheumatology, its biologic basis has remained unknown. Fibromyalgia shares many symptoms with SFPN, a recognized cause of chronic widespread pain for which there are accepted, objective tests.
Designed to investigate possible connections between the two conditions, the current study enrolled 27 adult patients with fibromyalgia diagnoses and 30 healthy volunteers. Participants went through a battery of tests used to diagnose SFPN, including assessments of neuropathy based on a physical examination and responses to a questionnaire, skin biopsies to evaluate the number of nerve fibers in their lower legs, and tests of autonomic functions such as heart rate, blood pressure and sweating.
The questionnaires, exam assessments, and skin biopsies all found significant levels of neuropathy in the fibromyalgia patients but not in the control group. Of the 27 fibromyalgia patients, 13 had a marked reduction in nerve fiber density, abnormal autonomic function tests or both, indicating the presence of SFPN. Participants who met criteria for SFPN also underwent blood tests for known causes of the disorder, and while none of them

had results suggestive of diabetes, a common cause of SFPN, two were found to have hepatitis C virus infection, which can be successfully treated, and more than half had evidence of some type of immune system dysfunction.

"Until now, there has been no good idea about what causes fibromyalgia, but now we have evidence for some but not all patients. Fibromyalgia is too complex for a 'one size fits all' explanation," says Oaklander, an associate professor of Neurology at Harvard Medical School. "The next step of independent confirmation of our findings from other laboratories is already happening, and we also need to follow those patients who didn't meet SFPN criteria to see if we can find other causes. Helping any of these people receive definitive diagnoses and better treatment would be a great accomplishment."

Anne Louise Oaklander, Zeva Daniela Herzog, Heather M. Downs, Max M. Klein. Objective evidence that small-fiber polyneuropathy underlies some illnesses currently labeled as fibromyalgia. PAIN, 2013; DOI: 10.1016/j.pain.2013.06.001

http://www.eurekalert.org/pub_releases/2013-07/slu-nti073113.php

New therapy improves life span in melanoma patients with brain metastases, SLU researchers find

In a retrospective study, Saint Louis University researchers have found that patients with melanoma brain metastases can be treated with large doses of interleukin-2 (HD IL-2), a therapy that triggers the body's own immune system to destroy the cancer cells.

ST. LOUIS -- The study that was recently published in Chemotherapy Research and Practice, reviews cases of eight patients who underwent this therapy at Saint Louis University.

John Richart, M.D., associate professor of internal medicine at SLU and principal investigator of the study, first treated a patient with the disease using the HD IL-2 treatment in 1999.

"Traditionally, melanoma patients with brain metastases have not been considered for HD IL-2 because treatment was thought to be futile," Richart said. "Our study shows that having this condition does not exclude a patient from getting this treatment and can in fact improve the length of their life."

Melanoma is the most dangerous form of skin cancer that begins in the melanin-producing cells called melanocytes. In some melanoma patients, the cancer spreads to the brain, causing multiple tumors that are difficult to treat. According to the CDC, melanoma is the third most common cancer causing brain metastases in the U.S. Richart said the median overall survival of patients with melanoma brain metastases is approximately four months whereas in the study, the median overall survival for patients was 8.7 months.

During the treatment, patients are given an IV medication -- a chemical the body naturally makes that stimulates the immune system to recognize and destroy melanoma cells -- for a period of six days while they are admitted to the hospital and are closely monitored by doctors and nurses. A patient requires four such six-day admission cycles in order to complete the course of the treatment.

To be eligible for HD IL-2 treatment, melanoma patients with brain metastases have to be in healthy shape with good brain function -- that is they cannot have brain lesions that are growing rapidly or show any symptoms of brain lesions. In the past, melanoma patients with brain metastases have been considered ineligible for this treatment because doctors thought that the treatment would cause life-threatening cerebral edema, a complication that causes excess accumulation of fluids in the brain, and neurotoxicity, or irreversible damage to the brain or the nervous system.

"In this review, we found that there were no episodes of treatment-related mortality. Our findings demonstrate that HD IL-2 can be considered as an option for patients with melanoma brain metastases," said Melinda Chu, M.D., a first year dermatology resident at SLU and first author of the study. SLU is the only medical center in the region that provides this treatment.

"We need a highly skilled nursing staff for the HD-IL-2 program to be successful," Richart said. "Our nursing team at SLU is with each patient every step of the way, 24 hours a day. They help patients get through and continue the treatment."

http://www.eurekalert.org/pub_releases/2013-07/uoh-tn073113.php

The naked mole-rat's secret to staying cancer free

Not a single incident of cancer has been detected makes the naked mole rat a fitting model for finding novel ways to fight cancer

Mice and rats have long since been a standard animal model for cancer research, mainly due to their short lifespan of four years on average and high incidence of cancer. Naked mole rats however, are a mystery among mammals. This social tiny African subterranean rodent has a maximum lifespan exceeding 30 years and most surprisingly, is cancer-resistant. The fact that so far, not a single incident of cancer has been detected makes the naked mole rat a fitting model for finding novel ways to fight cancer.

Recently, a team of researchers from the University of Rochester in New York and the University of Haifa found the naked mole rat's unique mechanism to staying cancer free- a super sugar called high-molecular-mass Hyaluronan (HMM-HA). They discovered that when secreted from the naked mole rat's cells, HMM-HA prevents cells from overcrowding and forming tumors. "Contact inhibition, a powerful anticancer mechanism, discovered by the Rochester team, arresting cell growth when cells come into contact with each other, is lost in cancer cells", explains Prof. Eviatar Nevo, from the Institute of Evolution at the University of Haifa, "The experiments showed that when HMM-HA was removed from naked mole rat cells, they became susceptible to tumors and lost their contact inhibition".

HMM-HA is a form of Hyaluronan- a long sugar polymer, naturally present as a lubricant in the extracellular matrix of the human body. It is commonly used in the treatment of arthritis or in anti-wrinkle skin care products. According to the current results, the naked mole rat cells secrete extremely high-molecular mass HA, which is over five times larger than human or mouse HA. This high-molecular-mass HA accumulates abundantly in naked mole rat tissues, owing to a more robust synthesis by a protein called HAS2 and a decreased activity of HA-degrading enzymes. When researchers compared the Has2 gene between the naked mole rat and other mammals, they discovered that two unique amino acids, (asparagines), that are 100% conserved among mammals, were replaced by two other amino acids (serines), in the naked mole rat. These unique amino acid changes may be responsible for the high processivity of the naked mole rat HAS2 protein- in charge of HA synthesis. The naked mole rat cells display a two-fold higher affinity to HA than mouse or human cells, contributing to the higher sensitivity of naked mole rat cells to HA signaling. Remarkably, explains Professor Nevo, "the cells of the Israeli solitary blind mole rat, Spalax, which is phylogenetically closer to mice and rats than to naked mole rats, also secreted HMM-HA. This highlights a parallel evolution in unrelated subterranean mammals, presumably a shared adaptation to life underground".

The researchers speculate that naked mole rats evolved higher concentrations of HA in the skin to provide the skin elasticity needed for life in underground tunnels. So far, experiments in human cells have been very limited. However, there has been some evidence showing there is reason for hope. In one of their experiments, the researchers noticed that when naked mole rat HAS2 synthesis protein was overexpressed in human cell tissues, the cells began secreting HMM-HA. This opens new avenues for cancer prevention and life extension in human medicine.

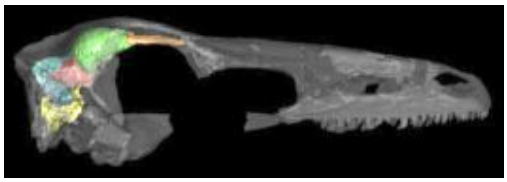
http://www.eurekalert.org/pub_releases/2013-07/amon-bbp072913.php

Bird brains predate birds themselves

New research based on CT scans indicates that 'flight-ready' brain was present in some non-avian dinosaurs

New research provides evidence that dinosaurs evolved the brainpower necessary for flight well before they actually took to the air as birds. Based on high-resolution X-ray computed tomographic (CT) scans, the study, published today in Nature, takes a comprehensive look at the so-called "bird brain." Contrary to the cliché, the term describes a relatively enlarged brain that has the capacity required for flight and was present in one of the earliest known birds, Archaeopteryx. In the new study, scientists reveal that at least a few non-avian dinosaurs had brains that were as large or larger than that of Archaeopteryx, indicating that some dinosaurs already suspected of possessing flight capability would have had the neurological hardwiring necessary for this behavior.

"Archaeopteryx has always been set up as a uniquely transitional species between feathered dinosaurs and modern birds, a halfway point," said lead author Amy Balanoff, a research associate at the American Museum of Natural History and a postdoctoral researcher at Stony Brook University. "But by studying the cranial volume of closely related dinosaurs, we learned that Archaeopteryx might not have been so special."



This CT scan shows the transparent skull and opaque brain cast of Zanabazar junior, a troodontid dinosaur. The endocast is partitioned into the following neuroanatomical regions: brain stem (yellow), cerebellum (blue), optic lobes (red), cerebrum (green), and olfactory bulbs (orange). ©AMNH/A. Balanoff

Birds can be distinguished from other living reptiles by their brains, which are enlarged compared to body size. This "hyperinflation," most obvious in the forebrain, is important for providing the superior vision and coordination required to fly. But scientists are increasingly finding that features once considered exclusive to modern birds, such as feathers and the presence of wishbones, are now known to have first appeared in non-avian dinosaurs. The new study provides more evidence to add the hyperinflated brain to that list.

The researchers used CT scanners at the University of Texas, Ohio University, Stony Brook University, and the Museum to peer inside the braincases of more than two dozen specimens, including modern birds,

Archaeopteryx, and closely related non-avian dinosaurs like tyrannosaurs. By stitching together the CT scans, the scientists created 3-D reconstructions of the skulls' interiors. In addition to calculating the total volume of each digital brain cast, the research team also determined the size of each brain's major anatomical regions, including the olfactory bulbs, cerebrum, optic lobes, cerebellum, and brain stem.
"The story of brain size is more than its relationship to body size," said coauthor Gabriel Bever, an assistant professor of anatomy at the New York Institute of Technology. "If we also consider how the different regions of the brain changed relative to each other, we can gain insight into what factors drove brain evolution as well as what developmental mechanisms facilitated those changes."
The researchers found that in terms of volumetric measurements, Archaeopteryx is not in a unique transitional position between non-avian dinosaurs and modern birds. Several other non-avian dinosaurs sampled, including bird-like oviraptorosaurs and troodontids, actually had larger brains relative to body size than Archaeopteryx.
"If Archaeopteryx had a flight-ready brain, which is almost certainly the case given its morphology, then so did at least some other non-avian dinosaurs," Balanoff said.
The researchers also examined another factor that is important to flight in modern birds: a neurological structure called the wulst, which is used in information processing and motor control. The team identified an indentation in the digital brain cast of Archaeopteryx that might be homologous to the wulst seen in living birds. But this indentation is not found in non-avian dinosaurs that have bigger brains than Archaeopteryx, presenting the research team with a new question to explore in the future.

http://www.eurekalert.org/pub_releases/2013-07/uoz-tft073113.php

The flexible tail of the prion protein poisons brain cells

Prion proteins are the infectious pathogens that cause Mad Cow Disease and Creutzfeldt-Jakob disease.

They occur when a normal prion protein becomes deformed and clumped. The naturally occurring prion protein is harmless and can be found in most organisms. In humans, it is found in our brain cell membrane. By contrast, the abnormally deformed prion protein is poisonous for the brain cells. Adriano Aguzzi, Professor of Neuropathology at the University of Zurich and University Hospital Zurich, has spent many years exploring why this deformation is poisonous. Aguzzi's team has now discovered that the prion protein has a kind of «switch» that controls its toxicity. This switch covers a tiny area on the surface of the protein. If another molecule, for example an antibody, touches this switch, a lethal mechanism is triggered that can lead to very fast cell death.

Flexible tail induces cell death

In the current edition of «Nature», the scientists demonstrate that the prion protein molecule comprises two functionally distinct parts: a globular domain, which is tethered to the cell membrane, and a long and unstructured tail. Under normal conditions, this tail is very important in order to maintain the functioning of nerve cells. By contrast, in the case of a prion infection the pathogenic prion protein interacts with the globular part and the tail causes cell death – this is the hypothesis put forward by the researchers.
Aguzzi and his team tested this by generating mimetic antibodies in tissue sections from the cerebellum of mice which have a similar toxicity to that of a prion infection. The researchers found that these antibodies tripped the switch of the prion protein. «Prion proteins with a trimmed version of the flexible tail can, however, no longer damage the brain cells, even if their switch has been recognized by antibodies», explains Adriano Aguzzi. «This flexible tail is responsible for causing cell death.» If the tail is bound and made inaccessible using a further antibody, activation of the switch can likewise no longer trigger cell death.
«Our discovery has far-reaching consequences for understanding prion diseases», says Aguzzi. The findings reveal that only those antibodies that target the prion protein tail are suitable for use as potential drugs. By contrast, antibodies that trip the switch of the prion are very harmful and dangerous.

http://theconversation.com/meddling-gut-bacteria-get-in-the-way-of-drug-therapy-16370

Meddling gut bacteria get in the way of drug therapy

Bacteria in the human gut, which are present in the billions, can change the effect of medicine. This has been demonstrated for at least 40 drugs. But, until now, nobody knew exactly how.

Ian Wilson PhD student at University of Liverpool

Bacteria in the human gut, which are present in the billions, can change the effect of medicine. This has been demonstrated for at least 40 drugs. But, until now, nobody knew exactly how.
New research, published in the journal Science by the lab of Peter Turnbaugh at Harvard University, helps solve this riddle, at least for one drug. The team looked at digoxin, which is used to treat heart failure and arrhythmia (irregular beats). Digoxin is only effective within a narrow range of concentrations. This makes getting the right digoxin dose very tricky — a challenge made more difficult by the gut bacteria

The drugs don't work

Digoxin is inactivated by a bacterium found in the gut called Eggerthella lenta. The bug changes the drug's structure so it cannot interact normally with its target. This inactive form, called dihydrodigoxin, is also quickly excreted by the patient. Turnbaugh aimed to find out how E. lenta inactivated the drug and how to prevent it from doing so.

To do this, he and his colleagues used a technique called RNA sequencing. Messenger RNA sequences are copies of genes that are used to build proteins. By reading an RNA sequence, scientists can figure out which genes are active in a cell population. The frequency of RNA sequences can indicate the level of activity, and thus the level of the corresponding protein.

With this in mind, the team grew one strain of E. lenta in two different conditions, one containing digoxin and the other not. They then looked to see which E. lenta genes were more active in the presence of the drug.

They found that digoxin induced a 100-fold increase in the expression of two linked genes. These genes encoded for enzymes called cytochromes, which are capable of inactivating digoxin.

Scanning electron micrograph of E. lenta Manfred Rohde/Standards in Genomic Science

The team later found that only the strain they studied was involved in inactivating digoxin. Two other strains of E. lenta that they checked later were found to be incapable of the former's ability. These different digoxin-degrading abilities may explain why it is so difficult to find an effective digoxin dose for patients. Turnbaugh says it was once hoped that knowing the number of E. lenta cells in a patient's gut would be enough to predict inactivation rates. It is now clear that this is not enough.

To be sure, the team compared the number of copies of the cytochrome genes with the number of E. lenta cells present in a group of human test subjects. The statistics showed that not every cell possessed the two genes. Clearly, a more comprehensive test is required if predictions are to be made on an individual basis.

The effect of diet on drugs

While working with E. lenta, Turnbaugh found that the bacteria grew better if fed the amino acid arginine, which is a component of most proteins. However, too much arginine led to reduced expression of the two cytochrome genes that inactivated digoxin. So Turnbaugh's team predicted that eating more protein would increase the arginine in the gut, which would limit the inactivation of digoxin by E. lenta. They tested this by colonising two sets of mice with the inactivating E. lenta strain, and feeding them different amounts of protein. The mice with higher protein intake had higher levels of active digoxin in their blood.

Turnbaugh believes that the work may show a way to improve delivery of cardiac drugs. He feels that the findings demonstrate the importance of understanding how drugs are inactivated. One day, he suggests, patients may find their prescriptions are accompanied by recommended diets or supplements, such as arginine, that improve the effectiveness of the drugs.

Disclosure Statement *Ian Wilson does not work for, consult to, own shares in or receive funding from any company or organisation that would benefit from this article, and has no relevant affiliations.*

http://www.scientificamerican.com/article.cfm?id=why-we-got-milk

Why We "Got Milk"

When a single genetic mutation first let ancient Europeans drink milk, it set the stage for a continental upheaval

By Andrew Curry and Nature magazine | Wednesday, July 31, 2013 | 5

In the 1970s, archaeologist Peter Bogucki was excavating a Stone Age site in the fertile plains of central Poland when he came across an assortment of odd artifacts. The people who had lived there around 7,000 years ago were among central Europe's first farmers, and they had left behind fragments of pottery dotted with tiny holes. It looked as though the coarse red clay had been baked while pierced with pieces of straw.

Looking back through the archaeological literature, Bogucki found other examples of ancient perforated pottery. "They were so unusual — people would almost always include them in publications," says Bogucki, now at Princeton University in New Jersey. He had seen something similar at a friend's house that was used for straining cheese, so he speculated that the pottery might be connected with cheese-making. But he had no way to test his idea.

The mystery potsherds sat in storage until 2011, when Mélanie Roffet-Salque pulled them out and analyzed fatty residues preserved in the clay. Roffet-Salque, a geochemist at the University of Bristol, UK, found signatures of abundant milk fats — evidence that the early farmers had used the pottery as sieves to separate fatty milk solids from liquid whey. That makes the Polish relics the oldest known evidence of cheese-making in the world.

Roffet-Salque's sleuthing is part of a wave of discoveries about the history of milk in Europe. Many of them have come from a €3.3-million ($4.4-million) project that started in 2009 and has involved archaeologists,

chemists and geneticists. The findings from this group illuminate the profound ways that dairy products have shaped human settlement on the continent.

During the most recent ice age, milk was essentially a toxin to adults because — unlike children — they could not produce the lactase enzyme required to break down lactose, the main sugar in milk. But as farming started to replace hunting and gathering in the Middle East around 11,000 years ago, cattle herders learned how to reduce lactose in dairy products to tolerable levels by fermenting milk to make cheese or yogurt. Several thousand years later, a genetic mutation spread through Europe that gave people the ability to produce lactase — and drink milk — throughout their lives. That adaptation opened up a rich new source of nutrition that could have sustained communities when harvests failed.

This two-step milk revolution may have been a prime factor in allowing bands of farmers and herders from the south to sweep through Europe and displace the hunter-gatherer cultures that had lived there for millennia. "They spread really rapidly into northern Europe from an archaeological point of view," says Mark Thomas, a population geneticist at University College London. That wave of emigration left an enduring imprint on Europe, where, unlike in many regions of the world, most people can now tolerate milk. "It could be that a large proportion of Europeans are descended from the first lactase-persistent dairy farmers in Europe," says Thomas.

Strong stomachs

Young children almost universally produce lactase and can digest the lactose in their mother's milk. But as they mature, most switch off the lactase gene. Only 35% of the human population can digest lactose beyond the age of about seven or eight. "If you're lactose intolerant and you drink half a pint of milk, you're going to be really ill. Explosive diarrhea — dysentery essentially," says Oliver Craig, an archaeologist at the University of York, UK. "I'm not saying it's lethal, but it's quite unpleasant."

Most people who retain the ability to digest milk can trace their ancestry to Europe, where the trait seems to be linked to a single nucleotide in which the DNA base cytosine changed to thymine in a genomic region not far from the lactase gene. There are other pockets of lactase persistence in West Africa (see Nature 444, 994–996; 2006), the Middle East and south Asia that seem to be linked to separate mutations (see 'Lactase hotspots').

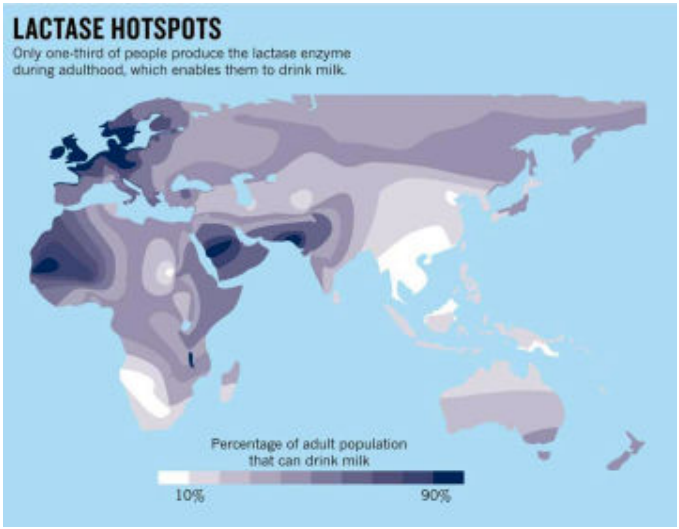


Image: Courtesy of Nature Magazine

The single-nucleotide switch in Europe happened relatively recently. Thomas and his colleagues estimated the timing by looking at genetic variations in modern populations and running computer simulations of how the related genetic mutation might have spread through ancient populations. They proposed that the trait of lactase persistence, dubbed the LP allele, emerged about 7,500 years ago in the broad, fertile plains of Hungary.

Powerful gene

Once the LP allele appeared, it offered a major selective advantage. In a 2004 study, researchers estimated that people with the mutation would have produced up to 19% more fertile offspring than those who lacked it. The researchers called that degree of selection "among the strongest yet seen for any gene in the genome". Compounded over several hundred generations, that advantage could help a population to take over a continent. But only if "the population has a supply of fresh milk and is dairying", says Thomas. "It's gene–culture co-evolution. They feed off of each other."

To investigate the history of that interaction, Thomas teamed up with Joachim Burger, a paleogeneticist at the Johannes Gutenberg University of Mainz in Germany, and Matthew Collins, a bioarchaeologist at the University of York. They organized a multidisciplinary project called LeCHE (Lactase Persistence in the early Cultural History of Europe), which brought together a dozen early-career researchers from around Europe.

By studying human molecular biology and the archaeology and chemistry of ancient pottery, LeCHE participants also hoped to address a key issue about the origins of modern Europeans. "It's been an enduring question in archaeology — whether we're descended from Middle Eastern farmers or indigenous hunter-gatherers," says Thomas. The argument boils down to evolution versus replacement. Did native populations of hunter-gatherers in Europe take up farming and herding? Or was there an influx of agricultural colonists who outcompeted the locals, thanks to a combination of genes and technology?

One strand of evidence came from studies of animal bones found at archaeological sites. If cattle are raised primarily for dairying, calves are generally slaughtered before their first birthday so that their mothers can be milked. But cattle raised mainly for meat are killed later, when they have reached their full size. (The pattern, if not the ages, is similar for sheep and goats, which were part of the dairying revolution.)
Image: Courtesy of Nature Magazine
On the basis of studies of growth patterns in bones, LeCHE participant Jean-Denis Vigne, an archaeozoologist at the French National Museum of Natural History in Paris, suggests that dairying in the Middle East may go all the way back to when humans first started domesticating animals there, about 10,500 years ago. That would place it just after the Middle Eastern Neolithic transition — when an economy based on hunter-gathering gave way to one devoted to agriculture. Dairying, says Roz Gillis, also an archaeozoologist at the Paris museum, "may have been one of the reasons why human populations began trapping and keeping ruminants such as cattle, sheep and goats". (See 'Dairy diaspora'.)
Dairying then expanded in concert with the Neolithic transition, says Gillis, who has looked at bone growth at 150 sites in Europe and Anatolia (modern Turkey). As agriculture spread from Anatolia to northern Europe over roughly two millennia, dairying followed a similar pattern.

Image: Courtesy of Nature Magazine

On their own, the growth patterns do not say whether the Neolithic transition in Europe happened through evolution or replacement, but cattle bones offer important clues. In a precursor study, Burger and several other LeCHE participants found that domesticated cattle at Neolithic sites in Europe were most closely related to cows from the Middle East, rather than indigenous wild aurochs. This is a strong indication that incoming herders brought their cattle with them, rather than domesticating locally, says Burger. A similar story is emerging from studies of ancient human DNA recovered at a few sites in central Europe, which suggest that Neolithic farmers were not descended from the hunter-gatherers who lived there before.
Taken together, the data help to resolve the origins of the first European farmers. "For a long time, the mainstream of continental European archaeology said Mesolithic hunter-gatherers developed into Neolithic farmers," says Burger. "We basically showed they were completely different."

Milk or meat

Given that dairying in the Middle East started thousands of years before the LP allele emerged in Europe, ancient herders must have found ways to reduce lactose concentrations in milk. It seems likely that they did so by making cheese or yogurt. (Fermented cheeses such as feta and cheddar have a small fraction of the lactose found in fresh milk; aged hard cheeses similar to Parmesan have hardly any.)
To test that theory, LeCHE researchers ran chemical tests on ancient pottery. The coarse, porous clay contains enough residues for chemists to distinguish what type of fat was absorbed during the cooking process: whether it was from meat or milk, and from ruminants such as cows, sheep and goats or from other animals. "That gave us a way into saying what types of things were being cooked," says Richard Evershed, a chemist at the University of Bristol.
Evershed and his LeCHE collaborators found milk fat on pottery in the Middle Eastern Fertile Crescent going back at least 8,500 years, and Roffet-Salque's work on the Polish pottery offers clear evidence that herders in Europe were producing cheese to supplement their diets between 6,800 and 7,400 years ago. By then, dairy had become a component of the Neolithic diet, but it was not yet a dominant part of the economy.
That next step happened slowly, and it seems to have required the spread of lactase persistence. The LP allele did not become common in the population until some time after it first emerged: Burger has looked for the mutation in samples of ancient human DNA and has found it only as far back as 6,500 years ago in northern Germany.
Models created by LeCHE participant Pascale Gerbault, a population geneticist at University College London, explain how the trait might have spread. As Middle Eastern Neolithic cultures moved into Europe, their farming

and herding technologies helped them to out-compete the local hunter-gatherers. And as the southerners pushed north, says Gerbault, the LP allele 'surfed' the wave of migration.
Lactase persistence had a harder time becoming established in parts of southern Europe, because Neolithic farmers had settled there before the mutation appeared. But as the agricultural society expanded northwards and westwards into new territory, the advantage provided by lactase persistence had a big impact. “As the population grows quickly at the edge of the wave, the allele can increase in frequency,” says Gerbault.
The remnants of that pattern are still visible today. In southern Europe, lactase persistence is relatively rare — less than 40% in Greece and Turkey. In Britain and Scandinavia, by contrast, more than 90% of adults can digest milk.

Cattle conquest

By the late Neolithic and early Bronze Age, around 5,000 years ago, the LP allele was prevalent across most of northern and central Europe, and cattle herding had become a dominant part of the culture. “They discover this way of life, and once they can really get the nutritional benefits they increase or intensify herding as well,” says Burger. Cattle bones represent more than two-thirds of the animal bones in many late Neolithic and early Bronze Age archaeological sites in central and northern Europe.
The LeCHE researchers are still puzzling out exactly why the ability to consume milk offered such an advantage in these regions. Thomas suggests that, as people moved north, milk would have been a hedge against famine. Dairy products — which could be stored for longer in colder climes — provided rich sources of calories that were independent of growing seasons or bad harvests.
Others think that milk may have helped, particularly in the north, because of its relatively high concentration of vitamin D, a nutrient that can help to ward off diseases such as rickets. Humans synthesize vitamin D naturally only when exposed to the sun, which makes it difficult for northerners to make enough during winter months. But lactase persistence also took root in sunny Spain, casting vitamin D's role into doubt.
The LeCHE project may offer a model for how archaeological questions can be answered using a variety of disciplines and tools. “They have got a lot of different tentacles — archaeology, paleoanthropology, ancient DNA and modern DNA, chemical analysis — all focused on one single question,” says Ian Barnes, a paleogeneticist at Royal Holloway, University of London, who is not involved in the project. “There are lots of other dietary changes which could be studied in this way.”
The approach could, for example, help to tease apart the origins of amylase, an enzyme that helps to break down starch. Researchers have suggested that the development of the enzyme may have followed — or made possible — the increasing appetite for grain that accompanied the growth of agriculture. Scientists also want to trace the evolution of alcohol dehydrogenase, which is crucial to the breakdown of alcohol and could reveal the origins of humanity's thirst for drink.
Some of the LeCHE participants are now probing further back in time, as part of a project named BEAN (Bridging the European and Anatolian Neolithic), which is looking at how the first farmers and herders made their way into Europe. Burger, Thomas and their BEAN collaborators will be in Turkey this summer, tracing the origins of the Neolithic using computer models and ancient-DNA analysis in the hope of better understanding who the early farmers were, and when they arrived in Europe.
Along the way, they will encounter beyaz peynir, a salty sheep's-milk cheese eaten with nearly every Turkish breakfast. It is probably much like the cheese that Neolithic farmers in the region would have eaten some 8,000 years ago — long before the march of lactase persistence allowed people to drink fresh milk.

http://www.eurekalert.org/pub_releases/2013-08/jhm-flt073113.php

For lung transplant, researchers surprised to learn bigger appears to be better

Johns Hopkins-led research finds larger lungs associated with 30 percent increase in survival at 1 year

Transplant teams have long tried to match the size of donor lungs to the size of the recipient as closely as possible, concerned that lungs of the wrong size could lead to poor lung function and poor outcomes. But new Johns Hopkins-led research suggests that oversized donor lungs may instead be the best option for patients, finding they are associated with a 30 percent increased chance of survival one year after the operation.
The issue of lung size was brought into the spotlight recently with the case of a 10-year-old Pennsylvania girl in need of a lung transplant. Regulations have made children under the age of 12 ineligible to receive adult lungs, primarily because of the potential size mismatch. Her situation sparked a national debate on organ allocation procedures, and her family successfully petitioned the courts to enable her to receive lungs from an adult.
"Despite what we thought, bigger lungs turn out to be better," says Christian A. Merlo, M.D., M.P.H., a lung transplant expert at the Johns Hopkins University School of Medicine and senior author of a study published in the August issue of the The Annals of Thoracic Surgery. "The survival rates for lung transplant, unfortunately,

are not as good as with other solid organ transplants like liver, kidney and heart. But our study tells us that if we were to routinely transplant larger lungs into patients, we could potentially make a real impact on survival. And that's the goal of research."
Lung size can be estimated from the height and sex of the patients and is termed the "predicted total lung capacity." Taller people have bigger lungs and a man's lungs are larger than a woman's of the same height. The researchers defined lung size mismatch as the ratio of the predicted lung capacity of the donor relative to the recipient. For example, a ratio of 1.0 is a perfect size match, whereas a ratio of 1.3 indicates that the transplanted lung is significantly larger than the predicted total lung capacity for the recipient. Merlo's research found that double lung transplant recipients who received lungs with an average ratio of 1.3 were 30 percent less likely to die in the first year.
The research, led by Michael Eberlein, M.D., Ph.D., a former Johns Hopkins medical resident and fellow, was done by analyzing data from 4,520 double lung transplants and 2,477 single lung transplants performed between May 2005 and April 2010 in the United States. The findings were clearer about the benefits of larger lungs in double lung transplants than in single ones, though oversized lungs did convey some survival benefit in those cases as well, they found.
"Size is a more powerful predictor of survival than we ever thought," says Ashish S. Shah, M.D., surgical director of lung transplantation at The Johns Hopkins Hospital and another of the study's authors. "Fears of oversized lungs appear to be unfounded. We hope this research dispels some myths."
In lung transplant, the sickest patients move to the top of the list. Once an adult patient is atop the list, height and gender (along with blood type) are used to determine whether those lungs are suitable for that patient. Merlo and Shah say it might be better to build in a calculation for predicted lung capacity. That way, oversized lungs could be offered to patients instead of smaller lungs that may not work as well.
Lungs can be too large, they caution. If lungs are beyond a certain size, surgeons could have trouble closing the chest cavity, the lungs could be too compressed and collapse or could weigh too heavily on the heart, causing low blood pressure and other problems.
Currently, children under 12 cannot receive adult lungs and adults cannot receive lungs from pediatric donors. Shah, an associate professor of surgery at Johns Hopkins, says the findings suggest that there may be some benefit to removing age from the equation altogether when allocating lungs, putting children and adult donors and recipients into the same pool. Then, doctors could make decisions based on each individual case and the size of the donor organs that become available.
"This study tells us that rather than looking at things like age or height, you have to look at each patient very carefully and determine what their lung capacity is," Shah says. "There may be children who could take adult lungs that would be oversized for them with a good result. And there may be small adults who would do well with pediatric lungs."
Still, Shah points out, while larger lungs may be ideal, transplant candidates who don't get new organs are more likely to die, so smaller lungs are often better than none at all. There are currently more than 1,600 people listed for lung transplants in the United States and many die before getting new lungs. One-year survival after lung transplantation is 80 percent.
The research was supported in part by the Health Resources and Services Administration (contract 234-2005-370011C). Other Johns Hopkins researchers contributing to the study include George Arnaoutakis, M.D.; Jonathan B. Orens, M.D.; and Roy G. Brower, M.D.

http://bit.ly/1ck1YmB

Giant clouds of lead glimpsed on distant dwarf stars

A lead balloon may be a metaphor for something unpopular, but real life clouds of lead glimpsed in the atmosphere of two stars are having the opposite effect. The giant clouds – thought to be 100 kilometres thick – are helping to boost a theory of stellar evolution.

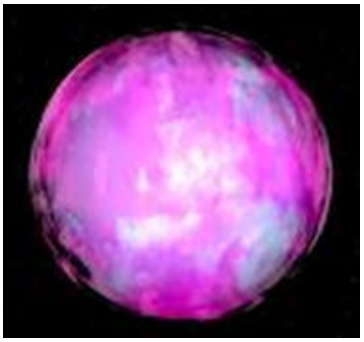
13:05 01 August 2013 by Anil Ananthaswamy

Although lead is one of the heaviest of the naturally occurring elements, clouds of the stuff were predicted to exist as part of a theory about the origins of a type of star called a hot subdwarf. These stars are about half as massive as our sun, and, unlike our sun, which fuses hydrogen to form helium, burn helium in their cores. Astronomers think that they form when bloated old red giant stars are stripped of the outer layers of their atmosphere, possibly because of interaction with a lower-mass companion star or even a planet. What's left behind in the immediate aftermath should be an extremely hot star whose outer layers are rich in helium.

Floating lead

The idea is that the helium, and other light elements heavier than hydrogen, then sink towards the core. And as part of this process of rearrangement, something strange happens to heavy elements. Depending on the star's

temperature, ions of heavy metals, including lead, can interact with the light streaming out of the star, causing them to rise to the surface. "Different ions will experience different forces from light and will float up and down," says Simon Jeffery of the Armagh Observatory in the UK. "Everything starts to sort itself into layers and those layers will migrate up and down depending on the temperature."



A heavy metal subdwarf **(Image: Royal Astronomical Society)**

The trouble was that until now the only hot subdwarfs glimpsed seemed to be at the end of this process – their atmospheres were made of hydrogen and had only traces of helium or heavy metals.

That changed when a team led Naslim Neelamkodan of the Academia Sinica Institute of Astronomy and Astrophysics in Taipei, Taiwan, which included Jeffery, glimpsed hot subdwarfs much earlier on in their evolution.

Missing link

When the team examined 134 hot subdwarfs in data collected by the Very Large Telescope in Chile, they found layers of heavy metals in two – one 800 light years from Earth and the other 1000 light years away, and both about seven times hotter than the sun. They discovered the metals by looking at the spectra of light from these stars. For example, the lead ions in the stars' atmospheres were absorbing light, leading to a telltale signature. The astronomers calculated that lead is 10,000 times more abundant in the atmosphere of these two stars than in the sun's atmosphere. They estimate that the layer of lead is about 100 kilometres thick and weighs 100 billion tonnes.

It wasn't just lead, though. One of the stars also had smaller layers of the heavy metals zirconium and yttrium, which is also predicted by the hot subdwarf theory.

Because the stars' atmospheres are also relatively rich in helium, the team say that they represent a key transition phase between being a red giant to being a normal hot subdwarf, in which most of the helium has settled in the core and the lead clouds have diffused throughout the star. "These stars present a missing link," says Jeffery. That strengthens the theory of subdwarf evolution.

"I have thought for a while that we should see a few stars that are transitioning between red giants and hot subdwarfs," says Simon O'Toole of the Anglo-Australian Observatory in Epping, Australia. "The intermediate helium subdwarfs seem to fit the bill."

Such stars can collectively be called heavy metal subdwarfs, the team suggests. If only stars could form rock bands.

Journal reference: Monthly Notices of the Royal Astronomical Society, DOI: 10.1093/mnras/stt1091

http://phys.org/news/2013-08-biggest-extinction-history-climate-changing-meteor.html

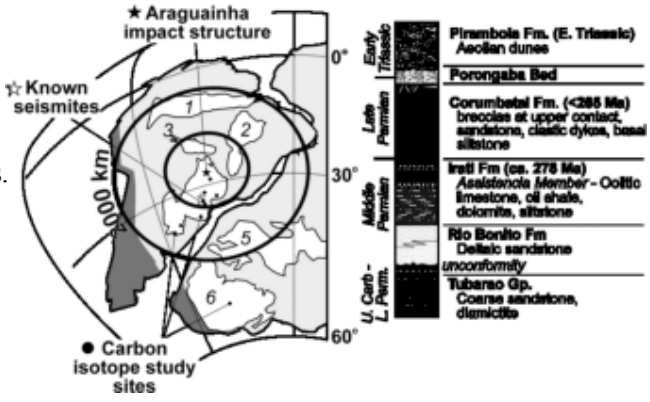
Biggest extinction in history caused by climate-changing meteor

It's well known that the dinosaurs were wiped out 66 million years ago when a meteor hit what is now southern Mexico but evidence is accumulating that the biggest extinction of all, 252.3m years ago, at the end of the Permian period, was also triggered by an impact that changed the climate.

Phys.org - While the idea that an impact caused the Permian extinction has been around for a while, what's been missing is a suitable crater to confirm it. Associate Professor Eric Tohver of the University of Western Australia's School of Earth and Environment believes he has found the impact crater which reveals though the trigger was the same, the details are significantly different.

Last year Dr Tohver redated an impact structure that straddles the border of the states of Mato Grosso and Goiás in Brazil, called the Araguainha crater, to 254.7m years, with a margin of error of plus or minus 2.5m years. Previous estimates had suggested Araguainha was 10m years younger, but Dr Tohver has put it within geological distance of the extinction date.

The Chicxulub crater in Mexico, is 180km in diameter while the Araguainha is 40 kilometres across and was thought to be too small to have caused the chain reaction which brought about such mass extinction.



Araguainha crater's location in Gondwana and geology

"I have been working with Fred Jourdan at Curtin University and UWA post-doctoral fellow Martin Schmieder to establish better ages for various impact structures in Australia and abroad. We were particularly interested in

the Araguainha crater, since the original age determined in the 1990s was relatively close to the Permo-Triassic boundary. The refinements in geochronological techniques that we are applying are helping to reveal the true age of these structures," Dr Tohver said.
The results of an extensive geological survey of the Araguainha crater funded by UWA and the Australian Research Council and published in Palaeogeography, Palaeoclimatology, Palaeoecology, revealed that a sizeable amount of the rock is oil shale.
The researchers calculated that the impact would have generated thousands of earthquakes of up to magnitude 9.9, significantly more powerful than the largest recorded by modern seismologists for hundreds of kilometres around, releasing huge amounts of oil and gas from the shattered rock.
Dr Tohver believes the explosion of methane released into the atmosphere would have resulted in instant global warming, making things too hot for much of the planet's animal life.
"Martin Schmieder and I are currently working on documenting some of the more extreme environmental effects of the impact, including giant tsunamis. In addition, ongoing work with Kliti Grice at Curtin University and her Ph.D. student Ines Melendez will be fundamental to documenting changes in the organic geochemistry of the target rocks," Dr Tohver said.
It's estimated more than 90 per cent of all marine species and about 70 per cent of land-based species disappeared in the Permian extinction.
More information: www.sciencedirect.com/science/article/pii/S0016703712001457

http://www.wired.com/autopia/2013/08/ambucycle/

When Ambulances Can't Get There in Time, the Nimble Ambucycle Saves Lives

Congestion kills. That's not hyperbole, it's a fact. In dozens of cities across the world, heavy traffic, construction, and poorly maintained roads keep first responders from getting to patients in time. That's where the Ambucycle comes in.

By Damon Lavrinc

With a dual-sport motorcycle and a surprising amount of lifesaving equipment on board, an Ambucycle and its medic rider can reach the scene of an accident or the home of a patient in an average of 90 seconds.
hat's lightspeed compared to the 20-30 minutes it could take a traditional ambulance to reach the same destination while dealing with traffic congestion and road closures.
The Ambucycle is the brainchild of Eli Beer, the founder and manager of United Hatzalah ("rescue" in Hebrew). At 15 he took his first EMT course and began volunteering with an ambulance service in Israel.
But he quickly realized that every minute that passed between leaving the station to arriving at a patient's door was a lifetime.
So at 17 he assembled a group of EMTs and a handful of emergency radio receivers to rush medical attention to those in need - sometimes on foot.

Video here**Photo: United Hatzalah**

Today, 25 years later, Beer's rogue band of first responders has evolved into United Hatzalah, a 2,000-volunteer army of medical technicians that can deploy on a moment's notice.
In just the last year the organization helped 207,000 patients, over 40,000 of which were treated for life-threatening emergencies.
The Ambucycles obviously can't carry a person, but they can stabilize a patient long enough for an ambulance to arrive, thanks to an on-board trauma kit, oxygen canister, defibrillator, and more.
The medics each have a smartphone equipped with GPS, allowing volunteers to be notified of an emergency in their vicinity and respond within minutes. Each year, the bikes serve almost 500 calls, one-quarter of which are life-threatening. And they do it all for free.
The cost of each bike - including the medical equipment, maintenance, and insurance - is around $26,000, and United Hatzalah is aiming to expand its fleet to 500 in order to meet demand in Jerusalem, Tel Aviv, and other cities throughout Israel.
Beer is already in talks with organizations in India and hopes to expand the Ambucycle's reach across the world. And if the terrain is too tough for their dual-sport, United Hatzalah has a four-wheel-drive Ambutractor in the fleet as well.

http://www.eurekalert.org/pub_releases/2013-08/ci-fwi072913.php

Future warming: Issues of magnitude and pace

Researchers reviewing climate change say continued warming at the current pacet may lead to the most rapid large climate change in the last 65 million years

Washington, DC- Researchers reviewed the likelihood of continued changes to the terrestrial climate, including an analysis of a collection of 27 climate models. If emissions of heat-trapping gases continue along the recent trajectory, 21st century mean annual global warming could exceed 3.6 °F (2 °C) over most terrestrial regions during 2046 to 2065 and 7.2 °F (4 °C) during 2081-2100. If warming occurs at this pace, it will probably be the most rapid large climate change in the last 65 million years.

The review, published in the August 2 issue of Science, was conducted by Stanford University's Noah Diffenbaugh and the director of the Carnegie Institution's Department of Global Ecology Chris Field.

"With a high scenario for future greenhouse gas emissions, the largest warming occurs over the high latitudes of the Northern Hemisphere, but all land areas warm dramatically," remarked Field

The scientists used the Coupled Model Intercomparison Phase 5 (CMIP5), which includes results from 27 different models. They reviewed information about the aspects of climate change that drive biological response; a comparison of current and future climate change with the past, including the rate and magnitude of the change; and the context in which the change is occurring. Results in the CMIP5 archive reflect the current state of understanding about the way the physics of the atmosphere and oceans respond to changes in concentrations of greenhouse gases released by human activity.

The researchers emphasize that there are numerous uncertainties about the magnitude of future climate change, such as energy feedbacks from clouds and the carbon cycle. The largest uncertainty is the level of greenhouse gas emissions from future human activity. Despite these uncertainties several existing conditions, especially ongoing demand for fossil fuels, makes some future climate change a certainty.

"What is perhaps most noteworthy is the rate of change," remarked Diffenbaugh. "For instance, the rapid global warming event that occurred some 55 million years ago was as large as these warming projections, but that event occurred over many thousands of years, not a mere century."

The duo emphasized that the rate of change will ultimately by determined by human decisions and innovations regarding greenhouse gas emissions. "The future of the planet lies in our hands," said Field.

http://bit.ly/13EgoVf

Y chromosome analysis moves Adam closer to Eve

Genetic studies push back age of men's most recent common ancestor

By Erin Wayman

Men might need some more pages in their family album.

The largest analyses to date of the human Y chromosome suggest that modern men can trace their family tree further back in time than previously thought. One of the studies, an analysis of 69 men from nine populations worldwide published in the Aug. 2 *Science*, finds that their most recent common ancestor lived 120,000 to 156,000 years ago. That's roughly the same time that the last common ancestor of women is estimated to have lived, researchers report.

The Y chromosome, passed down from father to son, and mitochondrial DNA, passed down from mother to child, are useful in retracing ancestry because they don't undergo genetic reshuffling as the rest of the genetic instruction book does. Researchers analyze mutations in these parts of the genome to assess when groups split apart. The hypothetical common ancestors of these genetic lineages are sometimes called Y Chromosome Adam and Mitochondrial Eve.

"We're not saying they're exact contemporaries or they actually met or all men and women descended from the same couple," says study coauthor Carlos Bustamante of Stanford University. Y Chromosome Adam and Mitochondrial Eve aren't the first human male and female but instead represent the common ancestors of the modern Y chromosome and modern mitochondrial DNA.

The findings may overturn previous results that suggested Y Chromosome Adam was only a half or a third as old as Mitochondrial Eve. Previous analyses date the Y chromosome common ancestor to between 50,000 and 115,000 years ago and the mitochondrial DNA common ancestor to between 150,000 and 240,000 years ago. Bustamante and colleagues also looked at mitochondrial DNA in their study population and found a common female ancestor 99,000 to 148,000 years ago.

Another study in the same issue of *Science* pushes the Y ancestor back even further in time. Paolo Francalacci of the University of Sassari in Italy and colleagues analyzed DNA from 1,204 Sardinian men and determined that Y Chromosome Adam lived 180,000 to 200,000 years ago.

Since the Y chromosome and mitochondrial DNA are inherited separately and have independent evolutionary histories, their trees do not necessarily spread from contemporaneous roots. Still, the apparent lag between the mitochondrial DNA and Y chromosome lineages has been a head-scratcher for researchers who expected the ancestors to be contemporaneous. "People tied themselves in knots to come up with an explanation," says Rebecca Cann, an evolutionary biologist at the University of Hawaii at Manoa.

One idea implicated mating differences between the sexes. Women bear approximately similar numbers of children, but men can vary widely in their fertility, Bustamante says. One man might leave behind hundreds of descendants, another only one or a few. That variation in the number of offspring of men and women could account for different patterns in the Y chromosome and mitochondrial DNA trees.

The studies look at longer stretches of the Y chromosome than earlier work, which could help explain why they find an older male ancestor, says Bustamante, whose team analyzed complete Y chromosome sequences.

But even these studies are missing pertinent data, says Michael Hammer of the University of Arizona in Tucson. In March, Hammer and colleagues reported in the *American Journal of Human Genetics* the discovery of a rare Y chromosome in an African-American and other Y chromosomes from the same lineage in 11 men in western Cameroon. Hammer's team traced the most recent common ancestor of the Y chromosome back 338,000 years. In this scenario, the Y chromosome ancestor is much older than the mitochondrial DNA ancestor — and even predates the earliest known fossils of *Homo sapiens* by more than 100,000 years. The great antiquity may imply that *H. sapiens* is older than the fossil evidence currently suggests or that early humans mated with a closely related hominid species that contributed to the Y chromosome gene pool.

The new studies didn't consider the Cameroonian population, so they are missing crucial genetic diversity in their analyses, Hammer says. In general, scientists are overlooking lots of Y chromosome diversity because populations in sub-Saharan Africa have been poorly sampled, he says.

Melissa Wilson Sayres, a geneticist at the University of California, Berkeley, agrees there are still a lot of data to collect. Part of the problem has been the complicated nature of the Y chromosome itself. It's highly repetitive and therefore has taken a long time to properly read. In fact, she says, it took almost as long to sequence the Y chromosome as it did to sequence all the rest of the human genome.

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Moderate kidney disease costs medicare tens of billions of dollars each year

Significant costs arise even before patients develop kidney failure

Washington, DC - Even early stages of kidney disease come with steep medical costs, according to a study appearing in an upcoming issue of the Journal of the American Society of Nephrology (JASN). The study found that expenses related to moderate chronic kidney disease (CKD) cost Medicare tens of billions of dollars each year.

Approximately 60 million people globally have CKD. Most of the costs of CKD are thought to arise when the disease progresses to kidney failure, also known as stage 5 CKD. The Centers for Disease Control and Prevention funded investigators from RTI International to study whether people who had early stages of CKD also incurred considerable medical costs that could be attributed to their disease.

"It was difficult to answer this question, because early stages of CKD often go undiagnosed. However, by using a sample of participants from the National Health and Nutrition Examination Survey III, or NHANES III, we were able to obtain lab measurements and estimate stages of CKD for persons in the sample," explained first author Amanda Honeycutt, PhD. The researchers then received permission to have Medicare payment data merged with the NHANES III data to determine the impact of diseases and other factors on Medicare spending. The lab data used in the analyses were from 1988 through 1994, and they were linked to Medicare costs for 1991 through 1994.

Among the major findings:

Medicare spending attributable to CKD stages 2 through 4 is likely to exceed $48 billion per year.

Medicare costs attributable to stage 2 CKD amounted to $1700 per person per year. Costs attributable to stage 3 CKD were $3500 per person per year, and for stage 4 CKD they were $12,700 per person per year, adjusted to 2010 dollars.

"This study is important because we were able to identify that even early stages of CKD—before people progress to full end-stage renal disease—contribute to high Medicare costs," said Dr. Honeycutt. The findings suggest that efforts to prevent the development of CKD may lead to significant savings. In addition, the study highlights the need to identify CKD in its earliest stages to prevent disease progression and avoid the high medical costs attributable to the latter stages of the disease.

Study co-authors include Joel E. Segel, BA, Xiaohui Zhuo, PhD, Thomas Hoerger, PhD, Kumiko Imai, PhD, and Desmond Williams, MD PhD.

Disclosures: The authors reported no financial disclosures.

The article, entitled "Medical Costs of Chronic Kidney Disease in the Medicare Population," will appear online at http://jasn.asnjournals.org/ on August 1, 2013, doi: 10.1681/ASN.2012040392.

http://www.eurekalert.org/pub_releases/2013-08/uom-ecc080113.php

Existing cropland could feed 4 billion more

New University of Minnesota research shows reallocating croplands away from fuels and animal feed could boost food available for people by 70 percent without clearing more land

The world's croplands could feed 4 billion more people than they do now just by shifting from producing animal feed and biofuels to producing exclusively food for human consumption, according to new research from the Institute on the Environment at the University of Minnesota.

Even a smaller, partial shift from crop-intensive livestock such as feedlot beef to food animals such as chicken or pork could increase agricultural efficiency and provide food for millions, the study says.

"We essentially have uncovered an astoundingly abundant supply of food for a hungry world, hidden in plain sight in the farmlands we already cultivate," says graduate research assistant Emily Cassidy, lead author of the paper published in Environmental Research Letters. "Depending on the extent to which farmers and consumers are willing to change current practices, existing croplands could feed millions or even billions more people."

Demand for crops is expected to double by 2050 as population grows and increasing affluence boosts meat consumption. Meat takes a particularly big toll on food security because it takes up to 30 crop calories to produce a single calorie of meat. In addition, crops are increasingly being used for biofuels rather than food production. This study sought to quantify the benefit to food security that would accrue if some or all of the lands used to produce animal feed and fuel were reallocated to directly produce food for people.

To get at that question, Cassidy and colleagues first mapped the extent and productivity of 41 major crops between 1997 and 2003, adjusting numbers for imports and exports and calculating conversion efficiencies of animal feed using U.S. Department of Agriculture data. The researchers assumed humans need an average of 2,700 calories per day, and grazing lands and animals were not included in the study. Among the team's findings:

Only 12 percent of crop calories used for animal feed end up as calories consumed by humans.

Only 55 percent of crop calories worldwide directly nourish people.

Growing food exclusively for direct human consumption could boost available food calories up to 70 percent

U.S. agriculture alone could feed an additional 1 billion people by shifting crop calories to direct human consumption.

When calculated on the basis of protein rather than calories, results were similar. For instance, of all plant protein produced, 49 percent ends up in human diets.

In addition to the global findings, the research team looked at allocation of crop calories in four key countries: India, China, Brazil and the U.S. They found that while India allocates 90 percent of calories to feeding people, the other three allocate 58 percent, 45 percent, and 27 percent, respectively.

Noting the major cultural and economic dimensions involved, the researchers acknowledged that while a complete shift from animal to plant-based diets may not be feasible, even a partial shift would benefit food security. Quantifying the impact of various strategies, they found that a shift from crop-intensive beef to pork and chicken could feed an additional 357 million people, and a shift to nonmeat diets that include eggs and milk could feed an additional 815 million people.

The researchers emphasized that they are not making diet prescriptions or recommendations, just pointing out opportunities for gains in food production. They noted that humans can completely meet protein needs with plant-based diets, but that crop systems would need to shift (e.g., toward more production of protein-rich legumes) to meet human dietary needs.

"The good news is that we already produce enough calories to feed a few billion more people," Cassidy says. "As our planet gets more crowded or we experience disasters like droughts and pests, we can find ways of using existing croplands more efficiently."

To view a video explaining the research, please visit http://www.youtube.com/watch?v=LmBVbqEPeC0&feature=c4-overview&list=UUXzMUZRZtBE0GtF1RCOWMbw.

http://www.eurekalert.org/pub_releases/2013-08/bumc-sfp080113.php

Study finds physicians need to better recognize use of herbal supplements while breastfeeding

The importance of physicians recognizing that many mothers use herbal supplements while breastfeeding

Boston – In an article published in this month's issue of Pediatrics In Review, researchers from Boston University School of Medicine (BUSM) stress the importance of physicians recognizing that many mothers use herbal supplements while breastfeeding in order to make accurate health assessments for both mother and child. In the US, no existing regulatory guidelines set a standardized risk assessment of herbal supplement use during breastfeeding. Because of the highly limited number of studies on herb use during lactation, numerous resources have mixed reports and safety recommendations, making it confusing for both mother and clinician. After completing a systematic review of human lactation and herbal medicine literature, the researchers found poor methodology in the few available studies and concluded that further research is needed to assess the prevalence, efficacy and safety of commonly used herbs during breastfeeding.

"It is important for physicians and clinicians to be more aware that mothers are using herbal supplements and how vital it is to ask the mothers, who are seeking a doctor's opinion when having trouble breastfeeding, about their use before making an assessment," said senior author Paula Gardiner, MD, MPH, assistant professor at BUSM and a physician of family medicine at Boston Medical Center.

Although there is little scientific evidence to support the efficacy or safety of herbal supplements, it is a common practice both nationally and internationally. "The use of herbal supplements while breastfeeding is two-sided—there are benefits, but there are also safety concerns," she added. "About 18 percent of the US population use herbs and dietary supplements. We just want to make sure physicians and clinicians are aware of this prevalent use when communicating with breastfeeding mothers about their health."

Herbal remedies may be used to increase the milk supply, relieve engorgement, treat mastitis, or for other therapeutic uses unrelated to lactation.

"Since there is very limited research, it is difficult to develop accurate information on the safety and effectiveness of specific herbs during breastfeeding," said Gardiner. "It is crucial that more research is conducted in this area, including national prevalence studies and safety and efficacy studies."

Gardiner is supported by grant K07AT005463 from the National Center for Complementary & Alternative Medicine. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Center for Complementary & Alternative Medicine or the National Institutes of Health

http://www.eurekalert.org/pub_releases/2013-08/wcmc-nds080113.php

Novel drug shuts down master protein key to lymphoma

Weill Cornell scientists reveal how the protein works and how the drug gums it up, offering new hope for treatment of aggressive cancer

NEW YORK - Researchers have discovered how an experimental drug is capable of completely eradicating human lymphoma in mice after just five doses. The study, led by researchers at Weill Cornell Medical College, sets the stage for testing the drug in clinical trials of diffuse large B-cell lymphoma (DLBCL), the most common subtype of non-Hodgkin lymphoma, itself the seventh most frequently diagnosed cancer in the U.S.

In the journal Cell Reports, published today online, the scientists describe how the powerful master regulatory transcription factor Bcl6 regulates the genome, ensuring that aggressive lymphomas survive and thrive. They also show how the Bcl6 inhibitor, developed at Weill Cornell, effectively gums up the protein, stopping it from working.

While Bcl6 is active in a number of cancers, including leukemia and breast cancer, work testing a Bcl6 inhibitor is most advanced in DLBCL. "That's because we desperately need a new strategy to treat this lymphoma -- many patients are resistant to currently available treatments," says the study's senior investigator, Dr. Ari Melnick, Gebroe Family Professor of Hematology/Oncology and director of the Raymond and Beverly Sackler Center for Biomedical and Physical Sciences at Weill Cornell.

Dr. Melnick developed the first BCL6 inhibitors nine years ago, and has continued to improve upon the design of these drugs so they could be used to treat cancer patients. He has since collaborated with colleagues at many institutions in a systemic effort to understand how both Bcl6 and its inhibitor drugs function.

In a study published in March in Nature Immunology, Dr. Melnick and his team reported that it is possible to shut down Bcl6 in DLBCL without affecting its vital role in the T cells and macrophages needed to support a healthy immune system. The protein has long been considered too complex to target with a drug as it also is crucial to proper function of many immune system cells, not just B cells gone bad.

That finding suggested Bcl6 inhibiting drugs may have few side effects, says Dr. Melnick, who is also a hematologist-oncologist at NewYork-Presbyterian Hospital/Weill Cornell Medical Center.
The latest study was designed to understand exactly how Bcl6 promotes DLBCL.
Transcription factors are responsible for either inhibiting or promoting the expression of genes, and master regulatory transcription factors are like transcription factors on steroids: their actions regulate thousands of genes in different kinds of cells. Bcl6 can control the type of immune cell that develops in the bone marrow -- pushing them to become B cells, T cells, or macrophages -- and it has a primary role in the developmental phase of B cells, during which they generate specific antibodies against pathogens.
The researchers found that in order to help B cells produce antibodies against an infection, Bcl6 "builds a huge shopping mall-style complex" that sits on top of a stretch of the genome. By binding onto these genes, Bcl6 deactivates the DNA, stopping genes from producing RNA and proteins. "Bcl6 acts like a barcode reader. When it sees that barcode -- the DNA sequence -- it attaches there," Dr. Melnick.
Normally, the protein complex goes away after an immune reaction has been successfully mounted against the pathogen. But when it doesn't, and remains stuck to the genes, DLBCL can result. That's because Bcl6 is inhibiting genes that stop cells from dividing and that sense damage to the genome, Dr. Melnick says. "We now know the genes that Bcl6 is repressing and how that helps lymphoma develop and survive."
Bcl6 also has a second, independent function that Dr. Melnick says acts like a switch on railroad track that routes a train in one direction or another. One track is needed when antibodies are required for an immune response, while the other keeps B cells in a constant state of division.
The researchers found that in order for DLBCL to survive, Bcl6 needs to maintain both its shopping mall protein complex and keep the train tracks on the path toward B cell division. To their surprise, they also found that both the complex and the train switch attach to the Bcl6 protein at the same site. "They fit into the same keyholes on Bcl6," Dr. Melnick says. "There are two identical binding sites on the protein surface."
Even better, the Bcl6 inhibitor they developed was designed to fit into that same keyhole.
"This is wonderfully serendipitous -- our drug just happens to be able to overcome both of the biological mechanisms that are key to survival of aggressive lymphoma," Dr. Melnick says, adding that the inhibitor completely eradicated DLBCL in mice in a short time, with no detectable side effects. The team is conducting additional research toward an investigational new drug application from the federal Food and Drug Admission.
The study was supported by grants from the National Cancer Institute (NCI R01 CA104348 and NCI R01 CA071540), a National Science Foundation CAREER grant 1054964, the Chemotherapy Foundation, the Burroughs Wellcome Foundation and a Sass Foundation Judah Folkman Fellowship, among other funding sources.
Dr. Olivier Elemento from Weill Cornell Medical Center is the study's co-senior investigator, and Dr. Katerina Hatzi, also from Cornell Weill, is the lead investigator. Other study authors are Yanwen Jiang, Chuanxin Huang, Francine Garrett-Bakelman, Christopher E. Mason, Leandro Cerchietti, Eugenia G. Giannopoulou, Paul Zumbo, and Matthias Kormaksson, from Weill Cornell; Micah D. Gearhart and Vivian J. Bardwell from the University of Minnesota, Minneapolis; Kevin Kirouac and Gilbert G. Prive from the Ontario Cancer Institute, Toronto; Srividya Bhaskara and Scott W. Hiebert from Vanderbilt University, Nashville; Jose M. Polo from Monash University, Victoria, Australia; and Alexander D. MacKerell, Jr. and Fengtian Xue from the University of Maryland, Baltimore.

http://www.sciencedaily.com/releases/2013/08/130801125018.htm

Researchers Find Home of Best Stem Cells for Bone Marrow Transplants

McMaster University researchers have revealed the location of human blood stem cells that may improve bone marrow transplants. The best stem cells are at the ends of the bone.

It is hoped this discovery will lead to lowering the amount of bone marrow needed for a donation while increasing regeneration and lessening rejection in the recipient patients, says principal investigator Mick Bhatia, professor and scientific director of the McMaster Stem Cell and Cancer Research Institute.
In a paper published online today by the journal Cell Stem Cell, his team reports that human stem cells (HSC) residing in the end (trabecular region) of the bones display the highest regenerative ability of the blood and immune system.
"Like the best professional hockey players, our findings indicate blood stem cells are not all equal," said Bhatia. "We now reveal the reason why -- it's not the players themselves, but the effect the arena has on them that makes them the highest scorers."
Bone marrow transplants have been done for more than 50 years and are routine in most hospitals, providing a life saving treatment for cancer and other diseases including leukemia, anemia, and immune disorders.
Bhatia, who also holds a Canada Research Chair in Human Stem Cell Biology, said that cells surrounding the best blood stem cells are critically important, as these "stem cell neighbors" at the end of the bone provide the unique instructions that give these human blood stem cells their superior regenerative abilities.
The research was funded by the Canadian Institutes of Health Research and Ontario Cancer Research Institute.

Borhane Guezguez, Clinton J.V. Campbell, Allison L. Boyd, Francis Karanu, Fanny L. Casado, Christine Di Cresce, Tony J. Collins, Zoya Shapovalova, Anargyros Xenocostas, Mickie Bhatia. Regional Localization within the Bone Marrow Influences the Functional Capacity of Human HSCs. Cell Stem Cell, 2013; 13 (2): 175 DOI: 10.1016/j.stem.2013.06.015

http://www.sciencedaily.com/releases/2013/08/130801142428.htm

Advance in Regenerative Medicine Could Make Reprogrammed Cells Safer While Improving Their Function

The enormous promise of regenerative medicine is matched by equally enormous challenges. But a new finding by a team of researchers led by Weill Cornell Medical College has the potential to improve both the safety and performance of reprogrammed cells.

The researchers' study, published in today's issue of the journal Nature, found that an enzyme, activation-induced cytidine deaminase (AID), helps in the process that changes an adult human cell into an induced pluripotent stem cell (iPS cell). These iPS cells can then be developed into any kind of cell needed to therapeutically restore tissues and organs.

The finding settles an ongoing controversy regarding use of AID to reprogram cells, says the study's senior investigator, Dr. Todd Evans, vice chair for research and professor of cell and developmental biology in the Department of Surgery at Weill Cornell Medical College.

"The dispute was whether AID is required to make iPS cells, and we found that the enzyme does make reprogramming very efficient, although it is not absolutely necessary," says Dr. Evans, an internationally-recognized authority on regenerative medicine. "In fact, we plan to test if reprogramming iPS cells without AID may even be helpful."

One reason is that AID can cause genetic mutations that can lead to cancer. AID is best known as a master regulator of antibody diversity in B cells, and in order to create varied types of beneficial antibodies, it routinely mutates antibody genes. But sometimes the process goes awry, resulting in development of B cell lymphoma, Dr. Evans says. "That leads us to believe that if you can reprogram cells without AID, it could reduce risk of potential mutations, and thus be safer."

iPS Cells Without AID Remember What They Once Were

In order to push a cell, such as a fibroblast, to revert to an iPS cell, the epigenetic "markers" that define an adult cell must be removed. "All cells of the body have the same genes, but they are used differently in different tissues," Dr. Evans explains. "If an undifferentiated cell becomes a heart cell, somehow it has to lock in and stabilize that particular adult phenotype and not forget what it is."

One way that function is accomplished is by placing a methylation group on top of certain genes that activate other cell destinations -- such as to become a liver cell -- usually switching those genes off. "We have known how these marks are put on genes, but we didn't know how they were taken off in the process of pushing an adult cell to revert back to a stem-cell-like state," Dr. Evans says.

Dr. Evans and his colleagues found that the AID enzyme removed those epigenetic markers.

They then created a mouse that did not produce AID to see if the animal's adult fibroblast cells could be pushed back to iPS cells. "If you need AID to reprogram the cells, you shouldn't be able to do it, or do it well." Surprisingly, they found that the cells at first seemed to want to reprogram even faster than normal cells, but most never fully reverted to a stem-cell-like state. "They eventually crashed and differentiated back into a fibroblast," Dr. Evans says. "What that meant is that they never cleared their memory of being a fibroblast cell. AID efficiently removes that epigenetic memory, smoothing the way for a cell to morph into an undifferentiated state." But some of the mouse adult fibroblasts lacking AID -- those that Dr. Evans says they "babysat" -- did become iPS cells.

Despite the fact that reprogramming adult cells without AID is inefficient, the researchers say that the method may offer another advantage besides increased safety.

"It might be useful to allow epigenetic memory to be retained," Dr. Evans says. "If you want to make new cardiac cells to repair a patient's heart, it might be better to start with a cardiac cell and push it to become an iPS cell, from which other cardiac cells could be made. If these cells remember they were cardiac cells, they might make a better heart cell than if they came from reprogrammed fibroblasts."

The study was supported by National Institutes of Health grants (HL056182 and AI072194) and a National Science Foundation CAREER grant (1054964).

Other study co-authors include Ritu Kumar, Ting-Chun Liu, Philipp Franck and Olivier Elemento from Weill Cornell Medical College; Lauren DiMenna, Nadine Schrode, Silvia Muñoz-Descalzo, Anna-Katerina Hadjantonakis and Jayanta Chaudhuri from Memorial Sloan-Kettering Cancer Institute; and Ali A. Zarrin from Genentech.

Ritu Kumar, Lauren DiMenna, Nadine Schrode, Ting-Chun Liu, Philipp Franck, Silvia Muñoz-Descalzo, Anna-Katerina Hadjantonakis, Ali A. Zarrin, Jayanta Chaudhuri, Olivier Elemento & Todd Evans. AID stabilizes stem-cell phenotype by removing epigenetic memory of pluripotency genes. Nature, 01 August 2013 DOI: 10.1038/nature12299

http://www.bbc.co.uk/news/science-environment-23536567

Ice core data supports ancient space impact idea

New data from Greenland ice cores suggest North America may have suffered a large cosmic impact about 12,900 years ago.

By Simon Redfern Reporter, BBC News

A layer of platinum is seen in ice of the same age as a known abrupt climate transition, US scientists report.
The climate flip has previously been linked to the demise of the North American "Clovis" people.
The data seem to back the idea that an impact tipped the climate into a colder phase, a point of current debate.
Rapid climate change occurred 12,900 years ago, and it is proposed that this is associated with the extinction of large mammals - such as the mammoth, widespread wildfires and rapid changes in atmospheric and ocean circulation. All of these have previously been linked to a cosmic impact but the theory has been hotly disputed because there was a lack of clear evidence.
New platinum measurements were made on ice cores that allow conditions 13,000 years ago to be determined at a time resolution of better than five years, report Michail Petaev and colleagues from Harvard University.
Their results are published in the journal Proceedings of the National Academy of Sciences.
A 100-fold spike in platinum concentration occurs in ice that is around 12,890 years old, at the same moment that rapid cooling of the climate is indicated from oxygen isotope measurements. This coincides with the start of a climatic period called the "Younger Dryas".
The Younger Dryas started and finished abruptly, and is one of a number of shorter periods of climate change that appear to have occurred since the last glacial maximum of 20,000 years ago.
Each end of the Younger Dryas period may have involved very rapid changes in temperature as the climate system reached a tipping point, with suggestions that dramatic changes in temperature occurred over as short as timescale as a decade or so.

Asteroid apocalypse?

The observations lend credence to earlier, disputed, reports that finds of microscopic grains of diamond and a mineral called lonsdaleite in lake sediments dated to the same time as a possible meteorite impact. Those measurements resemble the most recent observations, reported last month, of remnants of the Tunguska meteorite impact in Siberia. Sphere-shaped particles have also been identified in other sites' sediments, which also have been dated to this event.
While the platinum data and the spherical particles add to evidence for an impact event, doubters have pointed out that - as yet - no impact site has been identified.
It has been suggested that debris thrown into the atmosphere as a result of an impact triggered global cooling at a rate as rapid as the climate changes recorded in the past century. Such rapid climate change makes it difficult for ecologies and societies to adjust. It is the fluctuation that has been cited as the cause of the extinction of massive mammals like the mammoth, and native cultures such as the Clovis people in North America.
The possible role of cosmic impacts in causing huge changes to life on Earth is receiving increased attention.
The mass extinction 66 million years ago that wiped out the dinosaurs is generally believed to be linked to a space strike in southern Mexico's Yucatan Peninsula.
Recently, a group of scientists led by Eric Tohver at the University of Western Australia reported that the biggest extinction of all, which occurred 252.3 million years ago at the end of the Permian period, could be explained by an asteroid impact in Brazil.
Nasa is now focusing resources towards detection of future Earth-threatening asteroids.
The US space agency received more than 400 responses to their recent request for ideas to feed into their Asteroid Grand Challenge, which includes plans to redirect a space rock and send humans to study it.

http://www.medscape.com/viewarticle/808812?src=rss

Every Slice of Drug-Rep Pizza Counts Starting Aug. 1

Today marks a new era in the relationship between physicians and the drug and device makers that give them consulting fees, honoraria for presentations, and lunches for the office staff.

Robert Lowes

From now on, companies must keep track of virtually every payment and gift bestowed on each clinician and report them to the Centers for Medicare & Medicaid Services (CMS), which will report them to the world.
This accounting exercise stems from a provision in the Affordable Care Act (ACA) that seeks to expose the financial dealings between industry and physicians and discourage conflicts of interest for the latter that might

skew education, research, and clinical decision-making. Under the ACA provision, called the Physician Payments Sunshine Act, drug and device makers must report any "transfer of value" of $10 or more made to a physician. Transfers of value under $10 — a cup of coffee, say — aren't reportable unless they add up to more than $100 in a year. Companies also must disclose whether physicians have any ownership stake in them.
The record-keeping starts today, so yesterday's drug-rep pizza doesn't count, but today's does. The Sunshine Act requires CMS to post the totals for each physician online by September 30, 2014.
Physicians have no legal duty to keep a tally of industry payments and gifts, but they may want to anyway. The Sunshine Act allows them to contest the dollar amounts that drug and device makers submit to CMS, especially if they think the numbers are inflated. Some medical societies fear that inaccurate information published by CMS could jeopardize the careers of their members.
In light of that worry, CMS released a free mobile app last month that physicians can use to record cash and in-kind payments from industry. More information on the Sunshine Act, including the mobile app, is available on the CMS Web site.

http://nyti.ms/13s5vue

Gene Sleuths Find How Some Naturally Resist Cholera

People living in the Ganges region have developed a natural genetic resistance to cholera over the last 5,000 to 30,000 years.

By NICHOLAS WADE

People living in the Ganges Delta, where cholera is an ancient, endemic and often lethal disease, have adapted genetically to the scourge through variations in about 300 genes, say researchers who have scanned their genomes for the fingerprints of evolution. The researchers also found unexpected changes in genes that protect against arsenic, suggesting that arsenic exposure in Bangladesh is not just a modern problem associated with deep tube wells but may have ancient roots.
These instances of natural selection probably took place within the last 5,000 to 30,000 years, the researchers say, and show how evolution has continued to mold human populations through the relatively recent past.
Pinpointing the genes responsible for natural resistance to cholera will help the development of better vaccines, said Dr. Regina C. LaRocque, an infectious disease expert at the Massachusetts General Hospital and an author of the study, published Wednesday in the journal Science Translational Medicine. Vaccines now in use do not stay effective for long and must constantly be readministered in regions where the disease is endemic.
The genes that showed fingerprints of natural selection were identified by two other authors of the study, Elinor K. Karlsson and Dr. Pardis C. Sabeti, computational biologists at Harvard, in the genomes of Bengalis, the majority population in Bangladesh.
The selected genes offer a road map to how the body defends itself against cholera. Toxin from the bacterium binds to cells in the victim's intestine, prizing open the channels through which chloride ions leave the cell and forcing the cells to excrete volumes of water and electrolytes — up to two liters an hour. The diarrhea benefits the organism, which can reach drinking water and spread further, but can be lethal for the host if unchecked.
One set of selected genes in the Bengalis affects control of the innate immune system, the body's first line of defense against microbes. Another set of genes affects the channels that control the flow of potassium ions in and out of cells. It is not yet known exactly how the variations in any of the selected genes affect the biology of resisting cholera. But variations in the potassium channel genes, for instance, could help reverse the outward flow of water caused by the cholera toxin's attack on the chloride channels.
These findings fit the expected biology of cholera but upset other predictions. Cystic fibrosis is caused by a mutation in a gene that controls the movement of chloride in and out of cells. Since the cholera toxin requires this gene to be in working order, the mutation might be protective against it. But the researchers found no evidence of selection on the cystic fibrosis gene in the Bengali population.
People with blood group O are particularly susceptible to cholera, and indeed few Bengalis have blood group O. In scanning blood group genes, the researchers were not able to pick up any negative selection against the O group genes. But they unexpectedly found evidence of natural selection having favored a minor blood type known as the Kell blood group. The genes of this group have no known connection with cholera but seem to offer a defense against arsenic. The poison contaminates the groundwater of Bangladesh, having been released by the tube wells dug to secure clean water to protect against cholera. The presence of protective genes in the Bengali population, if verified, would suggest arsenic is not just a modern problem but has been unleashed by monsoons or other natural phenomena for thousands of years.
As a necessary preliminary to testing for natural selection, the researchers looked at the racial composition of the Bengali population and found that they are an Indian population with a 9 percent admixture of East Asian genes, probably Chinese. The admixture occurred almost exactly 52 generations ago, according to statistical

calculation, or around A.D. 500, assuming 29 years per generation. The Gupta empire in India was in decline at this time, but it is unclear whether the intermarriage with East Asians took place through trade or conquest.
"We can now go back to the historians and see what happened then," Dr. Karlsson said.
John Mekalanos, a cholera expert at the Harvard Medical School, said the new finding was one of several that "are starting to give a strong impression that the human genome has been dramatically shaped by responses to microorganisms." The discovery that Bengalis enjoy special resistance to cholera may help explain why much stronger doses of vaccine are needed to immunize them than are required for North American populations, Dr. Mekalanos said. The difference is usually attributed to differences in gut bacteria, but genetics now offers an alternative explanation.

http://www.eurekalert.org/pub_releases/2013-08/r-lnn080213.php

Largest neuronal network simulation to date achieved using Japanese supercomputer

Exploiting the full computational power of the Japanese supercomputer, K Computer, researchers have carried out the largest general neuronal network simulation

By exploiting the full computational power of the Japanese supercomputer, K Computer, researchers from the RIKEN HPCI Program for Computational Life Sciences, the Okinawa Institute of Technology (OIST) in Japan and Forschungszentrum Jülich in Germany have carried out the largest general neuronal network simulation to date.

By exploiting the full computational power of the Japanese supercomputer, K Computer, researchers have carried out the largest general neuronal network simulation to date. **Credit: RIKEN**

The simulation was made possible by the development of advanced novel data structures for the simulation software NEST. The relevance of the achievement for neuroscience lies in the fact that NEST is open-source software freely available to every scientist in the world.
Using NEST, the team, led by Markus Diesmann in collaboration with Abigail Morrison both now with the Institute of Neuroscience and Medicine at Jülich, succeeded in simulating a network consisting of 1.73 billion nerve cells connected by 10.4 trillion synapses. To realize this feat, the program recruited 82,944 processors of the K Computer.
The process took 40 minutes, to complete the simulation of 1 second of neuronal network activity in real, biological, time.
Although the simulated network is huge, it only represents 1% of the neuronal network in the brain. The nerve cells were randomly connected and the simulation itself was not supposed to provide new insight into the brain - the purpose of the endeavor was to test the limits of the simulation technology developed in the project and the capabilities of K. In the process, the researchers gathered invaluable experience that will guide them in the construction of novel simulation software.
This achievement gives neuroscientists a glimpse of what will be possible in the future, with the next generation of computers, so called exa-scale computers.
"If peta-scale computers like the K Computer are capable of representing 1% of the network of a human brain today, then we know that simulating the whole brain at the level of the individual nerve cell and its synapses will be possible with exa-scale computers hopefully available within the next decade," explains Diesmann.

Memory of 250,000 PCs

Simulating a large neuronal network and a process like learning requires large amounts of computing memory. Synapses, the structures at the interface between two neurons, are constantly modified by neuronal interaction and simulators need to allow for these modifications.
More important than the number of neurons in the simulated network is the fact that during the simulation each synapse between excitatory neurons was supplied with 24 bytes of memory. This enabled an accurate mathematical description of the network.
In total, the simulator coordinated the use of about 1 petabyte of main memory, which corresponds to the aggregated memory of 250,000 PCs.
NEST is a widely used, general-purpose neuronal network simulation software available to the community as open source.
The team ensured that their optimizations were of general character, independent of a particular hardware or neuroscientific problem. This will enable neuroscientists to use the software to investigate neuronal systems using normal laptops, computer clusters or, for the largest systems, supercomputers, and easily exchange their model descriptions.

A large, international project

Work on optimizing NEST for the K Computer started in 2009 while the supercomputer was still under construction. Shin Ishii, leader of the brain science projects on K at the time, explains that "Having access to the established supercomputers at Jülich, JUGENE and JUQUEEN, was essential, to prepare for K and cross-check results."

Mitsuhisa Sato, of the RIKEN Advanced Institute for Computer Science, points out that "Many researchers at many different Japanese and European institutions have been involved in this project, but the dedication of Jun Igarashi now at the Okinawa Institute of Technology, Gen Masumoto now at the RIKEN Advanced Center for Computing and Communication, Susanne Kunkel and Moritz Helias now at Forschungszentrum Jülich was key to the success of the endeavor."

Paving the way for future projects

Kenji Doya of OIST, currently leading a project aiming to understand the neural control of movement and the mechanism of Parkinson's disease, says "The new result paves the way for combined simulations of the brain and the musculoskeletal system using the K Computer. These results demonstrate that neuroscience can make full use of the existing peta-scale supercomputers."

The achievement on K provides new technology for brain research in Japan and is encouraging news for the Human Brain Project (HBP) of the European Union, scheduled to start this October. The central supercomputer for this project will be based at Forschungszentrum Jülich.

The researchers in Japan and Germany are planning on continuing their successful collaboration in the upcoming era of exa-scale systems.

http://www.eurekalert.org/pub_releases/2013-08/acoe-hts080213.php

How to stop bleeding in the ER caused by warfarin

Prothrombin complex concentrates are faster and more effective than fresh frozen plasma at reversing hemorrhage caused by the anti-coagulant warfarin

WASHINGTON - Prothrombin complex concentrates (PCCs) are faster and more effective than fresh frozen plasma at reversing hemorrhage caused by the anti-coagulant warfarin, despite plasma being the most commonly used therapy. A literature review published last month in Annals of Emergency Medicine suggests that physicians in the United States should join those around the world in following recommendations of multiple specialty organizations to use PCCs as the first line of defense in this common and life-threatening emergency ("Rapid Reversal of Warfarin-Associated Hemorrhage in the Emergency Department by Prothrombin Complex Concentrates").

"The typical remedies for hemorrhage caused by warfarin are slow and unpredictable," said author Kenneth Frumkin, PhD, MD of the Naval Medical Center in Portsmouth, Va. "By contrast, prothrombin complex concentrates reverse warfarin anticoagulation in minutes rather than hours. Its relative underuse in the U.S. compared to other countries seems to derive from lack of familiarity and infrequent availability."

PCCs (products made from pooled human plasma) were initially developed to treat hemophilia. They can be infused rapidly and generally reverse anticoagulation three to five times faster than fresh frozen plasma, which must be thawed. Recombinant Activated Factor VII (Factor rVIIa), while approved in the United States only for surgery or bleeding in hemophiliacs, has been used to reverse warfarin-associated bleeding. Factor rVIIa works faster than fresh frozen plasma, but carries more risk and costs much more.

"The April 2013 approval by the Food and Drug Administration of a form of PCC specifically intended for warfarin reversal should expand the use of these life-saving products," said Dr. Frumkin.

The views expressed by Dr. Frumkin are his own, and do not necessarily reflect the official policy or position of the Department of the Navy, Department of Defense, or the United States Government.

http://www.eurekalert.org/pub_releases/2013-08/wifb-nct080213.php

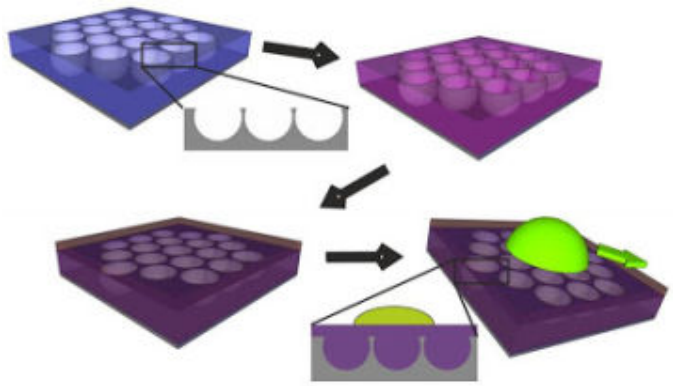
New coating turns ordinary glass into super glass

Resilient, ultraslippery glass could lead to self-cleaning, scratch-resistant windows, lenses, and solar panels

A new transparent, bioinspired coating makes ordinary glass tough, self-cleaning and incredibly slippery, a team from the Wyss Institute for Biologically Inspired Engineering at Harvard University and Harvard School of Engineering and Applied Sciences (SEAS) reported online in the July 31 edition of Nature Communications. The new coating could be used to create durable, scratch-resistant lenses for eyeglasses, self-cleaning windows, improved solar panels and new medical diagnostic devices, said principal investigator Joanna Aizenberg, Ph.D., who is a Core Faculty Member at the Wyss Institute, Amy Smith Berylson Professor of Materials Science at SEAS, and a Professor of Chemistry and Chemical Biology.

The new coating builds on an award-winning technology that Aizenberg and her team pioneered called Slippery Liquid-Infused Porous Surfaces (SLIPS) -- the slipperiest synthetic surface known. The new coating is equally

slippery, but much more durable and fully transparent. Together these advances solve longstanding challenges in creating commercially useful materials that repel almost everything.
SLIPS was inspired by the slick strategy of the carnivorous pitcher plant, which lures insects onto the ultraslippery surface of its leaves, where they slide to their doom. Unlike earlier water-repelling materials, SLIPS repels oil and sticky liquids like honey, and it resists ice formation and bacterial biofilms as well.
While SLIPS was an important advance, it was also "a proof of principle" – the first step toward a commercially valuable technology, said lead author Nicolas Vogel, Ph.D., a postdoctoral fellow in applied physics at Harvard SEAS.
"SLIPS repels both oily and aqueous liquids but it's expensive to make and not transparent," Vogel said. The original SLIPS materials also need to be fastened somehow to existing surfaces, which is often not easy. "It would be easier to take the existing surface and treat it in a certain way to make it slippery," Vogel explained.



Researchers create the ultraslippery coating by creating a glass honeycomb-like structure with craters (top), coating it with a Teflon-like chemical (purple) that binds to the honeycomb cells to form a stable liquid film. That film repels droplets of both water and oily liquids (bottom). Because it's a liquid, it flows, which helps the coating repair itself when damaged. **Nicolas Vogel, Wyss Institute.**

Vogel, Aizenberg, and their colleagues sought to develop a coating that accomplishes this and works as SLIPS does. SLIPS's thin layer of liquid lubricant allows liquids to flow easily over the surface, much as a thin layer of water in an ice rink helps an ice skater glide.
To create a SLIPS-like coating, the researchers corral a collection of tiny spherical particles of polystyrene, the main ingredient of Styrofoam, on a flat glass surface like a collection of Ping-Pong balls. They pour liquid glass on them until the balls are more than half buried in glass. After the glass solidifies, they burn away the beads, leaving a network of craters that resembles a honeycomb. They then coat that honeycomb with the same liquid lubricant used in SLIPS to create a tough but slippery coating.
"The honeycomb structure is what confers the mechanical stability to the new coating," said Aizenberg.
By adjusting the width of the honeycomb cells to make them much smaller in diameter than the wavelength of visible light, the researchers kept the coating from reflecting light. This made a glass slide with the coating completely transparent.
These coated glass slides repelled a variety of liquids, just as SLIPS does, including water, octane, wine, olive oil and ketchup. And, like SLIPS, the coating reduced the adhesion of ice to a glass slide by 99 percent. Keeping materials frost-free is important because adhered ice can take down power lines, decrease the energy efficiency of cooling systems, delay airplanes and lead buildings to collapse.
Importantly, the honeycomb structure of the SLIPS coating on the glass slides confers unmatched mechanical robustness. It withstood damage and remained slippery after various treatments that can scratch and compromise ordinary glass surfaces and other popular liquid-repellent materials, including touching, peeling off a piece of tape, wiping with a tissue.
"We set ourselves a challenging goal: to design a versatile coating that's as good as SLIPS but much easier to apply, transparent, and much tougher -- and that is what we managed," Aizenberg said.
The team is now honing its method to better coat curved pieces of glass as well as clear plastics such as Plexiglas, and to adapt the method for the rigors of manufacturing.
"Joanna's new SLIPS coating reveals the power of following Nature's lead in developing new technologies," said Don Ingber, M.D., Ph.D., the Wyss Institute's Founding Director. "We are excited about the range of applications that could use this innovative coating." Ingber is also the Judah Folkman Professor of Vascular Biology at Harvard Medical School and Boston Children's Hospital, and Professor of Bioengineering at Harvard SEAS.
This work was funded by the Advanced Research Projects Agency-Energy (ARPA-E), the Air Force Office of Scientific Research, and the Wyss Institute. Nicolas Vogel received funding from the Leopoldina Fellowship program. In addition to Vogel and Aizenberg, the research team included: Rebecca A. Belisle, a former Wyss research assistant who is now a graduate student in Materials Science and Engineering at Stanford University; Benjamin Hatton, Ph.D., formerly a Technology Development fellow at the the Wyss Institute and a research appointee at SEAS who is now an assistant professor of materials science and engineering at the University of Toronto; and Tak-Sing Wong, Ph.D., a former postdoctoral research fellow at the Wyss Institute who is now an Assistant Professor of Mechanical and Nuclear Engineering at Penn State University.

http://www.sciencedaily.com/releases/2013/08/130802094852.htm

Necrostatin-1 Counteracts Aluminum's Neurotoxic Effects

Investigators have linked aluminum accumulation in the brain as a possible contributing factor to neurodegenerative disorders such as Alzheimer's disease.

A new study published in Restorative Neurology and Neuroscience sheds light on the mechanism underlying aluminum-induced neuronal cell death and identifies necrostatin-1 as a substance which counteracts several of aluminum's neurotoxic effects.

Researchers have long focused on why neurons die in degenerative diseases. One process is apoptosis, a form of gene-directed programmed cell death which removes unnecessary, aged, or damaged cells. When neurons die as a result of stroke, trauma, or other insult, the process is known as necrosis. Recently, a new type of necrosis, necroptosis (programmed necrosis), has been implicated in the cell demise process. In this report, the results of several experiments support the hypothesis that aluminum-induced neuronal cell death is, to a large extent, due to necroptosis, says lead investigator Qinli Zhang, PhD, of the Department of Occupational Health, Ministry of Education Key Laboratory, School of Public Health of Shanxi Medical University in Taiyuan China.

For instance, when aluminum was added to mouse cortical neurons grown in cell culture, the cells began to die. By adding inhibitors of apoptosis (zVAD-fmk), of autophagy (3-methyladenin, 3-MA), or of necroptosis (necrostatin-1, Nec-1), investigators showed that all treatments enhanced cell viability although Nec-1 demonstrated the strongest protection. Using fluorescent microscopy, in which surviving neural cells stain green, apoptotic cells stain orange, and necrotic cells stain red, the investigators demonstrated Al-induced cell death as well as dose-dependent reduction of necroptosis with Nec-1.

When aluminum was injected into the cerebral ventricles of living mice, brain tissue analysis revealed shrunken and abnormal-looking neurons. When Nec-1 was injected simultaneously with aluminum into the ventricles, more surviving neurons could be seen, especially when higher doses of Nec-1 were used. When the investigators measured cell death-related proteins in the brain, a marker protein of necroptosis known as RIP1 showed the most changes, compared to marker proteins of apoptosis or autophagy. Similar findings were found for Alzheimer-related proteins: aluminum exposure increased the expression of mGluR2, mGluR5, Aβ, and Tau levels while Nec-1 treatment resulted in dose-dependent reductions of these protein levels.

Noting that "progressive cell loss in specific neuronal populations associated with typical learning and memory dysfunction is a pathological hallmark of neurodegenerative disorders, especially in AD," principal investigator Qiao Niu, MD, PhD, Director, Department of Occupational Health and Director, Institute of Preventive Medicine, Shanxi Medical University, and the team evaluated learning and memory in mice using the Morris Water Maze test. Al-treated mice performed poorly on the test and performance significantly improved if the mice were treated with Nec-1. Interestingly, if Nec-1 treatment was delayed for 2, 4, or 8 hours after the aluminum was introduced, Nec-1 had a protective effect less than simultaneous administration. Impaired cognitive performance was also correlated with reduced mGluR2 and mGluR5 protein in the cortex. "Nec-1, in addition to its use as a therapeutic agent for cell death, might therefore be of use in slowing the progression of the cognitive deficits associated with neuronal degeneration," says Dr. Niu.

The study demonstrates that Nec-1 may be useful for future prevention of and therapy for neurodegenerative disorders.

Zhang Qinli, Li Meiqing, Jiao Xia, Xu Li, Guo Weili, Ji Xiuliang, Ji Junwei, Yang Hailan, Zhang Ce and Niu Qiao. Necrostatin-1 inhibits the degeneration of neural cells induced by aluminum exposure. Restorative Neurology and Neuroscience, 2013; DOI: 10.3233/RNN-120304

http://www.sciencedaily.com/releases/2013/08/130802151835.htm

Japanese Vehicle Delivers New Hardware for NASA's Robotic Refueling Mission

It may be called the Robotic Refueling Mission (RRM), but NASA's RRM was built to demonstrate much more than the clever ways space robots can fill up satellites.

With the launch of new hardware to the International Space Station on Aug. 3, RRM -- recently named a "Top Exploration Technology Application From the International Space Station in 2012" -- will be outfitted to practice a new set of satellite-servicing activities.

New Hardware for a New Era of Satellite-Servicing Demonstrations

Earlier in 2013, RRM demonstrated remotely controlled robots using today's technology could refuel satellites not designed to be serviced. RRM tests from January 14 to 25 culminated in a first-of-its-kind robotic fluid transfer.

Following the success of completing this namesake task, in 2014 RRM will demonstrate how space robots can replenish cryogen (a type of refrigerant) in the instruments of legacy satellites -- existing, orbiting spacecraft not originally designed to be serviced.

"Just like robotic refueling, there were a lot of folks who said that this simply couldn't be done," says Benjamin Reed, deputy project manager of the Satellite Servicing Capabilities Office (SSCO) at NASA's Goddard Space Flight Center in Greenbelt, Md.
"But that's the whole point of the RRM demonstrations -- and the beauty of being able to execute them on such an extraordinary test bed as the space station. RRM is allowing us to show that the robotic satellite-servicing tools, technologies and techniques are mature and ready, because we've proven them on orbit."

Delivery to Space Station and Installation

New hardware deliveries to the space station will outfit the RRM module for this upcoming set of operations. The Japanese HTV cargo vehicle, currently scheduled to launch on Aug. 3, will deliver a new task board and the RRM On-orbit Transfer Cage (ROTC), an original device designed to transfer hardware outside of the space station.
Astronauts will mount the ROTC on the sliding table within the Japanese airlock and then install the task board onto the ROTC, giving the Canadian Dextre robot an easy platform from which to retrieve and subsequently install the new hardware.
A second shipment in 2014 will bring a second task board and a new device called the Visual Inspection Poseable Invertebrate Robot (VIPIR). This SSCO-built borescope inspection tool provides a set of eyes for internal satellite repair jobs. Both also will be transferred and installed on RRM via the Japanese airlock, ROTC and Dextre.
With the help of the twin-armed Dextre robot, the newly installed RRM task boards, and the RRM tools, the RRM team will then work its way through intermediate steps leading up to cryogen replenishment.
After retrofitting valves with new hardware, peering into dark places with the aid of VIPIR and creating a pressure-tight seal, the RRM and Dextre duo will stop short of actual cryogen transfer for this round of tasks. RRM Phase 2 operations are scheduled to begin in 2014.
Initial activities to demonstrate this in-orbit capability -- cutting wires and removing caps -- were completed in 2012 with the aid of the original RRM tools and activity boards.

Expanding Capabilities and Fleet Flexibility in Space

Cryogenic fluids are used on the ground and in space to make very sensitive cameras work better. However, in time this extremely cold substance leaks out, and the camera no longer performs well. Robotically replenishing these reserves, explains Reed, would allow spacecraft instruments to last past their expiration date and ultimately permit satellites to perform longer.
"It's all about expanding options for fleet operators, in both the government and the commercial sectors," Reed said. "Instead of retiring an aging observatory or spacecraft -- and perhaps launching a new, costly, one -- [operators] could choose to extend their lives by calling on a future cryogen-toting space tow truck. The RRM demonstrations are an important step to eventually enabling this capability."

Preparing for a Servicing-Enabled Future

"Since its launch to the ISS in 2011 on the last shuttle mission, RRM has been steadily practicing robotic satellite-servicing activities on orbit," says Jill McGuire, RRM project manager at SSCO. "A joint effort with the Canadian Space Agency, RRM uses the space station as a test bed for technology research and development."
On July 17, RRM was named a "Top Exploration Technology Application from the International Space Station in 2012" at the second international ISS Research and Development Conference in Denver. McGuire accepted on behalf of the team.
NASA developed RRM to demonstrate how remotely-operated robot mechanics could extend the lives of the hundreds of satellites residing in geosynchronous-Earth orbit (GEO).
Costly assets traveling about 22,000 miles above Earth, GEO spacecraft deliver such essential services as weather reports, cell phone communications, television broadcasts, government communications and air traffic management.
Servicing capabilities could greatly expand the options for government and commercial fleet operators in the future. They could potentially deliver satellite owners significant savings in spacecraft replacement and launch costs.
NASA continues to test capabilities for a new robotic servicing frontier. In conjunction with RRM, the SSCO team has been studying a conceptual servicing mission while building the necessary technologies, including an autonomous rendezvous and capture system, a propellant transfer system and specialized algorithms to orchestrate and synchronize satellite-servicing operations.

http://www.bbc.co.uk/news/health-23408949

Biting back: Taking the sting out of spider venom

Brown recluse spiders bite more than 7,000 people in Brazil every year causing serious skin lesions and even death. The anti-venom used as treatment comes at the expense of many animal lives. But could a breakthrough in synthetic spider venom lead to a more humane solution?

By Ben Tavener São Paulo, Brazil

"The first time I was bitten, I nearly died," says Adelaide Fabienski Maia, a school assistant from Curitiba. "I put my shorts on in the morning and felt a bite but didn't realise what it was. It wasn't until the evening that my face started burning up. I looked at the bite area and it was red."

Adelaide was soon rushed to hospital with the classic target-shaped lesion caused by the venom eating away at her skin. It was only thanks to a dose of anti-venom that she's still around to tell the tale. But the anti-venom currently available comes with its own risks - mostly to the animals involved in the production process.

Venom is milked from thousands of brown spiders before being injected into horses. This triggers an immune response that creates life-saving anti-venom for humans - while drastically reducing the horses' own lifespan.

Now scientists in Brazil have come up with a synthetic venom alternative that could save many of those lives.

Not so incy-wincy

The Loxosceles family of venomous brown and recluse spiders is found in North and South America, Africa, Australia and some parts of Europe. At 6-20mm long, they are by no means the world's biggest spiders. Even their bite is almost painless. But their venom can cause large sores and lesions through dermo-necrosis - literally "death of the skin". It is the only family of spiders in the world to cause the skin to die in this way. Scientists have linked it to a rare enzyme in the venom called sphingomyelinase D, which damages and kills skin tissue.

In a small percentage of cases where anti-venom is not administered quickly enough, people can die through organ failure. But many more deaths - of spiders and horses - are caused through the anti-venom production itself. "We milk the spiders once a month for three to four months," says Dr Samuel Guizze, a biologist at the Butantan Institute, Sao Paulo's pioneering centre for anti-venom production.

It involves one technician gingerly picking up a spider and giving it an electric shock while a second scientist rushes to draw the venom into a syringe. As only a tiny squirt of venom is surrendered each time, it means that tens of thousands of individuals must be bred for milking.

"The amount of venom obtained per spider is very small," says Dr Guizze. "We then inject the venom into horses and after 40 days the horses are bled and the antibodies [anti-venom] separated from the blood."

Unsurprisingly, being injected with brown spider venom has an effect on the horses' health over time. Their lifespan is reduced from around 20 years to just three or four.

Sadly, the spiders fare even worse - dying after just three or four venom extractions.

Alternatives to animals

Six hundred miles away at the Federal University of Minas Gerais, a breakthrough in venom technology promises to greatly reduce the anti-venom industry's reliance on animals.

Dr Carlos Chavez-Olortegui is a senior biologist and spider venom specialist. "We identified the parts of the venom responsible for creating antibodies, and we made a protein chain containing only these parts," he told the BBC.

By making a man-made copy of the active venom ingredient, it means that real spiders could soon be

World's Most Dangerous Spiders

Brazilian wandering spider (Phoneutria fera) - (pictured) According to the Guinness Book of Records it has the most active neurotoxic venom in the world. Just 0.006mg is enough to kill a mouse. If you're lucky enough to survive then a bite can cause extreme pain for days, including a painful erection which can lead to impotence.

Brown recluse spider (Loxosceles spp.) - Found on all continents except Antarctica, this spider bites causes necrotic wounds (see main article).

Southern black widow spider (Latrodectus mactans) - The spider that kills most people each year in the US, it has venom 14-15 times more powerful than that of a rattlesnake.

Sydney funnel web spider (Atrax robustus) - They have one of the most toxic venoms to humans of any spider, but there have thankfully been no known deaths since the introduction of anti-venom. They are aggressive when threatened. They also have a habit of falling into swimming g pools where they can survive for many hours.

Red back spider (Latrodectus hasseltii) Red backs are one of the most recognisable species in Australia. It is the female that is most likely to bite. Children and the elderly are most at risk of succumbing to the venom and should seek immediate medical attention.

completely superfluous to the process. And, although horses will still be needed for the foreseeable future, the synthetic venom is non-toxic. This means that horses will still make the right anti-venom in their blood but without experiencing the poisoning effects of being injected with real venom.
Dr Chavez-Olortegui says this new technique will enable horses to be retired after a few years and go on to live a full life Indeed in the future, he hopes animals can be removed from the process altogether.

A vaccine for the future?

But the study has also shown tantalising possibilities for creating a vaccine. Trials have shown that animals injected with synthetic spider venom start to produce antibodies that protect them from the effects of real brown spider bites.
Chavez-Olortegui hopes that these results could eventually pave the way for a human vaccine. "More tests are required to see if the level of immunisation is maintained long-term, but we believe we are on the right path to making a human vaccine soon," says Chavez-Ororteguí.
The potential vaccine is seen as a major breakthrough for science but could have only limited applications in the real world - as the cost of developing the vaccine is weighed against the chance of being bitten.
But in a country where 26,000 spider bites were reported in 2012 alone - 7,000 of which involved brown spiders - there could well prove to be quite a demand. Adelaide Fabienski Maia, who has the dubious honour of living in the "brown spider capital" of Brazil, has since been bitten a second time. Although they're not naturally aggressive, brown spiders have a nasty habit of sleeping inside people's clothes. Unsurprisingly, Adelaide doesn't fancy taking any more chances. "If there were a vaccine, I'd take the whole family today."

http://ars.to/15Dp2HP

University of California to allow open access to new academic papers

On November 1, faculty will be automatically enrolled in the UC's open access policy.

by Megan Geuss - Aug 4 2013, 5:45am TST

The University of California—an enormous institution that encompasses 10 campuses and over 8,000 faculty members—introduced an Open Access Policy late last week. This policy grants the UC a license to its faculty's work by default, and requires them to provide the UC with copy of their peer-reviewed papers on the paper's publication date. The UC then posts the paper online to eScholarship, its open access publishing site, where the paper will be available to anyone, free of charge.
Making the open access license automatic for its faculty leverages the power of the institution—which publishes over 40,000 scholarly papers a year—against the power of publishers who would otherwise lock content behind a paywall. “It is much harder for individuals to negotiate these rights on an individual basis than to assert them collectively,” writes the UC. “By making a blanket policy, individual faculty benefit from membership in the policy-making group, without suffering negative consequences. Faculty retain both the individual right to determine the fate of their work, and the benefit of making a collective commitment to open access.”
Faculty members will be allowed to opt out of the scheme if necessary—if they have a prior contract with a journal, for example. Academic papers published in traditional journals before the enactment of this policy will not be made available on eScholarship at this time.
“As faculty members, we are asserting our control over the publication of scholarly research and recognize the responsibility for making that process sustainable and true to the intentions of scholars,” explained the UC on a FAQ page. “The faculty are also sending a strong collective message to publishers about the values and the system we would like in the future.”
The move comes at a time when the US federal government is heavily promoting open access. In February 2013, the White House announced that all science papers produced through federal funding would be made available to the public one year after their publication, and the Obama Administration is working to extend that policy to cover the information published by all federal agencies. Many other institutions have adopted open access policies, including 177 other universities and the World Bank.
As Chris Kelty, associate professor at the Department of Information Studies at UCLA, explained in a series of videos on the UC's eScholarship site: ”Everybody benefits from this really, the faculty benefit from this because their work's more widely available, it might come in for higher citations. The University benefits because the profile of the University is higher and it might send a message to Sacramento about our commitment to research. And the public benefits—whether you're a K-12 teacher, or someone in an emergency room looking for an article, or someone in business trying to get a patent, everyone in the public benefits from wider availability of our research.” In addition, Kelty explained, publishers “are quite reconciled to this” after seeing 177 other universities take a similar path.

http://www.bbc.co.uk/news/world-asia-23565121

Kirobo is world's first talking robot sent into space

Japan has launched the world's first talking robot into space to serve as companion to astronaut Kochi Wakata who will begin his mission in November.

The android took off from the island of Tanegashima in an unmanned rocket also carrying supplies for crew onboard the International Space Station (ISS).
Measuring 34cm (13 inches), Kirobo is due to arrive at the ISS on 9 August.
It is part of a study to see how machines can lend emotional support to people isolated over long periods.
The launch of the H-2B rocket was broadcast online by the Japan Aerospace Exploration Agency (Jaxa).
The unmanned rocket is also carrying drinking water, food, clothing and work supplies to the six permanent crew members based at the ISS.

Tomotaka Takahashi with his creation

'Giant leap'

Kirobo's name derives from the Japanese words for "hope" and "robot". The small android weighs about 1kg (2.2 pounds) and has a wide range of physical motion. Its design was inspired by the legendary animation character Astro Boy. Kirobo has been programmed to communicate in Japanese and keep records of its conversations with Mr Wakata who will take over as commander of the ISS later this year.
In addition, it is expected to relay messages from the control room to the astronaut.
"Kirobo will remember Mr Wakata's face so it can recognise him when they reunite up in space," the robot's developer, Tomotaka Takahashi said. "I wish for this robot to function as a mediator between a person and machine, or a person and the Internet, and sometimes even between people."
The biggest challenge was to make the android compatible with space, Mr Takahashi added.
Dozens of tests were carried out over nine months to ensure Kirobo's reliability.
Kirobo has a twin robot on Earth called Mirata, which will monitor any problems its electronic counterpart may experience in space. "It's one small step for me, a giant leap for robots," Mirata said of the mission last month.
The endeavour is a joint project between Mr Takahashi, car producer Toyota and advertising company Dentsu.

http://www.scientificamerican.com/podcast/episode.cfm?id=portion-size-label-influences-inges-13-08-03

Portion-Size Label Influences Ingestion Intake

People ate less of a portion of food if it was labeled "double-sized" rather than "regular." Karen Hopkin reports.

Download MP3

The mayor of New York famously tried to ban super-sized sodas. But instead of legislating a drink's volume, maybe we should change its name. Because a new study shows that the words we use to describe portion size affect how much we actually consume. The findings are in the journal Health Economics. [David R. Just And Brian Wansink, One Man's Tall Is Another Man's Small: How The Framing Of Portion Size Influences Food Choice]
As portion sizes at many restaurants grow larger, so do our waistlines. Of course, no one says we have to finish that three-quarter pound burger or chug an entire Big Gulp. But what determines when we lay down the fork and push away from the table?
To find out, researchers led by Brian Wansink of the Cornell Food and Brand Lab served up some spaghetti. Some volunteers received a portion labeled "regular," others got a dish described as "double size." Although both plates contained the same amount of pasta, people ate more when they thought their serving size was normal. Participants who thought they'd gotten the piggy-sized portion left 10 times more food on their plates. So if a big beverage were called, say, Double the Size of your Stomach, maybe we'd think twice about draining every last drop.