http://www.eurekalert.org/pub_releases/2014-12/uoc--mca120414.php

Major complications after abortion are extremely rare, study shows

UCSF research is the first to use complete data on post-abortion care

In the most comprehensive look yet at the safety of abortion, researchers at UC San Francisco have concluded that major complications are rare, occurring less than a quarter of a percent of the time, about the same frequency as colonoscopies.

The study, published online on Monday, Dec. 8, 2014, in Obstetrics & Gynecology, analyzed data from more than 50,000 women enrolled in the Medi-Cal fee-for-service program who obtained abortions from 2009 to 2010, and looked for complications that occurred within six weeks of the procedure.

The rate is similar to what has been found in previous studies, but this is the first study in which researchers have based their conclusions on complete data on all of the health care used by women who have received abortions. Since some women must often travel long distances to find abortion providers, they tend to receive follow-up care at facilities closer to where they live. For many women, this means their local emergency department. But, up until now, no study has systematically examined emergency department use for post-abortion care.

The researchers said they expect the study will contribute to the national debate over abortion safety. Many state legislatures have recently passed laws that have the effect of reducing access to abortion by requiring providers to have transfer agreements or admitting privileges with hospitals or to construct their clinics so that they meet the requirements of an ambulatory surgical center. But the researchers said that these restrictions were likely to make women travel further to get abortions or induce them on their own using unsafe methods, both of which may increase the risks for women.

"Our study had very complete follow-up data on all of the women in it, and we still found a very low complication rate," said Ushma Upadhyay, PhD, MPH, an assistant professor at Advancing New Standards in Reproductive Health (ANSIRH), a program of the Department of Obstetrics, Gynecology and Reproductive Sciences at UCSF. "Abortion is very safe as currently performed, which calls into question the need for additional regulations that purportedly aim to improve safety."

California is one of 17 states that cover abortion and follow-up care for women enrolled in Medicaid, the state-federal health insurance program for the poor. Billing data from the Medi-Cal fee-for-service program gave researchers a complete picture of all the health care that women received in the six weeks following their abortion procedures.

California has more than 500 abortion providers, most of them practicing in an outpatient setting, and 97 percent of the abortions studied were performed in an outpatient clinic or a doctor's office. Only 3 percent were performed in hospitals.

Of the 54,911 abortions studied, just 126 cases involved major complications, which the researchers defined as conditions that required hospital admission, surgery or a blood transfusion. In all, a little less than two percent of the abortions, or 1,030 cases, resulted in minor complications in the six weeks following the procedure.

Women in their 30's were somewhat more likely than those in their early 20's to experience complications. Medication abortions also had a higher rate of complications compared to aspiration or surgical abortion. This was mostly due to needing an aspiration after a medication abortion, a well known, but not serious, risk of the method.

Researchers said the complication rate may be somewhat overstated in comparison to the total group of women seeking abortions around the country, since the women in the study were all low income. A wealthier population with private insurance may be healthier and less inclined to have abortion-related complications.

Other authors of the study include Tracy A. Weitz, PhD, MPA, and Patricia Anderson, MPH, of ANSIRH; Sheila Desai, MPH, who did the research while at ANSIRH; Diana Taylor PhD, RNP, an emeritus professor in the UCSF School of Nursing; Daniel Grossman, MD, of the UCSF Department of Obstetrics, Gynecology and Reproductive Sciences and Ibis Reproductive Health; and Vera Zlidar, MHS, who did the research while at John Snow, Inc.

http://www.eurekalert.org/pub_releases/2014-12/tl-tlc120514.php

The Lancet: Combining insecticide spraying and bed nets no more protective against malaria than nets alone

The combined use of spraying insecticide inside homes and insecticide-treated bed nets is no better at protecting children against malaria than using bed nets alone, a study in The Gambia suggests.

The findings, published in The Lancet, should encourage donors to invest their limited resources in additional bed nets, the more cost-effective solution to tackling malaria*.

Lead author Professor Steve Lindsay, a disease ecologist at Durham University in the UK explains, "Our findings do not support any universal recommendation for indoor residual spraying as an addition to long-lasting insecticidal nets (LLINs) across sub-Saharan Africa. High bed net use is sufficient to protect people against malaria in areas that have low or moderate levels of malaria like The Gambia."**

In 2012, there were an estimated 207 million cases of malaria and 627 000 deaths worldwide, mostly among African children. Low-cost solutions to prevent the

disease include LLINs or indoor residual spraying, which involves spraying insecticide on walls and roofs where mosquitoes are likely to land. Both have been shown to reduce the number of deaths due to malaria. But, until now, there has been little evidence to address whether combining these interventions would give better results.

This cluster-randomised trial involved almost 8000 children aged 6 months to 14 years in 70 clusters of villages in the Upper River region of The Gambia. Village clusters were randomly assigned to receive either LLINs alone or LLINs plus indoor spraying with dichlorodiphenyltrichloroethane (DDT). Cases of clinical malaria were measured in a group of children in each cluster in 2010 and 2011 using passive case detection (identifying cases that present at reporting health facilities) and annual surveys. Mosquito traps in houses were used to establish exposure to malaria-carrying mosquitoes and parasites. Coverage of indoor spraying (>80%) and LLINS (83-95%) were high in both years of the study.

The researchers found that clinical cases of malaria were similar in both groups. In year 1, incidence of clinical malaria was 0•047 per child-month at risk in the LLIN group and 0•044 in the spraying plus LLIN group. In year 2, incidence was 0•032 per child-month at risk in the LLIN group and 0•034 in the spraying plus LLIN group (see table 4, page 6 in the Article).

What is more, insecticide spraying did not reduce the number of malaria-carrying mosquitoes collected from the treated homes, suggesting that spraying has no additional effect in deterring or killing mosquitoes.

The researchers say that in order to get a proper measure of impact, further studies are needed to assess the effectiveness of combining LLINs with indoor spraying in areas with different levels of malaria transmission. They also recommend that where net coverage is low, the cost-effectiveness of additional control with indoor insecticide spraying should be considered.

Writing in a linked Comment, Jo Lines and Immo Kleinschmidt from the London School of Hygiene & Tropical Medicine in the UK discuss the mixed results of published trials. They caution, "All four experimental trials (including Pinder and colleagues' study in The Gambia) were designed to test the null hypothesis of no difference between the study groups, and because of this, those that did not find a significant difference should not be interpreted as proof of the absence of a benefit. The reason for this mixture of findings is not immediately clear, and a range of possible explanations related to differences in the trial settings and methods can be suggested, including vector species, insecticides used for indoor residual spraying, effective coverage (of each intervention), and insecticide resistance to one or other of the insecticides used... In view of the uncertainties that persist, it is advisable that all national malaria control programmes investing in the combined use of the two methods should include a rigorous component of monitoring and assessment."

This study was funded by UK Medical Research Council.

**Median financial costs per person per year (in 2009 US$) of $2.20 for bed nets and $6.70 for indoor residual spraying http://www.malariajournal.com/content/10/1/337*

http://www.eurekalert.org/pub_releases/2014-12/uoh-vcm120814.php

Vitamin C may help people who suffer from respiratory symptoms after exercise

Physical activity increases oxidative stress, and therefore, as an antioxidant vitamin C might have particularly evident effects on people who are participating in vigorous exercise.

In several studies, vitamin C administration attenuated the increases in oxidative stress markers caused by exercise. Furthermore, vitamin C is involved in the metabolism of histamine, prostaglandins, and cysteinyl leukotrienes, all of which appear to be mediators in the pathogenesis of exercise-induced bronchoconstriction.

A meta-analysis of three studies found that vitamin C halved post-exercise FEV1 decline in participants who suffered from exercise-induced bronchoconstriction. Five other studies examined subjects who were under short-term, heavy physical stress and a meta-analysis revealed that vitamin C halved the incidence of respiratory symptoms. Another trial reported that vitamin C halved the duration of the respiratory symptoms in male adolescent competitive swimmers.

FEV1 is the standard pulmonary function outcome for assessing whether a person suffers from exercise-induced bronchoconstriction. However, exercise-induced decline in FEF25-75 is twice as great as the decline in FEV1. FEV1 measures the large-airway obstruction, whereas FEF25-75 measures small-airway obstruction. Therefore, FEF25-75 or the closely related FEF50 might provide relevant additional information about the possible effects of vitamin C.

Harri Hemila, MD, PhD, of the University of Helsinki, Finland, carried out a secondary analysis of a study which had 12 participants. The participants had asthma, were on average 26 years, and suffered from exercise-induced bronchoconstriction. The FEV1 and FEF60 levels before and after exercise were reported on vitamin C and placebo days, but the data was not thoroughly analyzed originally.

In five out of the 12 participants, exercise caused a decline greater than 60% in FEF60. Such a dramatic FEF60 decline indicates that the absolute post-exercise level of FEF60 becomes an important outcome in its own right, in addition to its change from the pre-exercise level. Vitamin C administration increased the post-exercise FEF60 level in these 5 participants by between 50% and 150%. In

contrast, no mean difference between the vitamin C and placebo days was detected in the other 7 participants. The increase in post-exercise FEF60 level by vitamin C is a novel finding, which indicates that vitamin C may have substantial effects on the small airways, Dr. Hemilä states.

Dr. Hemila concludes that "given the safety and low cost of vitamin C, and the consistency of positive findings in the nine randomized trials on vitamin C against exercise-induced bronchoconstriction and respiratory symptoms, it seems reasonable for physically active people to test whether vitamin C is beneficial on an individual basis, if they have documented exercise-induced bronchoconstriction or suffer from respiratory symptoms such as cough or sore throat after taking vigorous exercise."

http://www.eurekalert.org/pub_releases/2014-12/mu-rih120414.php

Researchers identify hormone that reduces calorie burning, contributes to obesity

Researchers from McMaster University have identified an important hormone that is elevated in obese people and contributes to obesity and diabetes by inhibiting brown fat activity.

Hamilton, ON - Brown adipose tissue, widely known as brown fat, is located around the collarbone and acts as the body's furnace to burn calories. It also keeps the body warm. Obese people have less of it, and its activity is decreased with age. Until now, researchers haven't understood why.

There are two types of serotonin. Most people are familiar with the first type in the brain or central nervous system which affects mood and appetite. But this makes up only five per cent of the body's serotonin.

The lesser-known peripheral serotonin circulates in the blood and makes up the other 95 per cent of the body's serotonin. McMaster researchers have discovered that this kind of serotonin reduces brown fat activity or "dials down" the body's metabolic furnace.

The study, published today in Nature Medicine, is the first to show that blocking the production of peripheral serotonin makes the brown fat more active.

"Our results are quite striking and indicate that inhibiting the production of this hormone may be very effective for reversing obesity and related metabolic diseases including diabetes," said Gregory Steinberg, the paper's co-author and professor of medicine at the Michael G. DeGroote School of Medicine. He is also co-director of MAC-Obesity, the Metabolism and Childhood Obesity Research Program at McMaster.

"Too much of this serotonin acts like the parking brake on your brown fat," he explained. "You can step on the gas of the brown fat, but it doesn't go anywhere."

The culprit responsible for elevated levels of peripheral serotonin may also have been found.

"There is an environmental cue that could be causing higher serotonin levels in our body and that is the high-fat western diet," said Waliul Khan, co- author, associate professor of pathology and molecular medicine for the medical school and a principal investigator at Farncombe Family Digestive Research Institute. "Too much serotonin is not good. We need a balance. If there is too much, it leads to diabetes, fatty liver and obesity."

The majority of serotonin in the body is produced by tryptophan hydroxylase (Tph1). The McMaster team found that when they genetically removed or inhibited this enzyme that makes serotonin that mice fed a high-fat diet were protected from obesity, fatty liver disease and pre-diabetes due to an enhanced ability of the brown fat to burn more calories.

Notably, inhibiting the peripheral serotonin doesn't affect the serotonin in the brain or central nervous system functioning, said Steinberg.

This is in contrast to earlier weight loss drugs which worked to suppress appetite by affecting levels of brain serotonin, but were associated with problems including cardiac complications and increased risk of depression and suicide.

"Moving forward, we think it's a much safer method to work with increasing energy expenditure instead of decreasing the appetite, which involves more risks," said Steinberg.

The researchers conclude that reducing the production of serotonin by inhibition of Tph1 "may be an effective treatment for obesity and its comorbidities," and so the team is now working on a pharmacological "enzyme blocker."

This study, conducted over five years, was supported by funding from the Canadian Diabetes Association, the Canadian Institutes of Health Research, Crohn's and Colitis Canada, MAC-Obesity and the Natural Sciences and Engineering Research Council of Canada.

http://www.eurekalert.org/pub_releases/2014-12/uoc--nth120514.php

New therapy holds promise for restoring vision

Hybrid chemical/genetic therapy restores light sensitivity to retina in blind mice & dogs

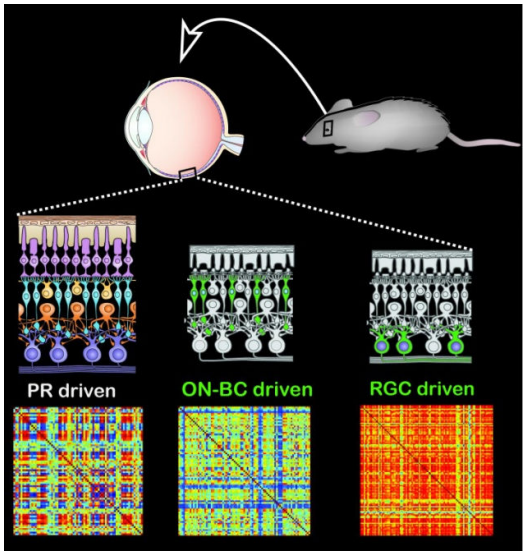
A new genetic therapy not only helped blind mice regain enough light sensitivity to distinguish flashing from non-flashing lights, but also restored light response to the retinas of dogs, setting the stage for future clinical trials of the therapy in humans.

The therapy employs a virus to insert a gene for a common ion channel into normally blind cells of the retina that survive after the light-responsive rod and cone photoreceptor cells die as a result of diseases such as retinitis pigmentosa. Photoswitches - chemicals that change shape when hit with light -are then

attached to the ion channels to make them open in response to light, activating the retinal cells and restoring light sensitivity.

Afflicting people of all ages, retinitis pigmentosa causes a gradual loss of vision, akin to losing pixels in a digital camera. Sight is lost from the periphery to the center, usually leaving people with the inability to navigate their surroundings. Some 100,000 Americans suffer from this group of inherited retinal diseases.

In a paper appearing online this week in the early edition of the journal Proceedings of the National Academy of Sciences, University of California, Berkeley, scientists who invented the photoswitch therapy and veterinary colleagues at the School of Veterinary Medicine of the University of Pennsylvania (UPenn) report that blind mice regained the ability to navigate a water maze as well as normal mice. The treatment worked equally well to restore light responses to the degenerated retinas of mice and dogs, indicating that it may be feasible to restore some light sensitivity in blind humans.



In normal mice with working photoreceptors (PR driven), stimulating the retina produces a variety of responses in retinal ganglion cells, the output of the eye. This can be seen in the colorful lower square, where measurements of the activity of different retinal ganglion cells are shown in response to the same stimulation. This is because the retinal circuit mediates different operations. Photoswitches inserted into retinal ganglion cells (RGC) of blind mice produce much less variety of response (all evenly red means the cells fire at the same time), while blind mice with photoswitches inserted into bipolar cells (ON-BC driven) exhibit much more variety in their retinal response to light, closer to that of normal mice. Future chemical/gene therapy should probably focus on bipolar cells in order to capture this retinal processing before signals are relayed to the brain. **Isacoff & Flannery/UC Berkeley and Beltran/PennVet**

"The dog has a retina very similar to ours, much more so than mice, so when you want to bring a visual therapy to the clinic, you want to first show that it works in a large animal model of the disease," said lead researcher Ehud Isacoff, professor of molecular and cell biology at UC Berkeley. "We've now showed that we can deliver the photoswitch and restore light response to the blind retina in the dog as well as in the mouse, and that the treatment has the same sensitivity and speed of response. We can reanimate the dog retina."

Advantages over other gene therapies

The therapy has several advantages over other sight restoration therapies now under investigation, says vision scientist John Flannery, UC Berkeley professor of vision science and of molecular and cell biology. It uses a virus already approved by the Food & Drug Administration for other genetic therapies in the eye; it delivers an ion channel gene similar to one normally found in humans, unlike others that employ genes from other species; and it can easily be reversed or adjusted by supplying new chemical photoswitches. Dogs with the retinal degeneration provide a key test of the new therapy.

"Our ability to test vision is very, very limited in mice because, even in the healthy state, they are not very visual animals, their behaviors are largely driven by their other senses," he says. "Dogs have a very sophisticated visual system, and are being used already for testing ophthalmic gene therapy."

The dogs were chosen because they have inherited a genetic disease caused by the same gene defect as some patients with human retinitis pigmentosa. Several of them at the PennVet colony were treated and are currently undergoing tests to determine what degree of light sensitivity they now have.

"Seeing that some of the UC Berkeley results with this pharmaco-optogenetic strategy that worked so nicely in mice could be reproduced by our group at PennVet in dogs with late stage retinal degeneration was really exciting," said William Beltran, an associate professor of ophthalmology at the UPenn School of Veterinary Medicine. "Use of such a clinically-relevant large animal model allows us to begin tackling the next challenges on the road to translating this novel therapeutic strategy to human patients."

Hybrid chemical-genetic therapy

Genetic diseases like retinitis pigmentosa destroy the photosensitive cells of the eye, the photoreceptors, but often leave intact the other cells in the retina: the bipolar cells that the photoreceptors normally talk to, and the ganglion cells that are the retina's output to the brain. Isacoff, Flannery and UC Berkeley colleagues have developed several optogenetic techniques for restoring light-sensitivity to surviving retinal cells other than the photoreceptors. These involve using the adeno-associated virus - a common and harmless vector or carrier for gene therapy - to successfully carry a modified gene into these cells. The virus inserts the therapeutic gene into the cell's DNA and uses its instructions to produce a receptor protein - a modified version of a common glutamate receptor ion channel- that they display on their surface.

The researchers then inject a chemical photoswitch into the eye, "basically, a glutamate dangling on a light-sensitive string," says Isacoff, "which anchors to the modified receptor and stuffs the glutamate into its docking site on the receptor when activated by light." The newest version of the photoswitch is fast enough to turn the activity of retinal neurons on and off at a rate that approaches video rate of 30 frames per second.

In mice, they can successfully insert the gene into almost every one of the million or so retinal ganglion cells. This, the researchers say, should restore useful vision. "So we have reasonable speed and a lot of pixels, now the question is: What can the treated animals see? So far we can say that the treated mice can distinguish between steady light and flashing light. Our next step is to figure out how good they are at telling images apart," says Isacoff, who holds the Class of 1933 Chair.

Which cells get gift of sight?

One key question the researchers wanted to answer is whether it is best to insert photoswitches into ganglion cells or bipolar cells. Viruses can be made to target one or the other. Because activity flowing from upstream bipolar cells to the retina's output ganglion cells undergoes a lot of processing in the retinal circuit, the researchers were hoping that this same processing would occur when bipolar cells were given a new function they never had before, light-sensitivity.

The answer seems to be yes.

"When we put the photoswitched channels into bipolar cells and record the output of the ganglion cells, we see complicated patterns that look a lot like the activity you get in a normal retina, compared to the on-off activity you get when you put the same photoswitch into a ganglion cell," Isacoff said.

"The dogs' behavior should show us if there is a functional difference between driving the system from the bipolar cells versus the ganglion cells," Flannery says.

He notes that the therapy works only for about a week after a single "charging" with the photoswitch, because the protein and attached chemical get recycled by the cell. While the modified receptors are replaced continually, since the new gene remains forever in the DNA, the chemical photoswitch - maleimide-azobenzene-glutamate, or MAG - must be resupplied by injection into the eyeball. Right now this means injection every week or so, with the future development of a slow release formulation less often.

"This is not necessarily a disadvantage," Isacoff said, "because the therapy can be stopped, and new photo-sensitive chemicals can be tried as they are improved."

The researchers continue to study the effects of treatment in both mice and dogs, improve the photoswitch, and develop ways of attaching the photoswitch to other receptors, including some that could amplify the signal and allow perception of fainter light, as occurs normally in rods and cones.

NIH funding keeps giving

The experiments, analysis and much of the design of the study were performed by first co-authors Benjamin Gaub, a graduate student, and Michael Berry, a technician, along with post-doctoral fellows Michael Keinzler and Andreas Reiner and technician Amy Holt, all from UC Berkeley and Natalia Dolgova and Sergei Nikonov in the labs of Gustavo Aguirre and William Beltran of UPenn.

The work was funded by a nine-year grant from the National Institutes of Health for the Nanomedicine Development Center for the Optical Control of Biological Function (PN2EY018241), as well a NIH grants RO1EY06855 and P30EY001583, and by a grant from the Foundation Fighting Blindness, USA.

"The NIH funding got us all the way from designing the chemical photoswitch to an experimental therapy in the dog," Flannery says, noting the essential role played by a UC Berkeley interdisciplinary team of chemists, molecular biologists and vision scientists.

"And along the way, we developed tools that could be applied to the basic science of how synapses work and how neural circuits work," Isacoff adds. "These are spinoffs that themselves could have implications for the clinic."

These tools are now the basis of new UC Berkeley projects recently funded by NIH and NSF through President Obama's BRAIN Initiative.

http://bit.ly/1wdbgdp

How Did Life Become Complex, And Could It Happen Beyond Earth?

When astrobiologists contemplate life on nearby planets or moons, they often suggest such life would be simple.

By Elizabeth Howell - Dec 8, 2014

Instead of there being some kind of multicellular organism on, say, Jupiter's moon Europa, scientists instead aim to find something more like a microbe.

But from such simple life, more complex life forms could eventually come to be. That's what happened here on planet Earth, and that's what could happen in other locations as well. How did the chemistry evolve to get life to where we are today? What transitions took place?

Frank Rosenzweig, an evolutionary geneticist at the University of Montana, is looking into such questions over the next five years with funding from the NASA Astrobiology Institute. His lab studies how life evolves "complex traits," factors that influence everything from lifespan to biodiversity.

"Over my career, I've been interested in what are the genetic bases of adaptation and how do complex communities evolve from single clones," Rosenzweig said. "Related to these questions are others such as how do the genetic 'starting point' and ecological setting influence the tempo and trajectory of evolutionary change."

Shopping for life in the Solar System

Complex life is only known to exist on Earth, but scientists aren't ruling out other locations in the Solar System. Our understanding of life's evolution could be informed by studying the Saturnian moon Titan, whose hydrocarbon chemistry is considered a precursor to a living system. Researchers recently tried to replicate a substance in Titan's atmosphere called tholins, which are organic aerosols created from solar radiation hitting the methane and nitrogen atmosphere.

Understanding how tholins and other substances are formed on Titan could give researchers a picture of how early Earth evolved life. Also, studying how Earthly life-forms and their biochemical precursors evolved from simple subunits to successively more complex and interdependent systems could give hints of how life might evolve on other moons or planets.

On Earth, examples of these transitions include collections of single proteins evolving into protein networks. For example, single-celled bacteria evolve into eukaryotic cells that contain two, or even three genomes. Also, competing microbes come together to form cooperative systems, such as microbial mats in hot springs and microbial biofilms lining the human gut. Each of these transitions results in increased bio-complexity, interdependence and a certain degree of autonomy for a new whole that is more than the sum of its parts.

Rosenzweig's research developed out of previous NASA grants over the past six years.

"There is, and still needs to be a lot of work done on chemical evolution, prebiotic (pre-life) evolution, extreme environments and bio-signatures," Rosenzweig said. "It struck me that it might be worthwhile trying to convince NASA to add to its research portfolio a set of proposals focused on understanding the genetic basis underlying major evolutionary transitions that have led to higher-order complexity."

As such, Rosenzweig's new research will focus on four areas where a complex system has arisen from simpler elements: metabolism, the eukaryotic cell, mutualism (co-operating species) and multicellularity. He will also look into a fifth area - mutations and gene interactions - that critically determines how quickly such complex systems can arise. He believes that lab experiments aimed at replicating key aspects of the evolution of life on Earth can better inform how we search in life-friendly locations on Mars, Europa, Saturn's moon Titan, or elsewhere.

Rosenzweig plans to have eight different teams focusing on questions of evolution and changes from simple to more complex life. To integrate his teams' experimental results into a broader framework he recruited theoreticians in the areas of population genetics and statistical physics.

Applications beyond Earth

Rosenzweig's previous NASA funding came from the Exobiology and Evolutionary Biology Program. The first project, initiated in 2007, examined how genetic material (or genomes) evolve in yeast species that were cultured under limited resources. A second project, initiated in 2010, is investigating how founder cells in E. coli genotypes, and the environment in which they evolve, influence the diversity and stability of subsequent populations.

The first project led to an unexpected finding: stress may increase the frequency with which genome sequences are rearranged. Stress introduces new chromosomal variants into the species' population that could prove beneficial under challenging circumstances. Indeed, previous studies have indicated that new chromosomal variants are stress resistant. In 2013, Rosenzweig's team, led by University of Montana research professor Eugene Kroll, began studying how yeast cultures respond to starvation.

This new line of inquiry has already led to one major publication entitled, "Starvation-associated genome restructuring can lead to reproductive isolation in yeast," which was published in PLoS One in 2013. Therein, Kroll and Rosenzweig further show that yeast containing stress-adaptive genomic rearrangements become "reproductively isolated" from their ancestors, suggesting that, at least in lower fungi, geographic isolation may not be required to generate new species. A new project through NASA's Exobiology and Evolutionary Biology Program, awarded Summer 2014, will enable the team to tease out the genetic mechanisms that underlie adaptation and reproductive isolation in starved yeast.

A distinguishing feature of this research, Rosenzweig notes, is that whereas most studies look at species' performance in relatively benign environments, the yeast are studied under near-starvation conditions. This kind of severe stress may be a closer analog to what real species face in nature as populations genetically adapt to drastically altered circumstances. Inasmuch as starvation may serve as a cue to any kind of stress, from diminished resources to greatly altered temperature to an invasion by superior competitors, the results of this study should have implications for life on other planets.

Indeed, a major theme that runs through all of these investigations is that by studying evolutionary processes in the laboratory using simple unicellular species, we can expect to uncover rules that govern the tempo and trajectory of evolution in any population of self-replicating entities whose structure and function are programmed by information molecules.

"What I would like fellow astrobiology researchers to be alert to is evidence of differentiation, either at the level of different proteins in a metabolic network,

different genotypes in a population of a given species, different genomes in a single cell, or different cells in a multicellular organism. In each case differentiation opens the door not only to competition but also to cooperation between variants, enabling a division of labor." he said. "We should be mindful that, however they may be encoded, lifeforms are likely to have differentiated on other worlds. Therefore, we should be alert to the signatures left by these more complex forms of life."

http://bit.ly/1z6qdOg

Curiosity Rover's Mars Crater May Have Cradled Large Lakes

Signs of water on Mars aren't new, but now scientists think water may have been there for a long time

By Marissa Fessenden

NASA's Mars Curiosity rover is on a mountain, more than three miles high, that is built out of sedimentary rock in the enormous Gale Crater of the Red Planet. How exactly that mountain, officially dubbed Aeolis Mons but called Mount Sharp, got to be there is somewhat a of a mystery, writes Kenneth Chang for the *New York Times*. On Earth, mountains push up as erupting volcanos or as collisions between the plates of the crust. "Mars lacks plate tectonics, and volcanoes do not spew out of sedimentary rock. So how did this 18,000-foot mountain form?" Chang asks.

Curiosity is slowly crawling up the side of the mountain, passing layers and layers of sedimentary rock to find the answer. And along the way, the rover has found many signs that Gale Crater once contained large freshwater lakes, explains Rachel Feltman for the *Washington Post*. New images from Curiosity show that patterns seen in lake-floor sediment and signs of rivers flowing down the crater rim. The discovery that there was once water on Mars isn't actually new. For Aeon, Lee Billings writes:

Every mission sent to Mars seeking water has found it and, as a result, we now know that our neighboring world used to be a warmer, wetter, more habitable place. Billions of years ago, that all changed, as the planet cooled and lost most of its air and water, and settled into a quiet senescence. But present-day Mars still harbors a slumbering aquasphere, locked in the ground as ice, which may stir every so often, erupting to the surface in evanescent briny flows.

But the latest findings indicate that the water of that warmer, wetter time may have stuck around long enough to create conditions favorable for life.

"If our hypothesis for Mount Sharp holds up, it challenges the notion that warm and wet conditions were transient, local, or only underground on Mars," Ashwin Vasavada, Curiosity's deputy project scientist at NASA's Jet Propulsion Laboratory in Pasadena said in a NASA press release. "A more radical explanation is that Mars' ancient, thicker atmosphere raised temperatures above freezing globally, but so far we don't know how the atmosphere did that."

Gale Crater was shaped by millions or possibly tens of millions of years of flowing rivers, deltas and large lakes, reports Marc Kaufman for the *New York Times*. The layers of Mount Sharp alternate between deposits laid by wind, rivers and lakes. It seems the cycles slowly built the mountain up and carved away deposits around the edge of the crater. Now we have a sedimentary mountain rising out of the crater floor.

Curiousity can keep scratching and drilling away, but it's ill-equipped to determine if life once lived in the shifting environment of lakes, rivers and sculpted mountain. To answer that question, Kenneth S. Edgett of Malin Space Science Systems, which helped build an orbiter to investigate Mars' geology, says we will need more than robots and satellites. "I'd like to think it would take only a few months," to solve the questions raised by Mount Sharp, he told the *Times*, "with a few people on the ground."

http://bit.ly/1yzTFcT

On Pluto's Doorstep, NASA's New Horizons Spacecraft Awakens for Encounter

NASA's New Horizons spacecraft came out of hibernation on Dec. 6

After a voyage of nearly nine years and three billion miles - the farthest any space mission has ever traveled to reach its primary target – NASA's New Horizons spacecraft came out of hibernation on Dec. 6 for its long-awaited 2015 encounter with the Pluto system.

Operators at the Johns Hopkins University Applied Physics Laboratory in Laurel, Md., confirmed at 9:53 p.m. (EST) that New Horizons, operating on pre-programmed computer commands, had switched from hibernation to "active" mode. Moving at light speed, the radio signal from New Horizons – currently more than 2.9 billion miles from Earth, and just over 162 million miles from Pluto – needed four hours and 26 minutes to reach NASA's Deep Space Network station in Canberra, Australia.

"This is a watershed event that signals the end of New Horizons crossing of a vast ocean of space to the very frontier of our solar system, and the beginning of the mission's primary objective: the exploration of Pluto and its many moons in 2015," said Alan Stern, New Horizons principal investigator from Southwest Research Institute, Boulder, Colo.

Since launching on January 19, 2006, New Horizons has spent 1,873 days - about two-thirds of its flight time - in hibernation. Its 18 separate hibernation periods, from mid-2007 to late 2014, ranged from 36 days to 202 days in length. The team

used hibernation to save wear and tear on spacecraft components and reduce the risk of system failures. “Technically, this was routine, since the wake-up was a procedure that we’d done many times before,” said Glen Fountain, New Horizons project manager at APL. “Symbolically, however, this is a big deal. It means the start of our pre-encounter operations.”

The wake-up sequence had been programmed into New Horizons’ onboard computer in August, and started aboard the spacecraft at 3 p.m. EST on Dec. 6. About 90 minutes later, New Horizons began transmitting word to Earth on its condition, including the report that it is back in “active” mode.

The New Horizons team will spend the next several weeks checking out the spacecraft, making sure its systems and science instruments are operating properly. They’ll also continue to build and test the computer-command sequences that will guide New Horizons through its flight to and reconnaissance of the Pluto system. With a seven-instrument science payload that includes advanced imaging infrared and ultraviolet spectrometers, a compact multicolor camera, a high-resolution telescopic camera, two powerful particle spectrometers and a space-dust detector, New Horizons will begin observing the Pluto system on Jan. 15.

New Horizons’ closest approach to Pluto will occur on July 14, but plenty of highlights are expected before then, including, by mid-May, views of the Pluto system better than what the mighty Hubble Space Telescope can provide of the dwarf planet and its moons.

“New Horizons is on a journey to a new class of planets we’ve never seen, in a place we’ve never been before,” says New Horizons Project Scientist Hal Weaver, of APL. “For decades we thought Pluto was this odd little body on the planetary outskirts; now we know it’s really a gateway to an entire region of new worlds in the Kuiper Belt, and New Horizons is going to provide the first close-up look at them.”

The Johns Hopkins Applied Physics Laboratory manages the New Horizons mission for NASA’s Science Mission Directorate. Alan Stern, of the Southwest Research Institute (SwRI) is the principal investigator and leads the mission; SwRI leads the science team, payload operations, and encounter science planning. New Horizons is part of the New Frontiers Program managed by NASA’s Marshall Space Flight Center in Huntsville, Alabama. APL designed, built and operates the New Horizons spacecraft.

A Musical Wake-Up

New Horizons joins the astronauts on four space shuttle missions who “woke up” to English tenor Russell Watson’s inspirational “Where My Heart Will Take Me” – in fact, Watson himself recorded a special greeting and version of the song to honor New Horizons! ***Listen to it here*** The song was played in New Horizons mission operations upon confirmation of the spacecraft’s wake-up on Dec. 6.

The Sleeping Spacecraft: How Hibernation Worked

During hibernation mode, much of the New Horizons spacecraft was unpowered. The onboard flight computer monitored system health and broadcast a weekly beacon-status tone back to Earth. Onboard sequences sent in advance by mission controllers woke New Horizons two or three times each year to check out critical systems, calibrate instruments, gather some science data, rehearse Pluto-encounter activities, and perform course corrections.

New Horizons pioneered routine cruise-flight hibernation for NASA. Not only has hibernation reduced wear and tear on the spacecraft’s electronics, it also lowered operations costs and freed up NASA Deep Space Network tracking and communication resources for other missions.

http://bit.ly/1x1Uy2k

Viking Women Colonized New Lands, Too

Vikings may have been family men who traveled with their wives to new lands, according to a new study of ancient Viking DNA.

by Tia Ghose, Staff Writer | December 07, 2014 07:01 pm ET

Maternal DNA from ancient Norsemen closely matches that of modern-day people in the North Atlantic isles, particularly from the Orkney and Shetland Islands. The findings suggest that both Viking men and women sailed on the ships to colonize new lands. The new study also challenges the popular conception of Vikings as glorified hoodlums with impressive seafaring skills.

"It overthrows this 19th century idea that the Vikings were just raiders and pillagers," said study co-author Erika Hagelberg, an evolutionary biologist at the University of Oslo in Norway. "They established settlements and grew crops, and trade was very, very important."

Vikings hold a special place in folklore as manly warriors who terrorized the coasts of France, England and Germany for three centuries. But the Vikings were much more than pirates and pillagers. They established far-flung trade routes, reached the shores of present-day America, settled in new lands and even founded the modern city of Dublin, which was called Dyfflin by the Vikings.

Some earlier genetic studies have suggested that Viking males traveled alone and then brought local women along when they settled in a new location. For instance, a 2001 study published in the American Journal of Human Genetics suggested that Norse men brought Gaelic women over when they colonized Iceland.

Modern roots

To learn more about Norse colonization patterns, Hagelberg and her colleagues extracted teeth and shaved off small wedges of long bones from 45 Norse

skeletons that were dated to between A.D. 796 and A.D. 1066. The skeletons were first unearthed in various locations around Norway and are now housed in the Schreiner Collection at the University of Oslo.

The team looked at DNA carried in the mitochondria, the energy powerhouses of the cell. Because mitochondria are housed in the cytoplasm of a woman's egg, they are passed on from a woman to her children and can therefore reveal maternal lineage. The team compared that material with mitochondrial DNA from 5,191 people from across Europe, as well as with previously analyzed samples from 68 ancient Icelanders.

The ancient Norse and Icelandic genetic material closely matched the maternal DNA in modern North Atlantic people, such as Swedes, Scots and the English. But the ancient Norse seemed most closely related to people from Orkney and Shetland Islands, Scottish isles that are quite close to Scandinavia.

Mixed group

"It looks like women were a more significant part of the colonization process compared to what was believed earlier," said Jan Bill, an archaeologist and the curator of the Viking burial ship collection at the Museum of Cultural History, a part of the University of Oslo.

That lines up with historical documents, which suggest that Norse men, women and children - but also Scottish, British and Irish families - colonized far-flung islands such as Iceland, Bill told Live Science. Bill was not involved with the new study.

"This picture that we have of Viking raiding - a band of long ships plundering - there obviously would not be families on that kind of ship," Bill said. "But when these raiding activities started to become a more permanent thing, then at some point you may actually see families are traveling along and staying in the camps."

As a follow-up, the team would like to compare ancient Norse DNA to ancient DNA from Britain, Scotland and the North Atlantic Isles, to get a better look at exactly how all these people are related, Hagelberg said.

The findings were published today (Dec. 7) in the journal Philosophical Transactions of the Royal Society B.

http://bit.ly/1DgHkly

How Placebos Can Help You Run Faster

Just believing that you're blood doping is enough to help you run faster, recent research found.

Dec 8, 2014 02:00 PM ET // by Sheila M. Eldred

When the runners found out that they'd been given nothing more powerful than an injection of salt water, many were red-faced and a little embarrassed, lead author Ramzy Ross said. While the subjects may have felt duped, however, it's actually another testament to the power of expectation on our health, placebo experts said. Other work has shown that placebos can soothe a baby's cough, relieve migraine pain, and even mend torn knee cartilage as well as surgery.

One of the key issues in placebo research is parsing out what makes them work, said John Kelley, deputy director of the Program in Placebo Studies at Harvard Medical School and an associate professor of psychology at Endicott College. The two most common components, he said, are conscious expectations and classical conditioning.

Think of the first as what you could verbalize: In the case of the runners, for example, most would say that taking erythropoietin (EPO) would improve their aerobic capacity and delay fatigue.

As for classical conditioning, just as Pavlov's dogs started salivating when the physiologist entered the room in anticipation of being fed, people experience physical responses to certain associations.

In fact, even when researchers tell subjects they're taking a placebo, so-called open label studies still show a positive placebo effect. Researchers attribute it to the conditioning response, Kelley said. It works best in people who have been treated previously for a condition.

People with migraine headaches who experienced pain relief by taking a certain drug in the past also felt better when taking a pill that looked similar -- even when they knew it was not the actual drug.

By that rationale, athletes who have previously blood doped for real might fare even better on sham EPO, Kelley said.

Previous research on cyclists showed that the benefits of taking morphine during workouts were maximized when the cyclists were preconditioned to using it first.

Ramzy's team also delivered the placebo to the runners via injections instead of pills, knowing that most people have a stronger reaction to more invasive procedures.

The runners who were "really into what we were doing and understood how EPO could work" had the best results, Ramzy said.

The average improvement over the 3,000-meter races was 1.2 percent, or about 10 seconds. The study will be published in Medicine & Science in Sports & Exercise.

Because placebos tend to work best in situations that contain some type of psychological component, such as pain, the results of the running study make sense, Kelley said.

There could be a bonus after-effect, too: After the subjects in the running study recovered from the initial shock of realizing they had not taken a performance enhancement, most took it as a confidence boost. "They said, I know that I can do it now," Ramzy said. "There's this belief system that wasn't there before."

http://bit.ly/1vHdSvd

Formation of life's building blocks recreated in lab

Talk about making an impact. One of the meteorites that slammed into the planet early in its history could have kick-started life: the collision may have generated all four of the bases in RNA.

20:00 08 December 2014 by Colin Barras

Life appeared on Earth around 4 billion years ago, about the same time that the planet was experiencing a beating from large meteorites - an event called the Late Heavy Bombardment. As far as Svatopluk Civiš at the Academy of Sciences of the Czech Republic in Prague and his colleagues are concerned, that's no coincidence.

They simulated a meteorite impact on early Earth by firing a high-power laser at samples of formamide – a liquid that would have existed on our primordial planet. The sample temperatures soared to 4200 °C, generating X-rays and extreme ultraviolet radiation that reacted with the formamide to create chemical radicals. These radicals, in turn, reacted with hydrogen and the remaining formamide to generate 2,3-diaminomaleonitrile – DAMN for short – which is a chemical precursor to the nucleobases. When Civiš and his colleagues examined the end products of their reaction, they found all four RNA bases: adenine, guanine, cytosine and uracil – three of which are also found in DNA.

The work "nicely correlates the Late Heavy Bombardment and the energy that it delivered to Earth with the formation of RNA and DNA nucleobases from formamide", says Steven Benner at the Foundation For Applied Molecular Evolution in Gainesville, Florida.

What an impact

It was two Italian researchers – Raffaele Saladino at the University of Tuscia and Ernesto Di Mauro at the Sapienza University of Rome – who first suggested, in 2001, that formamide played an important role in the origin of life.

It forms when hydrogen cyanide, which was present in Earth's early atmosphere, reacts with water. Although Saladino and Di Mauro have shown other ways that formamide can generate the four nucleobases, Di Mauro says "this is the first time that solid theoretical treatment and experimental data are presented together".

He adds that even more biologically important molecules can be generated if these experiments consider the role that various minerals inside the meteorites might have played as catalysts – something his latest, still unpublished work has explored.

"The obtained products are astonishingly rich and variegated," Di Mauro says.

Saladino and Di Mauro suggested formamide would have concentrated in warm lagoons on our young planet – particularly because formamide has a higher boiling point than water, so would concentrate as water evaporated.

Donald Lowe, a geologist at Stanford University who studies the Late Heavy Bombardment, says such environments did exist on early Earth – despite the disruption caused by the impacts.

Living the dry life

"Although the impact frequency may have been 10s or 100s of times greater than it is today, your chance of experiencing a large impact at the height of the LHB would have been small," says Lowe. "Lagoons or, in more general terms, shallow-water protected settings, are likely to have been well developed on the early Earth."

The work still doesn't quite answer the question of how the RNA bases came together with other complex molecules to form RNA, though. "This is what we are working on right now," says Civiš. For instance, they hope to generate carbohydrates through similar laser experiments.

But if huge impact events were critical for the generation of life's key molecules, water was apparently not. Saladino and Di Mauro's work on formamide suggested that the first, small RNA molecules were most likely to come together in a relatively water-free environment – like a formamide-rich lagoon.

Benner points out that some geologists think early Earth had too much water to allow these environments to exist, which last year led him to suggest that these formamide reactions may actually have occurred on the much drier early Mars, before life later rode through space on Martian meteorites to reach Earth.

The idea is compatible with Civiš and his colleagues' work emphasising the role of impact events. "The current view is that all of the inner planets experienced the Late Heavy Bombardment," says Benner.

Journal reference: PNAS, DOI: 10.1073/pnas.1412072111

http://nyti.ms/1Aksi8D

A One-Way Trip to Mars? Many Would Sign Up

When Seth Shostak, an astronomer who scans the cosmos for signs of extraterrestrial intelligence, asks middle school students how many of them want to go to Mars, all hands shoot up.

By NATALIE ANGIER

When he asks how many would rather design robots that go to Mars, most hands drop back to their desks. And when he asks general audiences how many would go to Mars even if it meant dying a few weeks after arriving, he invariably finds volunteers in the crowd. “I kid you not,” said Dr. Shostak, the director of the

Center for SETI Research. “People are willing to risk everything just to see Mars, to walk on the surface of our little ruddy buddy.”

His experience accords with what many say is a distinct surge in public enthusiasm for space travel generally, and a manned mission to Mars in particular. Or make that a *human* mission: Women, too, are wholly on board. “I would totally love to go to Mars,” said Pamela A. Melroy, a former NASA astronaut who piloted two space shuttle missions and commanded a third.

But the questions of when and who the “we” will be remain very much up in the air. A “global exploration road map” prepared by NASA and 15 other space agencies envisions a presumably international team of astronauts bouncing over the frigid rouge dustscape of Mars by the 2030s.

Private companies like SpaceX and Virgin Galactic say they may get there first, or better, or more democratically. Among the bolder if farther-fetched plans comes from a Dutch nonprofit venture called Mars One, which insists it will land four people on Mars - two men and two women - by 2025. As the project leaders see it, the technology needed to reach and colonize the red planet already exists, so why not go ahead and start loading the moving van?

There is a catch, they say. Where NASA-style flight plans are designed on the Apollo moonshot model of round-trip tickets, the “one” in Mars One means, starkly, one way. To make the project feasible and affordable, the founders say, there can be no coming back to Earth. Would-be Mars pilgrims must count on living, and dying, some 140 million miles from the splendid blue marble that all humans before them called home.

Nevertheless, enthusiasm for the Mars One scheme has been of middle-school proportions. Last year, the outfit announced that it was seeking potential colonists and that anybody over age 18 could apply, advanced degrees or no. Among the few stipulations: Candidates must be between 5-foot-2 and 6-foot-2, have a ready sense of humor and be “Olympians of tolerance.” More than 200,000 people from dozens of countries applied. Mars One managers have since whittled the pool to some 660 semifinalists.

Many space experts and Mars aficionados remain deeply skeptical about the program’s odds of success. They point out that Mars One doesn’t build rockets or any other aeronautic equipment, as SpaceX does. Nor does it have the tycoon portfolio of Virgin’s Sir Richard Branson. “I don’t take Mars One seriously at all,” said Andy Weir, author of “The Martian,” a novel about a stranded astronaut struggling to survive on Mars that is so revered by engineers and techno-space geeks that it has been called “competence porn.”

“I think they honestly believe in what they’re doing,” he added, “but I don’t think they have any chance of accomplishing it.”

Others have complained that the group’s emphasis on the colonist selection process over financial or technical details of the mission is little more than a publicity stunt.

Karen Cumming, 52, a Canadian journalist and teacher who is among the Mars One semifinalists, said she recently met the Canadian astronaut Chris Hadfield, who won fame on the International Space Station by singing David Bowie songs and showing the world how water behaves in low gravity.

“I told him who I was, and I asked if he had any advice,” Ms. Cumming said. “He said: ‘Be relentless in your questioning about the hardware. Astronaut selection is the least of their worries.’ ”Bas Lansdorp, 37, who conceived of Mars One as an engineering student at the University of Twente in the Netherlands, admitted that its founders sought publicity, but said nobody paid attention when they announced last year that they had formed a partnership with Lockheed Martin.

James B. Garvin, a chief scientist with NASA, discusses the history of Mars exploration, current technological advances and what is still to come in understanding our planetary neighbor. David Corcoran and Claire Maldarelli

Choosing the right people for the expedition, he said, is not the least of their worries, but ultimately the only worry. The mission’s success or failure hinges on assembling a team of people who can live together in extreme circumstances, he said, “without losing their minds.”

The various reasons offered for sending humans to Mars, at a cost of billions if not hundreds of billions of dollars - “but less expensive than the war in Iraq!” insisted Andrew Rader, a Mars One candidate and expert in human spaceflight with a doctorate from M.I.T. - include elements both practical and profound, optimistic and dystopian. Ellen Stofan, NASA’s chief scientist, said that for all the success of robots like Curiosity, sending humans to the surface “may be the only way to prove life evolved on Mars and what the nature of it is.”

And demonstrating that some form of life arose at least twice in our solar system would lend ballast to the argument that the universe teems with life. Humans will soon need more space and more resources than Earth can offer, Dr. Shostak said, adding, “If you want to have Homo sapiens for the long run, you have to move out somewhere.” Whatever hardships the Mars homesteaders endure, Mr. Lansdorp argued, may well improve life for those back on Earth. “We’re a species that explores and pushes boundaries,” he said.

“By exploring our own planet, we’ve developed technology to make our life more comfortable. Mars is the next logical step, the boundary to push, to make us more developed still.”

Scientists agree that of all the places in the solar system where a few expatriate earthlings might settle, Mars is the least hostile. It’s roughly one-sixth the size of

Earth, but given its lack of oceans, it nearly matches us in landmass. It rotates on an Earthlike tilt of 24 degrees and so has seasons, the length of its day is similar to ours, and its soil is about 2 percent frozen water, which in theory could be melted out and put to use. Its gravity is about 40 percent that of Earth - enough to keep inhabitants from the severe bone and muscle loss caused by long-term stints in outer space, but still of sufficient levity, said Norbert Kraft, chief medical officer for Mars One, "that maybe your knees won't hurt and your wrinkles will go away."

Yet Mars remains a forbidding, frigid place, with an average temperature of minus 50 degrees Fahrenheit and an unbreathable atmosphere just 1 percent the density of Earth's and consisting largely of carbon dioxide.

Colonists would live in artificial podlike habitats, grow vegetables in greenhouses and get their protein from insects. No pets, sorry. And if you plan on going outside - as you will, often, to repair infrastructure battered by the chronic Martian wind, or to wipe off solar panels encrusted with the ubiquitous Martian dust - you must wear your spacesuit at all times.

"No more smell of fresh grass, or the ocean," Ms. Melroy said. "Giving that up would be a huge deal." Another sacrifice, said Stephan Guenther, 46, a flight instructor and software developer in Cologne, Germany, and a Mars One semifinalist, would be the sound of silence. "There will always be some sound in the background, because the life support systems have to run," he said. "If there's real silence on Mars, something is going very badly."

Yet oh, how he wants to go to Mars. "I was not yet 1 year old when Neil Armstrong landed on the moon," he said. "I was standing on the couch watching it on TV, and my mother wasn't able to pull me away." All he ever wanted to do in life was fly and go to space. "I had my pilot's license before my driver's license," he said.

At 64, Jan Millsapps, a professor of cinema at San Francisco State University, is among the older candidates on the Mars One list. "I'm at a point in my life where I'm ready for a new adventure," she said. "I don't feel like I'm running away. It's more like I'm running toward."

Kellie Gerardi, 26, who works in the commercial spaceflight industry, says that even if Mars One never gets off the ground, it has already succeeded, elevating "the conversation about the need for space settlements to a global scale."

Ms. Gerardi is planning to get married in September, and a NASA astronaut is to officiate at the ceremony. Yet she would be willing to leave her husband behind should a Mars passport bear her name.

Why doesn't he apply to the program, too? For one thing, she said, "he doesn't think it would be fun." For another, he's an inch too tall.

http://bit.ly/1vHfN2M

Bouncy Gait Improves Mood

If you're in an up mood, you may walk more energetically. But a study finds that purposefully walking more energetically may improve your mood. Christie Nicholson reports

December 8, 2014 |By Christie Nicholson

Download MP3

A good mood may put a spring in your step. But the opposite can work too: purposefully putting a spring in your step can improve your mood. That's the finding from a study in the Journal of Behavior Therapy and Experimental Psychiatry. [Johannes Michalak, Katharina Rohde and Nikolaus F. Troje, How we walk affects what we remember: Gait modifications through biofeedback change negative affective memory bias]

Scientists showed volunteers a list of negative and positive words, like afraid and anxious, or sunny and pretty. Then the subjects had to walk on a treadmill while watching a gauge that moved left or right.

But here's what the participants did not know: if their stance - for example, slumped shoulders - seemed to indicate a down mood the gauge moved to the left. If their walk was more upbeat, say with swinging arms, the gauge moved to the right. The scientists asked half the subjects to adjust their walking style until the gauge moved to the right, and the other half so that the gauge went the left. Each group quickly learned what adjustments moved the gauge in the desired direction. Then the subjects had to write down as many words from the list that they remembered. And those who walked with a depressed gait recalled more negative terms, while the ones who were asked to walk in a more upbeat style came up with many more positive words.

Past research has shown that depressed people tend to remember negative words and happier people tend to remember happy words. So this study suggests that the way we walk influences our mental state. And that we can change our state by changing our gait.

http://www.eurekalert.org/pub_releases/2014-12/mu-cow120914.php

Controlling obesity with potato extract

Extract of Irish potatoes, rich in polyphenols, reduces weight gain to a surprising extent

Take a look in your pantry: the miracle ingredient for fighting obesity may already be there. A simple potato extract may limit weight gain from a diet that is high in fat and refined carbohydrates, according to scientists at McGill University. The results of their recent study were so surprising that the investigators repeated the experiment just to be sure.

Investigators fed mice an obesity-inducing diet for 10 weeks.

The results soon appeared on the scale: mice that started out weighing on average 25 grams put on about 16 grams. But mice that consumed the same diet but with a potato extract gained much less weight: only 7 more grams. The benefits of the extract are due to its high concentration of polyphenols, a beneficial chemical component from the fruits and vegetables we eat.

"We were astonished by the results," said Prof. Luis Agellon, one of the study's authors. "We thought this can't be right - in fact, we ran the experiment again using a different batch of extract prepared from potatoes grown in another season, just to be certain."

The rate of obesity due to over-eating continues to rise in Canada, affecting 1 in every 4 adults. Obesity increases the risk of cardiovascular disease and cancer. According to this study, potato extracts could be a solution for preventing both obesity and type 2 diabetes.

Extract derived from 30 potatoes

"The daily dose of extract comes from 30 potatoes, but of course we don't advise anyone to eat 30 potatoes a day," says Stan Kubow, principal author of the study, "as that would be an enormous number of calories." What the investigators envisage instead is making the extract available as a dietary supplement or simply as a cooking ingredient to be added in the kitchen. Popularly known for its carbohydrate content, the potato is also a source of polyphenols. "In the famous French diet, considered to be very healthy, potatoes - not red wine - are the primary source of polyphenols," says Kubow. "In North America, potatoes come third as a source of polyphenols - before the popular blueberries."

A low-cost solution

"Potatoes have the advantage of being cheap to produce, and they're already part of the basic diet in many countries," Kubow explains. "We chose a cultivated variety that is consumed in Canada and especially rich in polyphenols."

En route to the airport one day to catch the same flight, Stan Kubow, Associate Professor in the School of Dietetics and Human Nutrition and an expert on polyphenols, and Danielle Donnelly, Associate Professor in the Department of Plant Science and an expert on potatoes, had the bright idea of crossing their research interests, and together with Prof. Agellon, they carried out this study.

Although humans and mice metabolize foods in similar ways, clinical trials are absolutely necessary to validate beneficial effects in humans. And the optimal dose for men and women needs to be determined, since their metabolisms differ. The team hopes to patent the potato extract, and is currently seeking partners, mainly from the food industry, to contribute to funding clinical trials.

This study was funded by the Natural Sciences and Engineering Research Council of Canada, the Canadian Institutes of Health Research and the Canada Foundation for Innovation.

Extract of Irish potatoes (Solanum tuberosum L.) decreases body weight gain and adiposity and improves glucose control in the mouse model of diet-induced obesity

Molecular Nutrition & Food Research, November 2014 Stan Kubow, Luc Hobson, Michèle M. Iskandar, Kebba Sabally, Danielle J. Donnelly and Luis B. Agellon

http://onlinelibrary.wiley.com/doi/10.1002/mnfr.201400013/abstract;jsessionid=5F563E95E6DFF9E7A9883EF79F1F79F1.f02t04

http://www.eurekalert.org/pub_releases/2014-12/cmc-csm120914.php

Computer system more effective than doctors at producing comprehensive patient reports

A web-based questionnaire highlights the potential of computers to improve quality of care and medical outcomes by collecting and translating accurate patient data

LOS ANGELES - A computer system was more effective than doctors at collecting information about patient symptoms, producing reports that were more complete, organized and useful than narratives generated by physicians during office visits, according to a Cedars-Sinai study. Investigators said the research, published in the American Journal of Gastroenterology, highlights the potential of computers to enhance the quality of medical care and improve outcomes by harnessing accurate and thorough patient information.

The authors said they did not expect technology to replace physicians in the exam room. Instead, they said that computers can empower doctors to practice medicine more efficiently and effectively as they face growing requirements to document symptoms, diagnoses and other patient data.

"Our results suggest that computers can help clinicians focus on what they do best - practicing the distinctly human art of medicine," said Brennan Spiegel, MD, a study author and director of Health Services Research. "This study offers initial proof that a computer can create meaningful and relevant patient histories that are useful in the clinical setting."

The researchers conducted their study in outpatient gastrointestinal clinics in Los Angeles, identifying 75 patients who reported a variety of active symptoms, including abdominal pain, heartburn, reflux, nausea, vomiting, constipation and diarrhea.

Patients were seen initially by doctors, who typed or dictated information about illness histories into the electronic health record system. The patients later answered questions about their conditions on a website called My GI Health. An algorithm on the website collected the answers and translated them into patient narratives.

The reports generated by the doctors and the computer system were evaluated by a separate group of physicians who had no knowledge of the study, including the fact that half of the patient histories were written by a computer. The reviewers were told only that they were auditing the quality of reports in gastrointestinal clinics.

The reviewers concluded that the computer-generated summaries were superior, describing them as better organized, more complete, succinct, comprehensive and useful. "The computer-generated narratives were of higher quality overall," said Christopher V. Almario, MD, a Cedars-Sinai-based gastroenterology fellow and a lead author of the study.

The researchers said that computers offer a solution to the problem of doctors entering incomplete or inaccurate information into patients' records. The technology also frees physicians to focus more on patients during office visits and to catch important bits of information and nonverbal cues that might otherwise be missed.

The investigators suggested that patients are comfortable disclosing health information in "virtual human" interviews through the web-based questionnaire. "The study reveals that computers can lift at least some of the burden from doctors by collecting and analyzing data," Spiegel said.

The research was funded in part by the National Institutes of Health Patient Reported Outcomes Measurement Information System.

http://www.eurekalert.org/pub_releases/2014-12/uoa-yaf120914.php

Yeast are first cells known to cure themselves of prions

Yeast cells can sometimes reverse the protein misfolding and clumping associated with diseases such as Alzheimer's, according to new research from the University of Arizona.

The new finding contradicts the idea that once prion proteins have changed into the shape that aggregates, the change is irreversible.

"It's believed that when these aggregates arise that cells cannot get rid of them," said Tricia Serio, UA professor and head of the department of molecular and cellular biology. "We've shown that's not the case. Cells can clear themselves of these aggregates."

Prions are proteins that change into a shape that triggers their neighbors to change, also. In that new form, the proteins cluster. The aggregates, called amyloids, are associated with diseases including Alzheimer's, Huntington's and Parkinson's.

"The prion protein is kind of like Dr. Jekyll and Mr. Hyde," said Serio, senior author of the paper published Dec. 9 in the open-access journal eLife. "When you get Hyde, all the prion protein that gets made after that is folded in that bad way."

For yeast, having clumps of amyloid is not fatal. Serio and her students exposed amyloid-containing cells of baker's yeast to 104 F (40 C), a temperature that would be a high fever in a human. When exposed to that environment, the cells activated a stress response that changed the clumping proteins back to the no-clumping shape.

The finding suggests artificially inducing stress responses may one day help develop treatments for diseases associated with misfolded prion proteins, Serio said. "People are trying to develop therapeutics that will artificially induce stress responses," she said. "Our work serves as a proof of principal that it's a fruitful path to follow."

First author on the paper "Spatial quality control bypasses cell-based limitations on proteostasis to promote prion curing" is Serio's former graduate student Courtney Klaips, now at the Max Planck Institute for Biochemistry in Munich. The other authors are Serio's students Megan Hochstrasser, now at the University of California, Berkeley, and Christine Langlois of Brown University. The paper is available here: http://dx.doi.org/10.7554/eLife.04288. National Institute of Health grants R01 GM069802001, F31 AG034754 and F31 GM099383 funded the research.

To accomplish their jobs inside cells, proteins must fold into specific shapes. Cells have quality-control mechanisms that usually keep proteins from misfolding. However, under some environmental stresses, those mechanisms break down and proteins do misfold, sometimes forming amyloids.

Cells respond to environmental stress by making specific proteins, known as heat-shock proteins, which are known to help prevent protein misfolding.

Serio and her students wanted to know whether particular heat-shock proteins could make amyloids revert to the normal shape. To that end, the team studied yeast cells that seemed unable to clear themselves of the amyloid form of the prion protein Sup35.

The researchers were testing one heat-shock protein at a time in an attempt to figure out which particular proteins were needed to clear the amyloids. However, the results weren't making sense, she said.

So she and Klaips decided to stress yeast cells by exposing them to a range of elevated temperatures - as much as 104 F (40 C) - and let the cells do what comes naturally.

As a result, the cells made a battery of heat-shock proteins. The researchers found at one specific stage of the cell's reproductive cycle, the yeast could turn aggregates of Sup35 back into the non-clumping form of the protein.

Yeast cells reproduce by budding. The mother cell partitions off a bit of itself into a much smaller daughter cell, which separates and then grows up.

The researchers found in the heat-stressed yeast, just when the daughter was being formed, the mother cell retained most of the heat-shock proteins called chaperones, especially Hsp-104. As a result, the mother had a particularly high concentration of Hsp-104 because little of the protein was shared with the daughter.

The mother cells ended up "curing" themselves of the Sup35 amyloid, although the daughters did not. The degree of curing was correlated with the concentration of Hsp-104 in the cell, and the higher the temperature the more Hsp-104 the cells had.

The Hsp-104 takes the protein in the amyloid and refolds it, Serio said. But she and her colleagues found that just inducing high levels of Hsp-104 in cells by itself does not change the amyloid protein back to the non-clumping form.

"Clearly the heat-shock proteins are collaborating in some way that we don't understand," she said.

Having the amyloid-forming version of the protein is not automatically bad, she said. It may be that shape is good under some environmental conditions, whereas the non-aggregating form is good under others.

Even in humans, amyloid forms of a protein can be helpful, she said. Amyloid proteins are associated with skin pigmentation and with hormone storage.

To clear the amyloid from yeast cells, these experiments triggered cells to make many different heat-shock proteins. Serio now wants to figure out the minimal system necessary to clear amyloids from a cell. Knowing that may help the development of drug therapies for amyloid-related human diseases, she said.

http://bit.ly/1xdEdrn

The Mongol army was no match for bad weather

Two storms changed the course of history more than 700 years ago

By Mary Beth Griggs Posted Yesterday at 6:00am

A massive storm is currently battering northern California just after another storm bombed the United Kingdom. These weather events are huge news for the people living through them, but they are nothing compared to two storms that changed the course of history more than 700 years ago.

In the 13th century, the Mongol Empire, led by Kublai Khan, thought it would be a great idea to invade Japan. They tried in 1274, launching a fleet of hundreds boats filled with 30,000 armed men. But while they were on their way to the island nation, legend has it that a Kamikaze or 'divine wind' intercepted the fleet and destroyed it. Not ones for giving up, the Mongols tried again in 1281, this time with more than 140,000 men and thousands of ships, only to be met once again by another typhoon. The storms assumed a place of legend in Japanese history, exaggerated over the intervening centuries. Now, geologists have found evidence that the large storms really did occur.

A study published in Geology looked at layers of sediment dating back 2000 years in a lake near the site of the Mongol invasions of Japan. The researchers found two large deposits of marine sediments that corresponded with the typhoons. They also found evidence that there was a long period of increased flooding from 250 CE to 1600 CE, indicating that the large storms were more common in that area during that time period. In the paper, the authors write: "The Kamikaze typhoons may therefore serve as a prominent example for how past increases in severe weather associated with changing climate have had significant geopolitical impacts."

The Mongol Invasion Silk tapestry depicting the 13th Century Mongol Invasion

Walters Art Museum/Wikimedia Commons

This isn't the first evidence of the destroyed fleet to be unearthed. Underwater archaeology expeditions off the coast of Japan have yielded evidence of the destroyed ships, including human remains and early examples of explosive shells carried by the Mongol fleet. But the geological piece of the puzzle adds some context to the findings, showing that there were plenty of large, high intensity storms to help sink those ships.

http://www.eurekalert.org/pub_releases/2014-12/bmj-mei120514.php

Most exaggeration in health news is already present in academic press releases

The scientific community has the ability to improve this situation, say researchers

Most exaggeration in health related science news is already present in academic press releases, finds a study published in The BMJ this week.

The researchers suggest that improving the accuracy of academic press releases "could represent a key opportunity for reducing misleading health related news."

Health related news has widespread potential to influence health related behaviour but often misreports the science. It is not known whether exaggerations - claims going beyond those made in the research paper - originate in the news stories themselves or in press releases issued by academic institutions producing the research.

So a team, led by Professors Petroc Sumner and Chris Chambers at Cardiff University, set out to identify the source (press releases or news) of distortions,

exaggerations, or changes to the main conclusions drawn from research that could potentially influence a reader's health related behaviour.

They analysed 462 press releases on biomedical and health related science issued by 20 leading UK universities in 2011, alongside their associated peer reviewed research papers and 668 national news stories.

They focused on three common types of exaggeration: giving direct advice to readers to change their behaviour, making causal claims from correlational (observational) data, and making inference about humans from animal findings.

They found that 40% of press releases contained exaggerated advice, 33% contained exaggerated causal claims, and 36% contained exaggerated inference to humans from animal research, compared with the corresponding peer reviewed journal articles.

And when press releases contained exaggeration it was more likely that the news would too (58% for advice, 81% for causal claims, and 86% for inference to humans). But when press releases did not contain exaggeration, rates of exaggeration in news were only 17%, 18%, and 10%, respectively. However, there was little evidence that exaggeration in press releases increased the uptake of news.

The authors point out that this is an observational study so no definitive conclusions can be drawn about cause and effect.

Although it is common to blame media outlets and their journalists for news perceived as exaggerated, sensationalised, or alarmist, "our principle findings were that most of the inflation detected in our study did not occur de novo in the media but was already present in the text of the press releases produced by academics and their establishments," they write.

The blame - if it can be meaningfully apportioned - they say, "lies mainly with the increasing culture of university competition and self promotion, interacting with the increasing pressures on journalists to do more with less time."

The scientific community has the ability to improve this situation, they conclude. Press releases could be a primary target to improve the accuracy of science news, with potential benefit for public health.

In an accompanying editorial, Ben Goldacre, Research Fellow at the London School of Hygiene and Tropical Medicine and author of the book Bad Science, argues that academics should be made accountable for exaggerations in press releases about their own work.

Academic press releases should be treated as a part of the scientific publication, he says. They should include named individuals from the original research paper; they should be linked to the paper they are promoting; and presented as online data appendices, in full view of peers. There should also be opportunity for feedback in the publishing journal.

"Collectively this would produce an information trail, and accountability among peers and the public," he writes. And he speculates whether a public ranking of press releases "might change academic behaviour, and create an environment where researchers finally act to prevent patients and the public being routinely misled."

http://www.eurekalert.org/pub_releases/2014-12/luhs-wts120914.php

Why treating shoulder pain in baseball pitchers is so difficult

Results of shoulder pain treatments in throwers not as predictable as specialists would like to think

MAYWOOD, Ill. -- Results of treating shoulder pain in baseball pitchers and other throwing athletes are not as predictable as doctors, patients and coaches would like to think, according to a report in the journal Physical Medicine and Rehabilitation Clinics of North America.

Nickolas Garbis, MD, an orthopedic surgeon who specializes in shoulder and elbow injuries at Loyola University Medical Center, is the primary author.

Shoulder pain occurs in athletes who play sports that require rapid acceleration and deceleration of the throwing arm. They include baseball pitchers, tennis players, softball pitchers and javelin throwers, as well as athletes who play handball and water polo.

Overhead throwing generates a large amount of stress on the shoulder, which is one of the most mobile joints in the body. This makes it vulnerable to injury.

It is difficult to diagnose the cause of shoulder pain. The shoulder is comprised of four joints, and a problem with any of them can cause pain and affect performance. Moreover, many of these structures are deep in the shoulder and therefore difficult to examine by touch. Also, the same kind of pain can be due to multiple causes. For example, pain in the front of the shoulder can be due to rotator cuff tendinitis, rotator cuff tears, biceps tendinitis, shoulder instability, shoulder stiffness and several other causes.

"A systemic approach, and some experience, can help the clinician become more familiar with which constellation of findings in these athletes is not normal," Dr. Garbis and co-author Edward McFarland, MD, write.

Shoulder problems can begin during adolescence. Little League shoulder, an injury to the growth plate in the shoulder, is one of the most common. Adolescent pitchers most at risk for injuries are those who compete on traveling teams. Overuse injuries can lead to more serious mechanical injuries. Adhering to pitch counts should reduce injuries and decrease fatigue.

Treatment should be primarily nonsurgical. Nonsurgical options include icing the shoulder and judicial use of nonsteroidal anti-inflammatory medications such as ibuprofen and naproxen. Rehabilitation can restore a normal muscular balance. Rest can help, but it should not be prolonged, because the shoulder could become deconditioned.

If nonsurgical options fail, arthroscopic surgery can be considered. For example, surgical repair or trimming of partial rotator cuff tears can be highly successful, returning as many as 89 percent of college and professional pitchers back to play. However, the type of surgery needed depends upon the patient's shoulder problem.

Dr. Garbis is an assistant professor in the Department of Orthopaedic Surgery and Rehabilitation at Loyola University Chicago Stritch School of Medicine. Dr. McFarland is a professor in the Department of Orthopaedic Surgery at Johns Hopkins University.

http://www.eurekalert.org/pub_releases/2014-12/asfm-sfv120914.php

Seasonal flu vaccines boost immunity to many types of flu viruses

Seasonal flu vaccines may protect individuals not only against the strains of flu they contain but also against many additional types

WASHINGTON, DC - Seasonal flu vaccines may protect individuals not only against the strains of flu they contain but also against many additional types, according to a study published this week in mBio®, the online open-access journal of the American Society for Microbiology.

The work, directed by researchers at St. Jude Children's Research Hospital in Memphis, Tenn., found that some study participants who reported receiving flu vaccines had a strong immune response not only against the seasonal H3N2 flu strain from 2010, when blood samples were collected for analysis, but also against flu subtypes never included in any vaccine formulation.

The finding is exciting "because it suggests that the seasonal flu vaccine boosts antibody responses and may provide some measure of protection against a new pandemic strain that could emerge from the avian population," said senior study author Paul G. Thomas, PhD, an Associate Member in the Department of Immunology at St. Jude.

"There might be a broader extent of reactions than we expected in the normal human population to some of these rare viral variants."

Because avian influenza viruses have an important role in emerging infections, Thomas and colleagues tested whether exposure to different types of birds can elicit immune responses to avian influenza viruses in humans. They studied blood samples taken from 95 bird scientists attending the 2010 annual meeting of the American Ornithologist Union.

They exposed plasma from the samples to purified proteins of avian influenza virus H3, H4, H5, H6, H7, H8 and H12 subtypes using two laboratory tests to see how many different viruses participants reacted to, and how strongly. The first test, ELISA, measures if any antibodies -- proteins produced by the body that are used by the immune system to identify and neutralize foreign objects such as bacteria and viruses - combine in any way to a protein called HA on the surface of the virus. The second, HAI, measures if antibodies can bind to HA and interrupt its association with a substance viruses use to get inside human cells.

In the ELISA tests, 77 percent of participants had detectable antibodies against avian influenza proteins. Most individuals tested had a strong antibody response to the seasonal H3N2 human virus-derived H3 subtype, part of that year's vaccine (2009-2010), but many also had strong measurable antibody responses to group 1 HA (avian H5, H6, H8, H12) and group 2 HA (avian H4, human H7) subtypes. Sixty-six percent of participants had some level of detectable antibodies against four or more HA proteins, and a few had responses to all subtypes tested, most of which have not previously been detected in the human population.

In additional experiments, the scientists found that participants who had significant antibody responses did not necessarily also have significant immune system T cell responses to avian viruses, indicating that these two arms of immunity can be independently boosted after vaccination or infection; that individuals who reported receiving seasonal influenza vaccination had significantly higher antibodies to the avian H4, H5, H6, and H8 subtypes; and that participants with exposure to poultry had significantly higher antibody responses to the H7 subtype, but to none of the other subtypes tested. Exposure to other types of birds did not play a role in immunity.

A person's immune response on the ELISA test did not necessarily predict response on the HAI test, and vice versa. As HAI antibodies only target the "head" of the HA while ELISA antibodies can be against the head or the relatively conserved "stalk" domain, this result indicated that some individuals were more likely to target the conserved stalk region (i.e. show greater reactivity in ELISA than in HAI).

The work has opened up a lot of questions in figuring out why people mount different types of responses, and potentially how the seasonal vaccine may play a role in boosting these responses, Thomas said. He has started additional studies in other groups of people with varied vaccination and infection histories to tease apart what exposures boost immunity against avian influenza viruses.

The study was supported by the National Institutes of Health Centers of Excellence for Influenza Research and Surveillance (St. Jude CEIRS, contract HHSN272201400006C) and the American Lebanese Syrian Associated Charities (ALSAC), a fund-raising organization for the hospital. The article can be found online at http://bit.ly/mBiodec9.

http://nyti.ms/1GlwQ2B

Special K, a Hallucinogen, Raises Hopes and Concerns as a Treatment for Depression

It is either the most exciting new treatment for depression in years or it is a hallucinogenic club drug that is wrongly being dispensed to desperate patients in a growing number of clinics around the country.

By ANDREW POLLACK DEC. 9, 2014

It is called ketamine — or Special K, in street parlance.

While it has been used as an anesthetic for decades, small studies at prestigious medical centers like Yale, Mount Sinai and the National Institute of Mental Health suggest it can relieve depression in many people who are not helped by widely used conventional antidepressants like Prozac or Lexapro.

And the depression seems to melt away within hours, rather than the weeks typically required for a conventional antidepressant.

But some psychiatrists say the drug has not been studied enough to be ready for use outside of clinical trials, and they are alarmed that clinics are springing up to offer ketamine treatments, charging hundreds of dollars for sessions that must be repeated many times.

“We don’t know what the long-term side effects of this are,” said Dr. Anthony J. Rothschild, a professor of psychiatry at the University of Massachusetts Medical School.

Pharmaceutical companies hope to solve the problem by developing drugs that work like ketamine but without the side effects, which are often described as out-of-body experiences.

On Tuesday, at a medical conference in Phoenix, a privately held company called Naurex reported that its drug caused no such psychotic side effects in a midstage trial involving about 400 patients. The drug, called GLYX-13, showed signs of reducing depression in about half the patients tested.

“It’s definitely the most promising compound in the depression space in terms of effect and durability,” said Harry M. Tracy, the publisher of the newsletter NeuroPerspective, which follows companies developing drugs for psychiatry.

Naurex, based in Evanston, Ill., recently raised $80 million and will start a Phase 3 trial to confirm the safety and efficacy of GLYX-13 next year with hopes of receiving approval from the Food and Drug Administration in 2019, said Norbert G. Riedel, the chief executive.

GLYX-13 is given by intravenous injection every week or two weeks. Naurex is also working on a version that can be taken orally. Cerecor, a privately held company in Baltimore, hopes to have results from a midstage study of a once-a-day pill this month. Johnson & Johnson is in midstage trials of a nasal spray containing esketamine, a derivative of ketamine.

But achieving safety and efficacy for this type of drug can be challenging, and some attempts have failed. About a year ago, AstraZeneca dropped an experimental drug after it failed in a clinical trial.

Some doctors and patients are not waiting for the pharmaceutical industry.

Because ketamine has long been approved for anesthesia, doctors are allowed to use it off-label to treat depression. Clinics charge from $300 to more than $1,000 per treatment. Insurance rarely covers the cost. Schedules vary by clinic and by patient, but some patients are treated every few days at first, then every two weeks to two months.

Critics say that severely depressed patients might be too desperate to adequately weigh the risks of the experimental therapy.

“We are talking about a population that is particularly vulnerable,” said Dominic A. Sisti, an assistant professor of medical ethics at the University of Pennsylvania, who was one of the authors of a recent commentary in a journal expressing concern about the clinics.

He and other critics say that some clinics are run by anesthesiologists who are familiar with ketamine but do not provide overall psychiatric treatment. Others are run by psychiatrists who might not have experience administering the drug.

Besides the psychoticlike effects, ketamine can raise blood pressure and heart rate. Evidence from people who abuse the drug indicates that it can cause a decline in brain function and bladder problems.

Some patients say they are ready to take that risk.

“I look at the cost of not using ketamine — for me it was certain death,” said Dennis Hartman, 48, a businessman from Seattle.

He said that after a lifetime of severe depression, he had chosen a suicide date when he entered a clinical trial of ketamine at the National Institutes of Health two years ago.

His depression lifted and since then he has gone to a clinic in New York every two months or so for infusions. He started the Ketamine Advocacy Network to raise awareness of the treatment.

Advocates say that the dose used for depression is smaller than that used for anesthesia or by abusers and can be given safely.

Dr. David Feifel, a professor of psychiatry at the University of California, San Diego, said that what is essentially a psychedelic trip is over quickly after the treatment is ended.

“More often than not, they really like it,” said Dr. Feifel, who is one of the only academic psychiatrists to offer ketamine as a treatment, as opposed to in a clinical

trial, though only to people who have exhausted other options. He said that if he did not offer the drug, "I'm consigning you to lose another decade until ketamine might be ready. I just don't feel that presumptuous."

One of his patients, Maggie, said that when she got her first infusion she was aware enough to change the tunes on her iPod, albeit slowly, but was "transported into a completely different dimension." She added, "Everything there is completely vibrant or molten."

The trip ended quickly, but within hours, a lifetime of depression began to lift. "Never ever ever before have I felt like that," said Maggie, 53, who lives in Orange County, Calif., and spoke on the condition that her full name not be used because of the stigma associated with depression. "I woke up the next morning, and I didn't take an antidepressant for the first time in 20 years."

A common refrain among ketamine advocates is that questions about its safety are emanating from drug companies, which have no financial incentive to develop ketamine because it is generic, but see it as a threat to their proprietary products.

"Let's trash ketamine to justify producing something patentable and turn it into a blockbuster," said Dr. Glen Z. Brooks, an anesthesiologist who runs NY Ketamine Infusions, a clinic in Manhattan.

Drug company executives say that ketamine itself has too many problems to ever gain wide acceptance for long-term use, especially as an off-label treatment.

There is clearly a need for new drugs. "Almost half of depressed patients are not being treated adequately by existing drugs," said Dr. Sheldon H. Preskorn, a professor of psychiatry at the University of Kansas School of Medicine-Wichita. That, he said, is because virtually all the antidepressants used in the last 60 years work essentially the same way. They raise levels of serotonin or one or two other neurotransmitters, chemicals that transmit signals in the brain.

Ketamine would represent a new mechanism of action. It is believed to work mainly by blocking receptors in the brain for N-methyl-D-aspartate, or NMDA, which interact with a different neurotransmitter called glutamate.

The blockage sets off a cascade of changes that are not yet completely understood. "Synaptic connections that help us to cope seem to grow back," said Dr. John H. Krystal, chairman of psychiatry at Yale and a pioneer in the study of ketamine for depression.

He dismissed any suspicions that people are simply getting high and not experiencing a true antidepressant effect, saying the lifting of depression occurs after the side effects end.

Naurex says its drug avoids the side effects because it interacts with the NMDA receptor in a different way, not totally blocking it. Cerecor says its drug blocks only a particular subunit of the receptor.

Dr. Feifel said the biggest obstacle to ketamine use is not the side effects but that its effect on depression wears off so quickly.

To stretch the time between visits, some clinics are now providing ketamine that patients can inject themselves at home, or ketamine capsules prepared by a compounding pharmacy. That is a departure from the standard practice of closely monitoring patients while they take the drug.

The need for repeated treatments has been a problem for Tiffaney Israel-Ritchey, 41, of Lubbock, Tex., who said she was suicidal until she first tried ketamine in December 2012. "It saved my life," she said.

But she had to stop in October 2013 because she could no longer afford the infusions, which cost $750 to $1,000. Now her depression is back, she said, though it is not as bad as before.

http://www.eurekalert.org/pub_releases/2014-12/uops-dda120914.php

Drug developed at Pitt proves effective against antibiotic-resistant 'superbugs'

CVR develops far more effective treatment than antibiotics to inhibit the growth of drug-resistant bacteria

PITTSBURGH - A treatment pioneered at the University of Pittsburgh Center for Vaccine Research (CVR) is far more effective than traditional antibiotics at inhibiting the growth of drug-resistant bacteria, including so-called "superbugs" resistant to almost all existing antibiotics, which plague hospitals and nursing homes.

The findings, announced online in the journal Antimicrobial Agents and Chemotherapy and funded by the National Institutes of Health, provide a needed boost to the field of antibiotic development, which has been limited in the last four decades and outpaced by the rise of drug-resistant bacterial strains.

"Very few, if any, medical discoveries have had a larger impact on modern medicine than the discovery and development of antibiotics," said senior author Ronald C. Montelaro, Ph.D., professor and co-director of Pitt's CVR.

"However, the success of these medical achievements is being threatened due to increasing frequency of antibiotic resistance. It is critical that we move forward with development of new defenses against the drug-resistant bacteria that threaten the lives of our most vulnerable patients."

Each year in the U.S., at least 2 million people are infected with drug-resistant bacteria, and at least 23,000 die as a direct result of these infections, according to the U.S. Centers for Disease Control and Prevention.

On the tail end of HIV surface protein, there is a sequence of amino acids that the virus uses to "punch into" and infect cells. Dr. Montelaro and his colleagues developed a synthetic and more efficient version of this sequence - called engineered cationic antimicrobial peptides, or "eCAPs"--that can be chemically synthesized in a laboratory setting.

The team tested the two leading eCAPs against a natural antimicrobial peptide (LL37) and a standard antibiotic (colistin), the latter being used as a last-resort antibiotic against multidrug resistant bacterial infections.

The scientists performed the tests in a laboratory setting using 100 different bacterial strains isolated from the lungs of pediatric cystic fibrosis patients of Seattle Children's Hospital and 42 bacterial strains isolated from hospitalized adult patients at UPMC.

The natural human antimicrobial peptide LL37 and the colistin drug each inhibited growth of about 50 percent of the clinical isolates, indicating a high level of bacterial resistance to these drugs. In marked contrast, the two eCAPS inhibited growth in about 90 percent of the test bacterial strains.

"We were very impressed with the performance of the eCAPs when compared with some of the best existing drugs, including a natural antimicrobial peptide made by Mother Nature and an antibiotic of last resort," said Dr. Montelaro. "However, we still needed to know how long the eCAPs would be effective before the bacteria develop resistance."

The team challenged a highly infectious and pathogenic bacterium called Pseudomonas aeruginosa - which flourishes in medical equipment, such as catheters, and causes inflammation, sepsis and organ failure - with both the traditional drugs and eCAPs in the lab.

The bacterium developed resistance to the traditional drugs in as little as three days. In contrast, it took 25 to 30 days for the same bacterium to develop resistance to the eCAPs. In addition, the eCAPs worked just as effectively at killing Pseudomonas aeruginosa after it became resistant to the traditional drugs.

"We plan to continue developing the eCAPs in the lab and in animal models, with the intention of creating the least-toxic and most effective version possible so we can move them to clinical trials and help patients who have exhausted existing antibiotic options," said Dr. Montelaro.

Additional researchers on this study are Berthony Deslouches, M.D., Ph.D., Jonathan D. Steckbeck, Ph.D., M.B.A., Jodi K. Craigo, Ph.D., and Yohei Doi, M.D., all of Pitt; and Jane L. Burns, M.D., of Seattle Children's Research Institute.

This research was supported by NIH grants P30DK072506, R01AI104895, R21AI107302 and P30 DK089507, as well as funds from Pitt's Center for Vaccine Research and Cystic Fibrosis Research Center.

http://www.eurekalert.org/pub_releases/2014-12/acon-brc120214.php

Brain reward circuits respond differently to 2 kinds of sugar

The brain responds differently to two kinds of sugar

Phoenix, AZ - The brain responds differently to two kinds of sugar, according to a report today at the American College of Neuropsychopharmacology annual meeting in Phoenix Arizona. The study suggests that fructose heightens the response of brain reward circuits to food cues, promoting feeding behavior.

Currently, roughly two out of three U.S. adults are overweight and one out of three is obese. Changes in lifestyle and dietary intake during the past quarter century are thought to be the main culprits, with the increase in fructose consumption of particular concern. Fructose is the simple sugar found in fruit, but it is added to many foods as a "refined sugar" in the form of high-fructose corn syrup. By comparison, glucose, the primary energy source for the body, is usually produced through the breakdown of complex carbohydrates. Fructose ingestion produces smaller increases in circulating satiety hormones than glucose ingestion. Further, administration of fructose directly into the brain provokes feeding in rodents, whereas glucose administered this way promotes satiety, or the feeling of being full. Preliminary studies in people have also shown that glucose reduces activity in the hypothalamus, an event that is associated with metabolic satiety, whereas fructose does not.

Using functional magnetic resonance imaging (fMRI), Kathleen Page at the Keck School of Medicine of the University of Southern California (USC) and her colleagues in the Department of Psychology at the University of Southern California extended this work. They examined brain responses and motivation to eat when research volunteers viewed images of food (like chocolate cake) after they drank a beverage containing either glucose or fructose. The participants were 24 young men and women, 16 to 25 years of age. They viewed images of food during fMRI scans of their brains and reported how much they wanted to eat. The food cues produced activation in the nucleus accumbens, a part of the brain's "reward circuit", and increased the desire for food. Activation in the nucleus accumbens was greater after consuming the fructose drink compared to the glucose drink. The fructose drink also resulted in greater ratings of hunger and motivation to eat compared to the glucose drink. These neural and behavioral responses to high-calorie food stimuli could promote eating, and more so after consuming fructose compared to glucose.

These studies have important public health implications in a society that is inundated with high-sugar foods and tantalizing food stimuli. They suggest that consumption of fructose may promote overeating.

This work was supported by the Doris Duke Charitable Foundation Grant #2012068, the American Heart Association, and the SC CTSI (NIH/NCRR/NCATS) Award #UL1TR000130.

http://www.eurekalert.org/pub_releases/2014-12/jhm-bia120914.php

Brain inflammation a hallmark of autism, large-scale analysis shows

Johns Hopkins study is largest so far of gene expression in autism brains

While many different combinations of genetic traits can cause autism, brains affected by autism share a pattern of ramped-up immune responses, an analysis of data from autopsied human brains reveals. The study, a collaborative effort between Johns Hopkins and the University of Alabama at Birmingham, included data from 72 autism and control brains. It will be published online Dec. 10 in the journal Nature Communications.

"There are many different ways of getting autism, but we found that they all have the same downstream effect," says Dan Arking, Ph.D. , an associate professor in the McKusick-Nathans Institute for Genetic Medicine at the Johns Hopkins University School of Medicine. "What we don't know is whether this immune response is making things better in the short term and worse in the long term."

The causes of autism, also known as autistic spectrum disorder, remain largely unknown and are a frequent research topic for geneticists and neuroscientists. But Arking had noticed that for autism, studies of whether and how much genes were being used -- known as gene expression -- had thus far involved too little data to draw many useful conclusions. That's because unlike a genetic test, which can be done using nearly any cells in the body, gene expression testing has to be performed on the specific tissue of interest -- in this case, brains that could only be obtained through autopsies.

To combat this problem, Arking and his colleagues analyzed gene expression in samples from two different tissue banks, comparing gene expression in people with autism to that in controls without the condition. All told, they analyzed data from 104 brain samples from 72 individuals -- the largest data set so far for a study of gene expression in autism.

Previous studies had identified autism-associated abnormalities in cells that support neurons in the brain and spinal cord. In this study, Arking says, the research team was able to narrow in on a specific type of support cell known as a microglial cell, which polices the brain for pathogens and other threats. In the autism brains, the microglia appeared to be perpetually activated, with their genes for inflammation responses turned on. "This type of inflammation is not well understood, but it highlights the lack of current understanding about how innate immunity controls neural circuits," says Andrew West, Ph.D., an associate professor of neurology at the University of Alabama at Birmingham who was involved in the study.

Arking notes that, given the known genetic contributors to autism, inflammation is unlikely to be its root cause. Rather, he says, "This is a downstream consequence of upstream gene mutation." The next step, he says, would be to find out whether treating the inflammation could ameliorate symptoms of autism.

Other authors on the study are Simone Gupta, Shannon E. Ellis, Foram N. Ashar, Anna Moes, Joel S. Bader and Jianan Zhan, all of The Johns Hopkins University.

http://www.eurekalert.org/pub_releases/2014-12/uoz-awi121014.php

Anyone who is good at German learns English better

"A tree must be bent while it is young," as one saying about learning a foreign language goes.

In other words, the earlier you start learning a foreign language systematically, the better the language level will be in the long run. The second widely held view is that you need to be solid in your first language (L1) in order to develop good literacy skills in the foreign language. Linguist Simone Pfenninger from the University of Zurich has been examining these two myths in her five-year study involving Swiss high-school children in order to identify the optimal starting age for learning German as a language of literacy and English as a foreign language. The partial results she has just published reveal that anyone who reads and writes German well is likely to carry over this advantage to English - and, interestingly, regardless of the age of onset of foreign language learning or the biological age. The study also shows that students who are given early exposure to English do not maintain a clear advantage for more than a relatively short period over students who begin to learn the language only at secondary level. In fact, early foreign language learning can even have a negative impact on the L1 in the short run.

Positive and negative influences of German on English researched

For five years, the UZH scientist has been studying the extent to which starting age, biological age and L1 skills - Swiss or High German - influence the development of English proficiency. In order to test their skills in German and English, the literacy skills of 200 randomly selected high-school children in the Canton of Zurich were tested at the beginning and towards the end of their obligatory schooling in the senior grades. One group had begun English lessons in primary school at the age of eight, while the second group had only started English in high school at the age of thirteen.

Besides the positive influence of German on English, the negative influences and transfer of structures from the L1 to the foreign language were also studied in the areas of syntax and morphology. "After all, as the mother tongue becomes

increasingly entrenched, you might also expect an increasing negative influence of the L1 on English," explains Pfenninger.

As the results showed, foreign language lessons at an early age did not have a beneficial impact either in the long or in the short term. Already after six months learners who had started five years later had caught up with the early learners and sometimes even surpassed them, e.g. in terms of morpho-syntactic accuracy and complexity, syntactic fluency, grammaticality judgment, and content-related and structural aspects of written expression. However, the early learners had a larger vocabulary at the first measurement and less of a tendency to fill the gaps in their vocabulary in the foreign language with so-called "code-switching" into German. "By the second assessment, shortly before the final high-school exams, there were no longer any differences between early and late starters," says Pfenninger.

Late starters had better German writing skills

According to the study's author, the slightly disappointing results for early foreign language learning can be attributed to the following reasons (among others): at the beginning of high school, the late learners exhibited significantly better German writing skills than the early learners, who had already been taught German, English and French in elementary school. The late learners therefore began foreign language lessons with a more favorable foundation in the language of literacy. By the second assessment five years later, however, this advantage had disappeared.

Moreover, the link between German and English writing skills also displayed a positive and significant correlation: "Anyone who is good at German can carry over this advantage to the foreign language, utterly regardless of the age when they start learning the foreign language or their biological age," sums up Pfenninger. Therefore, the results of this study have shown so far that, where success is concerned, this does not relate for the most part to age of onset or length of the exposure to the foreign language

Pfenninger, Simone E. The Literacy Factor in the Optimal Age Debate: a 5-Year Longitudinal Study. International Journal of Bilingual Education and Bilingualism. December 10, 2014. doi: 10.1080/13670050.2014.972334

http://www.eurekalert.org/pub_releases/2014-12/tjnj-ict120914.php

Islet cell transplantation after pancreas removal may help preserve normal blood sugar

Removing all or part of the pancreas and transplanting a patient's own islet cells appears safe and effective in alleviating pain from severe chronic pancreatitis

Surgery to remove all or part of the pancreas and then transplant a patient's own insulin-producing islet cells appears to be a safe and effective final measure to alleviate pain from severe chronic pancreatitis and to help prevent surgically induced diabetes, according to a report published online by JAMA Surgery.

Chronic pancreatitis (CP) is an inflammatory disease that over time leads to loss of function of the pancreas and manifests with intractable pain, malabsorption and diabetes. While medical management and pain control are the initial approaches to CP, some patients need to undergo more invasive procedures to relieve ductal pressure in the pancreas. If those measures fail, surgical options can include total removal of the pancreas (total pancreatectomy, TP) or the Whipple procedure to remove part of the pancreas. Total pancreas removal produces diabetes because insulin-secreting cells are removed. Autologous islet transplantation (AIT) was first described in the 1970s as a potential way to preserve normal blood glucose levels after near-total or total pancreas removal. However, few medical centers worldwide offer such treatment for patients with CP, according to background information in the study.

Denise S. Tai, M.D., of the University of California, Los Angeles, and co-authors examined the outcomes of nine patients (5 male) who underwent pancreatic resection and AIT at the UCLA Center for Pancreatic Diseases between March 2007 and December 2013. It was a two-center collaboration with the University of California, San Francisco, handling isolation of the islet cells from the pancreatic tissue after removal.

Results show that eight of nine patients had successful procedures to isolate islet cells after their total or partial pancreas removal. Two of the patients did not require insulin and one required a low dose. All nine patients had less pain or were pain free two months after surgery.

"Pancreatic resection with AIT for severe CP is a safe and effective final alternative to ameliorate debilitating pain and to help prevent the development of surgical diabetes. It is practiced at only a few specialized centers worldwide because of the need for multidisciplinary coordination and care of these patients. ... However, with the practice of geographically remote islet isolation by means of institutional collaboration, many more patients with CP may have access to and may greatly benefit from this procedure," the authors conclude.

(JAMA Surgery. Published online December 10, 2014. doi:10.1001/jamasurg.2014.932. Available pre-embargo to the media at http://media.jamanetwork.com.)

http://www.eurekalert.org/pub_releases/2014-12/bmj-asl120814.php

Added sugars likely to have greater role than salt in high blood pressure and heart disease

Dietary guidelines should focus more on sugar, and less on salt, say doctors

Dietary guidelines should emphasise the role played by added sugars, particularly fructose, in the fight to curb the prevalence of cardiovascular, they insist.

Cardiovascular disease is the number one cause of premature death in the developed world. And high blood pressure is its most important risk factor,accounting for almost 350,000 deaths in the US in 2009 and costing more than $50 billion US dollars every year. Dietary approaches to lower high blood pressure have historically focused on cutting salt intake. But the potential benefits of this approach "are debatable," say the authors.

This is because the average reductions in blood pressure achieved by restricting salt intake tend to be relatively small, and there is some evidence to suggest that 3-6 g salt daily may be optimal for health, and that intake below 3 g may actually be harmful, they write. Most salt in the diet comes from processed foods, which also happen to be a rich source of added sugars, they point out.

"Sugar may be much more meaningfully related to blood pressure than sodium, as suggested by a greater magnitude of effect with dietary manipulation," they state. "Compelling evidence from basic science, population studies, and clinical trials implicates sugars, and particularly the monosaccharide fructose, as playing a major role in the development of hypertension [high blood pressure]," they write. "Moreover, evidence suggests that sugars in general, and fructose in particular, may contribute to overall cardiovascular risk through a variety of mechanisms," they add.

They point the finger in particular to high fructose corn syrup, which is the most frequently used sweetener in processed foods, particularly fruit-flavoured and fizzy drinks. "Worldwide, sugar sweetened beverage consumption has been implicated in 180,000 deaths a year," they write. Around 300 years ago, people only consumed a few pounds of sugar a year, they add, whereas current estimates suggest that average consumption in the US is 77-152 pounds a year--equivalent to 24-47 teaspoons a day.

The evidence suggests that people whose dietary intake of added sugars adds up to at least a quarter of their total daily calories have almost triple the cardiovascular disease risk of those who consume less than 10%.

And a daily intake of more than 74 g of fructose is associated with a 30% greater risk of blood pressure above 140/90 mm Hg and a 77% increased risk of blood pressure above 160/100 mm Hg.

A high fructose diet has also been linked to an unfavourable blood fat profile, higher fasting blood insulin levels, and a doubling in the risk of metabolic syndrome. Some dietary guidelines do include recommendations about daily intake of added sugars, but are not stringent enough, nor do they make specific recommendations about fructose, say the authors. And it's high time they did.

Of particular concern, they say, is that UK and US teens may be consuming added sugars up to 16 times the recommended limit.

They emphasise that naturally-occurring sugars found in fruit and vegetables are not harmful to health. Eating fruit and vegetables is almost certainly beneficial.

"Just as most dietary sodium does not come from the salt shaker, most dietary sugar does not come from the sugar bowl; reducing consumption of added sugars by limiting processed foods containing it, made by corporations, would be a good place to start," write the authors.

And they go on to warn: "The evidence is clear that even moderate doses of added sugar for short durations may cause substantial harm."

http://www.eurekalert.org/pub_releases/2014-12/bmj-mbl120814.php

Midriff bulge linked to heightened risk of sudden, often fatal, heart malfunction

Those with highest waist to hip ratio twice as likely to be affected as those with ratio in the normal range

Those with the largest waists and hips combined are twice as likely to be affected as those with measurements in the normal range, the findings indicate.

Sudden cardiac death, or SCD for short, occurs without warning, and is caused by a sudden unexpected loss of heart function, which rapidly reduces blood flow around the body, including to the brain. It is distinct from a heart attack, and kills around 300,000 people in the USA every year.

Obesity has long been associated with various unfavourable changes in cardiovascular health, including SCD. But the researchers wanted to find out if a persistent midriff bulge may carry a greater risk of SCD than general obesity as the evidence suggests this body fat distribution may be more dangerous.

They therefore studied almost 15,000 middle aged men and women (45-64 years of age), all of whom were taking part in the Atherosclerosis Risk in Communities (ARIC) study.ARIC has been tracking the causes of artery narrowing in middle aged Americans since 1987.

All the participants (55% women; 26% African American) underwent a detailed health assessment in 1987-9, and then again in 1990-92, 1993-5, 1996-8, and 2011-13. This included measurements of weight, height, waist circumference, and the waist to hip ratio.

During the monitoring period, which averaged 12.5 years, 253 SCDs occurred. Those affected were in their mid-fifties, on average; one in three was female; and four out of 10 were of African American heritage. Unsurprisingly, those who died suddenly tended to have a higher prevalence of known risk factors for cardiovascular disease, such as high blood pressure and high cholesterol. They also had a higher BMI (body mass index), larger waist circumference, and a larger

waist to hip ratio--an indicator of central obesity--than those who did not sustain an SCD.

The risk of SCD was associated with general obesity, but only in non-smokers.

And of the measures of obesity--BMI, waist circumference, and waist to hip ratio--waist to hip ratio was the most strongly associated with SCD risk after taking account of other influential factors. Those with the highest waist to hip ratio had double the risk of SCD of those with a normal ratio.

And unlike BMI and waist circumference, the association between waist to hip ratio was independent of existing coronary heart disease, diabetes, or high blood pressure and other known risk factors.

This is an observational study so no definitive conclusions can be drawn about cause and effect, added to which the precise mechanisms for the association between SCD and central obesity are not known, say the researchers.

But fat around the midriff is thought to be more critical than fat stored elsewhere in the body, because of its influence on inflammation.

http://bit.ly/1GyA6Ga

Massive Study Reveals Schizophrenia's Genetic Roots

The largest-ever genetic study of mental illness reveals a complex set of factors

Oct 16, 2014 |By Simon Makin

Schizophrenia is a distressing disorder involving hallucinations, delusions, paranoia and agitation. It affects around one in 100 people in the U.S., with symptoms usually first appearing between the ages of 16 and 30. Its causes have long been debated, particularly regarding whether genetics plays a role. It is known to be highly heritable, but small sample sizes and other methodology hurdles stymied early attempts to discern a genetic link.

Now the biggest-ever genetic study of mental illness has found 128 gene variants associated with schizophrenia, in 108 distinct locations in the human genome. The vast majority of them had never before been linked to the disorder. This finding lays to rest any argument that genetics plays no role.

The study, published in July in Nature, is the result of a collaboration among more than 300 scientists from 35 countries, named the Schizophrenia Working Group of the Psychiatric Genomics Consortium. The researchers compared the whole genomes of nearly 37,000 people with schizophrenia with more than 113,000 people without the disorder, in a so-called genome-wide association study (GWAS). Genetic material, or DNA, is made up of a sequence of molecular pairs, thousands of which string together to form genes. The GWAS involves tallying known common mutations in these pairs, in people with and without a condition. Variants that show up significantly more often in people with the condition are said to be “associated” with it. The GWAS “potentially provides a more comprehensive view of the biological players in disease than previous genetic studies,” says Benjamin Neale of the Broad Institute in Cambridge, Mass., one of the study's lead authors.

The technique cannot identify the exact mutations that cause illness or even pinpoint specific genes. Rather it flags areas of the genome that contribute to risk. Genes in these regions warrant further investigation to uncover the biological processes underlying the condition. “We've prised open lots of windows for people to climb in and attack the biology of schizophrenia,” says Michael O'Donovan of Cardiff University in Wales, another lead author.

Treatments for schizophrenia have not advanced in more than 50 years, since the discovery of drugs that reduce the activity of the chemical messenger dopamine. A leading theory has therefore focused on overactive dopamine signaling. Sure enough, one of the identified regions contains a gene that produces the type of dopamine receptor that is blocked by antipsychotic drugs.

Another of the brain's chemicals, glutamate, has also received attention, but drugs that target it have not fared well in clinical trials. The new study implicated several glutamate-related genes. “This is important confirmatory evidence that glutamate is relevant to schizophrenia,” O'Donovan says. “Exactly how is another question.” Past drugs may have failed because, for instance, they targeted the wrong kind of glutamate receptor; the genetic results will help drug developers focus their efforts.

The meaning of some of the other findings is less clear. Immune system genes were implicated, as were genes previously associated with smoking. These findings do not necessarily mean that schizophrenia is related to immunity or that smoking causes schizophrenia. The area of the genome related to immunity contains hundreds of genes, some of which affect other aspects of biology. Genes can also perform distinct roles in various tissues. “A lot of immune system proteins probably have different functions in the brain,” O'Donovan says. The link with smoking is similarly opaque. For instance, one genetic variant might both predispose people to smoking and increase the risk of schizophrenia, without one causing the other.

An important overall conclusion is that schizophrenia is a complex trait like any other, but its complexity does not mean it will remain mysterious. Past GWAS research has led to breakthroughs for other health conditions with tangled genetic and environmental roots, such as diabetes and Crohn's disease, and experts believe that this study will do the same for schizophrenia. “That there are lots of small, common genetic effects, scattered across the genome, is itself an important finding,” Neale says. “There are many different biological processes involved.”

http://www.eurekalert.org/pub_releases/2014-12/ru-pg121014.php

Patients given less blood during transfusions do well

Rutgers-led research finds similar survival rates whether transfusions are large or small

Patients with heart disease who receive transfusions during surgeries do just as well with smaller amounts of blood and face no greater risk of dying from other diseases than patients who received more blood, according to a new Rutgers study. The research, published in the journal Lancet, measures overall mortality and mortality from cardiovascular disease, cancer and severe infection, and offers new validation to a recent trend toward smaller transfusions.

For the study, led by Jeffrey Carson, chief of the Division of Internal Medicine at Rutgers Robert Wood Johnson Medical School, researchers followed 2,016 patients for as long as four years. Half received larger quantities of transfused blood; half received transfusions that were smaller by as much as two thirds. Carson and his team found no evidence of increased mortality from cardiovascular disease, cancer or severe infection due to the amount of the blood given after surgery. This study supports Carson's 2011 research published in the New England Journal of Medicine which demonstrated the safety of fewer transfusions in the short term - 60 days - and was one of the driving forces behind a change in blood transfusion practice nationally.

"There has been a steady decline in the amount of blood in transfusions given to patients in the past three to five years," Carson says. "I think it is very reassuring that we have found that using less blood is okay not just from a short term perspective, but also a long term perspective."

In the United States, an estimated 5 million people receive transfusions each year, according to the Centers for Disease Control and Prevention. They include surgery patients; accident, burn and trauma victims; mothers and babies during and after childbirth; and others whose blood counts reach levels low enough to threaten their health.

Carson says physicians performing surgeries and other procedures judge whether blood is needed based on how much they have seen the patient lose and by closely watching vital signs such as blood pressure. If physicians overestimate and provide too much blood, the patient's circulatory system can be overloaded and breathing can be affected. The risk of infection can also increase. "There are definite risks associated with transfusion," says Carson. "The classic ones are hepatitis and HIV. They are as rare as being hit by lightning, but even so - why give more blood to anyone if you can't show it benefits them?"

Carson - who chaired the American Association of Blood Banks' official guidelines committee in 2012 - says the rule he follows is that fewer transfusions are better than more, as long as rigorous studies show no added health risk. Fewer transfusions also benefit society, he says, by preserving the blood supply and preventing shortages.

Medical experts had worried that larger amounts of transfused blood might suppress immune function - which could lead to death from infection or cancer - or whether smaller transfusions might worsen a patient's chronic heart disease by depriving the heart of oxygen and other nutrients that it might have absorbed by pumping more blood. But in both instances Carson found no difference in long term death rates regardless of the number of transfusions.

There still are health conditions, like heart attacks, that need further research, he says. Preliminary evidence suggests those patients need more blood, not less. "We need additional studies; we need a big trial to settle that question," Carson says.

http://www.eurekalert.org/pub_releases/2014-12/ncsu-na121014.php

New 'high-entropy' alloy is as light as aluminum, as strong as titanium alloys

Researchers from North Carolina State University and Qatar University have developed a new "high-entropy" metal alloy that has a higher strength-to-weight ratio than any other existing metal material.

High-entropy alloys are materials that consist of five or more metals in approximately equal amounts. These alloys are currently the focus of significant attention in materials science and engineering because they can have desirable properties. The NC State research team combined lithium, magnesium, titanium, aluminum and scandium to make a nanocrystalline high-entropy alloy that has low density, but very high strength.

"The density is comparable to aluminum, but it is stronger than titanium alloys," says Dr. Carl Koch, Kobe Steel Distinguished Professor of Materials Science and Engineering at NC State and senior author of a paper on the work. "It has a combination of high strength and low density that is, as far as we can tell, unmatched by any other metallic material. The strength-to-weight ratio is comparable to some ceramics, but we think it's tougher - less brittle - than ceramics."

There are a wide range of uses for strong, lightweight materials, such as in vehicles or prosthetic devices. "We still have a lot of research to do to fully characterize this material and explore the best processing methods for it," Koch says. At this point, the primary problem with the alloy is that it is made of 20 percent scandium, which is extremely expensive. "One thing we'll be looking at is whether scandium can be replaced or eliminated from the alloy," Koch says.

The paper "A Novel Low Density, High Hardness, High-Entropy Alloy with Close-packed Single-phase Nanocrystalline Structures," is published online in the open-access journal

Materials Research Letters. Lead author of the paper is Dr. Khaled Youssef of Qatar University. Co-authors include Alexander Zaddach and Changning Niu, Ph.D. students at NC State; and Douglas Irving, an associate professor of material science and engineering at NC State. The work was supported in part by the National Science Foundation under grant number DMR-1104930.

http://www.eurekalert.org/pub_releases/2014-12/nrao-sop121114.php

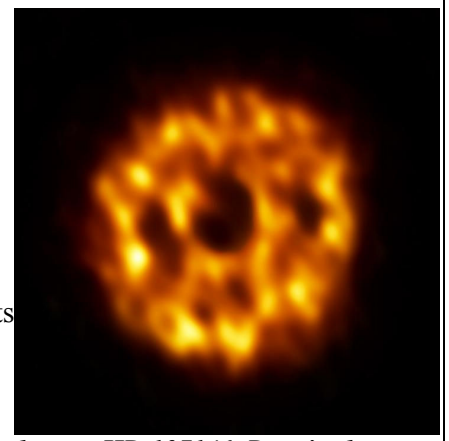
Swarms of Pluto-size objects kick-up dust around adolescent Sun-like star

Astronomers using the Atacama Large Millimeter/submillimeter Array (ALMA) may have detected the dusty hallmarks of an entire family of Pluto-size objects swarming around an adolescent version of our own Sun.

By making detailed observations of the protoplanetary disk surrounding the star known as HD 107146, the astronomers detected an unexpected increase in the concentration of millimeter-size dust grains in the disk's outer reaches.

This surprising increase, which begins remarkably far - about 13 billion kilometers - from the host star, may be the result of Pluto-size planetesimals stirring up the region, causing smaller objects to collide and blast themselves apart.

Dust in debris disks typically comes from material left over from the formation of planets Very early in the lifespan of the disk, this dust is continuously replenished by collisions of larger bodies, such as comets and asteroids.



This is an ALMA image of the dust surrounding the star HD 107146. Dust in the outer reaches of the disk is thicker than in the inner regions, suggesting that a swarm of Pluto-size planetesimals is causing smaller objects to smash together. The dark ring-like structure in the middle portion of the disk may be evidence of a gap where a planet is sweeping its orbit clear of dust. **L. Ricci; ALMA (NRAO/NAOJ/ESO); B. Saxton (NRAO/AUI/NSF)**

In mature solar systems with fully formed planets, comparatively little dust remains. In between these two ages - when a solar system is in its awkward teenage years - certain models predict that the concentration of dust would be much denser in the most distant regions of the disk. This is precisely what ALMA has found.

"The dust in HD 107146 reveals this very interesting feature -- it gets thicker in the very distant outer reaches of the star's disk," said Luca Ricci, an astronomer at the Harvard-Smithsonian Center for Astrophysics in Cambridge, Massachusetts, and lead author on a paper accepted for publication in the Astrophysical Journal. At the time of the observations, Ricci was with the California Institute of Technology in Pasadena.

"The surprising aspect is that this is the opposite of what we see in younger primordial disks where the dust is denser near the star. It is possible that we caught this particular debris disk at a stage in which Pluto-size planetesimals are forming right now in the outer disk while other Pluto-size bodies have already formed closer to the star," said Ricci.

According to current computer models, the observation that the density of dust is higher in the outer regions of the disk can only be explained by the presence of recently formed Pluto-size bodies. Their gravity would disturb smaller planetesimals, causing more frequent collisions that generate the dust ALMA sees.

The new ALMA data also hint at another intriguing feature in the outer reaches of the disk: a possible "dip" or depression in the dust about 1.2 billion kilometer wide, beginning approximately 2.5 times the distance of the Sun to Neptune from the central star.

Though only suggested in these preliminary observations, this depression could be a gap in the disk, which would be indicative of an Earth-mass planet sweeping the area clear of debris. Such a feature would have important implications for the possible planet-like inhabitants of this disk and may suggest that Earth-size planets could form in an entirely new range of orbits than have ever been seen before.

The star HD 107146 is of particular interest to astronomers because it is in many ways a younger version of our own Sun. It also represents a period of transition from a solar system's early life to its more mature, final stages where planets have finished forming and have settled into their billions-of-years-long orbits around their host star.

"This system offers us the chance to study an intriguing time around a young, Sun-like star," said ALMA Deputy Director and coauthor Stuartt Corder. "We are possibly looking back in time here, back to when the Sun was about 2 percent of its current age."

The star HD 107146 is located approximately 90 light-years from Earth in the direction of the constellation Coma Berenices. It is approximately 100 million years old. Further observations with ALMA's new long baseline, high resolution capabilities will shed more light on the dynamics and composition of this intriguing object.

Additional authors on the paper include John M. Carpenter and B. Fu, Caltech; A. M. Hughes, Wesleyan University; and Andrea Isella, Rice University.

http://www.eurekalert.org/pub_releases/2014-12/uos-rbe121114.php

Rapid bird evolution after the age of dinosaurs unprecedented, study confirms

The most ambitious genetic study ever undertaken on bird evolution has found that almost all modern birds diversified after the dinosaurs became extinct 66 million years ago.

"The popular view until now has been that the extraordinary diversity of birds began during the dinosaur age but we found little support for this," said Associate Professor Simon Ho, from the University of Sydney who led a major component of the research looking at evolutionary timescale.

An international collaboration of scientists worked for four years to sequence, assemble and compare the full genomes of 48 bird species representing all major branches of modern birds. It is the largest whole genomic study across a single vertebrate class ever undertaken.

Their results appear in a special edition of Science on 12 December (with simultaneous publications of related articles in other high profile journals).

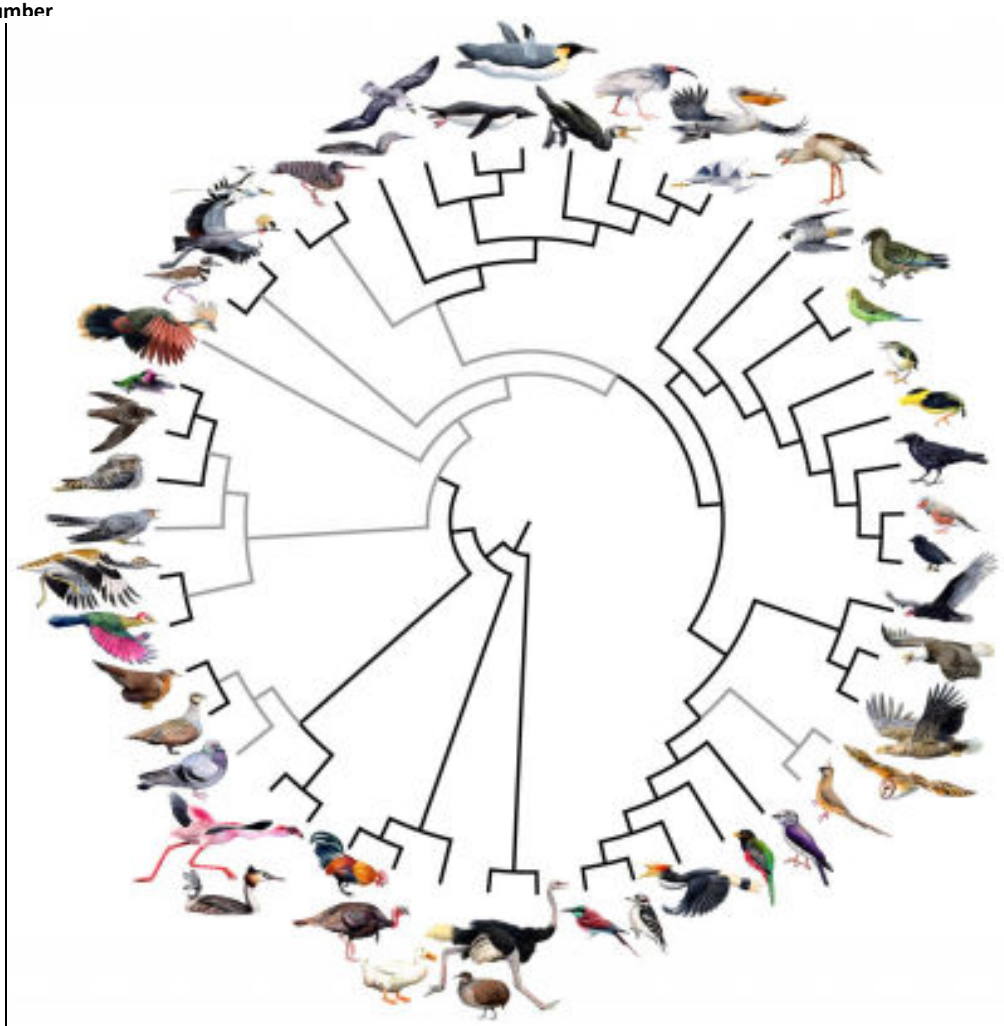
Associate Professor Ho, from the University's School of Biological Sciences, is an author on a Science paper and two articles in GigaScience. He contributed his expertise in using a technique known as 'molecular clock' analysis to estimate birds' evolutionary timescales, using genome data and fossil evidence.

His research helped confirm that some of the first lineages of modern birds appeared about 100 million years ago but that almost all of the modern groups of birds diversified in a small window of less than 10 million years, just after the dinosaurs were wiped out by an asteroid.

"Our team had to develop a range of new methods to handle the largest bird data set ever assembled. These required the equivalent of more than 400 years of computing power across nine supercomputers," said Associate Professor Ho.

"The team was able to work out the relationships among the major groups of modern birds, showing that our previous understanding of birds had been clouded by the appearance of similar traits and habits in distantly related groups. "So while grebes and cormorants are both waterbirds with webbed feet that dive to catch their prey they are, despite these similarities, from completely distinct lineages."

Another significant finding is that the ancestor of most of the land birds we see today is probably an apex predator that gave rise to raptors, eagles, owls and falcons in rapid succession before leading to land birds such as songbirds and woodpeckers. "With the demise of the dinosaurs, birds and mammals were able to become more diverse and to occupy all of the niches that had previously been dominated by dinosaurs," said Associate Professor Simon Ho.



The Avian Phylogenomics Consortium's work over four years has brought together more than 200 scientists to better understand the evolution of birds. **Jon Fjelds**

"This was one of the most significant episodes in the history of life on earth and it is tremendously exciting that this major scientific international effort has made these advances in our understanding," said Associate Professor Simon Ho.

Professor Eddie Holmes from the University of Sydney's School of Biological Sciences and Associate Professor Jaime Gongora and his research team from the Faculty of Veterinary Science also contributed to the international project and are authors on papers in Science and accompanying journals.

http://www.eurekalert.org/pub_releases/2014-12/epfd-rdp121114.php

Researchers detect possible signal from dark matter

EPFL scientists have picked up an atypical photon emission in X-rays coming from space, and say it could be evidence for the existence of a particle of dark matter.

Could there finally be tangible evidence for the existence of dark matter in the Universe? After sifting through reams of X-ray data, scientists in EPFL's Laboratory of Particle Physics and Cosmology (LPPC) and Leiden University believe they could have identified the signal of a particle of dark matter. This substance, which up to now has been purely hypothetical, is run by none of the standard models of physics other than through the gravitational force. Their research will be published next week in Physical Review Letters.

When physicists study the dynamics of galaxies and the movement of stars, they are confronted with a mystery. If they only take visible matter into account, their equations simply don't add up: the elements that can be observed are not sufficient to explain the rotation of objects and the existing gravitational forces. There is something missing. From this they deduced that there must be an invisible kind of matter that does not interact with light, but does, as a whole, interact by means of the gravitational force. Called "dark matter", this substance appears to make up at least 80% of the Universe.

Andromeda and Perseus revisited

Two groups have recently announced that they have detected the much sought after signal. One of them, led by EPFL scientists Oleg Ruchayskiy and Alexey Boyarsky, also a professor at Leiden University in the Netherlands, found it by analyzing X-rays emitted by two celestial objects - the Perseus galaxy cluster and the Andromeda galaxy. After having collected thousands of signals from the ESA's XMM-Newton telescope and eliminated all those coming from known particles and atoms, they detected an anomaly that, even considering the possibility of instrument or measurement error, caught their attention.

The signal appears in the X-ray spectrum as a weak, atypical photon emission that could not be attributed to any known form of matter. Above all, "the signal's distribution within the galaxy corresponds exactly to what we were expecting with dark matter, that is, concentrated and intense in the center of objects and weaker and diffuse on the edges," explains Ruchayskiy. "With the goal of verifying our findings, we then looked at data from our own galaxy, the Milky Way, and made the same observations," says Boyarsky.

A new era

The signal comes from a very rare event in the Universe: a photon emitted due to the destruction of a hypothetical particle, possibly a "sterile neutrino". If the discovery is confirmed, it will open up new avenues of research in particle physics. Apart from that, "It could usher in a new era in astronomy," says Ruchayskiy. "Confirmation of this discovery may lead to construction of new telescopes specially designed for studying the signals from dark matter particles", adds Boyarsky. "We will know where to look in order to trace dark structures in space and will be able to reconstruct how the Universe has formed."

These results are the outcome of a study conducted by EPFL's Laboratory of Particle Physics and Cosmology (LPPC), in collaboration with the Institute of Physics at Leiden University in the Netherlands. A video is available here: http://youtu.be/aogKkzESbgs

http://www.eurekalert.org/pub_releases/2014-12/bmj-sst121014.php

Study supports the theory that men are idiots

Sex differences in risk seeking behaviour, emergency hospital admissions, and mortality are well documented.

Males are more likely to be admitted to an emergency department after accidential injuries, more likely to be admitted with a sporting injury, and more likely to be involved in a fatal road traffic collision.

However, little is known about sex differences in idiotic risk taking behaviour. So researchers in north east England decided to test "male idiot theory" (MIT) that many of the differences in risk seeking behaviour may be explained by the observation that men are idiots and idiots do stupid things.

They reviewed data on idiotic behaviours demonstrated by winners of the Darwin Award over a 20 year period (1995 to 2014), noting the sex of the winner. To qualify, nominees must improve the gene pool by eliminating themselves from the human race using astonishingly stupid methods.

Worthy candidates include a man stealing a ride home by hitching a shopping trolley to the back of a train, only to be dragged two miles to his death before the train was able to stop; and the terrorist who posted a letter bomb with insufficient postage stamps and who, on its return, unthinkingly opened his own letter.

Of the 413 Darwin Award nominations, 332 were independently verified and confirmed by the Darwin Awards Committee. Of these, 14 were shared by male and female nominees - usually overly adventurous couples in compromising positions - leaving 318 valid cases for statistical testing.

Of these 318 cases, 282 Darwin Awards were awarded to males, and just 36 awards given to females. Males thus made up 88.7% of Darwin Award winners, and this sex difference is highly statistically significant, say the authors.

This finding is entirely consistent with male idiot theory (MIT) and supports the hypothesis that men are idiots and idiots do stupid things. However, this study has limitations, add the authors. For example, women may be more likely to nominate

men for a Darwin Award or the sex difference may reflect differences in alcohol use between men and women.

Despite this, it is puzzling that males are willing to take such unnecessary risks - simply as a rite of passage, in pursuit of male social esteem, or solely in exchange for "bragging rights," say the authors.

They believe male idiot theory deserves further investigation, and, "with the festive season upon us, we intend to follow up with observational field studies and an experimental study - males and females, with and without alcohol - in a semi-naturalistic Christmas party setting," they conclude.

http://www.eurekalert.org/pub_releases/2014-12/cp-anp120514.php

Affluence, not political complexity, explains the rise of moralizing world religions

Emergence of world religions was triggered by the rising standards of living in the great civilizations

The ascetic and moralizing movements that spawned the world's major religious traditions--Buddhism, Islam, Judaism, Hinduism, and Christianity--all arose around the same time in three different regions, and researchers reporting in the Cell Press journal Current Biology on December 11 have now devised a statistical model based on history and human psychology that helps to explain why. The emergence of world religions, they say, was triggered by the rising standards of living in the great civilizations of Eurasia.

"One implication is that world religions and secular spiritualities probably share more than we think," says Nicolas Baumard of the Ecole Normale Supérieure in Paris. "Beyond very different doctrines, they probably all tap into the same reward systems [in the human brain]."

It seems almost self-evident today that religion is on the side of spiritual and moral concerns, but that was not always so, Baumard explains. In hunter-gatherer societies and early chiefdoms, for instance, religious tradition focused on rituals, sacrificial offerings, and taboos designed to ward off misfortune and evil.

That changed between 500 BCE and 300 BCE--a time known as the "Axial Age"--when new doctrines appeared in three places in Eurasia. "These doctrines all emphasized the value of 'personal transcendence,'" the researchers write, "the notion that human existence has a purpose, distinct from material success, that lies in a moral existence and the control of one's own material desires, through moderation (in food, sex, ambition, etc.), asceticism (fasting, abstinence, detachment), and compassion (helping, suffering with others)."

While many scholars have argued that large-scale societies are possible and function better because of moralizing religion, Baumard and his colleagues weren't so sure. After all, he says, some of "the most successful ancient empires all had strikingly non-moral high gods." Think of Egypt, the Roman Empire, the Aztecs, the Incas, and the Mayans.

In the new study, the researchers tested various theories to explain the history in a new way by combining statistical modeling on very long-term quantitative series with psychological theories based on experimental approaches. They found that affluence--which they refer to as "energy capture"--best explains what is known of the religious history, not political complexity or population size. Their Energy Capture model shows a sharp transition toward moralizing religions when individuals were provided with 20,000 kcal/day, a level of affluence suggesting that people were generally safe, with roofs over their heads and plenty of food to eat, both in the present time and into the foreseeable future.

"This seems very basic to us today, but this peace of mind was totally new at the time," Baumard says. "Humans living in tribal societies or even archaic empires often experience famine and diseases, and they live in very rudimentary houses. By contrast, the high increase in population and urbanization rate in the Axial Age suggests that, for certain people, things started to get much better."

The researchers say that this transition is consistent with a shift from "fast" life strategies, focused on the immediate problems of the day, to those focused on long-term investments. They say that it will now be interesting to test whether other familiar characteristics of modern human society, such as high parental investment and long-term monogamy, might stem from the same historical change.

Current Biology, Baumard et al.: "Increased Affluence Explains the Emergence of Ascetic Wisdoms and Moralizing Religions"

http://www.eurekalert.org/pub_releases/2014-12/uoc--srg120514.php

Scientists reconstruct genome of common ancestor of crocodiles, birds, dinosaurs

Crocodiles found to have 1 of the most slowly evolving genomes, whereas the pace of genetic change has been much faster in birds

Crocodiles are the closest living relatives of the birds, sharing a common ancestor that lived around 240 million years ago and also gave rise to the dinosaurs. A new study of crocodilian genomes led by scientists at UC Santa Cruz reveals an exceptionally slow rate of genome evolution in the crocodilians (a group that includes crocodiles, caimans, alligators, and gharials).

The UC Santa Cruz team used the crocodilian genomes, combined with newly published bird genomes, to reconstruct a partial genome of the common ancestor of crocodiles, birds, and dinosaurs. The study, part of an ambitious international collaboration to analyze the genomes of modern birds and gain insights into their

evolution, is one of eight papers from the Avian Phylogenomics Consortium being published in a December 12 special issue of Science.

Richard E. (Ed) Green, lead author of the crocodilian genome paper and an assistant professor of biomolecular engineering at UC Santa Cruz, said the slow evolutionary rate in the crocodilian lineage was helpful in reconstructing the genome of the common ancestor. "The ticking of the molecular clock in the crocodilians is much slower than in other lineages we're used to looking at, like mammals, which means we can see back into their past more cleanly," Green said.

The reconstructed genome of the common ancestor will be a valuable tool for investigating the evolution of the "archosaurs," the group that includes all dinosaurs, pterosaurs, birds, and crocodilians. (Crocodilians are actually more closely related to birds and dinosaurs than they are to other reptiles, i.e., lizards, snakes, and turtles.) Green said the genome reconstruction effort, led by UC Santa Cruz research specialist Benedict Paten, yielded about half of the genome sequence of the common ancestor with an accuracy of about 91 percent, and he expects that to improve as more data on bird and crocodile genomes become available.

The team sequenced the genomes of three crocodilian species: the American alligator, the saltwater crocodile, and the Indian gharial. Their analysis indicates that the ancestor of all archosaurs probably had an extremely slow rate of molecular evolution, and that the rate of change sped up in the bird lineage. The rate of molecular evolution of crocodilians is an order of magnitude slower than that of mammals. The most likely reason for this relates to the relatively long time between generations in crocodilians, Green said.

"When it takes longer to get from one generation to the next, you expect the evolutionary rate to be slower, and big animals tend to have long generation times," he said. "We know from fossils that the body plan of crocs has remained largely unchanged for millions of years. Mammals, however, if you go back 50 or 60 million years there were no big mammals, so we see a faster rate of evolutionary change."

The slow rate of genome evolution in crocodilians also enabled the researchers to probe population sizes further into the past than is possible for faster evolving lineages, he said. They found that crocodile and gharial populations experienced sharp declines during the most recent ice age. Alligators, which inhabit more temperate latitudes than other crocodilians, showed a continuous decline in population throughout the Pleistocene epoch.

"Big-bodied, cold-blooded reptiles would have found the Earth a more hospitable place during warm periods like the Pliocene, and the cooling trend of the Pleistocene must have been bad news for crocodilians," Green said.

The new genome sequences are powerful tools for research on the fundamental biology of crocodiles and alligators, he said. Green is particularly interested in understanding the molecular basis of temperature-dependent sex determination in alligators (temperature rather than genetics determines whether a developing alligator becomes male or female). "There are a lot of questions about the evolutionary and molecular biology of crocodilians that we can now start to answer using genomics," he said.

The crocodilian genomes were also useful for the avian phylogenetic analyses, serving as a closely related "out group" for comparison with the bird genomes. Green and several other UC Santa Cruz researchers are coauthors of two articles on avian genomics that accompany the crocodile genomics paper in Science.

After the mass extinction that wiped out the dinosaurs 66 million years ago, the birds that survived experienced a rapid burst of evolution. As a result of this rapid diversification, the family tree of modern birds has confused biologists for centuries. The new genomics studies are helping to sort out those relationships and reveal the molecular details of how birds arrived at their spectacular biodiversity of more than 10,000 living species.

Coauthor David Haussler, professor of biomolecular engineering and director of the Genomics Institute at UC Santa Cruz, said the Avian Phylogenomics Project represents a significant step toward the vision of the Genome 10K Project (G10K) that he cofounded in 2009 with the goal of sequencing and analyzing the genomes of 10,000 vertebrate species. The G10K consortium helped organize the large international, interdisciplinary collaboration involved in carrying out this massive project.

Haussler and the other G10K leaders--Stephen O'Brien of St. Petersburg State University (Russia) and Oliver Ryder of the San Diego Zoo Institute for Conservation Research--published a commentary on the Avian Phylogenomics Project in the journal GigaScience, noting that the project has yielded "the most extensive comparative genomics analysis produced for any vertebrate group so far." In addition to the eight papers in Science, the project's initial findings are being reported in 15 other papers in Genome Biology, GigaScience, and other journals.

"G10K's contributions include a lot of work convincing people to work together, setting up collaborations, and holding meetings to get people to share ideas and get to know each other. In the end, of course, credit for this most recent work goes to the scientists most closely involved in the actual sequencing and analysis," Haussler said.

The Avian Phylogenomics Consortium is led by Guojie Zhang of the National Genebank at BGI in China and the University of Copenhagen, Erich D. Jarvis of Duke University and the

Howard Hughes Medical Institute, and M. Thomas P. Gilbert of the Natural History Museum of Denmark. Contributors to the crocodilian genomics paper include 54 scientists at dozens of institutions. The crocodilian research was supported by the National Science Foundation, and Green has funding from a Searle Scholarship and a Sloan Fellowship.

http://www.eurekalert.org/pub_releases/2014-12/eofr-maf121214.php

Male and female breast cancers are not identical

Results of the EORTC10085/TBCRC/BIG/NABCG International Male Breast Cancer Program

Results of the EORTC10085/TBCRC/BIG/NABCG International Male Breast Cancer Program conducted in both Europe and in the United States and presented at the 2014 San Antonio Breast Cancer Symposium found significant improvement in survival for men with breast cancer, but this improvement was not as good as that observed for women. The study, which included 1822 men treated for breast cancer between 1990 and 2010, provides much needed information about the clinical and biological characteristics of male breast cancer.

Dr. Fatima Cardoso of the Champalimaud Clinical Center in Lisbon and coordinator of this study says, "This study aims to characterize the biology of this rare disease; only with this crucial knowledge will men with breast cancer be properly treated in the future, which will definitely improve both their survival and quality of life".

Of all cancers diagnosed in males, breast cancer accounts for less than one percent, and male breast cancer also accounts for less than one percent of all breast cancer diagnoses. There are, however, African countries reporting a high incidence of male breast cancer, and these include Uganda, 5%, and Zambia, 15%.

Nevertheless, even though it is considered a rare disease, male breast cancer remains frequently lethal. In 2013 estimates indicated just 2,240 new cases of male breast cancer in the United States yet, alarmingly, 410 deaths.

Today, male breast cancer is not well understood, and the best way to treat this disease is not yet known. Currently, treatment strategies for men afflicted with this disease are based on those that have been used successfully for women, and research on the differences between men and women regarding the characteristics of this disease was sorely needed. Only case-control and retrospective studies with small numbers of male patients with breast cancer had been performed, and previous to this study there were no available data from randomized clinical trials, a consequence of the closing of all clinical trials for this patient population due to poor accrual.

Fortunately, the collaborative research strategy whereby the EORTC, Translational Breast Cancer Research Consortium (TBCRC), Breast International Group (BIG), and the North American Breast Cancer Groups (NABCG) have joined forces to launch this International Program on Male Breast Cancer, has provided a practical approach to learn more about this rare yet deadly form of cancer. The results of this study point out that male breast cancers are not identical to female breast cancers, and that men are not as well managed as female patients. For example, although the majority of male breast cancers are estrogen receptor (ER) positive, only 77 percent of male patients with this disease received hormonal therapy such as Tamoxifen, and despite the fact that slightly over half of all male breast cancers are diagnosed when the tumors are very small, only four percent of male breast cancer patients received breast-conserving surgery. The majority underwent mastectomies, a treatment decisions that can adversely affect quality of life, self-esteem and sexuality.

Analyses of tumor samples conducted as part of this study showed that 99 percent of male breast cancers were ER positive, seven percent were human epidermal growth factor receptor 2 (HER2) positive, and one percent were triple negative, meaning that they do not express the genes for ER, progesterone receptor (PR), or HER-2, and consequently do not respond to hormonal therapy nor anti-HER-2 therapies. For women, on the other hand, roughly 70 percent of breast cancers are ER-positive, 20 percent are HER2-positive, and 10 to 15 percent are triple-negative.

Additional findings were that grade 2 invasive ductal carcinomas were the most common histological type, and male breast cancers are usually androgen receptor positive, and of luminal A- like subtype (7% HER2 positive & 1% TNBC).

Overall, adjuvant radiotherapy appears to have been delivered properly, and anthracyclines were preferred as adjuvant chemotherapy and Tamoxifen for hormonal therapy following loco-regional treatment.

The second part of this male breast cancer program is now open: a prospective international registry of all male breast cancer patients treated at the participating institutions for a period of 30 months with collection of clinical data. Here, the number of patients who could be feasibly recruited for a future clinical trial will be evaluated, patterns of care will be described, and prospective sample collection will be performed in selected countries. A Quality of Life sub study is also ongoing, using the EORTC QLQ-30 questionnaire and items from the BR-23 and PR-25 questionnaires.

Discussions are already ongoing, for the opening of a prospective randomized clinical trial, as the first project of the third part of the International Male Breast Cancer Program.

The EORTC 10085 Male BC intergroup study is a fully academic study supported by the Breast Cancer Research Foundation, the EORTC Breast Cancer Group, the Dutch Pink

Ribbon, the EBCC Council, the Swedish Breast Cancer Association (BRO), and the Susan G. Komen For the Cure.

http://www.eurekalert.org/pub_releases/2014-12/ip-paf121214.php

Patient awakes from post-traumatic minimally conscious state after administration of depressant drug

First reported incidence and possible implications published in Restorative Neurology and Neuroscience

Amsterdam, NL - A patient who had suffered a traumatic brain injury unexpectedly recovered full consciousness after the administration of midazolam, a mild depressant drug of the GABA A agonists family. This resulted in the first recorded case of an "awakening" from a minimally-conscious state (MCS) using this therapy. Although similar awakenings have been reported using other drugs, this dramatic result was unanticipated. It is reported in Restorative Neurology and Neuroscience.

Traumatic brain injuries occur at high rates all over the world, estimated at 150-250 cases per 100,000 population per year. These injuries can result in several outcomes, ranging from vegetative state, minimally conscious state, severe disability to full recovery. In most cases, the outcome will cause catastrophic changes for his/her family and a significant drain on both human and financial resources.

Two years after the injury caused by a motor vehicle accident, the patient was mildly sedated, in order to undergo a CT scan, using midazolam instead of the more commonly used propofol. As the authors described in the article, the patient began to interact with the anesthetist and soon after with his parents. He talked by cellphone with his aunt and congratulated his brother when he was informed of his graduation; he recognized the road leading to his home. When he was asked about his car accident, he did not remember anything and apparently he was not aware of his condition. This clinical status lasted about two hours after drug administration and disappeared quickly thereafter, taking the patient back to the previous condition.

To further investigate this phenomenon, the researchers collected extensive EEG scans before, during, and after administration of midazolam. Using sophisticated data analysis, they were able to show the locations within the brain where the drug induced changes and followed the onset and the decline of the effects.

They noted that the patient could have also been diagnosed with the classic symptoms of catatonia, based on the similarity of the EEG sometimes observed in that pathology. Catatonia can be a manifestation of a non-convulsive status epilepticus (NCSE). The authors were thus faced with a two-fold mystery: Is this a case of catatonia mimicking a case of MCS or does the MCS, as a syndrome in itself, also include elements of a catatonic nature? Do the relative contributions of MCS versus catatonia in the individual patient determine whether or not he/she will respond to GABA A agonist drugs?

Maria Chiara Carboncini, MD, Medical Director of the Brain Injury Unit, Department of Neuroscience, University Hospital of Pisa and Adjunct Professor, University of Pisa, Italy, states, "Considering the MCS from this point of view could pave the way to new perspectives for both therapy and clinical management: at least a part of MCS patients could in fact benefit from treatment with non-selective GABA A agonists...." She also notes that as a practical consequence, "such patients should be tested not only with GABA A selective drugs like zolpidem, but also with GABA A non-selective drugs like benzodiazepines."

http://bit.ly/1GocIgj

2,400-Year-Old Coffin's 'Odd' Art Hints at Ancient Egypt's Brain Drain

An ancient Egyptian coffin with strange and amateurish decorations has been revealed, shedding light on a tumultuous period in Egyptian history when the Persian Empire was in control of the region.

by Owen Jarus, Live Science Contributor

A funerary scene from a 2,400-year-old Egyptian coffin. **Photo copyright: Mike Sigler**

TORONTO - In 525 B.C., Persian King Cambyses marched into Memphis, the Egyptian capital, inaugurating a period of Persian rule that would last for more than a century. The Persian Empire was a vast entity that stretched from modern-day Afghanistan to the west coast of Turkey. Ancient texts say that the Persian kings deported Egyptian artists and used them for building projects in Persia.

The coffin bears a series of unusual features that are likely related to the Persian Empire's deportation of artists. [See photos of the ancient Egyptian coffin]

"Many of the best artists in Egypt were taken by the Persians back to Persepolis and Susa as POWs and war booty — you can see their work in those places. There seems to have been a dearth of masters for some time, so that fewer and fewer artists got proper training," Gayle Gibson, an Egyptologist and educator at Toronto's Royal Ontario Museum, told Live Science in an email.

Gibson presented the coffin at the Society for the Study of Egyptian Antiquities Scholars' Colloquium, which was held Nov. 13 to 16 in Toronto.

Odd features

There are several odd features on the coffin that reflect the lack of knowledge the ancient artist had, Gibson said.

For instance, the deceased is depicted lying on a funerary bed, and the bed has a human-headed bird called a Ba. Flying over the deceased is a winged snake wearing a crown associated with the goddess Hathor. Below them are four jars bearing the heads of the four Sons of Horus, but the jars have a "goofy" appearance, Gibson said.

To an Egyptologist, this is a bizarre scene, Gibson said. "This is the only funerary bed I know of with a Ba's head," she told the Toronto audience, also noting that "we have a winged snake with Hathor's crown — very odd."

There are other oddities. The collar wrapped around the top of the coffin contains two creatures that look almost fishlike. The artist was likely trying to draw falcons, a symbol of the god Horus, but drew them very poorly, Gibson said.

A Mehen snake, a protective deity in Egypt, is also poorly drawn and actually stops at one point and starts in another, something strange for a protective deity. "The artist doesn't really understand the purpose of the Mehen snake," Gibson said. [Image Gallery: Egypt's Great Terrace of God]

Mike Sigler, a collector and Egyptian antiquities enthusiast who lives in Kentucky and now owns the coffin, sent a picture to Live Science showing that the ancient artist clumsily attempted to correct an error in an alternating pattern by scratching out an image of a scepter.

Ancient brain drain

Although there is no longer a mummy in the coffin, its inscriptions say that it belonged to someone named Denit-ast, or Dent-ast, likely a woman. Radiocarbon dating of her coffin indicates that she lived at a time when her country was under Persian control.

Ancient texts tell tales of the deportation of Egyptian artists to Persia during this time. Diodorus Siculus, who died around 30 B.C., said that Cambyses, the conqueror of Egypt, transferred both precious metals and artists from Egypt to Persia.

Additionally, Persian King Darius I bragged about the Egyptian artists he acquired in a text describing the construction of his palace at Susa. "The goldsmiths who wrought the gold, those were Mede and Egyptians. The men who wrought the wood, those were Sardians and Egyptians … the men who adorned the wall, those were Medes and Egyptians" Darius said (translation by Roland Kent).

Authentication

Gibson told the Toronto audience that when she first showed the coffin to other Egyptologists, some expressed skepticism and wondered if it was a fake created before Sigler owned it.

However, radiocarbon dating places the coffin in the Persian period and analysis of its wood indicates that it's sycamore, a wood that was commonly used in ancient Egypt. Additionally, an analysis of the coffin's blue pigments found that the pigment was Egyptian blue, which indicates that the coffin is authentic, Gibson said.

Sigler purchased the coffin in August 2013 from the Edgar L. Owen gallery, which sold it on behalf of a private collector. Paperwork that Sigler received indicates that the collector acquired it from the European art market in 1980. Its history before that is unknown.

Gibson is well-known for her Egyptological work. In the 1990s she helped identify a mummy in Niagara Falls, Canada, as likely being that of pharaoh Ramesses I. The mummy was later returned to Egypt with full military honors. Given Gibson's reputation, Sigler sought her out and asked her for help in understanding the coffin's strange features.

Despite its odd features, Gibson believes the coffin is not a fake. "I think there is really no doubt that this one is genuine," she said.

Sigler told Live Science that he hopes to find other examples of the coffin's unusual imagery. He said that he is interested in donating the coffin to a museum in the future.

The pigment and wood analysis was carried out by Microscopist William Randle while radiocarbon dating was conducted at the University of Georgia's Center for Applied Isotope Studies.

http://bit.ly/135LA6D

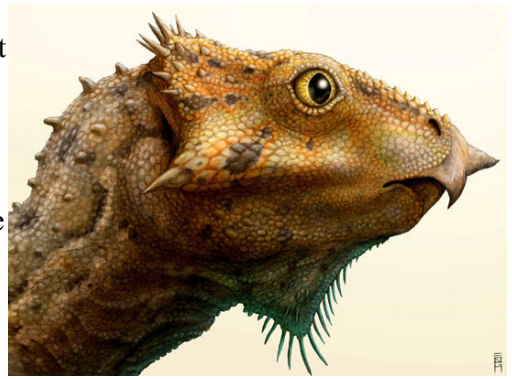
Aquilops Americanus – Oldest Species of North American Horned Dinosaur

A team of paleontologists has discovered the oldest "horned" dinosaur fossil from North America.

Named Aquilops americanus, the species is 40 million years older than the iconic Triceratops. A fossil skull small enough to fit in the palm of your hand represents the oldest species of horned dinosaur named from North America. The discovery, announced by a multi-institution team including the Raymond M. Alf Museum of Paleontology at The Webb Schools, is 40 million years older than the iconic Triceratops.

The new dinosaur is named Aquilops americanus, meaning "American eagle face." The name refers to the hook-like beak at the front of the skull, used to snip plants

during feeding. It lived around 108 million years ago, in what is now southern Montana. Aquilops (pronounced "uh-QUILL-ops") was about the size of a rabbit, weighing around 3.5 pounds and measuring around 2 feet in total length. It belongs to a group called ceratopsians, better known as horned dinosaurs. Unlike its famous relatives, such as Triceratops, Aquilops lacked horns and a bony neck frill. The animal is nearly 20 million years older than the previous oldest horned dinosaur named from North America.



"Aquilops is the first fossil to show what the earliest horned dinosaurs in North America looked like," said paleontologist Andrew Farke, Augustyn Family Curator at the Alf Museum and lead author on the scientific study. Farke continued, "Scattered teeth and bones from around the same time showed us that these animals were here, but not much else was known."

Aquilops Americanus Oldest Horned North American Dinosaur

Surprisingly, Aquilops turns out to be more closely related to ceratopsians from Asia than to other ceratopsians from North America. This is consistent with evidence from other animals, including carnivorous dinosaurs as well as early mammals, showing an immigration of species from Asia into North America sometime between 115 and 105 million years ago.

The fossils of Aquilops, including a partial skull and lower jaw, was found on an expedition led by Richard Cifelli, curator of vertebrate paleontology at the Sam Noble Oklahoma Museum of Natural History, Norman, Oklahoma, and the original fossil is housed there. Fieldwork was funded by a National Geographic Society Committee for Research and Exploration grant. Other researchers who co-authored the study included Desmond Maxwell (University of the Pacific) and Mathew Wedel (Western University of Health Sciences).

Publication: Andrew A. Farke, et al., "A Ceratopsian Dinosaur from the Lower Cretaceous of Western North America, and the Biogeography of Neoceratopsia," PLOS One, December 10, 2014; DOI: 10.1371/journal.pone.0112055

http://bit.ly/1AyBp5T

Massive volcanic eruptions set the stage for dinosaurs' demise

Deccan Traps spewed over a million cubic kilometers of rock just before impact.

by John Timmer - Dec 13 2014, 3:02am TST

It's now widely accepted that the impact of an asteroid at Chicxulub in Mexico's Yucatan region finished off any dinosaurs that we don't currently refer to as birds, while triggering a mass extinction that wiped out a lot of other species. But that hasn't ended the debate regarding the dynamics of the extinction event, with other ecological influences getting consideration as contributing to the dinosaurs' vulnerability.

One potential contributor that's hard to overlook is situated in western India: the Deccan Traps. These enormous deposits are built of layer upon layer of volcanic rock, suggesting a series of flood eruptions took place over thousands of years. These eruptions happened suspiciously close to the start of the mass extinction—close enough that some researchers argued that it was the eruptions that killed off the dinosaurs. There was, after all, precedent; the eruptions that formed the Siberian Traps have been blamed for a mass extinction that was so severe, it's known as the The Great Dying.

To help settle the issue, an international team of researchers has gone back and obtained the most precise dates for the eruptions yet. The dates show that the eruptions started nearly a quarter-million years before the onset of the mass extinction but continued for roughly 750,000 years, meaning they spanned the extinction event. This supports the idea that the eruptions helped set the stage for the end of the dinosaurs.

The dating techniques used in the work—uranium-lead dating of zircons—is pretty standard. But it's really the technical challenges of getting it right in multiple samples from a massive eruption that stand out. It was easy to find zircons and get dates from them, but a number of reasons to expect those dates wouldn't be very precise.

First, the researchers had to ensure that the zircons had formed in the magma involved in the eruptions rather than forming earlier and being included in them. This was handled by visually examining the crystals, which could eliminate non-volcanic zircons. But even then, some of the crystals seem to have taken an extended time to form, as the authors obtained a range of dates from their samples. So the authors looked at the presence of other elements in the sample, finding a set of zircons that had the same chemical signature and thus likely formed in the same magma.

To add an additional layer of control, the authors used the fact that each layer of rock must have erupted after the layers it was sitting on top of. So once dates were obtained, the researchers ordered them by rock layer and ran the whole stack through an analysis that discarded any dates that were out of order.

The authors conclude that it took 750,000 years to put about 80-90 percent of the rock that was ultimately erupted in place. That's a long time, but the Deccan Traps consist of at least 1.1 million cubic kilometers of rock, so that number still represents a pretty staggering series of eruptions. The dates also place the start of

the eruptions at 250,000 years prior to the mass extinction event at the Cretaceous-Paleogene boundary.

The start of the eruptions clearly didn't trigger the mass extinction. But a variety of ecological disruptions are apparent in the fossil record leading up to the mass extinction, and it's clear that the Deccan Traps eruptions could have contributed to these disruptions. The duration of the events also means that the eruptions could have been ongoing even as the Chicxulub impact occurred, which really provides just about any species out there a great excuse for dying.

Science, 2014. DOI: 10.1126/science.aaa0118

http://bit.ly/1wS6unS

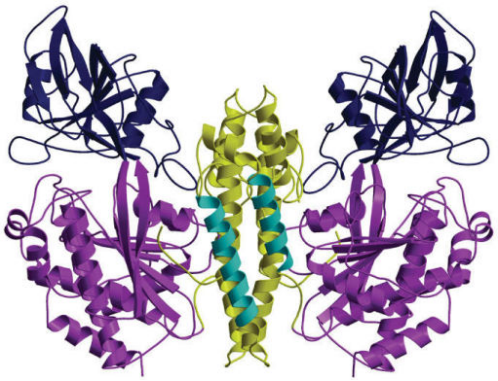
Yarr! Humans evolving to escape from bacterial iron piracy

An evolutionary arms race keeps humans and bacteria right where they started.

by Diana Gitig - Dec 13 2014, 10:15pm TST

Bacteria, like all living things, need iron for a variety of biochemical functions. Humans and other higher order organisms have plenty of iron; we limit bacterial access to it as a means of defending against bacterial infection. So when we need to transfer iron throughout our bodies, we keep it tightly sequestered in a protein called transferrin.

In order to infect us, bacterial pathogens must try to wrest that iron away; they have specialized transferrin binding proteins (Tbps) to do just that. Recent work demonstrates that transferrin "is engaged in ancient and ongoing evolutionary conflicts" with one of these Tbps, TbpA.



Transferrin, and the iron it carries, are brought inside human cells by this receptor. **NIH**

By comparing the genetic sequence of transferrin across twenty-one different primate species, researchers found that transferrin has undergone positive evolutionary selection in a manner often seen in molecular arms races between mammals and viruses. Fourteen of the sixteen rapidly evolving sites identified in transferrin are in amino acids that form direct contact with TbpA from bacterial all-stars like Neisseria meningitidis, which causes meningitis; Neisseria gonorrhoeae, which causes gonorrhea; and Haemophilus influenzae, which can cause pneumonia.

TbpA from these bugs can bind transferrin from humans and gorillas, but not from our next closest relatives the chimpanzees. Since the transferrin to which a given bacteria's Tbp can bind—and therefore, from which it can swipe a valuable iron molecule—is thought to dictate its host range, it seems plausible that positive selection in primate transferrin was mediated by interactions with an early form of this Tbp.

There are two common versions of the human transferrin gene—a major allele and a minor allele—which differ at a single nucleotide. Each creates a functional protein, with no discernible difference in their ability to bind iron. The more common variant (the major allele) has the same nucleotide in this position as chimpanzees, squirrel monkeys, and dusky titi monkeys. The less common variant (the minor allele) is found in between six and twenty-six percent of the human population, depending on geography. It has the same nucleotide in this position as Siamong gibbons, olive baboons, colobus monkeys, Spinx's tamarins, and night monkeys.

TbpA from Haemophilus influenzae was not able to bind the minor allele nearly as well as it bound the major allele; if this less common variant provides protection from infection, that could explain why it is still around. TbpA from Neisseria meningitidis and Neisseria gonorrhoeae could bind to both of these alleles of transferrin equally strongly, but neither could stick as strongly as Haemophilus influenzae's TbpA. So TbpA could be under positive selection too; different versions may balancing their affinity for one particular transferrin against the ability to bind a number of different transferrins.

Alice Liddell first encounters the Red Queen in Chapter 2 of Through the Looking Glass. Alice tries to catch her, but although they each run faster and faster, neither of them ever gets anywhere. They must run and run just to stay where they are. The evolutionary biologist Leigh Van Valen was thus inspired to call his theory of evolutionary arms races the Red Queen hypothesis; predator and prey, or host and pathogen, always co-evolve in tandem so neither one ever gets ahead of the other. Bacterial TbpA mutates to try to snatch the iron from primate transferrin, and transferrin mutates to teasingly hold the iron out of TbpA's reach. On and on. Neither one keeps the upper hand for long; everyone keeps evolving but ends up staying right where they are.

Science, 2014. DOI: 10.1126/science.1259329