http://www.eurekalert.org/pub_releases/2014-12/vcu-pia122914.php

Protein ID'd as possible universal therapeutic target for many infections, including Ebola

Conditions include Ebola, influenza, hepatitis and brain cancer

A protein called GRP78 could be a universal therapeutic target for treating human diseases like brain cancer, Ebola, Influenza, Hepatitis and superbug bacteria such as MRSE and MRSA, according to a Virginia Commonwealth University-led pre-clinical study published this month in the Journal of Cellular Physiology.

By using a drug combination of the clinically tested OSU-03012 (AR-12) and FDA approved Phosphodiesterase 5 Inhibitors (Viagra, Cialis) to target GRP78 and related proteins, researchers prevented the replication of a variety of major viruses in infected cells, made antibiotic-resistant bacteria vulnerable to common antibiotics and found evidence that brain cancer stem cells were killed.

Data were obtained in multiple brain cancer stem cell types, and using Influenza, Mumps, Measles, Rubella, RSV, CMV, Adenovirus, Coxsakie virus, Chikungunya, Ebola, Hepatitis, E. coli, MRSA, MRSE and N. gonorrhoeae, among others.

"Basically, we've got a concept that by attacking GRP78 and related proteins: (a) we hurt cancer cells; (b) we inhibit the ability of viruses to infect and to reproduce; and (c) we are able to kill superbug antibiotic-resistant bacteria," said the study's lead investigator, Paul Dent, Ph.D., Professor in the Department of Biochemistry and Molecular Biology at VCU School of Medicine, and Universal Chair for Signal Transduction.

GRP78 is part of a family of proteins called chaperones. The job of a chaperone is to help shape chains of amino acids into proteins and then to keep those proteins active in the correct 3D shape. The OSU/Viagra drug combination attacks GRP78 and other chaperones, thereby killing cancer cells. After learning of the drug combination's effect on GRP78 in cancer cells, Dent and his team began to target GRP78 for infectious diseases such as viruses and bacteria.

The chaperone proteins are very important in cancer cells or virus infected cells because these cells make extra protein compared to normal / uninfected cells. The team found that the OSU/Viagra drug combination reduced infectivity via reduced viral receptor expression on the surface of target cells and the prevention of virus replication in infected cells.

The drug combination was able to reduce expression of viral receptors for Ebola, Marburg, Hepatitis A, B and C, and Lassa fever viruses. In cancer cells the drug combination reduced the expression of oncogene receptors, too. In bacteria, the drug combination reduced expression of the equivalent GRP78 protein, in bacteria called Dna K, and induced cell death in pan-antibiotic resistant forms of E. coli, MRSE, MRSA and N. gonorrhoeae.

"The findings open an avenue of being able to treat viral infections, infections that certainly most people would say we'll never be able to treat; they prove that GRP78 is a "drugable" target to stop viruses from reproducing and spreading," Dent said. "And in the case of bacteria, we have a new antibiotic target, Dna K, that if we're careful and only use the OSU drug in hospitals, we've got something that can help to treat the superbugs."

Dent said that the next steps have already been taken and are leading to new discoveries: "we know in mice that the OSU/Viagra treatment can kill tumor cells but doesn't harm normal tissues like the liver and the heart. Of even more importance we've just discovered that the OSU/Viagra combination can reduce the levels of proteins called "pumps" in the mouse brain. Pumps are responsible for making tumor cells resistant to chemotherapy and for stopping life-saving brain cancer chemotherapy from entering into the brain and killing cancer."

VCU researchers previously have found Viagra drug combinations to be beneficial in many ways. In 2010, for example, Rakesh Kukreja, Ph.D., scientific director of the VCU Pauley Heart Center and the Eric Lipman professor in cardiology in the VCU School of Medicine, in collaboration with Dent, found that Viagra improved the effectiveness of the breast cancer treatment Doxorubicin while protecting the heart from harm caused by the chemotherapy. In 2013 and 2014 Dr. Dent obtained similar data with Viagra and conventional chemotherapy in bladder, pancreatic and pediatric brain cancer cells. Based on work from Dent's group, in the spring of 2015 a new phase I clinical trial will open at VCU Massey Cancer Center combining the colon cancer drug regorafenib with Viagra for all solid tumor patients.

The work undertaken to arrive at the current findings was made possible by support from the VCU Massey Cancer Center and, in part, by grants from the National Institutes of Health.

The full article is available online

http://www.eurekalert.org/pub_releases/2014-12/ggph-aca122914.php

American cities are many times brighter than German counterparts

German cities emit several times less light per capita than comparably sized American cities

German cities emit several times less light per capita than comparably sized American cities, according to a recent publication in the journal Remote Sensing. The size of the gap grew with city size, as light per capita increased with city size in the USA but decreased with city size in Germany. The study also examined

regional differences, and surprisingly found that light emission per capita was higher in cities in the former East of Germany than from those in the former West. The lead author, Dr. Christopher Kyba, studies visible light at night as a member of the Remote Sensing section of the German Research Center for Geosciences (GFZ). "The size of the difference in light emission is surprisingly large. This work will allow us to identify comparable cities in order to uncover the reasons behind the differences." These could include differences in the type of lamps, but also architectural factors like the width of the streets and the amount of trees. The LED lamps currently being installed in many cities are expected to greatly change the nighttime environment, for example by reducing the amount of light that shines upwards.

A main point of the study is to emphasize the great improvement in the quality of nighttime imagery of Earth since 2012. The European Space Agency's NightPod instrument has allowed astronauts to take high resolution images of individual cities. In addition, the entire world is now imaged nightly at 750 meter resolution by the Visible Infrared Imaging Radiometer Suite Day-Night Band onboard the Suomi National Polar-Orbiting Program weather satellite. This new imagery has made it possible to identify and measure the output of individual bright sources of light pollution for the first time. The study found that in Megacities in developing countries, the brightest light sources were typically airports or harbors. In contrast, the brightest areas in the capital cities of Europe are often associated with leisure, for example stadiums and city centers.

While artificial light at night is a problem for astronomers and nocturnal animals, it has the potential to be an important tool in understanding human activity. In order to make the most use out of it, the researchers say they will need to study urban light emissions in detail, including their spectrum, the directions in which light is emitted, and changes in light use and lit area over time.

The study demonstrated one practical use of the new data: since maps of nighttime light emission highlight the areas where light pollution is especially prevalent, they provide information about which areas can best be targeted for energy savings. Coauthor Dr. Franz Hölker from the Leibniz Institute for Freshwater Ecology and Inland Fisheries (IGB) explains, "artificial light is responsible for a sizable portion of all nighttime electricity consumption. Identifying areas where light could be more efficiently used will make it possible to save energy, reduce costs, and reduce the impact of artificial light on the nighttime environment."

Kyba, C.C.M., Garz, S., Kuechly, H., Sánchez de Miguel, A., Zamorano, J., Hölker, F., (2015) „High-resolution imagery of Earth at Night: new sources, opportunities, and challenges." Remote Sensing. 2015, 7(1), 1-23; doi:10.3390/rs70100001

The study was performed at the Leibniz Institute of Freshwater Ecology and Inland Fisheries, the Free University of Berlin, and the Universidad Complutense de Madrid.

http://www.eurekalert.org/pub_releases/2014-12/msu-tcc122914.php

Thanking customers can reap rewards

A sincere, well-timed "thank you" can reap huge rewards

EAST LANSING, Mich. - Companies rarely acknowledge customers who fill out those ubiquitous satisfaction surveys. But a sincere, well-timed "thank you" can reap huge rewards, finds first-of-its-kind research led by a Michigan State University marketing scholar.

According to the study, which focused on an upscale sit-down restaurant, satisfied customers who received an acknowledgement of their comments from the company president increased patronage to the business by more than 50 percent. The simple gesture of thanking customers was just as effective - and less damaging to the company's bottom line - as acknowledgements that included rewards in the form of gift cards and guaranteed reservations. "Sweetening the pot with rewards really didn't matter," said Clay Voorhees, MSU associate professor of marketing and lead author of the study. "These findings suggest that simple, sincere gestures are enough to drive feelings of gratitude among consumers."

Voorhees and his fellow researchers tracked patrons' attitudes and behaviors for a year after they gave the eatery high marks. While firms routinely collect customer feedback, few act on this information. Further, little attention is given to managing feedback from highly satisfied customers.

Within a week of completing the online satisfaction survey customers were sent a thank-you email from the company president. During the next 12 months, the number of repeat visits increased 50 percent for men and 57 percent for women. "In the restaurant industry, where 5 percent is a big deal, 50 percent blew our minds," Voorhees said.

In addition, the average size of the customers' party increased significantly. "So it wasn't just that they came back," he said, "but that they came back and brought more people with them." The increase in party size was particularly striking among women, jumping a whopping 79 percent (compared to a 42 percent increase among men). The study also found that sending an immediate automated response after customers completed the survey did not provide any value to the firm. "Delaying the acknowledgement is critical to ensure it comes across as being more personal and sincere," said Voorhees.

The study is available online through the Marketing Science Institute. Co-authors include Paul Fombelle of Northeastern University, Alexis Allen of the University of Kentucky, Sterling Bone of Utah State University and Joel Aach of Consumer Insights & Brand Strategy Consulting.

http://bit.ly/1vzIaA7

Yale Study Shows Metformin May be Safe for Patients with Kidney Disease

Diabetes Drug May be Safe for Patients with Kidney Disease

A newly published study from Yale University reveals that metformin (the most popular treatment for type 2 diabetes) may be safer for patients with mild to moderate kidney disease than guidelines suggest. The new study is published by Yale investigators in the Journal of the American Medical Association (JAMA).

For 20 years, metformin has been used in the United States to lower blood sugar in people with type 2 diabetes. Most experts consider it the best first agent to treat blood sugar increases in this disease. Despite its strong safety profile, the Food and Drug Administration (FDA) has long recommended that metformin not be prescribed to patients with mild to moderate kidney disease due to the risk of lactic acidosis, a potentially serious condition. But those decades-old guidelines have recently been called into question.

Yale professor of medicine Dr. Silvio E. Inzucchi and colleagues at Yale, the University of Texas Southwestern Medical Center, and Aston University in the United Kingdom conducted a systematic review of published research to assess the risk of lactic acidosis with metformin in diabetes patients with mild to moderate kidney disease. They found that the risk in these patients is extremely low - actually comparable to the risk in those who did not take metformin.

"What we found is that there is essentially zero evidence that this is risky," said Inzucchi, who is also medical director of the Yale Diabetes Center. "The drug could be used safely, so long as kidney function is stable and not severely impaired."

The finding is key because doctors often avoid or stop prescribing metformin to older patients with diabetes who need it. "They hit a certain age, their kidney function starts to decline, and the first thing most doctors do is to stop metformin," Inzucchi said. "What invariably happens next is their diabetes goes out of control. Other drugs may be substituted, but they are usually not generic products like metformin, and so are more expensive and may also have more side effects."

The JAMA review also noted that metformin is already being routinely prescribed to patients with type 2 diabetes and kidney disease despite the guidelines. "Many in the field know that metformin can be used cautiously in patients who have mild to moderate kidney problems," Inzucchi noted. "Most specialists do this all the time."

He cautions that the review findings do not apply to individuals with severe kidney disease. Should the guidelines change, as many in the field have recommended, dosage of metformin would probably need to be reduced at a certain level of kidney function, and patients would need to be more closely monitored to make sure kidney function remains stable.

If the FDA guidelines for metformin use are updated, as Dr. Inzucchi and colleagues have recommended, the drug could be made available to more than 2.5 million Americans living with type 2 diabetes. His group has assembled more than 100 signatures from diabetes experts throughout the country to petition the FDA to update its guidelines.

Other authors include Yale's Dr. Kasia J. Lipska; Clifford J. Bailey of Aston University; and Helen Mayo and Dr. Darren K. McGuire from the University of Texas Southwestern Medical Center.

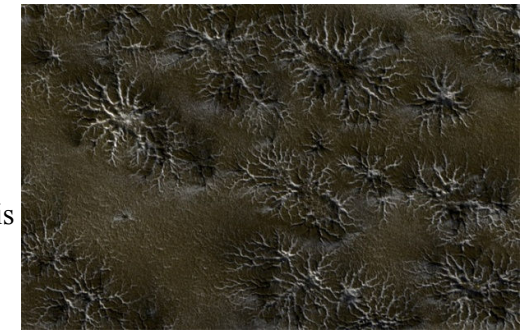
Publication: Silvio E. Inzucchi, et al., "Metformin in Patients With Type 2 Diabetes and Kidney Disease," JAMA, 2014, 312(24):2668-2675; doi:10.1001/jama.2014.15298

http://bit.ly/1tH9oLl

Mars Orbiter Spies Alien Ice 'Spiders'

The Martian surface is covered with a diverse array of landscapes and features, but this is one of the weirdest.

by Ian O'Neill



NASA/JPL-Caltech/University of Arizona

Imaged by the High-Resolution Imaging Science Experiment (HiRISE) camera on board NASA's Mars Reconnaissance Orbiter (MRO) that orbits the planet 150 miles overhead, strange spider-like formations cover this south polar region of Mars. And these are truly alien features that are found nowhere on Earth.

So what are they? Is Mars infested with arachnids? Or is it some sort of giant mold? Sadly, it's neither, it's actually a fascinating season-driven phenomena that HiRISE scientists call "araneiform" terrain.

Araneiform means, perhaps unsurprisingly, "spider-like" and the term applies to other features that have a "spider", "caterpillar" or "starburst"-like shape, according to planetary scientist Candice Hansen who described the same south pole region in an earlier HiRISE image release.

The Martian climate is so cold that even carbon dioxide will freeze from the atmosphere and accumulate as ice on the surface during winter. During spring, the carbon dioxide will sublimate back into the atmosphere as it is heated by a strengthening sun.

Carbon dioxide ice on Mars does not melt into a liquid state; it bypasses the liquid phase and sublimates straight from a solid into a vapor. This seasonal process therefore creates its own type of erosion on the Martian landscape.

"This particular example shows eroded channels filled with bright ice, in contrast to the muted red of the underlying ground," writes Hansen. "In the summer the ice will disappear into the atmosphere, and we will see just the channels of ghostly spiders carved in the surface."

Earth's atmospheric temperature does not drop as low as Mars', so carbon dioxide ice (or "dry ice") does not form naturally. Therefore, there is no terrestrial analog of these alien spider channels - it is purely a Mars phenomenon.

"This is truly Martian terrain - this type of erosion does not take place anywhere naturally on earth because our climate is too warm," adds Hansen.

Planetary scientists are therefore very interested in understanding these kinds of erosional processes; they provide us with a very privileged view into the changing seasons on the Red Planet and how very different erosional processes on an alien world continue to shape the dynamic Martian terrain.

http://bit.ly/1wIQSMJ

FBI's 2001 Anthrax Attack Probe Was Seriously Flawed

One genetic test had a 43 percent false negative rate, casting doubt on conclusions, says U.S. oversight report

By Rebecca Trager and ChemistryWorld

The scientific evidence that the US Federal Bureau of Investigation (FBI) relied upon to investigate the October 2001 anthrax attacks – and ultimately identify the culprit after his suicide – was deeply flawed, according to a new report from the congressional Government Accountability Office (GAO).

The GAO found that the FBI lacked a comprehensive approach or framework to standardize the genetic testing used to track down the culprit. It also found that each of the FBI's four contractors developed different tests and there was no statistical confidence for interpreting the results.

These genetic analyses were used to link the material found in the anthrax-laden letters to the laboratory of Bruce Ivins, a senior biodefence researcher at the US Army Medical Research Institute of Infectious Diseases. In February 2010, the FBI formally concluded that Ivins, who committed suicide in 2008, was solely responsible for the attacks.

'The lack of an understanding of how bacteria change (mutate) in their natural environment and in a laboratory is a key scientific gap that remains and could affect testing conducted in future incidents,' the GAO concluded. Specifically, the office said the significance of using such mutations as genetic markers to analyse samples to determine their origins remains unclear.

The GAO noted that the Department of Homeland Security is currently funding research on mutation in bacteria and genome sequencing methods. However, this research may not be complete for several years.

The investigation was undertaken partly because of questions raised by a National Academies study released in 2011, which determined that the FBI's scientific data did not rule out other possible sources of the weaponised anthrax spores in the letters.

The GAO also found that one of the four genetic tests the FBI used on the anthrax samples had a 43% false negative rate. 'That just really dropped my jaw, and it should be very embarrassing to the FBI that they still relied on that,' says Jim White, a now retired molecular biologist with expertise in fermentation technology and microbial growth. Two of the three other genetic tests that the FBI relied on had false negative rates in the 20% range.

The FBI issued a response saying it has 'complete confidence' in its scientific results. The agency said the genetic tests it used were 'well validated', and that it has reviewed the results of all scientific analysis conducted during the course of the investigation and is satisfied by its quality. The FBI further noted that the scientific results alone were not the sole basis for concluding that Ivins committed the attacks. But White and others argue that the information and questions that have surfaced in recent years warrant reopening the case.

Retiring congressman Rush Holt, whose New Jersey district was a target of the anthrax letters, requested the GAO study. Holt, who is set to be the next president of the American Association for the Advancement of Science, said the GAO findings confirm that the FBI's conclusions about the anthrax attacks are not definitive. Holt is quoted as saying that the US needs a 'comprehensive, independent review' of the FBI investigation to ensure that lessons have been learned.

http://bit.ly/1zYR95q

Venus Gets Weirder: CO2 Oceans May Have Covered Surface

Venus may have once possessed strange oceans of carbon dioxide fluid that helped shape the planet's surface, researchers say.

by Charles Q. Choi, Space.com

Venus is often described as Earth's twin planet because it is the world closest to Earth in size, mass, distance and chemical makeup. However, whereas Earth is a haven for life, Venus is typically described as hellish, with a crushing atmosphere and clouds of corrosive sulfuric acid floating over a rocky desert surface hot enough to melt lead.

Although Venus is currently unbearably hot and dry, it might have once had oceans like Earth. Prior research suggested that Venus possessed enough water in

its atmosphere in the past to cover the entire planet in an ocean about 80 feet deep (25 meters) - if all that water could somehow fall down as rain. But the planet was probably too warm for such water to cool down and precipitate, even if the planet did have enough moisture. Instead of seas of water, then, scientists now suggest that Venus might have once possessed bizarre oceans of carbon dioxide fluid.

Carbon dioxide is common on Venus. "Presently, the atmosphere of Venus is mostly carbon dioxide, 96.5 percent by volume," said lead study author Dima Bolmatov, a theoretical physicist at Cornell University in Ithaca, New York..

Most familiar on Earth as a greenhouse gas that traps heat, helping warm the planet, carbon dioxide is exhaled by animals and used by plants in photosynthesis. While the substance can exist as a solid, liquid and gas, past a critical point of combined temperature and pressure, carbon dioxide can enter a "supercritical" state. Such a supercritical fluid can have properties of both liquids and gases. For example, it can dissolve materials like a liquid, but flow like a gas.

To see what the effects of supercritical carbon dioxideon Venus might be, Bolmatov and his colleagues investigated the unusual properties of supercritical matter. A great deal remains uncertain about such substances, he said.

Scientists had generally thought the physical properties of supercritical fluids changed gradually with pressure and temperature.

However, in computer simulations of molecular activity, Bolmatov and his colleagues found that supercritical matter could shift dramatically from gaslike to liquidlike properties.

The atmospheric pressure on the surface of Venus is currently more than 90 times that of Earth, but in the early days of the planet, Venus' surface pressure could have been dozens of times greater. This could have lasted over a relatively long time period of 100 million to 200 million years. Under such conditions, supercritical carbon dioxide with liquidlike behavior might have formed, Bolmatov said. "This in turn makes it plausible that geological features on Venus like rift valleys, riverlike beds, and plains are the fingerprints of near-surface activity of liquidlike supercritical carbon dioxide," Bolmatov told Space.com.

The researchers found that depending on the pressure and temperature, clusters of gas-like supercritical carbon dioxide [Michael D1] might have formed in this supercritical carbon dioxide on Venus that "looked like soap bubbles," Bolmatov said. "A bubble of gas that is covered by a thick layer of liquid."

Bolmatov and his colleagues said they now hope to conduct experiments to detect this shift from gaslike to liquidlike properties in supercritical carbon dioxide. The scientists detailed their findings in the Aug. 21 issue of the Journal of Physical Chemistry Letters.

http://www.eurekalert.org/pub_releases/2014-12/e-baa122614.php

Bats are a possible source of the Ebola epidemic in West Africa

Ebola virus in West Africa may have originated from contact between humans and infected bats

HEIDELBERG - The outbreak of the Ebola virus disease occurring in West Africa may have originated from contact between humans and virus-infected bats, suggests a study led by researchers from the Robert Koch-Institute in Berlin, Germany. The report, published in EMBO Molecular Medicine, identifies insectivorous free-tailed bats as plausible reservoirs and expands the range of possible Ebola virus sources to this type of bats. The results also reveal that larger wildlife are not the source of infection.

Ebola virus disease epidemics are of zoonotic origin, transmitted to human populations either through contact with larger wildlife or by direct contact with bats. "We monitored the large mammal populations close to the index village Meliandou in south-eastern Guinea and found no evidence for a concurrent outbreak," says Fabian H. Leendertz of the Robert Koch Institute, who led the study. The second infection route appears more plausible as direct contact with bats is usual in the affected region.

Fruit bats are the commonly suspected Ebola virus reservoir as previous outbreaks in Africa show. Interviews with Meliandou locals revealed that exposure to fruit bats through hunting and consumption of meat in this area is common. Yet fruit bats seem an unlikely source of infection, as a food-borne transmission would have affected adults before or concurrently with the two-year-old boy - the index case. This suggests a source of infection unrelated to food.

Another opportunity for infection was a large colony of free-tailed insectivorous bats housed in a hollow tree nearby the home of the index case. Villagers reported that children often used to play in and around the tree. This may have resulted in a massive exposure to bats.

The multidisciplinary team of researchers led a four-week field mission in Guinea in April 2014 to examine human exposure to bats, to survey local wildlife and to capture and sample bats in Meliandou and in neighbouring forests. The index village is not located in the forest but rather in an area heavily modified by humans representing "modern" African settings.

The virus that spread from Meliandou into other areas of Guinea and Sierra Leone, Liberia, Nigeria and Senegal, represents the largest ever-recorded Ebola outbreak killing 7,800 people (as of 17 December 2014).

Investigating the Zoonotic Origin of the West African Ebola Epidemic

Almudena Marí Saéz, Sabrina Weiss, Kathrin Nowak, Vincent Lapeyre, Fee Zimmermann, Ariane Düx, Hjalmar S. Kühl, Moussa Kaba, Sebastien Regnaut, Kevin Merkel, Andreas

Sachse, Ulla Thiesen, Lili Villányi, Christophe Boesch, Piotr W. Dabrowski, Aleksandar Radoni?, Andreas Nitsche, Siv Aina J. Leendertz, Stefan Petterson, Stephan Becker, Verena Krähling, Emmanuel Couacy-Hymann, Chantal Akoua-Koffi, Natalie Weber, Lars Schaade, Jakob Fahr, Matthias Borchert, Jan F. Gogarten, Sébastien Calvignac-Spencer, Fabian H. Leendertz http://embomolmed.embopress.org/content/early/2014/12/29/emmm.201404792 *doi: 10.15252/emmm.201404792*

http://www.eurekalert.org/pub_releases/2014-12/e-mni122514.php

Molecular network identified underlying autism spectrum disorders

Molecular network identified that comprises many of the genes previously shown to contribute to autism spectrum disorders

Heidelberg - Researchers in the United States have identified a molecular network that comprises many of the genes previously shown to contribute to autism spectrum disorders. The findings provide a map of some of the crucial protein interactions that contribute to autism and will help uncover novel candidate genes for the disease. The results are published in Molecular Systems Biology.

"The study of autism disorders is extremely challenging due to the large number of clinical mutations that occur in hundreds of different human genes associated with autism," says Michael Snyder, Professor at the Stanford Center for Genomics and Personalized Medicine and the lead author of the study. "We therefore wanted to see to what extent shared molecular pathways are perturbed by the diverse set of mutations linked to autism in the hope of distilling tractable information that would benefit future studies."

The researchers generated their interactome - the whole set of interactions within a cell - using the BioGrid database of protein and genetic interactions. "We have identified a specific module within this interactome that comprises 119 proteins and which shows a very strong enrichment for autism genes," remarks Snyder. Gene expression data and genome sequencing were used to identify the protein interaction module with members strongly enriched for known autism genes. The sequencing of the genomes of 25 patients confirmed the involvement of the module in autism; the candidate genes for autism present in the module were also found in a larger group of more than 500 patients that were analyzed by exome sequencing. The expression of genes in the module was examined using the Allen Human Brain Atlas. The researchers revealed the role of the corpus callosum and oligodendrocyte cells in the brain as important contributors to autism spectrum disorders using genome sequencing, RNA sequencing, antibody staining and functional genomic evidence.

"Much of today's research on autism is focused on the study of neurons and now our study has also revealed that oligodendrocytes are also implicated in this disease," says Jingjing Li, Postdoctoral Fellow at the Stanford Center for Genomics and Personalized Medicine who helped to spearhead the work. "In the future, we need to study how the interplay between different types of brain cells or different regions of the brain contribute to this disease."

"The module we identified which is enriched in autism genes had two distinct components," says Snyder. "One of these components was expressed throughout different regions of the brain. The second component had enhanced molecular expression in the corpus callosum. Both components of the network interacted extensively with each other."

The working hypothesis of the scientists, which is consistent with other recent findings, is that disruptions in parts of the corpus callosum interfere with the circuitry that connects the two hemispheres of the brain. This likely gives rise to the different phenotypes of autism that result due to impairment of signaling between the two halves of the brain.

"Our study highlights the importance of building integrative models to study complex human diseases," says Snyder. "The use of biological networks allowed us to superimpose clinical mutations for autism onto specific disease-related pathways. This helps finding the needles in the haystack worthy of further investigation and provides a framework to uncover functional models for other diseases."

Integrated systems analysis reveals a molecular network underlying autism spectrum disorders *Jingjing Li, Minyi Shi, Zhihai Ma, Shuchun Zhao, Ghia Euskirchen, Jennifer Ziskin, Alexander Urban, Joachim Hallmayer, Michael Snyder doi: 10.15252/msb.20145487 http://dx.doi.org/10.15252/msb.20145487*

http://bit.ly/1AhyCip

New study explains how and why lung cancer spreads

Severed protein ties allow lung cancer cells to break loose and spread more easily than other types of cells

Chuck Bednar for redOrbit.com

Lung cancer cells can spread more easily than other types of cells because the protein ties that tether them together are severed, allowing them to break loose, a team of researchers from the Cancer Research UK Manchester Institute report in a new study.

Lung cancer cells can spread more easily than other types of cells because the protein ties that tether them together are severed, allowing them to break loose, a team of researchers from the Cancer Research UK Manchester Institute report in a new study.

In research published Wednesday in the journal *Cell Reports*, the study authors explained that microscopic images revealed that the ties that keep cells held

together, which are controlled by a protein known as TIAM1, are cut to pieces when cell maintenance goes wrong in cancer cells.

Typically, healthy cells routinely scrap older cell parts so that they can be broken down and reused. However, in lung cancer cells, the process spirals out of control and causes too many of the TIAM1 ties to be scrapped. Targeting this process could keep lung cancer cells from spreading by keeping them attached firmly to one another, the researchers said in their study.

"This important research shows for the first time how lung cancer cells sever ties with their neighbors and start to spread around the body, by hijacking the cells' recycling process and sending it into overdrive," said lead author Dr Angeliki Malliri from the Cancer Research UK Manchester Institute at the University of Manchester.

"Targeting this flaw could help stop lung cancer from spreading," she added.

According to the study authors, there are more than 43,000 new cases of lung cancer diagnosed in the UK each year. It is also that country's most common cause of cancer deaths, killing more than 35,000 patients annually.

"Lung cancer causes more than one in five of all cancer deaths in the UK and it's vital that we find effective new treatments to fight the disease and save more lives," said Nell Barrie, Cancer Research UK's senior science information manager.

In the US, the National Cancer Institute reports that the two main types of lung cancer (small cell lung cancer and non-small cell lung cancer) were responsible for a combined 159,260 deaths this year thus far. They also note that there have been nearly 225,000 new cases diagnosed in 2014.

"Early-stage research like this is essential to find treatments which could one day block cancer spread – which would be a game changer," she added. "It's also crucial that we find ways to diagnose the disease earlier, when treatment is more likely to be successful and the cancer is less likely to have spread."

According to International Business Times, World Health Organization statistics indicate that approximately 70 percent of all global lung cancer deaths are associated with tobacco use. Lung cancers killed a reported 1.59 million people worldwide, and the condition is difficult to treat as it can lie dormant for nearly 20 years before becoming aggressive, the publication added.

In August, researchers analyzed data from the Surveillance, Epidemiology, and End Results (SEER) program and revealed that US lung cancer rates are declining as a whole. However, they also found that lung cancer rates vary by subtype, sex, race/ethnicity and age, and reported that an estimated 90 to 95 percent of lung cancers in the US could be attributed to smoking.

http://www.eurekalert.org/pub_releases/2014-12/arrs-lcm123014.php

Lung cancer metastases may travel through airways to adjacent or distant lung tissue

A new study by researchers in Canada supports the hypothesis that lung cancer, particularly adenocarcinoma, may spread through the airways.

The putative occurrence of intrapulmonary aerogenous metastasis of lung cancer has staging, management, and prognostic implications.

Lung cancer is the most common and most lethal cancer worldwide. Its prognosis remains poor: The 5-year survival rate is 6-18%. Adenocarcinoma has surpassed squamous cell carcinoma as the leading histologic type, accounting for 30% of all cases of lung cancer. Hematogenous spread (i.e., carried by blood) is the most common mechanism of intrapulmonary metastasis. Although local venous spread can occur, systemic spread with secondary lung involvement is much more common.

"Cumulative evidence suggests that intrapulmonary aerogenous spread may exist and is underrecognized," say the authors of "Aerogenous Metastases: A Potential Game Changer in the Diagnosis and Management of Primary Lung Adenocarcinoma," published in the December 2014 issue of the American Journal of Roentgenology. "Aerogenous metastases must be differentiated from multiple synchronous lesions in the spectrum of lung adenocarcinoma, [and] imaging features are helpful in differentiating possible aerogenous spread of tumor."

http://www.eurekalert.org/pub_releases/2014-12/uor-rsn123014.php

Researchers show neutrinos can deliver not only full-on hits but also 'glancing blows'

In what they call a "weird little corner" of the already weird world of neutrinos, physicists have found evidence that these tiny particles might be involved in a surprising reaction.

Neutrinos are famous for almost never interacting. As an example, ten trillion neutrinos pass through your hand every second, and fewer than one actually interacts with any of the atoms that make up your hand. However, when neutrinos do interact with another particle, it happens at very close distances and involves a high-momentum transfer.

And yet a new paper, published in Physical Review Letters this week, shows that neutrinos sometimes can also interact with a nucleus but leave it basically untouched - inflicting no more than a "glancing blow" - resulting in a particle being created out of a vacuum.

Professor Kevin McFarland is a scientific co-spokesperson with the international MINERvA collaboration, which carries out neutrino scattering experiments at

Fermilab McFarland, who also heads up the Rochester team that was primarily responsible for the analysis of the results, compares neutrino interactions to the firing of a bullet at a bubble, only to find the bubble was left intact.

"The bubble - a carbon nucleus in the experiment - deflects the neutrino 'bullet' by creating a particle from the vacuum," McFarland explains. "This effectively shields the bubble from getting blasted apart and instead the bullet only delivers a gentle bump to the bubble."

Producing an entirely new particle - in this case a charged pion - requires much more energy than it would take to blast the nucleus apart - which is why the physicists are always surprised that the reaction happens as often as it does.

McFarland adds that even painstakingly detailed theoretical calculations for this reaction "have been all over the map."

"The production of pions from this reaction had not been observed consistently in other experiments," McFarland said. By using a new technique, they were able to measure how much momentum and energy were transferred to the carbon nucleus - showing that it remained undisturbed - and the distribution of the pions that were created.

"After analyzing the results, we now have overwhelming evidence for the process," McFarland says.

The two members of the collaboration who were primarily responsible for analyzing the results were Aaron Higuera, at the time a postdoc at Rochester and now at the University of Houston, and Aaron Mislivec, one of McFarland's Ph.D. students.

Working with Higuera, Mislivec wrote the computer code that allowed them to sift through the results and get a picture of the reaction. "Our detector gave us access to the full information of exactly what was happening in this reaction," Mislivec explains. "Our data was consistent with the unique fingerprint of this reaction and determined how these interactions happen and how often." The key to identifying the reaction was finding undisturbed carbon nuclei and then studying the two resulting particles - the pion, which is responsible for shielding the nucleus, and the muon.

Understanding this reaction, McFarland states, "is not going to make a better mousetrap, but it is exciting to learn that this weird reaction really does take place."

Researchers in the MINERvA collaboration measure low energy neutrino interactions both to support neutrino oscillation experiments and study the strong dynamics of the nucleon and nucleus that affect the interactions.

The work is funded by the Department of Energy, the National Science Foundation, and partnering scientific agencies in Brazil, Chile, Mexico, Switzerland, Peru and Russia.

http://bit.ly/1HkgaJb

Harvard coloring tech could be an attractive alternative to paint

New lightweight, low-cost coloring technology for both rough and smooth surfaces

By Ben Coxworth

Most people probably don't think of a coating of paint as being a particularly major component of a manufactured item. If the object is quite large, however, or if a lot of them are being made, paint can add considerably to its weight and/or production costs. With that in mind, researchers from Harvard University's Laboratory for Integrated Science and Engineering have created a new lightweight, low-cost coloring technology for both rough and smooth surfaces.

Developed by PhD student Mikhail Kats and his advisor Prof. Federico Capasso, the process involves using a machine known as an electron-beam evaporator to vaporize pieces of metal, by striking them with a stream of electrons. The vapor travels upwards through a vacuum chamber within the evaporator, and collects on the surface of a metallic item placed at the top (if the item *isn't* metallic, an initial base layer of vaporized metal vapor can first be applied). By repeating this process, multiple layers can be deposited on the item.

What results is an ultra-thin coating. Due to the nature in which that coating scatters reflected light, it appears to the human eye as a given color – exactly which color depends upon the metals used, and the ratios in which they're applied.

In a test of the technology, Kats coated a piece of paper with a film made up of gold and germanium. While a previous study had shown that the technique worked on smooth surfaces, this was the first time that it had been successfully applied to a rough surface.

The paper remained flexible, even after the coating was applied. Although the color appeared basically the same when viewed from different angles, the "hills and valleys" within its microstructure added some subtle variation to the light-scattering process. This caused it to have a somewhat pearlescent appearance, which could be desirable in many applications. Using a different application technique, however, the color could be made to appear completely uniform from any angle.

Although gold is an expensive metal, very little of it was required. Additionally, a number of other metals can be used, including not only germanium but also aluminum. "This is a way of coloring something with a very thin layer of material, so in principle, if it's a metal to begin with, you can just use 10 nanometers to color it, and if it's not, you can deposit a metal that's 30 nm thick and then another 10 nm," said Kats. "That's a lot thinner than a conventional paint coating that might be between a micron and 10 microns thick."

According to the university, the technology could be used to color virtually any material, including those that are rough or flexible. Additionally, because the coatings absorb a lot of light, they could find their way into optoelectronic devices such as photodetectors and solar cells.

http://bit.ly/13MC6xs

Banking Culture Encourages Dishonesty

What is it about the financial sector that encourages bad behavior?

December 30, 2014 |By Francesca Gino

Across the globe, many people and institutions suffered large costs from the 2008 financial meltdown. Among the victims is the financial sector itself - whose reputation has been questioned after scandals involving the manipulation of interest rates and fraudulent deals.

In trying to make sense of the crisis, some have pointed the fingers to individual bankers and banks, others to institutional pressures. But new research suggests that one important cause may reside elsewhere: in the banking culture itself. A paper recently published in Nature magazine found that the financial sector's culture encourages dishonesty.

This is an important finding, as it suggests that good conduct starts with having the right culture. Finance CEOs and upper management need to change cultural norms, so that they can model good behavior at all levels of banks and assure that performance incentives don't inadvertently reward dishonesty. But what, you may be wondering, is unique about banking culture? The fact that there is a lot of focus on money and number crunching.

For the study published in Nature, Alain Cohn and his colleagues divided 128 employees of a large bank into two groups. In the first group, bankers were primed to think about their professional identity, with questions such as "what is your function at this bank?" Bankers in the second group, instead, completed a survey about their wellbeing and everyday life that did not include questions about to their professional life.

Next they all tossed a virtual coin 10 times, in private, knowing each time which outcome would earn them $20 for the flip. They then had to report their results online to claim any winnings. The second group of bankers behaved honestly - reporting half heads, half tails - but there was cheating among those whose professional identity had been primed.

In their case, in fact, the percentage of winning tosses came in at an incredibly fortunate 58.2 percent. Interestingly, the researchers also conducted the same experiment in other industries but did not find the same skewing when employees were primed to think about their work.

The authors conclude that the prevailing business culture in the banking industry weakens and undermines honesty. Research in moral psychology and behavioral ethics, however, suggests that the dishonesty may be due something more basic: money and number crunching are an important part of the banking industry.

When people are focused on money, research shows, they behave in self-interested ways.

Even thinking about money leads people to be less helpful and fair in their dealings with others, to be less sensitive to social rejection, and to work harder toward personal goals. In fact, money can make us so focused on our selfish motives that it can even lead to unethical behavior. In my own research, for instance, I find that university students were more likely to cheat after seeing 7,000 dollar bills than after seeing 24. Similarly, study participants across a variety of studies were more likely to cheat when they were primed to think about money.

The banking industry is not only about money: it also involves a lot of number crunching. And, research suggests, even basic math calculations increase people's likelihood of engaging in selfish and unethical behavior. Research by Long Wang (City University of Hong Kong) Chen-Bo Zhong (University of Toronto), and J. Keith Murnighan (Northwestern University) finds that number crunching put people in a "calculative mindset" that makes them more likely to focus on a quantitative approach to solving a problem, overlooking a decision's moral consequences. This narrowly focused "crunch the numbers" approach, they show, has unintended consequences in the way that organizations approach decision-making.

After engaging in a calculative task, participants in their experiments were more likely to succumb to the temptations of higher payoffs by acting more selfishly or dishonestly. Thus, the mere act of calculating can activate a calculative mindset that crowds out moral concerns.

Together, this body of work may seem very discouraging. After all, money is ubiquitous in our daily lives, and number crunching is very prominent in our Western culture's psyche. But money is not the only ubiquitous resource. Another one is time. Benjamin Frank once said that "time is money," thus suggesting that the two resources are equal. Yet, we treat them differently. Whereas money is a self-serving resource, time is an interpersonally connecting and more personally meaningful resource. For instance, research by Cassie Mogilner and Jennifer Aaker shows that people induced to think about time, rather than money, are more likely to choose to spend time with loved ones over work obligations. Additionally, time is used in more intimate situations than money: people use money in transactions with everyone from close friends to

perfect strangers, but they use time almost exclusively for the people and things that really matter to who they are. Thinking about time triggers greater self-reflection than money. Such self-reflection may be a simple exercise, but it is an important one: it reminds us of that we want to be good people.

In my own research, I find that thinking about time encourage people to reflect on who they are, making them more conscious of how they conduct themselves. Given that people desire to see themselves as good people, triggers that encourage them to reflect on who they are affect their behavior.

Priming people to think about time, rather than money, lead to less selfish and more ethical behavior. For instance, in one study, half of the study participants completed a series of task while sitting in a cubicle with a mirror on their desk. Participants who had been primed to think about money cheated 39 percent of the time when a mirror was present but 67 percent when it was not. Those who had been primed to think about time cheated 32% of the time in the presence of the mirror and 36 percent in its absence - a percentage that is statistically the same. In this study, the mirror triggered self-reflection.

This made a difference for those participants thinking about money: they behaved more honestly. But for those participants thinking about time, it was the time prime who triggered self-reflection and thus the mirror was unnecessary.

The French author and philosopher Albert Camus once said, “Man is the only creature that refuses to be what he really is.” Having the strong desire to be a good person is important, but it may not be enough to assure our actions reflect such desire. By recognizing the pervasive effects money can have, we can be more mindful of our actions, and we can make sure we have opportunities in our busy lives to stop and reflect - to make time to think about time.

Francesca Gino is a behavioral scientist and professor of Business Administration at Harvard Business School. She is the author of “Sidetracked: Why Our Decisions Get Derailed, and How We Can Stick to the Plan.”

http://www.eurekalert.org/pub_releases/2014-12/uom-cwa123014.php

Children with autism who live with pets are more assertive

Dogs, cats and other animals may improve social skills of children with autism

COLUMBIA, Mo. - Dogs and other pets play an important role in individuals' social lives, and they can act as catalysts for social interaction, previous research has shown. Although much media attention has focused on how dogs can improve the social skills of children with autism, a University of Missouri researcher recently found that children with autism have stronger social skills when any kind of pet lived in the home.

"When I compared the social skills of children with autism who lived with dogs to those who did not, the children with dogs appeared to have greater social skills," said Gretchen Carlisle, research fellow at the Research Center for Human-Animal Interaction (ReCHAI) in the MU College of Veterinary Medicine. "More significantly, however, the data revealed that children with any kind of pet in the home reported being more likely to engage in behaviors such as introducing themselves, asking for information or responding to other people's questions. These kinds of social skills typically are difficult for kids with autism, but this study showed children's assertiveness was greater if they lived with a pet."

Pets often serve as "social lubricants," Carlisle said. When pets are present in social settings or a classroom, children talk and engage more with one another. This effect also seems to apply to children with autism and could account for their increased assertiveness when the children are living in a home with pets, Carlisle said.

"When children with disabilities take their service dogs out in public, other kids stop and engage," Carlisle said. "Kids with autism don't always readily engage with others, but if there's a pet in the home that the child is bonded with and a visitor starts asking about the pet, the child may be more likely to respond."

Carlisle also found that children's social skills increased the longer a family had owned a dog, yet older children rated their relationships with their dogs as weaker. When children were asked, they reported the strongest attachments to smaller dogs, Carlisle found.

"Finding children with autism to be more strongly bonded to smaller dogs, and parents reporting strong attachments between their children and other pets, such as rabbits or cats, serves as evidence that other types of pets could benefit children with autism as well," Carlisle said.

Carlisle surveyed 70 families who had children with autism between the ages of 8 and 18.The children were patients at the MU Thompson Center for Autism and Neurodevelopmental Disorders. Almost 70 percent of the families that participated had dogs, and about half of the families had cats. Other pets owned by participants included fish, farm animals, rodents, rabbits, reptiles, a bird and even one spider.

"Dogs are good for some kids with autism but might not be the best option for every child," Carlisle said. "Kids with autism are highly individual and unique, so some other animals may provide just as much benefit as dogs. Though parents may assume having dogs are best to help their children, my data show greater social skills for children with autism who live in homes with any type of pet."

"The Social Skills and Attachment to Dogs of Children with Autism Spectrum Disorder" was published in the Journal of Autism and Developmental Disorders. Sigma Theta Tau-Alpha Iota provided funding for the project.

http://bit.ly/1EUeSqF

Masculine-sounding lawyers less likely to win in court

Men masculine voices are less likely to win a US Supreme Court case than their more gentle-sounding peers

15:00 30 December 2014 by Andy Coghlan

In the adversarial, macho environment of the courtroom, a booming voice might seem like a good trait for a lawyer to cultivate. Not so - men who sound very masculine are actually less likely to win a US Supreme Court case than their more gentle-sounding peers.

It's well known that the sound of our voice shapes how people perceive us, which in turn may affect how successful we are in various walks of life. Men, for example, are more likely to vote for men with deeper, masculine voices in leadership contests, and both men and women prefer women with a more masculine tone as leaders. CEOs with deeper voices tend to manage larger companies and earn more money.

To explore whether the vocal characteristics of male lawyers affect trial outcomes, a team led by linguist Alan Yu of the University of Chicago and legal theorist Daniel Chen of ETH Zurich in Switzerland collected 60 recordings of male lawyers in the Supreme Court making the traditional opening statement: "Mister Chief Justice, may it please the court". Then 200 volunteers rated these clips for how masculine they thought the speaker was, as well as how attractive, confident, intelligent, trustworthy and educated they perceived the voice to be.

Bias in the court

After accounting for the age and experience of the lawyers, statistical analysis showed that only one of the traits could predict the court outcome. Lawyers rated as speaking with less-masculine voices were more likely to win. "It was a surprise to all of us," says Yu, whose results will be presented at the annual meeting of the Linguistic Society of America in Portland, Oregon, in January.

Although legal systems are based on the principle of fair, objective trials, we know that obscure factors, such as whether the judge has eaten recently, can bias a case. Yu's results suggest that the masculinity of the voice is another source of bias, but why remains a mystery.

Yu now wants to explore whether the perceived likelihood of winning affects how lawyers speak. "Lawyers who think they're going to lose may project a different kind of voice, perhaps overcompensating by sounding more masculine" says Yu, who is keen to stress that the findings are just the beginning of wider project looking at the impact of voice and gender in the courts.

If there is a genuine bias, it could be hard to overcome. "You could have legal writings without oral arguments, but that's not a feasible change," says Casey Klofstad, a political scientist at the University of Miami who carried out the studies on how voice affects voting preference. "The only way around it is to make people aware of the bias, and hope they are mindful of it when listening".

http://bit.ly/1zHHfQL

What Rare Disorder Is Hiding in Your DNA?

As comprehensive genetic tests become more widespread, patients and experts mull how to deal with unexpected findings

Dec 16, 2014 |By Dina Fine Maron

Last spring Laura Murphy, then 28 years old, went to a doctor to find out if a harmless flap of skin she had always had on the back of her neck was caused by a genetic mutation. Once upon a time, maybe five years ago, physicians would have focused on just that one question. But today doctors tend to run tests that pick up mutations underlying a range of hereditary conditions. Murphy learned not only that a genetic defect was indeed responsible for the flap but also that she had another inherited genetic mutation.

This one predisposed her to long QT syndrome, a condition that dramatically increases the risk of sudden cardiac death. In people with the syndrome, anything that startles them - say, a scary movie or an alarm clock waking them from a deep slumber - might kill by causing the heart to beat completely erratically.

Doctors call this second, unexpected result an “incidental finding” because it emerged during a test primarily meant to look for something else. The finding was not accidental, because the laboratory was scouring certain genes for abnormalities, but it was unexpected.

Murphy, whose name was changed for this story, will most likely have plenty of company very soon. The growing use of comprehensive genetic tests in clinics and hospitals practically guarantees an increasing number of incidental discoveries in coming years. Meanwhile the technical ability to find these mutations has rapidly outpaced scientists’ understanding of how doctors and patients should respond to the surprise results.

Unknown Unknowns

Incidental findings from various medical tests have long bedeviled physicians and their patients. They appear in about a third of all CT scans, for example. A scan of the heart might reveal odd shadows in nearby lung tissue. Further investigation of the unexpected results - either through exploratory surgery or yet more tests - carries its own risks, not to mention triggering intense anxiety in the patient. Follow-up exams many times reveal that the shadow reflects nothing at all - just normal variation with no health consequences.

What makes incidental findings from genetic tests different, however, is their even greater level of uncertainty. Geneticists still do not know enough about how

most mutations in the human genome affect the body to reliably recommend any treatments or other actions based simply on their existence. Furthermore, even if the potential effects are known, the mutation may require some input from the environment before it will cause its bad effects.

Thus, the presence of the gene does not necessarily mean that it will do damage. Genetics is not destiny.

In Murphy's case, her mutation means that she has a roughly 50 to 80 percent chance of developing long QT syndrome, and the presence of the mutation alone is not a sure indicator she will be afflicted, says her physician, Jim Evans, a genetics and medicine professor at the University of North Carolina School of Medicine. To be safe, he has advised her to meet with a cardiac specialist to talk about next steps, including possibly starting beta-blocker drugs to regularize her heart rate.

The incidence of hard-to-interpret results is expected to rise because the cost of surveying large swaths of the genome has dropped so low - to around $1,000. It is typically less expensive to get preselected information about the 20,000 or so genes that make up a person's exome - the section of the genome that provides instructions for making proteins - than to perform a more precision-oriented test that targets a single gene.

As a consequence, scientists and policy makers are now scrambling to set up guidelines for how much information from such testing to share with patients and for how best to help them deal with the inevitable incidental findings.

Before making any definitive recommendations, however, they need to know how often genetic results produce such findings. To that end, Evans is heading up the NCGENES clinical trial, part of a larger effort by three organizations, including the University of North Carolina School of Medicine.

Of the roughly 300 patients who have received genetic information since Evans started ordering whole exome tests a couple of years ago, he says, six of them (or 2 percent) had incidental findings that required further testing or decisions about treatment.

Separately, Christine Eng, medical director of the DNA Diagnostic Laboratory at the Baylor College of Medicine, says her team has conducted more than 2,000 whole exome tests since October 2011 with about 95 incidental findings. “That's an incidence of about 5 percent,” she notes. Most of the findings did not require immediate action. Usually they prompt more frequent screening tests, often for breast cancer or colorectal cancer.

Balancing Act

In the hope of minimizing the number of people forced to cope with incidental findings, the American College of Medical Genetics and Genomics (ACMG) in 2013 proposed regularly returning results on 56 genes from comprehensive genetic tests.

The professional group felt that there was enough - though by no means conclusive - information about these specific mutations to merit letting patients know if they had tested positive for them. In other words, the mutations “met a standard of relatively high likelihood of being disease-causing.”

The list included genetic variants that have been strongly linked to retinoblastoma (cancer of the eye), hereditary breast cancer and long QT syndrome. The ACMG believed that its guidance would give physicians a shortcut so they would not need to haphazardly guess which mutations had a strong enough link to a given malady to tell patients about the results.

Such advice is particularly important given how often children undergo genetic tests nowadays. “About 80 percent of our cases are pediatric-aged, so the incidental findings are being found in the children, and many of the conditions are adult-onset conditions,” Eng says. Families given such information about their children then may have to wait decades before they can do anything about it or decide when, if ever, to start considering treatment for a disorder that may not ever develop.

Yet a year after issuing its guidance, the ACMG produced an addendum: patients should have the opportunity to opt out of having information about even that short list of analyzed genes. “When families are given a choice, a very large percentage of them want this information, but there are some individuals who feel they do not want this information, so I think this option is a good one,” says Eng, who was not on that decision-making board.

For her part, Murphy is still grappling with how to respond to her incidental finding. She is not yet 30, and she finds it hard to imagine being young and carefree and on beta blockers. “Generally, I'm a very healthy person. I was doing just fine until now, so why does it matter that I found this out?” she asks. “I've been giving it a lot of thought, and if I hadn't gotten [the test] done, I might never have known about this. Now I'm wondering if I really want a lifestyle change. It's a lot to think about.”

Yet the hope is that Murphy's experience, and those of other patients, will help geneticists decide which tests to include in future gene scans and better prepare patients and health care workers for dealing with any unwelcome surprises.

The Best Gene Screen

Information about most rare genetic mutations is so uncertain as to be meaningless. As a result, geneticists recommend testing only for genes that clearly increase the risk of developing certain conditions. A list of these ailments and their associated genes appears below.

Cancers and Precancerous Conditions

Familial adenomatous polyposis - APC
Familial medullary thyroid cancer - RET
Hereditary breast and ovarian cancer - BRCA1, BRCA2
Li-Fraumeni syndrome - TP53
Lynch syndrome - MLH1, MSH2, MSH6, PMS2
Multiple endocrine neoplasia type 1 - MEN1
Multiple endocrine neoplasia type 2 - RET
MYH-associated polyposis and related conditions - MUTYH
Peutz-Jeghers syndrome - STK11
PTEN hamartoma tumor syndrome - PTEN
Retinoblastoma - RB1
Von Hippel–Lindau syndrome - VHL
WT1-related Wilms tumor - WT1

Heart and Vascular Disorders

Arrhythmogenic right ventricular cardiomyopathy - PKP2, DSP, DSC2, TMEM43, DSG2
Certain other cardiomyopathies - MYBPC3, MYH7, TNNT2, TNNI3, TPM1, MYL3, ACTC1, PRKAG2, GLA, MYL2, LMNA
Catecholaminergic polymorphic ventricular tachycardia - RYR2
Ehlers-Danlos syndrome (vascular type) - COL3A1
Long QT syndromes and Brugada syndrome - KCNQ1, KCNH2, SCN5A
Marfan syndrome and related conditions - FBN1, TGFBR1, TGFBR2, SMAD3, ACTA2, MYLK, MYH11

Noncancerous growths

Hereditary paraganglioma-pheochromocytoma syndrome - SDHD, SDHAF2, SDHC, SDHB
Neurofibromatosis type 2 - NF2
Tuberous sclerosis complex - TSC1, TSC2

Other

Familial hypercholesterolemia - LDLR, APOB, PCSK9
Malignant hyperthermia susceptibility - RYR1, CACNA1S

http://bit.ly/177ukAw

How to See This Green Comet With the Naked Eye

The "New Year's Comet" is taking astronomers by storm with an unexpected showing, and it should only get brighter through early January

By Victoria Jaggard

Terry Lovejoy is one hardworking comet hunter. The amateur astronomer based in Australia has been discovering new comets since 2007, and is perhaps most famous for first spotting the icy body known as C/2011 W3 - aka, the Great Christmas Comet of 2011. That comet roared to life as it made a close pass by the sun in late December, becoming almost as bright as the planet Venus and putting on stunning displays for sky-watchers in the Southern Hemisphere.

Now Lovejoy is at it again, and his latest find - formally known as C/2014 Q2 - has already been dubbed the New Year's Comet of 2014. (As with his past discoveries, C/2014 Q2 is also being called Comet Lovejoy.)

The New Year's Comet is getting brighter as it moves closer to the sun, because the increased heat is causing its ices to vaporize and release gases and dust, forming a brilliant hazy head and a faint, spiky tail. Astronomers originally predicted that Comet Lovejoy wouldn't get bright enough to be visible to naked eyes. But in a holiday surprise, the comet's glow has been rapidly intensifying, and it is now easily visible with binoculars even from urban areas, where light pollution makes all but the brightest stars difficult to spot.

In rural places where the skies are clear and very dark, viewers should now be able to see Comet Lovejoy without any optical aids - look for a green fuzzball a bit below the "belt" of the constellation Orion. The comet appears green because it is releasing cyanogen gas and a type of carbon gas, which both fluoresce when exposed to sunlight.

Lovejoy discovered C/2014 Q2 comet in August, and astronomers around the world have been tracking its movements since then. Gareth Williams at the Harvard-Smithsonian Center for Astrophysics even found the comet in archived pictures taken before its discovery and used them to help track its orbit. He calculates that the comet will get closest to the sun on January 18, passing within 120 million miles of the solar surface. But it will pass closest to Earth on January 7, getting within 43 million miles. For context, our nearest planetary neighbor, Venus, is 25 million miles away on average.

Astronomer David Levy famously quipped that comets are like cats, "they have tails, and they do precisely what they want." He was referring to the notorious difficulty of predicting what a comet will do as it nears the sun. If Lovejoy keeps brightening at the same rate, it should put on its best show in the weeks after the close approach to Earth. In mid-January the full moon will be waning, reducing glare in the night sky and making the comet easier to see. According to Sky & Telescope, observers in the Northern Hemisphere should watch for the comet as it passes through the constellations Taurus and Aries, skirting southeast of the Pleiades star cluster.

The comet is traveling on a very elongated elliptical orbit, which means it swings far out into the depths of the solar system and only rarely visits our neighborhood. Its route suggests that this Comet Lovejoy has been here before, probably last passing near the sun about 11,200 years ago. As it heads away from Earth in February, the gravitational pull of other objects it passes will drain some of its

orbital energy, shortening the comet's path. But we still won't see it again for at least another 8,000 years, astronomers predict. Here's hoping Terry Lovejoy finds yet more cometary wonders for us to admire in the meantime.

http://bbc.in/1AmuaAa

Nasa to hack Mars rover Opportunity to fix 'amnesia' fault

Mars rover Opportunity, which has been exploring the Red Planet for more than 10 years, is suffering from memory problems, Nasa has said.

The six-wheeled vehicle - not to be confused with Curiosity, which launched in 2011 - keeps resetting unexpectedly. The Opportunity team thinks an age-related fault affecting the flash memory used by the robot is to blame. It believes it has found a way to hack the rover's software to disregard the faulty part. Speaking to Discovery News, Nasa project manager John Callas outlined how his team intended to solve the issue.

'It forgets'

He explained how the rover, like a typical computer, has two key types of memory - volatile and non-volatile.

Non-volatile memory "remembers" its information even if it is powered down, making it ideal for long-term storage, similar to how a hard drive works on a PC

Volatile memory - comparable to a PC's random access memory, or RAM - is quicker to access but requires power, so when the machine turns off, any data stored within the volatile memory is lost

The problem with Opportunity is that its non-volatile memory is suffering from a fault, probably related to the hardware's age. It means that when the rover tries to save telemetry data to the flash memory it fails, and so it then writes it to the volatile memory instead. When the rover powers down, the information is then wiped. "So now we're having these events we call 'amnesia,'," explained Mr Callas in Discovery News. "Which is the rover trying to use the flash memory, but it wasn't able to, so instead it uses the RAM... it stores telemetry data in that volatile memory, but when the rover goes to sleep and wakes up again, all [the data] is gone. "So that's why we call it amnesia - it forgets what it has done."

Old rover

The problems are becoming more severe, Nasa says, with the memory issue causing the rover reset itself, and in some cases stop communicating with mission control altogether. In an attempt to solve the problem, the Nasa team is attempting to "hack" the rover's software so that it ignores the faulty part of its flash memory, and instead writes, permanently, to the healthy hardware.

The process will take a couple of weeks, Mr Callas told Discovery News. However, he added that Opportunity is ageing and could be heading towards the end of its useful life.

"It's like you have an aging parent, that is otherwise in good health - maybe they go for a little jog every day, play tennis each day - but you never know, they could have a massive stroke right in the middle of the night," he said.

"So we're always cautious that something could happen."

Even if the rover fails now, it will have comfortably exceeded the initial goal of spending three months on the Red Planet. Ten years after it first landed, Opportunity has covered 26 miles (41.8km) of the Mars surface, and sent back vital intelligence about the planet's biological make-up.

http://bit.ly/1AmuXkI

High and dry? Party drug could target excess drinking

A patent has been filed for a drug that produces some of ecstasy's euphoric effects – and seems to put the brakes on boozing

31 December 2014 by Michael Slezak

THINKING of taking a break from the booze? Many of us drink more than we probably should and wish we were better able to control our intake. Several drugs now in development could help us do just that.

In 2012, alcohol played a part in 3.3 million deaths worldwide. Awareness campaigns and prevention services have done little to reduce the amount that people drink overall, and consumption has remained steady or increased around the world. The scale of the problem has led people, including David Nutt, a psychopharmacologist at Imperial College London, to want to try a different approach.

Last month, a patent application was filed for a drug that is supposed to give people a pleasant intoxication as well as limit the amount they drink.

In an unlikely marriage, the compound was created by the drug designer behind mephedrone, a now widely banned substance that has caused at least one death and been implicated in 13 others in the UK. The man, who has asked to be referred to by his pseudonym, Dr Z, initially intended his creation to be sold as a legal high. But after having discussions with Nutt and trying it on himself, he now plans to gift the patent to Nutt's charitable research group DrugScience, in the hope it will be used as a "binge mitigation agent".

How it might finally be used will depend on the results of detailed testing – including how quickly it is absorbed and how it mixes with alcohol. But it might become something you'd take at the start of a night out, or perhaps even add to each drink.

Nutt and Dr Z have called the new drug "chaperon". Its less catchy name is MEAI or 5-methoxy-2-aminoindane. Structurally, it is closely related to two drugs you can buy as a legal high in some places – MDAI and MMAI. Both were invented

by David Nichols from Purdue University in West Lafayette, Indiana, and have some of ecstasy's euphoric effects.

Unpredictable effects

Nichols says chaperon also looks a bit like another drug, PMA, which is known to be highly toxic. And therein lies the risk: "There really is no good way to predict biological activity in a completely novel structure," he says. What it does to the brain is also hard to predict because small tweaks to a molecule can result in big changes to the neurotransmitters and pathways it acts on.

So far no lab tests have been done on the substance, but Dr Z and about 40 other people have tried it. One of those people was me (see "A night on chaperon").

According to Dr Z, there have been no serious problems, although one person didn't enjoy the experience. Several others said it made them feel euphoric.

The effects varied, but some of the experimenters reportedly lost the desire to drink. The effect didn't kick in immediately. The longest delay was 2 hours, and it took 5 hours before I felt like holding back on the booze – although this may have been because I took a very small dose to start with. This isn't necessarily a problem, says Dr Z, as long as people know that in advance so they don't keep taking it while waiting for it to work. However, he is concerned that the effect is so much like ecstasy: "Maybe the drug is too good?"

Nutt doesn't think chaperon's ability to induce euphoria is necessarily an obstacle. There are other drugs that help people with alcohol problems to drink less or that act as a less harmful substitute – including some that Nutt is involved with (see "The alcohol fighters"). But most cultures around the world use drugs for pleasure, so a drug like chaperon could be a "win-win" situation, he says, acting both as a binge mitigator and providing some of its desirable effects.

But "you need scientific tests", says Nutt. "Anecdotal evidence isn't enough." These would involve finding out what receptors it binds to, how it affects rats and working out a safe dosage profile, before raising funding to conduct clinical trials to see whether it really does reduce alcohol intake.

David Caldicott from the Australian National University College of Medicine says the safety bar for new medicines is high – and even higher for recreational products.

Caldicott is enthusiastic about the potential of a substance like chaperon, that has some of alcohol's desirable qualities, but he is worried about mixing drugs and alcohol: "From a harm minimisation perspective, mixing drugs and alcohol is never a good idea. It's one of the basic premises."

Alex Wodak of the Australian Drug Law Reform Foundation says it is hard to predict what a drug will do when widely released. Its success will depend on whether it lowers people's intake of alcohol or simply adds another dimension to a night out.

Of course, there's every chance the drug will simply be banned, like so many of Dr Z's creations. Nutt is philosophical. "Let's just hope they don't," he says. "We have to see this as an opportunity to reduce harms rather than a new drug that has hit the market."

http://bit.ly/1AmvS4w

Tracking the Fukushima radioactivity plume across the Pacific

How long did it take a radioactive plume to travel the waters of the Pacific from Fukushima, Japan, to the shores of North America?

Dec 31, 2014 by Deborah Netburn, Los Angeles Times

The answer, according to a new study published in PNAS, is about 2.1 years.

After an earthquake-triggered tsunami damaged the Fukushima Daiichi nuclear power plant in March 2011, a team of Canadian scientists saw an opportunity to put models of Pacific Ocean current speeds to the test.

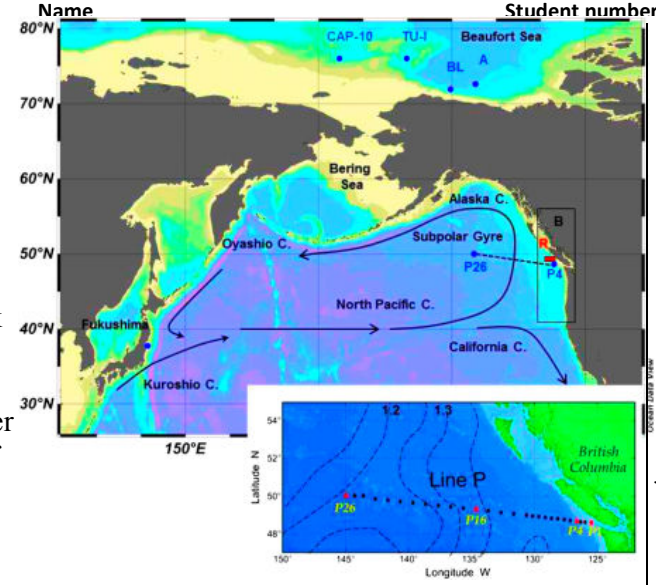
After the tsunami struck, the plant released cesium 134 and cesium 137 into the ocean. The researchers knew that a small percentage of this radioactive material would be carried by currents across the Pacific, eventually reaching the west coast of North America. Computer models could predict when this might happen, but by taking actual samples of the ocean water and testing them for cesium 134 and cesium 137 the scientists could see for certain when it happened.

"We had a situation where the radioactive tracer was deposited at a very specific location off the coast of Japan at a very specific time," said John Smith, a research scientist at the Bedford Institute of Oceanography in Dartmouth, Nova Scotia, and the lead author of the paper. "It was kind of like a dye experiment," he added. "And it is unambiguous - you either see the signal or you don't, and when you see it you know exactly what you are measuring."

Just three months after the tsunami, Smith and his team began sampling ocean water from as far as 1,500 kilometers (930 miles) off the coast of British Columbia. They took measurements from the same sites every June from 2011 to 2013, collecting 60 liters of water and then analyzing it for traces of cesium 134 and cesium 137.

In June of 2011 they detected no signature from the Fukushima disaster at any of the test sites. In June of 2012 they found small amounts of the Fukushima radiation at the westernmost station, but it had not moved any closer to shore. By June of 2013, however, it had spread all the way to the continental shelf of Canada. The amount of radiation that finally made it to Canada's west coast by June 2013 was very small - less than 1 Becquerels per cubic meter. (Becquerels are the number of decay events per second per 260 gallons of water.) That is more

than 1,000 times lower than acceptable limits in drinking water, according to the Environmental Protection Agency. Computer models that match fairly closely with the hard data that Smith collected suggest that the amount of radiation will peak in 2015 and 2016 in British Columbia, but it will never exceed about 5 Becquerels per cubic meter. "Those levels of cesium 137 are still well below natural levels of radioactivity in the ocean," said Smith.



Map showing the location of the site of the Fukushima Dai-ichi Nuclear Power Plant accident in Japan. Stations are indicated at which seawatersamples were collected in 2011–2014 on Line P and in 2012 in the Beaufort Sea. Box B represents the model domain for which Fukushima-derived 137Cs timeseriesconcentrations were estimated by Behrens and colleagues (6). Station R is the cross-shelf regime for which the Rossi and colleagues (7, 8) model resultsapply. (Inset) Sampling station locations along Line P. Dashed curves are time-averaged streamlines representing the mean dynamic height field for 2002–2012, indicating the northward geostrophic transport of the Alaska Current across Line P.

Because of the structure of the currents, the radiation levels in Southern California are expected to peak a few years later, but by that time they will be even smaller than the highest levels of radiation expected in Canada.

"Even when levels are small like this, it is important to collect systematic data so we can better predict how another event might move through the ocean," said Ken Buesseler, a marine chemist at Woods Hole Oceanographic Institute, who was not involved in the study.

Buesseler leads a citizen scientist group called Our Radioactive Oceans, to track the arrival of the Fukushima radioactivity plume in the U.S. He noted that his group's results matched Smith's. "What we really need for understanding what happens after events like Fukushima is data like this on a regular basis," he said.

http://www.eurekalert.org/pub_releases/2014-12/cp-psc122414.php

Patient stem cells used to make dementia-in-a-dish; help identify new treatment strategy

New strategy for treating an inherited form of dementia

Belgian researchers have identified a new strategy for treating an inherited form of dementia after attempting to turn stem cells derived from patients into the neurons most affected by the disease. In patient-derived stem cells carrying a mutation predisposing them to frontotemporal dementia, which accounts for about half of dementia cases before the age of 60, the scientists found a targetable defect that prevents normal neurodevelopment. These stem cells partially return to normal when the defect is corrected.

The study appears in the December 31st issue of Stem Cell Reports, the official journal of the International Society of Stem Cell Research published by Cell Press.

"Use of induced pluripotent stem cell (iPSC) technology"--which involves taking skin cells from patients and reprogramming them into embryonic-like stem cells capable of turning into other specific cell types relevant for studying a particular disease--"makes it possible to model dementias that affect people later in life," says senior study author Catherine Verfaillie of KU Leuven.

Frontotemporal disorders are the result of damage to neurons in parts of the brain called the frontal and temporal lobes, gradually leading to behavioral symptoms or language and emotional disorders. Mutations in a gene called progranulin (GRN) are commonly associated with frontotemporal dementia, but GRN mutations in mice do not mimic all the features of the human disorder, which has limited progress in the development of effective treatments.

"iPSC models can now be used to better understand dementia, and in particular frontotemporal dementia, and might lead to the development of drugs that can curtail or slow down the degeneration of cortical neurons," Verfaillie says.

Verfaillie and Philip Van Damme of the Leuven Research Institute for Neuroscience and Disease explore this approach in the Stem Cell Reports study by creating iPSCs from three patients carrying a GRN mutation. These immature cells were impaired at turning into mature, specialized cells called cortical neurons--the most affected cell type in frontotemporal dementia.

One of the top defective pathways in the iPSCs was the Wnt signaling pathway, which plays an important role in neuronal development. However, genetic correction or treatment with a compound that inhibits the Wnt signaling pathway restored the ability of the iPSCs to turn into cortical neurons. Taken together, the findings demonstrate that the GRN mutation causes the defect in cortical neuron formation by altering the Wnt signaling pathway.

"Our findings suggest that signaling events required for neurodevelopment may also play major roles in neurodegeneration," Van Damme says. "Targeting such pathways, as for instance the Wnt pathway presented in this study, may result in the creation of novel therapeutic approaches for frontotemporal dementia."

The researchers will now work to better understand what goes wrong in GRN-mutated cells, as well as identify precise molecular targets that could then be used for drug screens.

Stem Cell Reports, Raitano et al. Restoration of Progranulin Expression Rescues Cortical Neuron Generation in an Induced Pluripotent Stem Cell Model of Frontotemporal Dementia

http://bit.ly/1wJZliM

Remains of long-dead viruses in our genomes aid our immune response

Let B cells respond to pathogens without any help.

by Shalini Saxena Jan 1 2015, 4:00am TST

When foreign pathogens, such as bacteria or a virus, enter our body, our immune system responds in a concerted effort to eliminate them. B cells produce antibodies that recognize markers (called antigens) on the surface of the invaders; these antibodies are then used to tag foreign pathogens for destruction.

B cells typically require interaction with T cells for full activation and antibody production, which is critical to overcoming an infection. But there are some cases where the T cells are not required. Now, researchers have figured out how this works - and discovered that it relies on the remains of long-dead viruses that litter our genomes.

Large, repetitive sugar structures that are often found on the surface of bacteria and viruses are the key to activating antibody production without the help of a T cell. These sugary structures engage proteins called B cell receptors, which activate the B cells. B cells then grow, forming short-lived cells that produce antibodies and long-lived memory cells that will recognize the same invader upon subsequent infection.

Until recently, researchers have had little understanding of the processes that enable B cells to become activated in the absence of T cell mediation. After exposing mice to an antigen that B cell receptors respond to without T cell activation, researchers monitored the production of antibodies. From these studies, it was apparent that the chemical activates a signaling cascade that ends up making RNA from what are called endogenous retroviruses. Endogenous retroviruses are remnants of past infections that have been incorporated into our DNA.

The RNA made from these viruses then activates B cells through two distinct pathways. In the first pathway, the RNA directly triggers an antiviral signaling pathway. In the second pathway, the RNA is reverse transcribed into DNA, which triggers an antiviral pathway. This pathway later activates interferon genes, producing signaling molecules that evoke a general response to a foreign pathogen.

Ultimately, these sensors provide signals that promote the activation and expansion of antigen-specific B cells, which produce the specific antibodies.

Researchers were able to confirm the importance of these pathways using mice that were deficient in critical signaling proteins or by using chemicals that blocked the copying of the RNA into DNA.

Further studies were performed to gain a better understanding of the types of pathogens that activate this pathway. These demonstrated that when antigens from Streptococcus pneumonia and its commercial vaccine Pneumovax are used, endogenous retroviral RNA activates B cells using the second pathway.

These studies suggest that dead viruses are critical for specific response of B cells to this type of surface marker in the absence of T cell mediation. Ongoing work is looking into whether the location of B cells in the body influences the ability to activate this antibody-production pathway. But this study has also highlighted how evolution has harnessed past viral infections to defend itself against new infections.

Science, 2014. DOI: 10.1126/science.1257780 (About DOIs).

http://bit.ly/1K6PUo6

Cancer Deaths Continue to Fall in US: 22% Drop in 20 Years

Deaths from cancer continue to fall in the United States, and the American Cancer Society (ACS) estimates that the 22% drop in cancer mortality seen during the last 2 decades has resulted in more than 1.5 million cancer deaths being avoided in those years.

Zosia Chustecka

However, the burden continues to be substantial: the ACS estimates that 589,430 Americans will die from cancer in 2015, corresponding to about 1600 deaths per day. The figures come from the ACS's annual report on cancer statistics, scheduled to be published online in CA: A Cancer Journal for Clinicians early in 2015. For now, the ACS has highlighted a few points form the report in a press release.

For most of the 20th century, the overall cancer death rate was rising, reaching a peak in 1991. This was driven largely driven by rapid increases in lung cancer deaths among men as a consequence of the tobacco epidemic, the ACS explains. Since the 1991 peak, cancer mortality has been falling in the United States, and the steady decline is the result of fewer Americans smoking, as well as advances in cancer prevention, early detection, and treatment, the society comments.

Lung cancer death rates declined 36% between 1990 and 2011 among males and by 11% between 2002 and 2011 among females as a result of reduced tobacco use, the ACS points out.

However, lung cancer continues to be the most common cause of cancer death, accounting for more than one quarter (27%) of all cancer mortality. The next most common cause of cancer death is prostate cancer in men and breast cancer in women, and the third most common cause of cancer death is colorectal cancer in both sexes.

Although cancer deaths for the nation as a whole are falling, there is a large geographical variation between various states, with the states in the South generally showing the smallest decline (a fall of about 15% between 1991 and 2011) and those in the Northeast showing the largest decline (falls of 25% to 30% for Maryland, New Jersey, Massachusetts, New York, and Delaware).

"The continuing drops we're seeing in cancer mortality are reason to celebrate, but not to stop," said John R. Seffrin, PhD, chief executive officer of the ACS. "Cancer was responsible for nearly one in four deaths in the United States in 2011, making it the second leading cause of death overall. It is already the leading cause of death among adults aged 40 to 79, and is expected to overtake heart disease as the leading cause of death among all Americans within the next several years. The change may be inevitable, but we can still lessen cancer's deadly impact by making sure as many Americans as possible have access to the best tools to prevent, detect, and treat cancer."

http://www.eurekalert.org/pub_releases/2015-01/pu-fpt122914.php

Findings point to potential approach to treat virus causing illness, possible paralysis

Enterovirus D68 has stricken children with serious respiratory infections and might be associated with polio-like symptoms

WEST LAFAYETTE, Ind. - New research findings point toward a class of compounds that could be effective in combating infections caused by enterovirus D68, which has stricken children with serious respiratory infections and might be associated with polio-like symptoms in the United States and elsewhere.

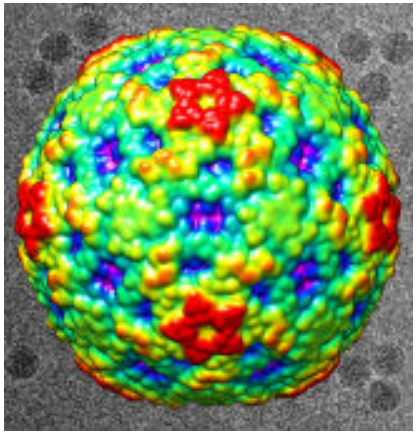
The researchers have used a technique called X-ray crystallography to learn the precise structure of the original strain of EV-D68 on its own and when bound to an anti-viral compound called "pleconaril."

The ongoing research could lead to the development of drugs that inhibit infections caused by the most recent strains of the virus, said Michael G. Rossmann, Hanley Distinguished Professor of Biological Sciences at Purdue University.

A molecule called a "pocket factor" is located within a pocket of the virus's protective shell, called the capsid. When the virus binds to a human cell, the pocket factor is squeezed out of its pocket resulting in the destabilization of the virus particle, which then disintegrates and releases its genetic material to infect the cell and to replicate itself.

The antiviral compound pleconaril also binds into the pocket, inhibiting infection.

"The compound and the normal pocket factor compete with each other for binding into the pocket," Rossmann said. "They are both hydrophobic, and they both like to get away from water by going into the pocket. But which of these is going to win depends on the pocket itself, the pocket factor and properties of the antiviral compound."



This color-coded image shows the surface view of enterovirus D68, which has stricken children with serious respiratory infections and might be associated with polio-like symptoms. Red regions are the highest peaks, and the lowest portions are blue. In the black-and-white background are actual electron microscopy images of the EV-D68 virus. A publication-quality image is available. **Purdue University image/Yue Liu and Michael G. Rossmann**

The findings are detailed in a paper appearing in the journal Science on Friday (January 2). The paper was authored by Yue Liu, a graduate student; Ju Sheng, a technical assistant; Andrei Fokine, Geng Meng, Woong-Hee Shin, and Feng Long, post doctoral research associates; Richard Kuhn, professor and head of Purdue's Department of Biological Sciences; Daisuke Kihara, a professor of biological sciences and computer science; and Rossmann.

"In this work we only focused on the very original EV-D68 isolate, which was discovered in 1962," Liu said. "Strains in the current outbreaks have minor differences."

Although pleconaril is not active against current strains of EV-D68 tested thus far, it is active against the original isolate. Small changes in the structure of pleconaril are likely to lead to anti EV-D68 inhibitors against a broader spectrum of isolates.

An upsurge of EV-D68 cases in the past few years has shown clusters of infections worldwide. In August 2014 an outbreak of mild-to-severe respiratory illnesses occurred among thousands of children in the United States of which 1,149 cases have been confirmed to be caused by EV-D68. The virus also has been associated with occasional neurological infections and "acute flaccid

myelitis," characterized by symptoms including muscle weakness and paralysis. Although EV-D68 has emerged as a considerable global public health threat, there is no available vaccine or effective antiviral treatment.

Research led by Rossmann, working with pharmaceutical companies, has resulted in antiviral drugs for other enteroviruses such as rhinoviruses that cause common cold symptoms. These drugs include pleconaril, which was developed in the 1990s but not approved by the U.S. Food and Drug Administration primarily because of a side effect that puts women using birth control drugs at risk of conception.

Purdue researchers became interested in studying pleconaril's potential effectiveness against EV-D68 after an outbreak of about 20 cases of acute flaccid paralysis was reported in California between 2012 and 2014. Out of those cases, two tested positive for EV-D68. "This suggests the potential association of EV-D68 with polio-like illness," Liu said.

The researchers are working with the Centers for Disease Control and Prevention and are studying these newer strains to determine their structures.

"The need for an effective antiviral agent for treatment of EV-D68 infections was made apparent by the widespread and large numbers of EV-D68 infections (in 2014), many of which were associated with significant morbidity," said Mark A. McKinlay, director of the Center for Vaccine Equity at the Task Force for Global Health. "The determination of the structure of the EV-D68 reported here by Michael Rossmann and his team represents an important step in this direction. The strain of EV-D68 used in the study is from 1962, and Michael's team along with Steve Oberste's group at CDC have shown that this strain is inhibited by pleconaril at clinically achievable concentrations. Testing of pleconaril against the current circulating strains at CDC thus far showed these strains are not susceptible to the antiviral compound."

McKinlay, who collaborates with the CDC on polio eradication efforts, has been a key figure in pharmaceutical-company collaborations with Rossmann's group to discover and develop pleconaril.Once the newer strains are better understood, the ongoing research could yield compounds that are effective against these strains.

"Designing the best possible compound for these newer strains will take more time, but I hope that in a year or so we might have something," Rossmann said.

Rossmann and Kuhn as well as David Stuart's team in Oxford, England, working with Zihe Rao's group in Beijing were among the first scientists to reveal important details of the structure of enterovirus 71, or EV71, which causes hand, foot and mouth disease, and is common throughout the world. Although that disease usually is not fatal, the virus has been reported to cause fatal encephalitis in infants and young children, primarily in the Asia-Pacific region.

Rossmann's and Kuhn's collaborative research has looked at virus structures in complex with receptors that permit entry of the virus into cells, and inhibitors of virus replication for a variety of viruses.

Like EV-D68 and EV71, poliovirus is an enterovirus and is within the large family called picornaviruses. Non-polio enteroviruses are common viruses and cause about 10 to 15 million infections in the United States each year, but most infected individuals have only mild illness, similar to a common cold, according to the CDC. *The research was supported by the National Institutes of Health.*

http://www.eurekalert.org/pub_releases/2015-01/uoc--fia122914.php

Fat isn't all bad: Skin adipocytes help protect against infections

Fat cells below the skin help protect us from bacteria

When it comes to skin infections, a healthy and robust immune response may depend greatly upon what lies beneath. In a new paper published in the January 2, 2015 issue of Science, researchers at the University of California, San Diego School of Medicine report the surprising discovery that fat cells below the skin help protect us from bacteria.

Richard Gallo, MD, PhD, professor and chief of dermatology at UC San Diego School of Medicine, and colleagues have uncovered a previously unknown role for dermal fat cells, known as adipocytes: They produce antimicrobial peptides that help fend off invading bacteria and other pathogens.

"It was thought that once the skin barrier was broken, it was entirely the responsibility of circulating (white) blood cells like neutrophils and macrophages to protect us from getting sepsis," said Gallo, the study's principal investigator. "But it takes time to recruit these cells (to the wound site). We now show that the fat stem cells are responsible for protecting us. That was totally unexpected. It was not known that adipocytes could produce antimicrobials, let alone that they make almost as much as a neutrophil."

The human body's defense against microbial infection is complex, multi-tiered and involves numerous cell types, culminating in the arrival of neutrophils and monocytes - specialized cells that literally devour targeted pathogens.

But before these circulating white blood cells arrive at the scene, the body requires a more immediate response to counter the ability of many microbes to rapidly increase in number. That work is typically done by epithelial cells, mast cells and leukocytes residing in the area of infection.

Staphylococcus aureus is a common bacterium and major cause of skin and soft tissue infections in humans. The emergence of antibiotic-resistant forms of S. aureus is a significant problem worldwide in clinical medicine.

Prior published work out of the Gallo lab had observed S. aureus in the fat layer of the skin, so researchers looked to see if the subcutaneous fat played a role in preventing skin infections.

Ling Zhang, PhD, the first author of the paper, exposed mice to S. aureus and within hours detected a major increase in both the number and size of fat cells at the site of infection. More importantly, these fat cells produced high levels of an antimicrobial peptide (AMP) called cathelicidin antimicrobial peptide or CAMP. AMPs are molecules used by the innate immune response to directly kill invasive bacteria, viruses, fungi and other pathogens.

"AMPs are our natural first line defense against infection. They are evolutionarily ancient and used by all living organisms to protect themselves," said Gallo. "However, in humans it is becoming increasingly clear that the presence of AMPs can be a double-edged sword, particularly for CAMP. Too little CAMP and people experience frequent infections. The best example is atopic eczema (a type of recurring, itchy skin disorder). These patients can experience frequent Staph and viral infections. But too much CAMP is also bad. Evidence suggests excess CAMP can drive autoimmune and other inflammatory diseases like lupus, psoriasis and rosacea."

The scientists confirmed their findings by analyzing S. aureus infections in mice unable to either effectively produce adipocytes or whose fat cells did not express sufficient antimicrobial peptides in general and CAMP in particular. In all cases, they found the mice suffered more frequent and severe infections.

Further tests confirmed that human adipocytes also produce cathelicidin, suggesting the immune response is similar in both rodents and humans. Interestingly, obese subjects were observed to have more CAMP in their blood than subjects of normal weight.

The potential clinical applications of the findings will require further study, said Gallo. "Defective AMP production by mature adipocytes can occur due to obesity or insulin resistance, resulting in greater susceptibility to infection, but too much cathelicidin may provoke an unhealthy inflammatory response.

"The key is that we now know this part of the immune response puzzle. It opens fantastic new options for study. For example, current drugs designed for use in diabetics might be beneficial to other people who need to boost this aspect of immunity. Conversely, these findings may help researchers understand disease associations with obesity and develop new strategies to optimize care."

Co-authors include Tissa Hata, UCSD; Christian F. Guerrero-Juarez, Paul Ramos and Maksim V. Plikus, UC Irvine; and Sagar P. Bapat, The Salk Institute for Biological Studies. Funding for this research came, in part, from the National Institutes of Health (grants R01A1083358, R01A052453, AR052728, DK096828, R01AR067273, GM055246, The Atopic Dermatitis Research Network, the Edward Mallinckrodt Jr. Foundation, the Dermatology Foundation, the National Science Foundation and the California Institute for Regenerative Medicine.

http://www.eurekalert.org/pub_releases/2015-01/jhm-lo123014.php

'Bad luck' of random mutations plays predominant role in cancer, study shows

Statistical modeling links cancer risk with number of stem cell divisions

Scientists from the Johns Hopkins Kimmel Cancer Center have created a statistical model that measures the proportion of cancer incidence, across many tissue types, caused mainly by random mutations that occur when stem cells divide. By their measure, two-thirds of adult cancer incidence across tissues can be explained primarily by "bad luck," when these random mutations occur in genes that can drive cancer growth, while the remaining third are due to environmental factors and inherited genes.

"All cancers are caused by a combination of bad luck, the environment and heredity, and we've created a model that may help quantify how much of these three factors contribute to cancer development," says Bert Vogelstein, M.D., the Clayton Professor of Oncology at the Johns Hopkins University School of Medicine, co-director of the Ludwig Center at Johns Hopkins and an investigator at the Howard Hughes Medical Institute.

"Cancer-free longevity in people exposed to cancer-causing agents, such as tobacco, is often attributed to their 'good genes,' but the truth is that most of them simply had good luck," adds Vogelstein, who cautions that poor lifestyles can add to the bad luck factor in the development of cancer.

The implications of their model range from altering public perception about cancer risk factors to the funding of cancer research, they say. "If two-thirds of cancer incidence across tissues is explained by random DNA mutations that occur when stem cells divide, then changing our lifestyle and habits will be a huge help in preventing certain cancers, but this may not be as effective for a variety of others," says biomathematician Cristian Tomasetti, Ph.D., an assistant professor of oncology at the Johns Hopkins University School of Medicine and Bloomberg School of Public Health. "We should focus more resources on finding ways to detect such cancers at early, curable stages," he adds.

In a report on the statistical findings, published Jan. 2 in Science, Tomasetti and Vogelstein say they came to their conclusions by searching the scientific literature for information on the cumulative total number of divisions of stem cells among 31 tissue types during an average individual's lifetime. Stem cells "self-renew," thus repopulating cells that die off in a specific organ.

It was well-known, Vogelstein notes, that cancer arises when tissue-specific stem cells make random mistakes, or mutations, when one chemical letter in DNA is incorrectly swapped for another during the replication process in cell division. The more these mutations accumulate, the higher the risk that cells will grow unchecked, a hallmark of cancer. The actual contribution of these random mistakes to cancer incidence, in comparison to the contribution of hereditary or environmental factors, was not previously known, says Vogelstein.

To sort out the role of such random mutations in cancer risk, the Johns Hopkins scientists charted the number of stem cell divisions in 31 tissues and compared these rates with the lifetime risks of cancer in the same tissues among Americans. From this so-called data scatterplot, Tomasetti and Vogelstein determined the correlation between the total number of stem cell divisions and cancer risk to be 0.804. Mathematically, the closer this value is to one, the more stem cell divisions and cancer risk are correlated.

"Our study shows, in general, that a change in the number of stem cell divisions in a tissue type is highly correlated with a change in the incidence of cancer in that same tissue," says Vogelstein. One example, he says, is in colon tissue, which undergoes four times more stem cell divisions than small intestine tissue in humans. Likewise, colon cancer is much more prevalent than small intestinal cancer.

"You could argue that the colon is exposed to more environmental factors than the small intestine, which increases the potential rate of acquired mutations," says Tomasetti. However, the scientists saw the opposite finding in mouse colons, which had a lower number of stem cell divisions than in their small intestines, and, in mice, cancer incidence is lower in the colon than in the small intestine. They say this supports the key role of the total number of stem cell divisions in the development of cancer.

Using statistical theory, the pair calculated how much of the variation in cancer risk can be explained by the number of stem cell divisions, which is 0.804 squared, or, in percentage form, approximately 65 percent.

Finally, the research duo classified the types of cancers they studied into two groups. They statistically calculated which cancer types had an incidence predicted by the number of stem cell divisions and which had higher incidence. They found that 22 cancer types could be largely explained by the "bad luck" factor of random DNA mutations during cell division. The other nine cancer types had incidences higher than predicted by "bad luck" and were presumably due to a combination of bad luck plus environmental or inherited factors.

"We found that the types of cancer that had higher risk than predicted by the number of stem cell divisions were precisely the ones you'd expect, including lung cancer, which is linked to smoking; skin cancer, linked to sun exposure; and forms of cancers associated with hereditary syndromes," says Vogelstein. "This study shows that you can add to your risk of getting cancers by smoking or other poor lifestyle factors. However, many forms of cancer are due largely to the bad luck of acquiring a mutation in a cancer driver gene regardless of lifestyle and heredity factors. The best way to eradicate these cancers will be through early detection, when they are still curable by surgery," adds Vogelstein.

The scientists note that some cancers, such as breast and prostate cancer, were not included in the report because of their inability to find reliable stem cell division rates in the scientific literature. They hope that other scientists will help refine their statistical model by finding more precise stem cell division rates.

The research was funded by the Virginia and D. K. Ludwig Fund for Cancer Research, the Lustgarten Foundation for Pancreatic Cancer Research, the Sol Goldman Pancreatic Cancer Research Center, and the National Institutes of Health's National Cancer Institute (grants P30-CA006973, R37-CA43460, RO1-CA57345 and P50-CA62924).

http://www.eurekalert.org/pub_releases/2015-01/uouh-dts122914.php

Defying textbook science, study finds new role for proteins

First demonstration that amino acids can be assembled without DNA or RNA

Open any introductory biology textbook and one of the first things you'll learn is that our DNA spells out the instructions for making proteins, tiny machines that do much of the work in our body's cells. Results from a study published on Jan. 2 in Science defy textbook science, showing for the first time that the building blocks of a protein, called amino acids, can be assembled without blueprints - DNA and an intermediate template called messenger RNA (mRNA). A team of researchers has observed a case in which another protein specifies which amino acids are added.

"This surprising discovery reflects how incomplete our understanding of biology is," says first author Peter Shen, Ph.D., a postdoctoral fellow in biochemistry at the University of Utah. "Nature is capable of more than we realize."

To put the new finding into perspective, it might help to think of the cell as a well-run factory. Ribosomes are machines on a protein assembly line, linking together amino acids in an order specified by the genetic code. When something goes wrong, the ribosome can stall, and a quality control crew is summoned to the site. To clean up the mess, the ribosome is disassembled, the blueprint is discarded, and the partly made protein is recycled.

Yet this study reveals a surprising role for one member of the quality control team, a protein conserved from yeast to man named Rqc2. Before the incomplete protein is recycled, Rqc2 prompts the ribosomes to add just two amino acids (of a total of 20) - alanine and threonine - over and over, and in any order. Think of an

auto assembly line that keeps going despite having lost its instructions. It picks up what it can and slaps it on: horn-wheel-wheel-horn-wheel-wheel-wheel-wheel-horn.

"In this case, we have a protein playing a role normally filled by mRNA," says Adam Frost, M.D., Ph.D., assistant professor at University of California, San Francisco (UCSF) and adjunct professor of biochemistry at the University of Utah. He shares senior authorship with Jonathan Weissman, Ph.D., a Howard Hughes Medical Institute investigator at UCSF, and Onn Brandman, Ph.D., at Stanford University. "I love this story because it blurs the lines of what we thought proteins could do."

Like a half-made car with extra horns and wheels tacked to one end, a truncated protein with an apparently random sequence of alanines and threonines looks strange, and probably doesn't work normally. But the nonsensical sequence likely serves specific purposes. The code could signal that the partial protein must be destroyed, or it could be part of a test to see whether the ribosome is working properly. Evidence suggests that either or both of these processes could be faulty in neurodegenerative diseases such as Alzheimer's, Amyotrophic lateral sclerosis (ALS), or Huntington's.

"There are many interesting implications of this work and none of them would have been possible if we didn't follow our curiosity," says Brandman. "The primary driver of discovery has been exploring what you see, and that's what we did. There will never be a substitute for that."

The scientists first considered the unusual phenomenon when they saw evidence of it with their own eyes. They fine-tuned a technique called cryo-electron microscopy to flash freeze, and then visualize, the quality control machinery in action. "We caught Rqc2 in the act," says Frost. "But the idea was so far-fetched. The onus was on us to prove it."

It took extensive biochemical analysis to validate their hypothesis. New RNA sequencing techniques showed that the Rqc2/ribosome complex had the potential to add amino acids to stalled proteins because it also bound tRNAs, structures that bring amino acids to the protein assembly line. The specific tRNAs they saw only carry the amino acids alanine and threonine. The clincher came when they determined that the stalled proteins had extensive chains of alanines and threonines added to them. "Our job now is to determine when and where this process happens, and what happens when it fails," says Frost.

Shen, Frost, Brandman, and Weissman conducted the work in collaboration with colleagues at the University of Utah (Krishna Parsawar, James Cox), University of California at San Francisco (Xueming Li, Yifan Cheng, Matthew Larson), Stanford University (Joseph Park), and the University of Texas at Austin (Yidan Qin, Alan Lambowitz).

The research was supported by grants from the Searle Scholars program, the National Institutes of Health, the Howard Hughes Medical Institute, Stanford University, and the University of Utah.

Rqc2p and 60S ribosomal subunits mediate mRNA-independent elongation of nascent chains. Peter S. Shen, Joseph Park, Yidan Qin, Xueming Li, Krishna Parsawar, Matthew H. Larson, James Cox, Yifan Cheng, Alan M. Lambowitz, Jonathan S. Weissman, Onn Brandman, Adam Frost. Science, Jan. 2, 2015

http://nyti.ms/17ay44t

Ebola Doctors Are Divided on IV Therapy in Africa

Experts who favor aggressive rehydration point to several hospitals that claim unusually low death rates as evidence that it is effective. Skeptics say other factors may be at work.

By DONALD G. McNEIL Jr. JAN. 1, 2015

Medical experts seeking to stem the Ebola epidemic are sharply divided over whether most patients in West Africa should, or can, be given intravenous hydration, a therapy that is standard in developed countries. Some argue that more aggressive treatment with IV fluids is medically possible and a moral obligation. But others counsel caution, saying that pushing too hard would put overworked doctors and nurses in danger and that the treatment, if given carelessly, could even kill patients.

The debate comes at a crucial time in the outbreak. New infections are flattening out in most places, better-equipped field hospitals are opening, and more trained professionals are arriving, opening up the possibility of saving many lives in Africa, rather than a few patients flown to intensive care units thousands of miles away.

The World Health Organization sees intravenous rehydration, along with constant measuring of blood chemistry, as the main reason that almost all Ebola patients treated in American and European hospitals have survived, while about 70 percent of those treated in West Africa have died.

Every hospital there should have “early, liberal use of intravenous fluid and electrolyte replacement,” said Dr. Robert A. Fowler, a Canadian critical care specialist who leads a W.H.O. Ebola team. Anything less, he said, is “not medically justified and will result in continued high case-fatality rates.”

Experts who favor aggressive rehydration point to several hospitals that claim unusually low death rates as evidence that it is effective. Skeptics say other factors may be at work. Even two of the most admired medical charities have squared off over the issue. Partners in Health, which has worked in Haiti and Rwanda but is just beginning to treat Ebola patients in West Africa, supports the aggressive treatment. Its officials say the more measured approach taken by Doctors Without Borders is overly cautious.

"M.S.F. is not doing enough," said Dr. Paul Farmer, one of the founders of Partners in Health, using the French initials for Doctors Without Borders, whose staff members have worked on the front lines of Ebola outbreaks for years. "What if the fatality rate isn't the virulence of disease but the mediocrity of the medical delivery?"

Doctors Without Borders representatives strongly disagreed, saying that Dr. Farmer's assumptions about Ebola were incorrect, that intensive rehydration would probably not save as many patients as he believes, and that the W.H.O.'s position has not been proved.

The group's overwhelmed doctors do what they can, officials said, but it is hard to insert needles while wearing three pairs of gloves and foggy goggles. IVs must be monitored, drawing virus-laden blood for tests is dangerous, and patients yank needles out - sometimes in delirium, sometimes just to go to the toilet when no nurse is around.

Ebola patients lose up to five quarts of fluid a day through diarrhea and vomiting. In that fluid are electrolytes like potassium, magnesium, sodium and calcium, and proteins like albumin. Electrolyte loss can stop the heart; protein loss can cause fatal internal swelling. Rehydrating patients and replacing those elements "is the antidote to the idea that everybody's going to die," Dr. Farmer said.

Every Ebola hospital, he argued, should have a team that specializes in inserting IVs - or, better yet, peripherally inserted central catheters, or PICC lines. These are thin plastic tubes, inserted in the arm or chest and threaded through a vein, that can be left in place for days and the needle discarded.

Along with doctors at the London School of Hygiene and Tropical Medicine, who published an article on rehydration in The Lancet on Dec. 4, Dr. Farmer has also called for the use of thick needles driven into bone marrow with surgical "guns." This procedure, known as intraosseous infusion, is slow, but it reinflates veins too shrunken to admit an intravenous line, and the needles are much harder for agitated patients to pull out.

However, not all doctors know how to use PICC lines or bone needles, or how to inject fluids into empty abdominal spaces, another technique endorsed in the Lancet article. (The article was accompanied by a video in which Dr. Ian Roberts, the chief author, had some of those techniques demonstrated on himself. He used minimal anesthesia, he said, to imitate field conditions in West Africa.)

Doctors Without Borders normally puts IV lines in as many Ebola patients as it can manage, said Dr. Armand Sprecher, an Ebola expert with the organization. That practice was temporarily stopped in September, when the disease was spreading so fast that doctors had only one minute per patient during the one hour they could work in their sweltering protective suits.

The fatality rate across the group's six Ebola treatment centers in West Africa was about 60 percent then, and is now 40 to 50 percent, Dr. Sprecher said. He disputed Dr. Farmer's contention that rehydration could bring it down to 10 percent.

"It would probably push it down some, but I'd be surprised if it were dramatic," Dr. Sprecher said. Dr. Farmer cited the treatment given at a unit in Hastings, Sierra Leone, as an example of the kind of care he endorses.

In a Dec. 24 letter to The New England Journal of Medicine, the Sierra Leonean doctors running that center with Western advisers said they had had a 48 percent fatality rate when they opened in September and had since reduced it to 24 percent. Each of the 581 patients the center has treated immediately received IV fluids with electrolytes, they wrote. Even without lab tests, each patient also received an antibiotic, an anti-parasitic drug, an antimalarial drug, an anti-vomiting drug, pain pills, vitamins, zinc and a nutrition supplement.

"That's effective case management," Dr. Farmer said. "We're cheering them on."

The fatality rate at the unit Partners in Health runs in Port Loko, Sierra Leone, is 35 to 40 percent, its director, Dr. Corrado Cancedda, estimated.

Up to 80 percent of patients there receive IV rehydration, Dr. Cancedda said, and some have had bone needles inserted; no PICC lines have been used. Battery-powered electrolyte monitoring machines are being introduced.

Dr. Sprecher said death rates at Doctors Without Borders' six hospitals in the region varied, with the lowest being 36 percent in Bo, Sierra Leone.

But he could not explain why. Some of the hospitals see more young adults, who tend to survive. At rural centers, the sickest patients die on the way there.

Rehydration was only one lifesaving factor for the handful of patients transported to American or European hospitals, Dr. Sprecher argued, because all of them also received intensive nursing, and some received dialysis, ventilation and experimental therapies. He was reluctant to have his doctors seen using bone-needle guns on patients. "Not long ago, we were being accused of stealing organs," he said. "You have to be sure people understand what the heck you're doing."

Dr. Sprecher also disputed Dr. Farmer's comparison of Ebola to cholera, which both medical charities fight with aggressive rehydration. Ebola, he said, does more organ damage and makes blood vessels leak fluid. "In cholera, you can get fatalities down from 50 percent to 1 percent," he said. We've been putting people on IVs for Ebola for 14 years. If just tanking them up worked, we'd be doing it."

Lab testing is a crucial issue. For example, while low potassium can kill, so can overdoses. Potassium is used in executions by lethal injection.

West Africa has at least eight laboratories run by various American, Canadian and European government agencies, Dr. Sprecher said. Until recently, they tested only for Ebola and diseases that mimic it, like malaria or Lassa fever.

Now, he said, about half can test for electrolytes.

Because heat and humidity knock out the machines that analyze blood chemistry, labs must be air-conditioned, said Dr. Thomas R. Frieden, director of the Centers for Disease Control and Prevention. The C.D.C. runs two large laboratories in the region, only one of which now tests for electrolytes. Sometimes, conservative guesswork is called for, Dr. Frieden said. His father, a physician, gave potassium to patients who needed IV rehydration long before such tests were routine.

The best-equipped treatment center in West Africa is the 25-bed United States Public Health Service hospital in Monrovia, Liberia, which is reserved for doctors, nurses, burial teams and others fighting the epidemic. It is fully air-conditioned and has 32 medical personnel, who wear high-tech protective gear that sucks in fresh air. Its on-site lab tests blood for electrolytes and proteins. The pharmacy has drugs to raise blood pressure or increase coagulation, and patients can be fed through tubes.

Since it opened in November, it has had 14 Ebola patients. Seven recovered, five died, one was transferred and one is in treatment, a spokeswoman said. (Ten other people who were admitted did not have Ebola.) That is a 42 percent fatality rate, though based on a small sample, for the 12 patients whose fates are clear.

Other units tread a middle ground, relying on what measures they have at hand. The fatality rate at the International Medical Corps hospital in Bong County, Liberia, is about 55 percent, said Dr. Pranav Shetty, the agency's international emergency health coordinator.

All patients who need IV lines get them, Dr. Shetty said. But when there are too few nurses around, usually at night, the IVs are unhooked, so patients may get only one quart of fluids a day. And only patients still urinating, indicating that their kidneys are working, receive electrolytes. Spending money on air-conditioning "doesn't even cross our minds," Dr. Shetty said, because other needs are more urgent. When IV lines are impractical, the W.H.O. urges doctors to make patients drink six quarts of rehydration solution a day. Nigeria's victory over its Ebola outbreak in September was attributed in part to that. Dr. Adaora Igonoh, a 28-year-old Nigerian physician who survived the disease, became a symbol for the cause: The W.H.O. distributed pictures of her giving a thumbs-up while drinking the solution, and Bill Gates blogged about her story, telling how she forced herself to drink despite the repulsive salty taste and her vomiting.

Still, even oral rehydration is hard, doctors say. Patients need anti-nausea drugs and must be pressured to drink. The solution tastes better when refrigerated. But, like air-conditioning, that requires electricity.

http://bit.ly/1BvliXr

India's Prototype Space Capsule Passes Big Test

In a two-in-one mission, the Indian Space Research Organisation (ISRO) successfully conducted the first experimental flight of its next-generation launch vehicle and demonstrated the re-entry and recovery of a prototype crew capsule.

K.S. Jayaraman, Space News

BANGALORE, India - The Dec. 18 maiden flight of the Geosynchronous Satellite Launch Vehicle Mark 3 (GSLV-3) began with a liftoff at 9:30 a.m local time from the Satish Dhawan Space Center on the southeastern coast of India and was over in 20 minutes.

ISRO said in a statement that this "suborbital" experimental mission was intended to test the vehicle performance during the critical atmospheric phase of its flight. The vehicle carried a passive, or nonfunctional, cryogenic upper stage.

The rocket carried a 3,775-kilogram unmanned crew module built by Indian industry. The module, designed to accommodate three astronauts, separated from the rocket at an altitude of 127 kilometers and, after being slowed by parachutes, splashed down in the Bay of Bengal.

The 42.4-meter tall GSLV-3 is a three-stage vehicle with a liftoff weight of 630 metric tons. The first stage consists of two solid-rocket motors, each with 200 tons of propellant. Its second stage uses two restartable engines, with 110 tons of liquid propellant.

As designed, the cryogenic upper stage of the rocket features a propellant loading of 25 tons of liquid-oxygen and -hydrogen. But in this flight only the first two stages were fired; the cryogenic upper stage was inert. The mission objective was to test the first two stages - they had never flown before - and validate the rocket's aerodynamic stability during the ascent phase through the atmosphere.

ISRO said in a statement that the flight aimed "to validate the re-entry technologies envisaged for crew module and enhance the understanding of blunt body re-entry aerodynamics and parachute deployment in cluster configuration." With the success the rocket "has moved a step closer to its first developmental flight with the functional cryogenic upper stage."

"It has been a significant day for ISRO," the agency's chairman, Koppilli Radhakrishnan, said in a post-launch speech. "The performance of solid and liquid stage motors and the unmanned crew module was as expected."

Radhakrishnan said the rocket's cryogenic upper stage is still in development and that he is confident the first full-fledged flight will take place in two years. Once ready, he said, the GSLV-3 will be able to launch satellites weighing 4 tons and could be used for the Indian manned spaceflight program.

The GSLV-3, in development since 2002, was initially expected to become operational by 2010 or 2011, with its first flight in 2009 or 2010. The demonstration flight was pushed back several times, one reason being the failure of the home-made cryogenic upper stage during a 2010 flight of the current-generation GSLV.

ISRO has sought about 125 billion rupees ($1.9 billion) for its human spaceflight endeavor but India's government has yet to approve the funding. Radhakrishnan has said that ISRO could send astronauts to space within seven to eight years of getting a government nod.

http://www.eurekalert.org/pub_releases/2015-01/cuot-ibd010215.php

Innate behavior determines how we steer our car

When maneuvering a steering wheel, both children and adults demonstrate a jerkiness that researchers have previously been unable to explain

Researchers at Chalmers University of Technology have solved a 70 year old mystery in traffic research: an until now inexplicable jerkiness when we steer a vehicle. The discovery may lead to safety systems in cars that can correct dangerous steering movements before they occur.

The ability to predict what a driver is going to do in the near future and to be able to prepare the car's system for this sounds a little bit like science fiction, and it would naturally be a dream come true for the safety departments at car manufacturers. The dream is now one step closer to becoming reality.

"With the driver model I have developed, it is possible to predict what drivers are going to do with the steering wheel before they do it. It is possible to predict how far the driver is going to turn the wheel, right when the person starts a wheel-turning movement. It's like looking into the future," says Chalmers researcher Ola Benderius.

As a result of the recently published discovery, several applications for car support systems can be developed to make our cars safer. Smarter anti-skid systems and systems for fatigued drivers are two examples of potential usage areas. "Imagine a fatigued driver on the verge of running off the road. He or she suddenly wakes up and reflexively initiates a very large corrective manoeuvre, a potential misjudgement that can lead to something very dangerous. Since we are now able to predict how far the driver is going to turn the wheel, the vehicle's support systems can identify potential misjudgements and intervene, which means a serious accident, such as the car travelling into approaching traffic, can be avoided," says Ola Benderius.

What is the mystery that Ola Benderius has solved? As early as 1947, the well-known British researcher Arnold Tustin (1899-1994) produced the first model for how a person steers towards a target. He identified a continuous and linear control behaviour. When a car is driven, this corresponds to the driver gently and continuously following the road with the steering wheel.

This behaviour is known as tracking within control theory, and it has been the prevailing theory for car driving ever since. However, when comparing the linear model with actual measured data, some deviations become apparent, namely jerkiness in the steering signal.

Tustin saw these deviations from the continuous prediction as well, but the mystery has remained unsolved until now. Ola Benderius and his colleague Gustav Markkula got the idea while they were attending a lecture on neurocognition at Sahlgrenska University Hospital. The lecture addressed the behavioural theory of reaching, which concerns the basic human behaviour when we reach for something.

When studying how we humans move our hand from Point A to pick up something from Point B, the speed of the movement has a direct relationship with the distance - the longer the distance, the quicker the movement. The interesting effect of this is that the time for the movement is the same regardless of the distance.

"We immediately recognised this pattern from our measured steer signals," says Ola Benderius. "It was a bit of a eureka moment. Was it possible that this basic human behaviour also controlled how we steer a car?"

With the idea in mind, Ola Benderius extracted over 1,000 hours of car and truck driving from real driving data, which resulted in 1.3 million steer corrections. It turned out that 95 per cent of these correspond with the reaching theory. Ola Benderius and Gustav Markkula had discovered that steering is not linear when the driver follows the road, but rather that the driver turns the wheel according to the special reaching pattern.

"We were able to use the theory to explain what researchers had been trying to solve for a long time. This was the answer to the previously inexplicable jerkiness in the control signal. Rather than looking upon steering as continuously following the road, steering corrections seem to be applied in a very predetermined manner," says Ola Benderius.

"The control behaviour has also proven to be very natural; I saw this in an earlier study where I examined driving behaviour in 12 year olds and their parents."

With this new knowledge, he was able to develop a mathematical model that can explain many observed steering behaviours, which means that the driver response to different situations can be predicted before it occurs.

Ola Benderius believes the discovery will have an impact on an entire research field. "This might completely change how we regard human control of vehicles, crafts and vessels. I hope and believe that many researchers will utilise the

findings and start to think in new ways. Control behaviour has traditionally been studied on the basis of control theory and technical systems. If it is instead studied on the basis of neuroscience with focus on the human, an entire new world opens up. This could push the research field in an entirely different direction," says Ola Benderius.

The research has been conducted within the Adaptive systems research group at the Department of Applied Mechanics at Chalmers University of Technology. It has been financed by the Safer Vehicle and Traffic Safety Centre at Chalmers and the FFI research programme.

The discovery of the innate steering behaviour was recently published as a scientific paper, "Evidence for a fundamental property of steering":

The study and mathematical model are part of Ola Benderius' doctoral thesis that was recently published: "Modelling driver steering and neuromuscular behaviour"

http://bit.ly/1xsPUt7

Vitamin D's benefit may lie in syncing our body clocks

ARE you spending enough time in the sun? As well as keeping our bones strong, vitamin D – the hormone our skin makes when exposed to ultraviolet rays – may also help regulate our body clocks.

We all have a small group of "clock genes" which switch on and off during the day. As a result, the levels of the proteins they code for rise and fall over a 24-hour period. Enforced routines such as night shift work can play havoc with our health – increasing our risk of a stroke, for example.

To find out whether a lack of vitamin D might be responsible, Sean-Patrick Scott and his colleagues at the Monterrey Institute of Technology and Higher Education in Mexico looked at the behaviour of two clock genes in human fat cells.

When the cells were immersed in blood serum, they acted as they would in the body: the clock genes' activity oscillated over a 24-hour period.

Dosing the cells with vitamin D instead produced the same effect. No such effect was seen in cells placed inside a nutrient broth.

"Vitamin D synchronises the cells," says Scott. "Our results explain some of the benefits of sunlight," he says.

"Vitamin D is one of the ways we might be able to maintain circadian rhythms in the body."

Julia Pakpoor of the University of Oxford says clinical trials are needed to confirm the effect in people, but she adds, "We should all make sure we are vitamin D replete regardless."

The work was presented at the World Stem Cell Summit in San Antonio, Texas, last month.

http://www.eurekalert.org/pub_releases/2015-01/ehs-hvs010215.php

HIV vaccines should avoid viral target cells, primate model study suggests

More CD4+ T cells in gateway tissues = increased risk of infection

Vaccines designed to protect against HIV can backfire and lead to increased rates of infection. This unfortunate effect has been seen in more than one vaccine clinical trial.

Scientists at Yerkes National Primate Research Center, Emory University, have newly published results that support a straightforward explanation for the backfire effect: vaccination may increase the number of immune cells that serve as viral targets. In a nonhuman primate model of HIV transmission, higher levels of viral target cells in gateway mucosal tissues were associated with an increased risk of infection.

The findings, published in Proceedings of the National Academy of Sciences, suggest that vaccine researchers, when evaluating potential HIV/AIDS vaccines, may need to steer away from those that activate too many viral target cells in mucosal tissues.

"One of the reasons why it has been so difficult to make an AIDS vaccine is that the virus infects the very cells of the immune system that any vaccine is supposed to induce," says senior author Guido Silvestri, chief of microbiology and immunology at Yerkes National Primate Research Center.

Silvestri is also a professor of pathology and laboratory medicine at Emory University School of Medicine and a Georgia Research Alliance Eminent Scholar.

The first author of the paper is senior research specialist Diane Carnathan, PhD, and colleagues from the Wistar Institute, Inovio Pharmaceuticals and the University of Pennsylvania contributed to the study.

A large part of the HIV/AIDS vaccine effort has been focused on developing vaccines that stimulate antiviral T cells. T cells come in two main categories, defined by the molecules found on their surfaces. CD8 is a marker for "killer" cells, while CD4 is a marker for "helper" cells. CD4+ T cells are known to be primary targets for HIV and SIV (simian immunodeficiency virus) infection, while several studies have proposed that CD8+ T cells could be valuable in controlling infection.

In this study, researchers immunized rhesus macaques with five different combinations of vaccines encoding SIV proteins found on the inside of the virus only. This experimental strategy was designed to examine the effects of cell-mediated immunity, without stimulating the production of neutralizing antibodies, in what scientists refer to as a "reductionist approach".

The monkeys received an initial immunization followed by two booster shots after 16 and 32 weeks. The monkeys were then exposed to repeated low-dose intrarectal challenge with SIV, once per week, up to 15 times. In general, the immunization regimens did not prevent SIV infection. While all the immunized monkeys had detectable levels of circulating "killer" CD8+ T cells, there was no correlation between these cells and preventing infection.

The most important result, however, was that the monkeys that became infected had higher levels of activated CD4+T cells in rectal biopsies before challenge, Silvestri says. "This study shows that if a vaccine induces high levels of activated CD4+ T cells in mucosal tissues, any potential protective effect of the vaccine may be hampered," he explains.

The study emphasizes the unique challenges that HIV poses in terms of vaccine development, and the importance of pursuing vaccine concepts and products that elicit strong antiviral immune responses without increasing the number of CD4+ T cells in the portals of entry for the virus.

http://bit.ly/1zLG82s

We Used to Recycle Drugs From Patients' Urine

Penicillin extracted from a patient's urine could be reused

By Colin Schultz

When penicillin was first used medically, in 1940, it was a time of austerity. While Alexander Fleming first discovered penicillin in 1928, his world-changing observations had garnered hardly any notice, and it wasn't until 1938 that another team of reserachers finally began to isolate and test the active chemical ingredients in the world's first antibiotic.* By that time, World War II was raging, and medical manufacturing capacity that could be devoted to experimental treatments was in short supply.

Producing usable penicillin from Penicillium notatum mold was no easy feat, says PBS: “In spite of efforts to increase the yield from the mold cultures, it took 2,000 liters of mold culture fluid to obtain enough pure penicillin to treat a single case of sepsis in a person.”

Pencilin production couldn't happen nearly fast enough to match rising demand. To make up the shortfall, writes Rebecca Kreston for her Body Horrors blog at Discover Magazine, researchers came up with a novel way to get the penicillin they needed: extracting and isolating it from patients' urine.

Not all of the penicillin given to a patient is broken down. Some - in fact, most - of the penicillin passes through the body unchanged. According to Kreston:

[A]nywhere from 40 to 99 percent of the antibiotic is excreted in urine in its fully functional form about 4 hours after administration thanks to our efficient and hardworking kidneys. Due to this distinct feature of its pharmacokinetics, penicillin could be extracted from the crystalized urine of a treated patient and then used to treat another patient in the throes of serious bacterial infection just next door.

Eventually, penicillin production reached a pace that could match doctors' needs. But even today, some portion of the active ingredient from many drugs passes through our bodies unchanged. Instead of isolating and recycling them, though, we send them down the toilet and out into the world.

As the Harvard Health Letter wrote back in 2011, some water experts are growing increasingly concerned about the flow of drugs from pharmacy to stream. More than just an issue of pharmaceutical waste, these drugs seem to be having an effect on the behavior and health of animals living downstream. Doctors are no longer short on antibiotics, but it might be worth considering how to revive those early recycling strategies, anyway.

http://www.space.com/28151-how-to-see-venus-2015.html

Planet Venus to Dazzle Stargazers in 2015 Night Sky

The planet Venus should be a dazzling object in the night sky of 2015. Here's how to see the bright planet in the night sky this year.

by Joe Rao, SPACE.com

Currently hovering very low in the southwest twilight sky near the setting sun these evenings is the most brilliant of the planets: Venus. And in the New Year, this planet will truly shine.

Venus, Earth's sister planet and nearest planetary neighbor, travels in a nearly perfect circle as it orbits the sun. This means the Venus circles the sun 13 times over eight Earth years, so that as seen from Earth the planet appears to make five circuits around our night sky. Each of the 8 years in this Venus-cycle (discovered by the Babylonians and the Mayans) has its pattern, so that the phenomena we will be seeing in 2015 will be a repeat of what we saw in 2007, and one we will see again in 2023.

As I just mentioned, Venus is quite low at the present time. But this current evening apparition of Venus is going to evolve into an exceptionally good one, so let's get into a fuller explanation as to what is to come.

Venus passed superior conjunction (appearing to go behind the sun as seen from Earth) back on Oct. 25. Since then, it has been mired deep in the brilliant glare of the sun. Nonetheless, with each passing day, it has been moving on a slow course toward the east, and pulling slowly away from the sun's vicinity.

And now Venus is getting ready for its evening ascendency as it has now begun climbing up out of the sunset glow in earnest. It will soon reclaim its role as the brilliant Evening Star, a title it has not held since the start of 2014.

You can look for Venus with binoculars shortly after sundown very low in the southwest. In early December, the planet was just a mere 6 degrees high in the

southwest at sundown (your clinched fist held at arm's length is roughly 10-degrees wide). At the time, Venus touched the horizon about 40 minutes after sunset.

But during the middle and latter part of December, Venus gradually became easier to see. Continuing its swing east of the sun in late December, the planet should have become plainly visible in the western evening sky even to the most casual of observers, weather permitting. Venus, appearing as a brilliant silvery-white starlike object of magnitude –3.9 on the brightness scale used by astronomers, slipped below the horizon just over an hour after the sunset on Christmas Day. By New Year's Eve, it will have improved to more than 70 minutes.

Venus in 2015

It is during the first seven months of 2015 that Venus will perform like a sequined showgirl in the night sky, starring each evening in a brilliant evening performance. Viewed in the western twilight with clear weather, Venus should always appear dazzlingly bright to the unaided eye, and more so in binoculars. It will slowly rise higher each evening and will continue to grow in prominence all during the winter and on into the spring. By April, Venus will also start becoming increasingly evident that the planet is making an unusual excursion into the deep night sky, setting more than 3.5 hours after the sun from late April through late May.

Some astronomy books will tell you that it's impossible to see Venus in the middle of the night. So it will be hard to believe that Venus can stay up as late as it will during the third week of May, when it will be setting at 11:45 p.m. your local time. This will translate after midnight for observers stationed in cities like Pittsburgh, Raleigh, Dallas and Salt Lake City. And in the most extreme cases, it could be around 12:30 a.m. on daylight saving clocks in those cities that are far to the west of their standard time meridians!

Venus' best show in 2015

Venus reaches its greatest elongation - its greatest angular distance - 45 degrees to the east of the sun on June 6. On the evenings of June 30 and July 1, it will team with Jupiter in a spectacularly close conjunction high in the western sky at dusk. Venus will be at its brightest in early summer as it heads back down toward the sun, reaching its greatest brilliancy for this apparition on the evening of July 10 at magnitude –4.5. The planet should be most striking then; shining almost twice as bright as it does now. But with this final burst of glory, Venus will quickly fade, sliding back into the solar glare and vanishing from our view at the start of August.

Between now and the beginning of August, repeated observation of Venus with a small telescope will show the complete range of its phases and disk sizes. Currently, Venus appears nearly full (it goes through phases like Earth's moon), and through the upcoming winter season will display nothing more than a tiny, dazzling gibbous disk. The planet will become noticeably less gibbous by the end of March.

By early June, Venus reaches dichotomy (displaying a "half moon" shape). In July, the planet shows us a large crescent as it swings near the Earth. Indeed, those using telescopes will note that while the Earth-Venus distance is lessening, the apparent size of Venus' disk will grow, doubling from its present size by May 21. When it has doubled again in size on July 14, its large crescent shape should be easily discernible even in steadily held 7-power binoculars.

But even after it passes inferior conjunction on Aug.15, the Venus show will not be over, for it dramatically reemerges as a dazzling "morning star" low in the southeast sky by month's end. Then, a repeat performance will begin in September, with the above sequence of events reversed. It continues right through to the end of 2015. Indeed, without a question of doubt, 2015 will be Venus' year!

http://www.scientificamerican.com/article/rebrand-stage-fright-to-overcome-it/

Rebrand Stage Fright to Overcome It

Call performance anxiety "excitement" and psych yourself up

Dec 18, 2014 |By Tori Rodriguez

Pounding heart, rapid breath, racing thoughts - is it anxiety or excitement? New studies at Harvard University found that by interpreting these sensations as excitement instead of anxiety, people performed better in three types of stressful situations: singing in front of strangers, speaking in public and solving difficult math problems.

In the experiments, some participants were told to either try to calm down or try to get excited before the task; others were given no such instructions. People who viewed their anxious arousal as excitement not only reported feeling more excited, they also performed better on all tasks than the other participants: their singing was about 30 percent more accurate, their scores on several dimensions of public speaking were approximately 20 percent higher, and their performance on a timed math test was about 15 percent better, according to the paper, which ran in the Journal of Experimental Psychology last June. Another Harvard study, published in Emotion in August 2014, also found performance-boosting effects for people with social anxiety who thought of their stress as being helpful during a public performance.

Most people try to calm down when facing high-stakes situations, but that approach backfires by increasing rumination about what could go wrong. Instead choose to focus on the potential high points of the scenario - for instance, look forward to making colleagues laugh during a presentation or knowing how to solve some problems on a test. "Getting excited about how things can go well will give you confidence and energy and increase the likelihood that the positive

outcomes you imagine will actually happen," says Alison Wood Brooks, an assistant professor of business administration at Harvard Business School and author of the June paper.

http://nyti.ms/1ymRyy0

If You Want to Meet That Deadline, Play a Trick on Your Mind

It's just a few days into the new year. How are you doing on your resolutions? Wait: Have you even started on them yet?

By PHYLLIS KORKKI JAN. 3, 2015

Recognizing that the hardest part of many tasks is beginning them at all, two researchers have sought to determine whether certain outside cues can jump-start us toward reaching our goals. Such cues, which manipulate our perception of time, are simple yet effective, according to a recent article in the Journal of Consumer Research.

In one study, conducted in 2010, the researchers asked two groups of farmers in India to set up a bank account and accumulate a certain amount of money by a deadline, offering extra money as an incentive. One group was approached in June, with a deadline of December that year. The second group was approached in July with a deadline of January the next year.

The farmers in the first group were more likely to set up an account immediately, even though both groups had the same amount of time. That's because the deadline was in the same year as the assignment and therefore seemed more like the present, said Yanping Tu, a Ph.D. candidate at the Booth School of Business at the University of Chicago. She performed the research along with Dilip Soman, a marketing professor at the Rotman School of Management at the University of Toronto. (Lest you think that only farmers in India would benefit from this approach, the two researchers also found similar results among undergraduates and M.B.A. students in North America.)

So the inventors of the New Year's resolution were on the right track when they had people set new goals on Jan. 1 rather than Dec. 31. But clearly that's not enough, since the past is littered with unachieved resolutions. Fortunately, there are other time-related cues that can give people that in-the-present feeling.

In a separate study, the researchers also found that people were "more likely to start working on a task whose deadline is in the current month than in the next month," even though the number of days to finish the task was the same, Ms. Tu said.

Color can also influence the perception of time, she said. She and Professor Soman found that simply by coding a stretch of calendar days in the same color — say, blue — with an assignment occurring on the first "blue" day and the deadline set for the last "blue" day, people were more likely to complete the tasks. Once again, this serves to make the future deadline seem more like the present. (Managers, are you listening? Get out your crayons.)

Research into procrastination has noted that people have much less concern about their future selves than their present selves — and are willing to sell their future selves down the river for the sake of present ease. But when the present marches into the future, and we are confronted with the work that our past selves refused to do, we pay the price in unmet deadlines, all-nighters and general torment.

So if a few little tricks can manipulate us into thinking that time is of the essence, why not give them a try?

http://nyti.ms/1xJmxF4

SpaceX's Next Frontier: Landing a Rocket on Earth

On Tuesday, SpaceX hopes to upend the economics of space travel by launching a Falcon 9 rocket and landing the rocket's 14-story-tall first stage on a barge.

By KENNETH CHANG JAN. 4, 2015

In rocketry, what goes up usually comes down in pieces.

The cost of getting to orbit is exorbitant, because the rocket, with its multimillion-dollar engines, ends up as trash in the ocean after one launching.

Elon Musk, the chief executive of the Space Exploration Technologies Corporation, better known as SpaceX, likens the waste to throwing away a 747 jet after a single transcontinental flight. "Reusability is the critical breakthrough needed in rocketry to take things to the next level," Mr. Musk said in October during a talk at the Massachusetts Institute of Technology.

On Tuesday, his company hopes to upend the economics of space travel.

At 6:20 a.m. Eastern time, one of SpaceX's Falcon 9 rockets is scheduled to lift off from the Cape Canaveral Air Force Station in Florida on what is otherwise a routine unmanned cargo run to the International Space Station.

But this time, the company will attempt to land the first stage of the rocket intact on a barge floating in the Atlantic Ocean. After the booster falls away and the second stage continues pushing the payload to orbit, its engines will reignite to turn it around and guide it to a spot about 200 miles east of Jacksonville, Fla.

SpaceX has attempted similar maneuvers on three earlier Falcon 9 flights, and on the second and third attempts, the rocket slowed to a hover before splashing into the water.

"We've been able to soft-land the rocket booster in the ocean twice so far," Mr. Musk said. "Unfortunately, it sort of sat there for several seconds, then tipped over and exploded. It's quite difficult to reuse at that point."

The first rocket stage, Mr. Musk noted, is as tall as a 14-story building. "When a 14-story building falls over, it's quite a belly flop," he said. "What we need to do is to be able to land on a floating platform."

So SpaceX built a floating platform, 300 feet long and 170 feet wide, for the rocket stage to land on.

A new addition to the rocket is a set of "grid fins" that will fold out after separation to help steer the rocket toward the platform. No people will be aboard the barge during the landing attempt. If SpaceX's gamble succeeds, the company plans to reuse the rocket stage on a later flight.

Mr. Musk put the chances of success at 50 percent or less. But, he added, over the dozen or so flights scheduled for this year, "I think it's quite likely, 80 to 90 percent likely, that one of those flights will be able to land and refly."

Eventually, SpaceX would like to land the first stage back at the launch site. A longer-term goal is to recover and reuse the second stage as well, and Mr. Musk has predicted that a fully reusable rocket could cut launch costs to a hundredth of what they are now.

This NASA cargo mission, SpaceX's fifth, is carrying more than 5,000 pounds of supplies and equipment, including an IMAX movie camera, a laboratory habitat for studying fruit flies, and an instrument to measure the distribution of clouds as well as particles of dust, smoke and air pollution. After four weeks docked to the space station, the SpaceX cargo capsule will carry experiments, trash and other items back to Earth.

This flight is also attracting scrutiny because the Orbital Sciences Corporation, the other company that NASA has hired to ferry cargo to the space station, suffered a catastrophic failure in October when its Antares rocket fell back to the ground moments after liftoff.

Among the items destroyed in the explosion were 18 student experiments, part of a program run by the National Center for Earth and Space Science Education. Some of the students had traveled to the Orbital's launching site in eastern Virginia and left crestfallen.

But Jeff Goldstein, the director of the center, and NanoRacks, the company that made arrangements for the experiments on the space station, were already working to juggle the manifests on future cargo flights.

Three weeks later, 17 of the 18 student teams had recreated their experiments and shipped them to Houston for NASA to add them to the SpaceX payload, then scheduled for launching on Dec. 19.

"It was nuts," Dr. Goldstein said. "NASA moved heaven and earth for this."

The 18th team, Dr. Goldstein said, decided to modify its experiment, requiring a new safety review.

The launching was subsequently postponed after a test firing of the Falcon 9's nine engines was cut short. After a later successful test firing, the launch date was set for Jan. 6.

http://nyti.ms/1xsRcok

Limiting Rest Is Found to Help Young Concussion Patients

Patients prescribed two days rest report fewer symptoms than those prescribed five days rest

By CATHERINE SAINT LOUIS JAN. 5, 2015

Experts recommend that young people who have suffered a concussion get one or two days of rest at home, until symptoms start resolving, before gradually returning to school and physical activity. But scientific evidence to support this approach is sparse, and some doctors have recommended that young patients remain inactive for even longer periods after a concussion.

Now a randomized trial has compared the approaches and found that among a group of patients ages 11 to 22, those with a concussion who were prescribed strict rest for five days by staff members of an emergency department actually reported more symptoms than those told to rest for one or two days. Recovery was also slower for the group receiving stricter rest, researchers reported Monday in the journal Pediatrics.

The study does not provide definitive guidance on how to manage pediatric concussions, experts say. But it does confirm that resting for longer than 24 to 48 hours is not beneficial for most young patients and suggests that "cocoon therapy" — which entails mostly lying in a dark room for multiple days - should not be recommended for most young people with mild traumatic brain injury.

"More isn't always better," said Dr. Christopher Giza, a professor of pediatric neurology at Mattel Children's Hospital at the University of California, Los Angeles, who was not involved in the research. He added, "There was no advantage to prolonged rest."

None of the study participants were admitted to the hospital, and the findings do not apply to patients with brain injuries so severe that they must be hospitalized.

The researchers had expected to find that more rest would be helpful. Instead, Dr. Danny G. Thomas, a pediatric emergency medicine doctor at Children's Hospital of Wisconsin who led the research, and his colleagues found that the patients advised to rest for five days reported more physical symptoms like headache and nausea in first few days, and more often experienced emotional symptoms like irritability and sadness over 10 days. "There are potential adverse consequences if you over-restrict activity without respect to individual symptoms," said Gerard Gioia, chief of pediatric neuropsychology at Children's National Medical Center in Washington, who was not involved with the study.

If rest is prolonged, adolescents worry because schoolwork is piling up, he said, and because "they're removed from their life support, their friends." Symptoms in most young patients improve over time. "If you are restricting them beyond what

they need," Dr. Gioia said, "they start to get worried and think, 'I can handle it, but I'm not being allowed.' Then you might see mood changes or anxiety."

For the study, 88 young patients who went to the emergency department at Children's Hospital of Wisconsin within a day of experiencing a concussion were advised to get cognitive and physical rest either for no more than 48 hours or for five days.

Each day, participants rated their symptoms. They also took computerized tests and paper exams to test their brain function. The researchers measured the participants' ability to balance. There was no difference between the groups in brain function or ability to maintain balance, the researchers found.

While praising the design of the study, Dr. William Meehan, the director of the Micheli Center for Sports Injury Prevention in Waltham, Mass., noted that it was not a blind experiment. "Those assigned to the strict rest group may have perceived themselves as sicker," which could have influenced their reporting of symptoms, said Dr. Meehan, who wrote a commentary accompanying the study.

The available evidence suggests that young patients with a concussion should rest away from school and work for the first 24 to 48 hours, experts said. If symptoms are improving, the patients may slowly resume normal activity.

But a return to school sports or exercise where they might be at risk for another concussion should happen only after the patients have been cleared by a doctor with experience in concussion management. "Ten years ago, we were doing very little management or restriction of activity, and kids were doing too much" after concussions, said Dr. Gioia. "I now see kids are actually being forced to do too little. The pendulum has to come back to the middle."

http://nyti.ms/1xsRcok

Heat and a drug do the trick

A Keio University team has developed what it says is an improved method of opening blood vessels that have narrowed and become clogged.

YUSUKE YAGI, Nikkei staff writer

TOKYO - Such blockages result from conditions like arteriosclerosis.

This device, developed at Keio University, widens blood vessels by heating them and applying a drug.

With the new technique, blood vessels are first softened by warming them up. They are then dilated by inserting a drug-coated balloon. The medicine prevents the vessels from narrowing again. The angioplasty procedure has been successfully tested on animals; according to the team, led by professor Tsunenori Arai, it does no damage to blood vessels.

The group aims to begin clinical trials in 2015, hoping to aid treatment of blood vessels in the legs.

Balloon angioplasty is not the only method of opening blood vessels. Stents, or tiny tubes, are also commonly used. Some types of stents are coated with drugs that control multiplication of cells and also prevent recurrent stenosis -- the re-narrowing of the blood vessels after they are opened.

Arai's research team noticed that when blood vessels are warmed, the collagen tissue that is part of their makeup softens. Armed with this knowledge, the team set out to create a better balloon angioplasty method. A laser is beamed from the tip of a catheter, and the resulting heat softens the vessel. This purportedly allows for damage-free balloon dilation.

Combining the heat method with drugs appears to have led to an even more potent dilation solution. For coating the balloon, the agent of choice is a cancer drug called paclitaxel. This can also be used with a drug-eluting balloon -- one that gradually discharges the agent.

When the scientists tested the procedure on hog carotid arteries, they heated them to 70 C and inserted the drug-coated balloon for one minute. The drug reached beyond the inner membrane of the vessel walls, confirming that this approach offers deeper penetration than methods that do not involve heat. The effect of the drug is expected to last for a month or longer.

Arai said that using a balloon with the drug results in a 10% or less chance of re-narrowing in leg blood vessels, even without heating. Use heat, and the team estimates an even lower probability.

With conventional stent or balloon methods, one issue has been the high probability of stenosis recurring in blood vessels below the knee, Arai said. Vessel damage has also been a concern: Stents, which are made with metal, can shift sometime after the procedure and potentially weaken vessel walls.

The team is currently working with the Tokorozawa Heart Center, near Tokyo, to prepare for clinical trials as a step toward commercialization.

 Name _____ **Student number** _____