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Evidence suggests life on Earth started after meteorites splashed into warm little ponds

Life on Earth began somewhere between 3.7 and 4.5 billion years ago, after meteorites splashed down and leached essential elements into warm little ponds

HAMILTON, ON - Life on Earth began somewhere between 3.7 and 4.5 billion years ago, after meteorites splashed down and leached essential elements into warm little ponds, say scientists at McMaster University and the Max Planck Institute in Germany. Their calculations suggest that wet and dry cycles bonded basic molecular building blocks in the ponds' nutrient-rich broth into self-replicating RNA molecules that constituted the first genetic code for life on the planet.

The researchers base their conclusion on exhaustive research and calculations drawing in aspects of astrophysics, geology, chemistry, biology and other disciplines. Though the "warm little ponds" concept has been around since Darwin, the researchers have now proven its plausibility through numerous evidence-based calculations.

Lead authors Ben K.D. Pearce and Ralph Pudritz, both of the McMaster's Origins Institute and its Department of Physics and Astronomy, say available evidence suggests that life began when the Earth was still taking shape, with continents emerging from the oceans, meteorites pelting the planet - including those bearing the building blocks of life - and no protective ozone to filter the Sun's ultraviolet rays. "No one's actually run the calculation before," says Pearce. "This is a pretty big beginning. It's pretty exciting."

"Because there are so many inputs from so many different fields, it's kind of amazing that it all hangs together," Pudritz says. "Each step led very naturally to the next. To have them all lead to a clear picture in the end is saying there's something right about this."

Their work, with collaborators Dmitry Semenov and Thomas Henning of the Max Planck Institute for Astronomy, has been published today in the Proceedings of the National Academy of Science.

"In order to understand the origin of life, we need to understand Earth as it was billions of years ago. As our study shows, astronomy provide a vital part of the answer. The details of how our solar system formed have direct consequences for the origin of life on Earth," says Thomas Henning, from the Max Planck Institute for Astronomy and another co-author.

The spark of life, the authors say, was the creation of RNA polymers: the essential components of nucleotides, delivered by meteorites, reaching sufficient concentrations in pond water and bonding together as water levels fell and rose through cycles of precipitation, evaporation and drainage. The combination of wet and dry conditions was necessary for bonding, the paper says.

In some cases, the researchers believe, favorable conditions saw some of those chains fold over and spontaneously replicate themselves by drawing other nucleotides from their environment, fulfilling one condition for the definition of life. Those polymers were imperfect, capable of improving through Darwinian evolution, fulfilling the other condition. "That's the Holy Grail of experimental origins-of-life chemistry," says Pearce.

That rudimentary form of life would give rise to the eventual development of DNA, the genetic blueprint of higher forms of life, which would evolve much later. The world would have been inhabited only by RNA-based life until DNA evolved.

"DNA is too complex to have been the first aspect of life to emerge," Pudritz says. "It had to start with something else, and that is RNA."

The researchers' calculations show that the necessary conditions were present in thousands of ponds, and that the key combinations for the formation of life were far more likely to have come together in such ponds than in hydrothermal vents, where the leading rival theory holds that life began in roiling fissures in ocean floors, where the elements of life came together in blasts of heated water. The authors of the new paper say such conditions were unlikely to generate life, since the bonding required to form RNA needs both wet and dry cycles.

The calculations also appear to eliminate space dust as the source of life-generating nucleotides. Though such dust did indeed carry the right materials, it did not deposit them in sufficient concentration to generate life, the researchers have determined. At the time, early in the life of the solar system, meteorites were far more common, and could have landed in thousands of ponds, carrying the building blocks of life. Pearce and Pudritz plan to put the theory to the test next year, when McMaster opens its Origins of Life laboratory that will re-create the pre-life conditions in a sealed environment.

"We're thrilled that we can put together a theoretical paper that combines all these threads, makes clear predictions and offers clear ideas that we can take to the laboratory," Pudritz says.

http://bit.ly/2xmQMaI

Methane made lakes on Mars, study claims

Geophysicists find a mechanism to explain big lakes in a dry climate on the Red Planet. Andrew Masterson reports.

The mystery of ancient lakes on Mars may have been solved, according to a study published in the journal Nature Geoscience.

The research, by a team led by geophysicist Edwin Kite from the University of Chicago in the US, provides a plausible explanation for an apparent data inconsistency that has puzzled scientists for a while.

Information compiled about ground layers on Mars – including that gathered by the rover Curiosity – indicate that fewer than three million years ago the planet had lakes full of liquid water. This has been perplexing, because other data, including the lack of weathering around the lake outflows, indicate that long before then most of the planet had become cold and dry.

For the lakes to form, therefore, there had to be a period of climate warming strong enough to induce ice to melt in sufficient quantities to form the gigantic lakes – and long enough to allow the lakes to endure for thousands of years, as sediment evidence suggests they did.

Kite and his colleagues used a numerical analysis to try to account for the apparent inconsistency, and posit one scenario that would explain it. They suggest that shifts in the planet's axis destabilised ice sheets, causing them to shrink and shift. Methane stored in the Martian soil and trapped beneath the ice was thus liberated and released into the atmosphere.

This, in turn, had a warming effect, melting ice and creating the lakes.

The researchers note that this proposed mechanism is "inconsistent with many previously proposed triggers for lake-forming climates" but fits well what they term a "methane-burst scenario".

In an accompanying editorial, Alberto Fairen of the Centro de Astrobiología in Madrid, Spain, says that while it is unlikely that any single mechanism is sufficient to explain the existence of Martian lakes during otherwise arid periods, the methane-burst scenario nevertheless provides a fresh means by which to approach the evidence.

http://bit.ly/2xnBUsq

Scientists find new source of radioactivity from Fukushima disaster

Scientists have found radioactive material from the Fukushima Dai-ichi nuclear power plant in sands and brackish groundwater beneath beaches up to 60 miles away

Scientists have found a previously unsuspected place where radioactive material from the Fukushima Dai-ichi nuclear power plant disaster has accumulated--in sands and brackish groundwater beneath beaches up to 60 miles away.

The research team sampled eight beaches in Japan within 60 miles of the crippled Fukushima Dai-ichi Nuclear Power Plant and found high levels of radioactive cesium discharged from the 2011 accident in the brackish groundwater beneath the beaches. The cesium did not constitute a public health concern, but it showed how radioactive material can be transported far from accidents sites, where it attaches to and is stored by sand grains. **Souichiro Teriyaki, Kanazawa University**

The sands took up and retained radioactive cesium originating from the disaster in 2011 and have been slowly releasing it back to the ocean.

"No one is either exposed to, or drinks, these waters, and thus public health is not of primary concern here," the scientists said in a study published October 2 in the Proceedings of the National Academy of Sciences. But "this new and unanticipated pathway for the storage and release of radionuclides to the ocean should be taken into account in the management of coastal areas where nuclear power plants are situated."

The research team--Virginie Sanial, Ken Buesseler, and Matthew Charette of Woods Hole Oceanographic Institution and Seiya Nagao of Kanazawa University--hypothesize that high levels of radioactive cesium-137 released in 2011 were transported along the coast by ocean currents. Days and weeks after the accident, waves and tides brought the cesium in these highly contaminated waters onto the coast, where cesium became "stuck" to the surfaces of sand grains. Cesium-enriched sand resided on the beaches and in the brackish, slightly salty mixture of fresh water and salt water beneath the beaches.

But in salt water, cesium no longer "sticks" to the sand. So when more recent waves and tides brought in salty seawater from the ocean, the brackish water underneath the beaches became salty enough to release the cesium from the sand, and it was carried back into the ocean.

"No one expected that the highest levels of cesium in ocean water today would be found not in the harbor of the Fukushima Dai-ichi nuclear power plant, but in the groundwater many miles away below the beach sands," said Sanial.

The scientists estimated that the amount of contaminated water flowing into the ocean from this brackish groundwater source below the sandy beaches is as large as the input from two other known sources: ongoing releases and runoff from the nuclear power plant site itself, and outflow from rivers that continue to carry cesium from the fallout on land in 2011 to the ocean on river-borne particles. All three of these ongoing sources are thousands of times smaller today compared with the days immediately after the disaster in 2011.

The team sampled eight beaches within 60 miles of the crippled Fukushima Dai-ichi Nuclear Power Plant between 2013 and 2016. They plunged 3- to 7-foot-long tubes into the sand, pumped up underlying groundwater, and analyzed its cesium-137 content. The cesium levels in the groundwater were up to 10 times higher than the levels found in seawater within the harbor of the nuclear power plant itself. In addition, the total amount of cesium retained more than 3 feet deep in the sands is higher than what is found in sediments on the seafloor offshore of the beaches.

Cesium has a long half-life and persists in the environment. In their analyses of the beaches, the scientists detected not only cesium-137, which may have come from the Dai-ichi plant or from nuclear weapons tested in the 1950s and 1960s, but also cesium-134, a radioactive form of cesium that can come only from the 2011 Fukushima accident.

The researchers also conducted experiments on Japanese beach samples in the lab to demonstrate that cesium did indeed "stick" to sand grains and then lost their "stickiness" when they were flushed with salt water.

"It is as if the sands acted as a 'sponge' that was contaminated in 2011 and is only slowly being depleted," said Buesseler.

"Only time will slowly remove the cesium from the sands as it naturally decays away and is washed out by seawater," said Sanial.

"There are 440 operational nuclear reactors in the world, with approximately one-half situated along the coastline," the study's authors wrote. So this previously unknown, ongoing, and persistent source of contamination to coastal oceans "needs to be considered in nuclear power plant monitoring and scenarios involving future accidents."

This research was funded by the Gordon and Betty Moore Foundation, the Deerbrook Charitable Trust, and the European Commission Seventh Framework Project "Coordination and implementation of a Pan-Europe Instrument for Radioecology."

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Adverse events spike after blood pressure meds go generic in Canada

Circulation: Cardiovascular Quality and Outcomes Journal Report

DALLAS - One month after generic versions of three widely-used blood pressure drugs became available in Canada, hospital visits for adverse events spiked in generic drug users, according to new research in Circulation: Cardiovascular Quality and Outcomes, an American Heart Association journal.

Researchers in Quebec compared hospital visits and emergency room consultations among 136,177 patients, aged 66 years and older, who took one of three hypertension medications before and after their generic versions became available. The drugs - losartan (Cozaar®), valsartan (Diovan®) and candesartan (Atacand®) - are also used in patients with heart failure.

They found:

Before generic versions were commercialized, the average proportion of adverse events was 10 percent.

The month when generics were commercialized, the rates of adverse events ranged from 8 percent to 14 percent for patients using generics, depending on the type of drug.

The increase was 8 percent for losartan, 11.7 percent for valsartan and 14 percent for candesartan, and the rates for losartan remained consistently higher for the study year.

"Because most users of a brand-name drug are switched to generic versions within two or three years after it becomes available, the observed increase in adverse events could reflect an acute response to equivalent, but not identical, generic drugs for newly switched patients," said Paul Poirier M.D., Ph.D., FAHA, study author and professor of pharmacy at Laval University in Quebec City.

The immediate increase of adverse events in these three generic drugs could, hypothetically, be explained by differences between drugs. "In our study, patients could have been substituted to a generic version that is pharmacokinetically 6 to 21 percent different from the brand-name version that was used," Poirer said. "The results must be interpreted cautiously because studies like this assessing adverse events over a fixed time period, combined with differences between patients, make drawing firm conclusions difficult. Also, because the findings were based on medical claims data, there may be inaccuracies."

After the first month, the difference between brand names and generics narrowed, but some differences persisted - primarily cardiovascular problems, he said. To some degree the findings might partially reflect various demographic differences between generic users, although clinical differences among very sick and lower socioeconomic patients were minimal, according to the authors.

"Although generic drugs are generally considered to be equivalent, patients and their physicians should be aware that they may not have exactly the same effect as their brand-name counterparts, especially during the first month as patients transition to the new medicine," Poirier said.

Co-authors are Jacinthe Leclerc, R.N., M.Sc.; Claudia Blais, Ph.D.; Louis Rochette, M.Sc.; Denis Hamel, M.Sc. and Line Guénette, B.Pharm., Ph.D. Author disclosures are on the manuscript.

The project is part of the continuous chronic disease surveillance mandate in Quebec.

Available multimedia is on the right column of the release link - https://newsroom.heart.org/news/adverse-events-spike-after-blood-pressure-meds-go-generic-in-canada?preview=17d196396c887c0bffda8bd1fcd13e66

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Observations of red aurora over 1770 Kyoto help diagnose extreme magnetic storm

Japanese researchers combine historic accounts of a rare red aurora with modern methods to describe an extreme magnetic storm over Kyoto in the 18th century

Auroras are lightshows that typically occur at high latitudes such as the Arctic and Antarctic; however, they expand equatorward under severe magnetic storms. Past observations of such unusual auroras can therefore allow us to determine the frequency and severity of magnetic storms. The more information that can be gathered about historic intense magnetic storms, the greater the opportunity to mitigate disruption of power grids in a future event.

The painting of the red aurora of Sept. 17 1770 in the premodern Japanese text "Seikai," which is owned by the Matsusaka City Museum of History and Traditional Crafts. A radial structure of stripes is shown, comprising small-scale rays inside the stripes. The bottom section and eastern/western edges of the stripes are somewhat darkened. The caption on the right-hand side may be translated as follows, "On 17 September 1770, at night, red vapor was active at northern sky. The figure was as it watched at midnight." **Matsusaka City, Mie Prefecture**

Historical documents are becoming much more accessible for research as newly discovered records surface from private collections across the world. Researchers centered at Tokyo's National Institute of Japanese Literature (NIJL) and National Institute for Polar Research (NIPR) examined a detailed painting from a Japanese manuscript Seikai ("understanding comets") with associated commentary describes a red aurora occurring over Kyoto on 17 September 1770. Also investigated were detailed descriptions of the event from a newly discovered diary of the Higashi-Hakura family of Kyoto.

"The enthusiasm and dedication of amateur astronomers in the past provides us an exciting opportunity," Kiyomi Iwahashi of NIJL says. "The diary was written by a kokugakusha [scholar of ancient Japanese culture], and provides a sophisticated description of the red aurora, including a description of the position of the aurora relative to the Milky Way."

Using astrometric calculations of the elevations of the Milky Way as it would have been viewed from Kyoto on 17 September 1770, the researchers were able to calculate the geometry of the red aurora and check the results against the details from the Seikai painting and the diary. The success of the description of the aurora according to the historical documents allowed the researchers to estimate the strength of the magnetic storm that caused the September 1770 aurora.

"The magnetic storm on 17 September 1770 was comparable with or slightly larger than the September 1859 magnetic storm that occurred under the influence of the Carrington solar flare. The 1859 storm was the largest magnetic storm on record, in which technological effects were widely observed, "Ryuho Kataoka of NIPR says." It was lucky for us that the 1770 storm predated our reliance on electricity."

So how likely are such magnetic storms? " We are currently within a period of decreasing solar activity, which may spell the end for severe magnetic storms in the near future," Kataoka says. "However, we actually witnessed an extremely fast coronal mass ejection only several days ago [10 September 2017], which might be powerful enough to cause extreme storms. Fortunately, it just missed the Earth."

Regardless of the specific likelihood of another perfect magnetic storm, interdisciplinary historical and scientific collaborations are invaluable in providing important physical details that could help us to understand the greatest magnetic storms in history and prepare for any potential future event.

The article, "Inclined zenith aurora over Kyoto on 17 September 1770: Graphical evidence of extreme magnetic storm" was published in Space Weather at DOI: 10.1002/2017SW001690

http://bit.ly/2xXBGYI

'Ideal biomarker' detects Alzheimer's disease before the onset of symptoms

The discovery that clinicians have long been waiting for

Croatia, New Mexico Absence of a prefrontal activation during sensory gating of simple tones detects the Alzheimer's disease (AD) before the occurrence of the first symptoms. Sanja Josef Golubic Ph.D., physicists at the Department of Physics, Faculty of Science, University of Zagreb, reveals the high potential, absolutely non-invasive biomarker of AD pathology in a new study published in the journal Human Brain Mapping. Josef Golubic found a discrete, individual biomarker of AD with "ideal" properties.

Highlights of the new biomarker:

Absolutely non-invasive

Detects the illness before the occurrence of the first symptoms (preclinical)

Discrete: localized/non-localized a prefrontal generator

Does not require estimation of uniform cut-off levels and standardization processes

Low sensitivity to individual heterogeneity and variability

Can follow the evolution of the pathophysiological process of AD

Individual

Topographic

Worldwide spread of Alzheimer's disease, a long-lasting morbid type of dementia, is one of the biggest global public health challenges facing this generation. A wealth of evidence emerged during over more than 110 years of disease research suggest that the pathological changes associated with AD start decades before the onset of clinical symptoms. This long progression of neurodegeneration that is irreversible by the stage of symptomatic disease, may account for failure to develop successful disease-modifying therapies. Currently, there is a pressing worldwide search for a marker of very early, possibly reversible, pathological changes related to AD in still cognitively intact individuals, before the occurrence of the first symptoms.

Reisa Sperling, chairman of the National Institute on Aging/Alzheimer's Association Workgroup on Preclinical AD and director of the Neuroimaging Program at Harvard Medical School, reviewing the extensive search for the biomarker of preclinical AD, emphasises: „An active line of research is the relationship of intrinsic neural networks and the "topographic" evolution of the pathophysiological process of AD. It is possible, just as in real estate, that "location, location, location" is key".*

Sanja Josef Golubic found the location of the key - it was hidden in the topography of auditory sensory gating network. She uncovered a topological biomarker of preclinical and clinical AD pathology at the individual level that shows a large effect size (0.98) and high accuracy, sensitivity and specificity (100%) in identifying symptomatic AD patients within a research sample. The new biomarker does not require estimation of cut-off levels or standardization processes what is the main problem with so far proposed AD markers. It is absolutely non-invasive, not based on the use of group means and is not associated with statistically significant changes in a continuous variable. Its strength lies in the simplicity of using a binary value, i.e. activated or not-activated a neural generator. The low sensitivity to individual heterogeneity and variability due to its binary nature is probably the most important property of the proposed biomarker.

"Three years ago we discovered the novel, third fast sensory processing pathway-gating loop, which directly links primary sensory areas to medial prefrontal cortex within first 80ms after auditory stimulation**. We provided strong evidences of the modulatory role of the medial prefrontal generator on the dynamics of generators in primary auditory cortices. We have also noticed the high sensitivity of the gating generators dynamic on AD pathology. It was inspiration to focus our AD biomarker search in the direction of prefrontal sensory gating generator activation", says Sanja Josef Golubic, who together

with Cheryl Aine, Selma Supek, Julia Stephen, John Adair and Janice Knoefel form the international research team. The team was formed by the University of Zagreb, New Mexico University, Mind Research Network and New Mexico VA Healthcare System.

"In the present study, we demonstrate the use of the localization of neural sources underlying neuromagnetic fields measured outside a head to detect AD even before the onset of symptoms. The healthy controls activated a prefrontal generator in response to both the deviant and repeating tones of an oddball paradigm. To the contrary, the symptomatic AD group was lacking any medial prefrontal gating generator activation to either the deviant or repeating tones. However, we detected a sub-group of controls characterized by the absence of prefrontal gating generator activation for the repeating tone only and significantly lower scores on a mini mental status exam and delayed visual memory test - Rey-Osterreith Complex Figure Test. It is highly probable that these individuals were captured in a preclinical AD phase since they show both neuropsychological and neurophysiological impairments characteristic of an AD type of dementia, although they did not yet meet clinical criteria for the early phase of symptomatic AD", emphasises Josef Golubic.

The localization of a discrete prefrontal gating activation is a highly promising biomarker of Alzheimer's disease at the individual level with potential of following the evolution of the pathophysiological process of disease. The next steps in evolving the biomarker include the testing in a large independent samples and assessment in longitudinal clinical studies. The large effect size, absolute non-invasiveness and statistical independence, properties of an "ideal" biomarker, will certainly launch this AD biomarker promptly into clinical use.

Original publication:

"MEG biomarker of Alzheimer's disease: Absence of a prefrontal generator during auditory sensory gating",Sanja Josef Golubic, Cheryl J Aine, Julia M Stephen, John C Adair, Janice E Knoefel, Selma Supek. Hum Brain Mapp 38:5180-5194, (2017).

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*** "Modulatory role of the prefrontal generator within the auditory M50 network", Sanja Josef Golubic, Cheryl J Aine, Julia M Stephen, John C Adair, Janice E Knoefel, Selma Supek.Neuroimage 9: 120-131 (2014).*

http://bit.ly/2yOHqRp

Vitamin D protects against severe asthma attacks

Taking oral vitamin D supplements in addition to standard asthma medication could halve the risk of asthma attacks requiring hospital attendance, according to research led by Queen Mary University of London (QMUL).

Asthma affects more than 300 million people worldwide and is estimated to cause almost 400,000 deaths annually. Asthma deaths arise primarily during episodes of acute worsening of symptoms, known as attacks or 'exacerbations', which are commonly triggered by viral upper respiratory infections.

Vitamin D is thought to protect against such attacks by boosting immune responses to respiratory viruses and dampening down harmful airway inflammation.

The new study, funded by the National Institute for Health Research, and published in The Lancet Respiratory Medicine, collated and analysed the individual data from 955 participants in seven randomised controlled trials, which tested the use of vitamin D supplements.

Overall, the researchers found that vitamin D supplementation resulted in:

a 30 per cent reduction in the rate of asthma attacks requiring treatment with steroid tablets or injections - from 0.43 events per person per year to 0.30.

a 50 per cent reduction in the risk of experiencing at least one asthma attack requiring Accident and Emergency Department attendance and/or

hospitalisation - from 6 per cent of people experiencing such an event to 3 per cent.

Vitamin D supplementation was found to be safe at the doses administered. No instances of excessively high calcium levels or renal stones were seen, and serious adverse events were evenly distributed between participants taking vitamin D and those on placebo.

Lead researcher Professor Adrian Martineau said: "These results add to the ever growing body of evidence that vitamin D can support immune function as well as bone health. On average, three people in the UK die from asthma attacks every day. Vitamin D is safe to take and relatively inexpensive so supplementation represents a potentially cost-effective strategy to reduce this problem."

The team's use of individual participant data also allowed them to query the extent to which different groups respond to vitamin D supplementation, in more detail than previous studies.

In particular, vitamin D supplementation was found to have a strong and statistically-significant protective effect in participants who had low vitamin D levels to start with. These participants saw a 55 per cent reduction in the rate of asthma exacerbations requiring treatment with steroid tablets or injections - from 0.42 events per person per year to 0.19.

However, due to relatively small numbers of patients within sub-groups, the researchers caution that they did not find definitive evidence to show that effects of vitamin D supplementation differ according to baseline vitamin D status.

Professor Hywel Williams, Director of the NIHR Health Technology Assessment Programme, said: "The results of this NIHR-funded study brings together evidence from several other studies from over the world and is an important contribution to reducing uncertainties on whether Vitamin D is helpful for asthma - a common condition that impacts on many thousands of people worldwide."

Dr David Jolliffe from QMUL, first author on the paper, added: "Our results are largely based on data from adults with mild to moderate asthma: children and adults with severe asthma were relatively under-represented in the dataset, so our findings cannot necessarily be generalised to these patient groups at this stage. Further clinical trials are on-going internationally, and we hope to include data from them in a future analysis to determine whether the promise of today's results is confirmed in an even larger and more diverse group of patients."

Research paper: 'Vitamin D supplementation to prevent asthma exacerbations: systematic review and meta-analysis of individual participant data'. David A Jolliffe, Lauren Greenberg, Richard Hooper, Christopher Griffiths, Carlos Camargo Jr, Conor Kerley, Megan Jensen, David Mauger, Iwona Stelmach, Mitsuyoshi Urashima, Adrian Martineau. The Lancet Respiratory Medicine. http://www.thelancet.com/journals/lanres/article/PIIS2213-2600(17)30306-5/fulltext?elsca1=tlxpr

http://bit.ly/2wECZrD

Predatory bacteria that engineer portholes and paint frescoes in harmful bacteria

Illuminating the mystery of how one bacterium could invade another and grow inside it without breaking the other bacterium instantly

A microbiological mystery of how one bacterium could invade another and grow inside it without breaking the other bacterium instantly has been illuminated by scientists at the University of Nottingham and Indiana University.

The Nottingham scientists are investigating the invasive predatory bacteria Bdellovibrio bacteriovorus as a potential therapeutic to kill antibiotic-resistant pathogenic bacteria. The Indiana scientists are investigating what bacterial cell structures are made of and how they are built. To do this they have developed and used fluorescent D amino-acids (FDAAs) – coloured substitutes for natural substances found in bacterial cell walls. This was combined with super-resolution microscopy to great effect in a new paper published today in Nature Microbiology.

The teams have joined forces and discovered that the invading Bdellovibrio bacterium forms a tiny reinforced molecular 'porthole' in the wall of the host bacterium, squeezes through this and then seals it

up from the inside. This process is like cutting and welding a porthole on a ship but on a molecular-scale.

Professor Liz Sockett from the University of Nottingham said: "The bacteria being invaded are 100 million times shorter than a ship like the Queen Mary 2, and the invading bacteria are 500 million times narrower. The materials used for the welding aren't metal of course, but are natural D-amino-acids. These are mirror image forms of the 'L' amino-acids found in the proteins of foods and of our bodies.

"We discovered a second process where the invading bacteria effectively 'plaster' the inside of the bacterium they are invading, again using the D amino-acids. This makes the inside of the bacterium a more reinforced home for the Bdellovibrio to live inside. This is important as a previous paper showed that the invaded bacterial walls are initially rounded-up and weakened early in the invasion process."

Erkin Kuru, a PhD student at the time, suggested to Liz during a lecture visit to Indiana, that she use coloured FDAAs to label the two different bacteria as the predators attacked. Adding a new colour just as invasion was beginning and later as it progressed, replaced the natural amino-acids being used and shone a new coloured light on how predation works.

FDAAs showed what was happening at each stage and gave the team a 'eureka moment' when they saw that the predatory bacteria make a 'porthole' with a central pore surrounded by a reinforcing ring containing D amino-acids. Bdellovibrio squeeze through this pore and fill it in with more D-amino-acid containing material so the invaded bacteria don't burst and all their internal cell contents can be privately eaten by the predators without leaking away to the outside.

As this is happening the predatory bacteria go on to add more FDAAs in all around the wall of the invaded bacterium, not just at the porthole ring. In the experimental conditions the predatory bacteria 'painted' this coloured FDAA, rather like a molecular scale 'fresco', to the walls of the invaded bacterium in a process which reinforces the wall of invaded bacterium so it doesn't collapse before the predator has eaten the nutritional contents inside. Dr Carey Lambert from Nottingham joined the project and was able to find some of the 'tools' that apply the frescos – these are a group of enzymes that have been little studied until recently.

Professor Sockett concludes: "It is remarkable to see this in action at such a tiny scale and also useful. Knowing more about the mechanisms used by the invading predatory bacteria could help design new ways of killing pathogens. Now that the invasion processes have been defined it should be possible to gather all the tools needed to invade and consume pathogenic bacteria without releasing large amounts of their pathogenic cell materials by them bursting."

Explore further: How bacterial predators evolved to kill other bacteria without harming themselves

More information: Erkin Kuru et al. Fluorescent D-amino-acids reveal bi-cellular cell wall modifications important for Bdellovibrio bacteriovorus predation, Nature Microbiology (2017). DOI: 10.1038/s41564-017-0029-y

http://bit.ly/2y0VPdN

Okinawan pit viper genome reveals evolution of snake venom

A bite from a pit viper, locally known as habu, can cause permanent disability and even death. Yet, much about its venom remains an enigma.

Highly variable in composition, even between littermates, this toxic cocktail keeps changing over generations.

A recent study in Genome Biology and Evolution sheds light on the evolution of snake venoms. For the first time, researchers have sequenced a habu genome, that of the Taiwan habu (Protobothrops mucrosquamatus), and compared it to that of its sister species, the Sakishima habu (Protobothrops elegans).

More than 50 instances of snake bites were recorded in the past year on Okinawa alone, prefectural government figures show. Globally, snake bites cause between 81,000 and 138,000 mortalities per year, according to the World Health Organization. In developing countries and rural areas with high exposure to venomous species and scant

medical resources, snake bites can be especially devastating. For such places, creating effective antivenom can be a matter of life or death.

"For many years it was known that snake venoms evolve very rapidly, and the most common explanation for this has been natural selection," said Alexander Mikheyev, senior author on the paper and head of the Ecology and Evolution Unit at the Okinawa Institute of Science and Technology (OIST), "but there are reasons to suspect that this might not be the only evolutionary force at work."

By taking samples of venoms and soft tissues from more than 30 specimens of the Taiwan and Sakishima habus, invasive but well-established species on Okinawa, researchers from OIST and the Okinawa Prefectural Institute of Health and Environment were able to map entire sequences of venom genes. Their study shows more than one factor at play in the evolution of this venom.

To understand how the chemical composition of a snake bite evolves, it is crucial to understand its redundancy. Like multiple engines that allow a plane to fly if one of them should fail, venom targets multiple systems, assuring the snake's success. This complex mixture of proteins and small organic molecules attacks crucial prey physiological systems, such as blood pressure or blood coagulation, at several points. Even if one venom component does not prove optimally effective, various others do.

Typically, a habu injects a small amount of venom, a drop the size of a pinhead. Yet, it is more than strong enough to paralyze a rodent. Evolutionary biologists call this surplus power, which prevents prey from injuring or killing a snake, "overkill."

Over time, as snakes reproduce, advantageous traits of venom are passed on to offspring in the process of natural selection. However, the offspring can also inherit other traits—not necessarily beneficial ones. Because the average dose of venom is so high—in some cases killing prey almost instantaneously—it can mask inefficiencies in the venom's chemical makeup. These inefficiencies can be passed down from generation to generation with relatively little effect on the venom's function. "You can think of venoms evolving over two axes," said Mikheyev. "One of those is pushing them to be more effective, but another axis actually pushes them to be less effective."

"We're only now coming up with analytical methods to look at venoms comprehensively," said Steven Aird, first author on the paper. "There's a tremendous amount we can learn." The researchers' work opens the door to new avenues of study as well as medical applications.

More information: Steven D. Aird et al. Population genomic analysis of a pitviper reveals microevolutionary forces underlying venom chemistry, Genome Biology and Evolution (2017). DOI: 10.1093/gbe/evx199

http://bit.ly/2z4onTP

New use for alcohol aversion drug in treatment of chemo resistant lung cancer found

Researchers were able to reverse chemotherapy resistance in non-small cell lung cancer

Scientists have had positive results from a laboratory-based study using a well-known alcohol aversion drug to try to combat chemotherapy resistance in the most common type of lung cancer, non-small cell lung cancer (NSCLC). The findings from the scientists at Trinity College Dublin and St James's Hospital, Dublin, Ireland, have been published in the leading international journal Oncotarget.

Chemotherapy forms the backbone of many treatment plans for lung cancer patients, however, treatment resistance has become a significant clinical challenge. While chemotherapy kills the majority of tumour cells within a tumour, some types of cancer cells, called cancer stem cells, continue to grow and divide and contribute to the development of drug resistance. This results in tumour recurrence or secondary tumours which often prove fatal.

The scientists from the Trinity Translational Medicine Institute at St James's Hospital Dublin, in collaboration with the Cancer Stem Cell Group, Coombe Hospital, Dublin, found that lung cancer cells that have high levels of ALDH activity, a recently identified marker of cancer stem cells became resistant to chemotherapy. This induces the

growth and expansion of a drug-resistant population of lung cancer cells, allowing the cancer cells to survive the effects of treatment. These findings may help explain why a large number of lung cancer patients receiving this type of chemotherapy eventually relapse resulting in progression of their disease.

The FDA-approved alcohol aversion drug Disulfiram (Antabuse), which has been used to treat alcohol addiction for over sixty years, works against ALDH by restricting its activity. Upon alcohol consumption, it prevents the body from metabolising alcohol and makes the person feel sick. When it comes to cancer cells, the drug was found to be effective in inhibiting the activity of ALDH, which resulted in decreased tumour cell growth and increased killing of lung cancer stem cells. The research team at Trinity and St James's found that the alcohol aversion drug Disulfiram in combination with chemotherapy, was significantly more effective in killing drug resistant lung cancer stem cells compared to treatment with the chemotherapy alone.

Dr Martin Barr, Adjunct Assistant Professor and a lead investigator in the Thoracic Oncology Research Group, St James's Hospital and Trinity said: "Disulfiram is an already approved drug with well tolerated side effects which can be taken orally. Its potential use may give chemotherapeutic drugs such as cisplatin, a new lease of life in the treatment of resistant lung tumours. We believe that our research findings show that this is a really important option that warrants further investigation and clinical testing. "

An alternative approach to seeking new drug treatments for cancer is not to start with molecular targets, but to assess those drugs approved for other therapeutic uses which show some evidence of anti-cancer activity. This is the field of drug repurposing in oncology and there is now an increasing interest in the use of non-cancer drugs as anti-cancer therapeutics.

"The development of novel anti-cancer drugs against various malignant tumours is both time-consuming and expensive and involves pre-clinical and clinical testing. Finding new uses for existing drugs, otherwise known as 'repurposing', may allow for new uses of an old drug that may lead to the discovery of new treatments. Such repurposing is a proven short cut between the research laboratory and the clinic," said Dr Lauren MacDonagh who carried out this study as part of her PhD at Trinity College Dublin.

Lung cancer is the leading cause of cancer-related deaths worldwide and accounts for more deaths than breast, colon and prostate cancers combined. In Ireland, there are more than 2,300 new cases of lung cancer per year and over 1,800 deaths. While incidence rates are decreasing in men, lung cancer incidence is increasing in women.

This study was funded by Molecular Medicine Ireland as part of the Clinical & Translational Research Scholars Programme under Cycle 5 of the Irish Government's Programme for Research in Third Level Institutions (PRTLI) and co-funded under the European Regional Development Fund (ERDF).

http://bit.ly/2z53tUI

Researchers find that accurately transcribing DNA overrides DNA repair

Fidelity of transcribing DNA comes at the expense of DNA repair

A groundbreaking and surprising discovery provides a major conceptual change of what is most important to cells: the fidelity of the DNA transcription process - accurately copying the DNA message into RNA, the precursor to proteins - or DNA repair, which saves broken chromosomes from being lost. As reported in the journal Nature, researchers found that in the model organism E. coli, the fidelity of transcribing DNA comes at the expense of DNA repair.

"If you asked a group of scientists which is more important for a cell, maintaining the integrity of its DNA containing all of the organism's genetic information, or the fidelity of transcription - the process that transcribes DNA into RNA, which leads to protein synthesis - the vast majority would agree that repairing DNA is more important," said corresponding author Dr. Christophe Herman, associate professor of molecular and human genetics and molecular virology and

microbiology at Baylor College of Medicine. "In this study we show the opposite."

It is well known that DNA breaks are troublesome for cells because they can cause major instability in the cell's genes or cell death, if not repaired correctly. In contrast, errors during transcription are generally considered less important because the transcript is temporary, and if one is defective, cells can make another one. For these reasons, most researchers consider that DNA break repair would outweigh transcription to protect DNA integrity, and keep cells from losing their chromosomes.

"Scientists have been studying DNA repair for decades and generated a great deal of information about it. In comparison, we know little about transcription fidelity," said Herman, who also is a member of the Dan L Duncan Comprehensive Cancer Center. "My lab has been studying fidelity of transcription for the last 12 years. We showed years ago that transcription errors can lead to heritable changes. That made us think that transcription fidelity might be more important than we had originally thought. In this study we wanted to investigate the consequences of removing GreA, a factor that helps ensure the fidelity of the transcription process on the bacterium E. coli, on DNA break repair."

An unexpected discovery

"After removing GreA, bacteria were hundreds of times more efficient at repairing DNA damage caused by drugs that mimic radiation," said first author Dr. Priya Sivaramakrishnan, a Ph.D. student in the Herman lab during the development of this project. "Bacteria can repair DNA breaks much faster when GreA is absent."

To pinpoint how the lack of transcription fidelity can lead to faster repair, the researchers developed a novel whole-genome sequencing method, which they have named eXOnucleases sequencing (XO-seq), to physically visualize the different steps of DNA repair in living cells. Using this and other methods, the researchers determined the molecular mechanism by which loss of GreA promotes DNA repair.

The finding that the transcription fidelity factor GreA prevents DNA repair represents a major paradigm shift in the DNA world because it implies that ensuring proper transcription fidelity comes at the cost of lowering the cell's ability to repair DNA. "That was completely unexpected," Herman said.

"To have a process that helps transcribe DNA into high-quality RNA that will produce high-quality proteins, bacteria are paying a hundred-fold price in DNA repair efficiency," said co-author Dr. Susan Rosenberg, Ben F. Love Chair in Cancer Research and professor of molecular and human genetics, of molecular virology and microbiology and of biochemistry and molecular biology at Baylor. Rosenberg also is leader of the Cancer Evolvability Program at the Dan L Duncan Comprehensive Cancer Center at Baylor.

"The conservation of the basic biology of nucleic acids from bacteria to humans is tremendous," said Rosenberg. "We hypothesize that this mechanism discovered in E. coli might also be present in other cells, which would have implications in a number of fields, from cancer to evolution."

Other contributors to this work include Leonardo A. Sepúlveda, Jennifer A. Halliday, Jingjing Liu, María Angélica Bravo Núñez and Ido Golding, who are affiliated with Baylor College of Medicine and the Dan L Duncan Comprehensive Cancer Center.

The study was supported by National Institutes of Health grant R01-GM088653, pilot grant from the Dan L Duncan Comprehensive Cancer Center and P30 CA125123 and was partly supported by the NIH Director's Pioneer Award DP1-CA174424. Further support was provided by a gift from the WM Keck Foundation, NIH grants R01-GM53158 and R01-839-GM082837, National Science Foundation grants PHY 1147498, PHY 1430124, and PHY 1427654, the Welch Foundation grant Q-1759, the John S. Dunn Foundation Collaborative Research Award and a Cullen Foundation Scholarship.

http://bit.ly/2z4STNs

Healing molecule discovery could reduce limb amputations for diabetes patients

Scientists have discovered new insights into a molecule which is part of the body's tissue repair system, in a finding which could help treat non-healing wounds and injuries, such as diabetic foot

The number of limbs amputated because of diabetes is at an all-time high of 20 each day in England alone. Intense research around the world is being carried out to discover new treatments that could help avoid such life-changing operations and reduce medical costs for society.

A study led by the universities of Exeter and Bath, and published in the journal Antioxidants and Redox Signalling has made great strides in understanding how the molecule deoxyribose-1-phosphate stimulates the formation of new blood vessels.

It has long been known that the formation of new blood vessels is critical during the body's response to tissue damage. Now, thanks to this project jointly funded by Biotechnology and Biological Sciences Research Council (BBSRC) and the Medical Research Council, the understanding of how deoxyribose-1-phosphate works could open new avenues of treatment in encouraging the body to heal- a discipline known as regenerative medicine.

Dr Giordano Pula, of the University of Exeter Medical School, led the team. He said: "We're very excited to provide new insights into how this crucial molecule works to stimulate the formation of blood vessels in people. We now hope to be able to use this knowledge to trigger the formation of new blood vessels in patients where this is required for tissue regeneration, such as diabetic foot."

This study demonstrates that deoxyribose-1-phosphate activates an enzyme called NADPH oxidase 2 (NOX2). This in turn leads to the stimulation of the transcription factor called NFkB, which is responsible for turning on genes specifically involved in the formation of new blood vessels.

Among the genes activated in the chain of events leading to blood vessel formation, the vascular endothelial growth factor receptor 2 (VEGFR2) play a central role. This is a key target in regenerative medicine, and the team hope that this discovery will provide a cost-effective treatment for manipulating blood vessel formation.

Dr Pula's team is now planning to focus their investigation on the ability of deoxyribose-1-phosphate to stimulate skin repair by increasing the vascularisation of wounds and non-healing ulcers. The team hopes this work will lead to new applications for treating conditions such as diabetic foot.

The paper, Direct activation of NADPH oxidase 2 by 2-deoxyribose-1-phosphate triggers nuclear factor kappa B-dependent angiogenesis, is now published in the journal Antioxidants and Redox Signalling. The full list of authors is D Vara D, JM Watt JM, TM Fortunato TM, H Mellor, M Burgess, K Wicks, K Mace, S Reeksting, AT Lubben, CP Wheeler-Jones CP, G Pula.

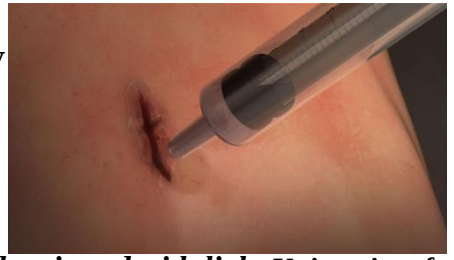
http://bit.ly/2xZF70X

'Squirtable' elastic surgical glue seals wounds in 60 seconds

Emergency treatments could be transformed, saving lives

A highly elastic and adhesive surgical glue that quickly seals wounds without the need for common staples or sutures could transform how surgeries are performed.

Biomedical engineers from the University of Sydney and the United States collaborated on the development of the potentially life-saving surgical glue, called MeTro.



MeTro is applied directly to the wound and activated with light **University of Sydney**

MeTro's high elasticity makes it ideal for sealing wounds in body tissues that continually expand and relax - such as lungs, hearts and arteries - that are otherwise at risk of re-opening.

The material also works on internal wounds that are often in hard-to-reach areas and have typically required staples or sutures due to surrounding body fluid hampering the effectiveness of other sealants.

MeTro sets in just 60 seconds once treated with UV light, and the technology has a built-in degrading enzyme which can be modified to determine how long the sealant lasts - from hours to months, in order to allow adequate time for the wound to heal.

The liquid or gel-like material has quickly and successfully sealed incisions in the arteries and lungs of rodents and the lungs of pigs, without the need for sutures and staples.

The results were published today in Science Translational Medicine, in a paper by the University of Sydney's Charles Perkins Centre and Faculty of Science; Boston's Northeastern University, the Wyss Institute for Biologically Inspired Engineering at Harvard University and the Beth Israel Deaconess Medical Center (BIDMC) in Boston.

MeTro combines the natural elastic protein technologies developed in collaboration with author and University of Sydney McCaughey Chair in Biochemistry Professor Anthony Weiss, with light sensitive molecules developed in collaboration with author and Director of the Biomaterials Innovation Research Center at Harvard Medical School Professor Ali Khademhosseini.

Lead author of the study, Assistant Professor Nasim Annabi from the Department of Chemical Engineering at Northeastern University, oversaw the application of MeTro in a variety of clinical settings and conditions. "The beauty of the MeTro formulation is that, as soon as it comes in contact with tissue surfaces, it solidifies into a gel-like phase without running away," she said. "We then further stabilise it by curing it on-site with a short light-mediated crosslinking treatment. This allows the sealant to be very accurately placed and to tightly bond and interlock with structures on the tissue surface."

The University of Sydney's Professor Anthony Weiss described the process as resembling that of silicone sealants used around bathroom and kitchen tiles. "When you watch MeTro, you can see it act like a liquid, filling the gaps and conforming to the shape of the wound," he said. "It responds well biologically, and interfaces closely with human tissue to promote healing. The gel is easily stored and can be squirted directly onto a wound or cavity.

"The potential applications are powerful - from treating serious internal wounds at emergency sites such as following car accidents and in war zones, as well as improving hospital surgeries."

Professor Khademhosseini from Harvard Medical School was optimistic about the study's findings.

"MeTro seems to remain stable over the period that wounds need to heal in demanding mechanical conditions and later it degrades without any signs of toxicity; it checks off all the boxes of a highly versatile and efficient surgical sealant with potential also beyond pulmonary and vascular suture and staple-less applications," he said. The next stage for the technology is clinical testing, Professor Weiss said.

"We have shown MeTro works in a range of different settings and solves problems other available sealants can't. We're now ready to transfer our research into testing on people. I hope MeTro will soon be used in the clinic, saving human lives."

Elastagen Pty Ltd is commercialising the technology.

Images and video https://cloudstor.aarnet.edu.au/plus/index.php/s/K4uNG7qdcoSG88J.

YouTube explainer https://www.youtube.com/watch?v=h7Ww805tUS8&feature=youtu.be

http://bit.ly/2xp1uNL

No clear evidence that most new cancer drugs extend or improve life

Study prompts calls to 'raise the evidence bar' for approval of new cancer drugs

Even where drugs did show survival gains over existing treatments, these were often marginal, the results show.

Many of the drugs were approved on the basis of indirect ('surrogate') measures that do not always reliably predict whether a patient will live longer or feel better, raising serious questions about the current standards of drug regulation.

The researchers, based at King's College London and the London School of Economics say: "When expensive drugs that lack clinically meaningful benefits are approved and paid for within publicly funded healthcare systems, individual patients can be harmed, important societal resources wasted, and the delivery of equitable and affordable care undermined."

The research team analysed reports on cancer approvals by the European Medicines Agency (EMA) from 2009 to 2013.

Of 68 cancer indications approved during this period, 57% (39) came onto the market on the basis of a surrogate endpoint and without evidence that they extended survival or improved the quality of patients' lives.

After a median of 5 years on the market, only an additional 8 drug indications had shown survival or quality of life gains.

Thus, out of 68 cancer indications approved by the EMA, and with a median 5 years follow-up, only 35 (51%) had shown a survival or quality of life gain over existing treatments or placebo. For the remaining 33 (49%), uncertainty remains over whether the drugs extend survival or improve quality of life.

The researchers outline some study limitations which could have affected their results, but say their findings raise the possibility that regulatory evidence standards "are failing to incentivise drug development that best meets the needs of patients, clinicians, and healthcare systems."

Taken together, these facts paint a sobering picture, says Vinay Prasad, Assistant Professor at Oregon Health & Science University in a linked editorial.

He calls for "rigorous testing against the best standard of care in randomized trials powered to rule in or rule out a clinically meaningful difference in patient centered outcomes in a representative population" and says "the use of uncontrolled study designs or surrogate endpoints should be the exception not the rule."

He adds: "The expense and toxicity of cancer drugs means we have an obligation to expose patients to treatment only when they can reasonably expect an improvement in survival or quality of life."

These findings suggest "we may be falling far short of this important benchmark."

This study comes at a time when European governments are starting to seriously challenge the high cost of drugs, says Dr Deborah Cohen, Associate Editor at The BMJ, in an accompanying feature.

She points to examples of methodological problems with trials that EMA has either failed to identify or overlooked, including trial design, conduct, analysis and reporting.

"The fact that so many of the new drugs on the market lack good evidence that they improve patient outcomes puts governments in a difficult position when it comes to deciding which treatments to fund," she writes. "But regulatory sanctioning of a comparator that lacks robust evidence of efficacy, means the cycle of weak evidence and uncertainty continues." In a patient commentary, Emma Robertson says: "It's clear to me and thousands of other patients like me that our current research and development model has failed."

Emma is leader of Just Treatment, a patient led campaign with no ties to the pharmaceutical industry, which is calling for a new system that rewards and promotes innovation, so that more effective and accessible cancer medicines are brought within reach.

http://bit.ly/2yvxcZP

We've finally seen how the sleeping brain stores memories

sleep

AT LAST, we've seen how the brain memories when we sleep. By scanning slumbering people, researchers have watched how the "trace" of a memory moves from one region of the brain to another.

By Jessica Hamzelou

"The initial memory trace kind of disappears, and at the same time, another emerges," says Shahab Vahdat at Stanford University in California. It is the first time memories have been observed being filed away in humans during sleep, he says.

Vahdat and his colleagues did this by finding people who were able to fall asleep in the confined, noisy space of an fMRI scanner, which is no easy undertaking. "We screened more than 50 people in a mock scanner, and only 13 made it through to the study," says Vahdat.

The team then taught this group of volunteers to press a set of keys in a specific sequence – in the same way that a pianist might learn to

play a tune. It took each person between about 10 and 20 minutes to master a sequence involving five presses. “They had to learn to play it as quickly and as accurately as possible,” says Vahdat. Once they had learned the sequence, each volunteer put on a cap of EEG electrodes to monitor the electrical activity of their brain, and entered an fMRI scanner – which detects which regions of the brain are active.

The team saw a specific pattern of brain activity while the volunteers performed the key-pressing task. Once they had stopped, this pattern kept replaying, as if each person was subconsciously revising what they had learned.

The volunteers were then asked to go to sleep, while the team monitored each of them for two-and-a-half hours. At first, the pattern of brain activity continued to replay in the outer region of the brain called the cortex, which is involved in higher thought.

When the volunteers entered non-REM sleep – known as the stage when we have relatively mundane dreams – the pattern started to fade in the cortex, but a similar pattern of activity started in the putamen, a region deep within the brain (eLife, doi.org/cdsz). “The memory trace evolved during sleep,” says Vahdat.

His team thinks that movement-related memories are transferred to deeper brain regions for long-term storage. This chimes with the hypothesis that the brain’s cortex must free up space so that it can continue to learn new information, says Christoph Nissen at University Psychiatric Services in Bern, Switzerland.

Non-REM sleep happens within a few hours of dozing off, says Vahdat. If you’re hoping for some night-time learning, it’s important to make sure that those first few hours are uninterrupted, he says.

Nissen hopes a better understanding of how memories are consolidated during sleep could lead to treatments for people with insomnia and similar sleep disorders. Such individuals tend to be treated with drugs that send them to sleep, but Nissen has found that this sleep doesn’t seem to be as good at consolidating memories as natural sleep.

http://bit.ly/2y1hZ2j

Researchers create molecule that could 'kick and kill' HIV

In lab animals, a particle developed by UCLA, Stanford, NIH scientists awakens dormant virus cells and then knocks them out

Current anti-AIDS drugs are highly effective at making HIV undetectable and allowing people with the virus to live longer, healthier lives. The treatments, a class of medications called antiretroviral therapy, also greatly reduce the chance of transmission from person to person.

But the medications do not actually rid the body of the virus, which has the ability to elude medications by lying dormant in cells called CD4+ T cells, which signal another type of T cell, the CD8, to destroy HIV-infected cells. When a person with HIV stops treatment, the virus emerges and replicates in the body, weakening the immune system and raising the likelihood of opportunistic infections or cancers that can sicken or kill the patient.

Researchers have been looking for ways to eliminate the "reservoirs" where the virus hides, and researchers from UCLA, Stanford University and the National Institutes of Health may have developed a solution. Their approach involves sending an agent to "wake up" the dormant virus, which causes it to begin replicating so that either the immune system or the virus itself would kill the cell harboring HIV.

Scientists call the technique "kick and kill."

Destroying the reservoir cells could rid some or all of the HIV virus from people who are infected. And although the scientists' approach has not been tested in humans yet, a synthetic molecule they developed has been effective at kicking and killing HIV in lab animals, according to a study published Sept. 21 in the peer-reviewed journal PLOS Pathogens.

"The latent HIV reservoir is very stable and can reactivate virus replication if a patient stops taking antiretroviral drugs for any reason," said Matthew Marsden, an assistant professor of medicine in

the division of hematology oncology at the David Geffen School of Medicine at UCLA, and the study's lead author. "Our study suggests that there may be means of activating latent virus in the body while the patient is on antiretroviral drugs to prevent the virus from spreading, and that this may eliminate at least some of the latent reservoir."

To test the approach, the researchers gave antiretroviral drugs to mice that had been infected with HIV, and then administered a synthetic compound called SUW133, which was developed at Stanford, to activate the mice's dormant HIV. Up to 25 percent of the previously dormant cells that began expressing HIV died within 24 hours of activation.

With further development, the technique could lower the viral reservoir enough for people with HIV to be able to discontinue their anti-viral therapy, Marsden said.

SUW133 is based on bryostatin 1, a natural compound extracted from a marine animal called Bugula neritina. The research determined that the new compound is less toxic than the naturally occurring version.

"The findings are significant because several previous attempts to activate latent virus have had only limited success," said senior author Jerome Zack, professor and chair of the UCLA department of microbiology, immunology and molecular genetics at the Geffen School, and director of the UCLA Center for AIDS Research. "Most studies showed weak activation of the virus, or severe toxicity, with little effect on the reservoir."

Marsden said results in mice will not necessarily translate to humans. In further studies, the scientists plan to learn how to make SUW133's less toxic, and to evaluate its effectiveness in larger animals, before it could be tested in humans.

The study's other authors are Xiaomeng Wu and Christina Ramirez of UCLA; Brian Loy, Adam Schrier, Akira Shimizu, Steven Ryckbosch, Katherine Near and Paul Wender of Stanford; and Danielle Murray and Tae-Wook Chun of the NIH's National Institute of Allergy and Infectious Diseases.

The research was funded by the NIH, a Bill and Melinda Gates Foundation Explorations grant, the James B. Pendleton Charitable Trust and the UCLA Center for AIDS Research.

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Largest twin study pins nearly 80 percent of schizophrenia risk on heritability

A new study in Biological Psychiatry looks at the risk for schizophrenia in twins

Philadelphia, PA - In the largest study of twins in schizophrenia research to date, researchers at the University of Copenhagen, Denmark, estimate that as much as 79% of schizophrenia risk may be explained by genetic factors. The estimate indicates that genetics have a substantial influence on risk for the disorder.

Published in Biological Psychiatry, the study used a new statistical approach to address one of the factors that contributes to inconsistencies across previous studies -- usually studies of heritability require that people be classified as either having schizophrenia or not, but some people at risk could still develop the disease after the study ends. Drs. Hilker, Helenius and colleagues applied a new method to take this problem into account, making the current estimates likely the most accurate to date.

"The new estimate of heritability of schizophrenia, 79%, is very close to the high end of prior estimates of its heritability," said Dr. John Krystal, Editor of Biological Psychiatry, referring to previous estimates that have varied between 50% and 80%. "It supports the intensive efforts in place to try to identify the genes contributing to the risk for developing schizophrenia," said Dr. Krystal, which have been built on the idea that schizophrenia is highly heritable based on the findings of generations of twin studies.

The study took advantage of the nationwide Danish Twin Register -- a record of all twins born in Denmark since 1870--coupled with

information from the Danish Psychiatric Central Research Register, to assess genetic liability in over 30,000 pairs of twins.

Because the diagnosis of schizophrenia is based on a narrow definition of symptoms, the researchers also estimated heritability using a broader illness category including related disorders on the schizophrenia spectrum. They found a similar estimate of 73%, indicating the importance of genetic factors across the full illness spectrum.

Dr. Hilker explained, "This study is now the most comprehensive and thorough estimate of the heritability of schizophrenia and its diagnostic diversity. It is interesting since it indicates that the genetic risk for disease seems to be of almost equal importance across the spectrum of schizophrenia," even though the clinical presentation may range from severe symptoms with lifelong disability to more subtle and transient symptoms. "Hence, genetic risk seems not restricted to a narrow illness definition, but instead includes a broader diagnostic profile," she added.

The article is "Heritability of schizophrenia and schizophrenia spectrum based on the nationwide Danish Twin Register," by Rikke Hilker, Dorte Helenius Mikkelsen, Birgitte Fagerlund, Kaare Christensen, Axel Skytthe, Thomas Werge, Merete Nordentoft, and Birte Glenthøj. It appears in Biological Psychiatry, published by Elsevier.

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A need for bananas? Dietary potassium regulates calcification of arteries

Low dietary potassium leads to calcified arteries and aortic stiffness, while increased dietary potassium alleviates that in a mouse model, suggesting dietary potassium may protect against heart disease and death from heart disease in humans

BIRMINGHAM, Ala. - Bananas and avocados -- foods that are rich in potassium -- may help protect against pathogenic vascular calcification, also known as hardening of the arteries.

University of Alabama at Birmingham researchers have shown, for the first time, that reduced dietary potassium promotes elevated aortic stiffness in a mouse model, as compared with normal-potassium-fed mice.

Such arterial stiffness in humans is predictive of heart disease and death from heart disease, and it represents an important health problem for the nation as a whole.

The UAB researchers also found that increased dietary potassium levels lessened vascular calcification and aortic stiffness. Furthermore, they unraveled the molecular mechanism underlying the effects of low or high dietary potassium.

Such knowledge of how vascular smooth muscle cells in the arteries regulate vascular calcification emphasizes the need to consider dietary intake of potassium in the prevention of vascular complications of atherosclerosis. It also provides new targets for potential therapies to prevent or treat atherosclerotic vascular calcification and arterial stiffness.

A UAB team led by Yabing Chen, Ph.D., UAB professor of pathology and a Research Career Scientist at the Birmingham VA Medical Center, explored this mechanism of vascular disease three ways: living mice fed diets that varied in potassium, mouse artery cross-sections studied in culture medium with varying concentrations of potassium, and mouse vascular smooth muscle cells grown in culture medium.

Working from living mice down to molecular events in cells in culture, the UAB researchers determined a causative link between reduced dietary potassium and vascular calcification in atherosclerosis, as well as uncovered the underlying pathogenic mechanisms.

The animal work was carried out in the atherosclerosis-prone mouse model, the apoliprotein E-deficient mice, a standard model that are prone to cardiovascular disease when fed a high-fat diet.

Using low, normal or high levels of dietary potassium -- 0.3 percent, 0.7 percent and 2.1 percent weight/weight, respectively, the UAB team found that the mice fed a low-potassium diet had a significant increase in vascular calcification.

In contrast, the mice fed a high-potassium diet had markedly inhibited vascular calcification. Also, the low-potassium mice had increased stiffness of their aortas, and high-potassium mice had decreased stiffness, as indicated by the arterial stiffness indicator called pulse wave velocity, which is measured by echocardiography in live animals. The different levels of dietary potassium were mirrored by different blood levels of potassium in the three groups of mice.

When researchers looked at arterial cross-sections in cultures that were exposed to three different concentrations of potassium, based on normal physiological levels of potassium in the blood, they found a direct effect for the potassium on arterial calcification within arterial rings. Arterial rings in low-potassium had markedly enhanced calcification, while high-potassium inhibited aortic calcification.

"The findings have important translational potential," said Paul Sanders, M.D., professor of nephrology in the UAB Department of Medicine and a co-author, "since they demonstrate the benefit of adequate potassium supplementation on prevention of vascular calcification in atherosclerosis-prone mice, and the adverse effect of low potassium intake."

Mechanistic details

In cell culture, low potassium levels in the culture media markedly enhanced calcification of vascular smooth muscle cells. Previous research by several labs including Chen's group has shown that calcification of vascular smooth muscle cells resembles the differentiation of bone cells, which leads to the transformation of smooth muscle cells into bone-like cells.

So the UAB researchers tested the effect of growing vascular smooth muscle cells in low-potassium cell culture. They found that the low-potassium conditions promoted the expression of several gene markers that are hallmarks of bone cells, but decreased the expression of vascular smooth muscle cell markers, suggesting the transformation of the vascular smooth muscle cells into bone-like cells under low-potassium conditions.

Mechanistically, they found that low-potassium elevated intracellular calcium in the vascular smooth muscle cells, via a potassium transport channel called the inward rectifier potassium channel.

This was accompanied by activation of several known downstream mediators, including protein kinase C and the calcium-activated cAMP response element-binding protein, or CREB.

In turn, CREB activation increased autophagy -- the intracellular degradation system -- in the low-potassium cells. Using autophagy inhibitors, the researchers showed that blocking autophagy blocked calcification.

Thus, autophagy plays an important role in mediating calcification of vascular smooth muscle cells induced by the low-potassium condition.

The roles of the CREB activation and autophagy signals were then tested in the mouse artery cross-section and living-mouse models, with low, normal or high levels of potassium in the media or diet. Results in both of those systems supported the vital role for potassium to regulate vascular calcification through calcium signaling, CREB and autophagy.

Besides Chen and Sanders, co-authors of the paper, "Dietary potassium regulates vascular calcification and arterial stiffness," published in JCI Insight, are Yong Sun, Chang Hyun Byon and Youfeng Yang, UAB Department of Pathology; Wayne E. Bradley, Louis J. Dell'Italia and Anupam Agarwal, UAB Department of Medicine; and Hui Wu, UAB Department of Pediatric Dentistry. Sanders, Agarwal and Chen are also members of the Research Department, Veterans Affairs Birmingham Medical Center.

The paper is also highlighted as an Editor's Pick in the November issue of JCI This Month.

At UAB, Agarwal holds the Marie S. Ingalls Endowed Chair in Nephrology Leadership, Dell'Italia holds the Elmer and Glenda Harris Endowed Chair in Cardiovascular Disease, and Sanders holds the Thomas E. Andreoli Endowed Chair in Nephrology.

Funding for this work came from National Institutes of Health grants HL092215, HL136165 and DK100847, as well as Veterans Affairs Research Department awards BX000369, BX003617 and BX001591.

http://bit.ly/2fUUddx

Do earthquakes have a 'tell'?

Data scientists and seismologists use 'deep tremor' to forecast strong earthquakes

Researchers have long had good reason to believe that earthquakes are inherently unpredictable. But a new finding from Northwestern University might be a seismic shift for that old way of thinking.

An interdisciplinary team recently discovered that "slow earthquakes," which release energy over a period of hours to months, could potentially lead to nearby "regular earthquakes." The finding could help seismologists better forecast some strong earthquakes set to occur within a certain window of time, enabling warnings and other preparations that may save lives.

"While the build-up of stress in the Earth's crust is largely predictable, stress release via regular earthquakes is more chaotic in nature, which makes it challenging to predict when they might occur," said Kevin Chao, a data science scholar in the Northwestern Institute on Complex Systems. "But in recent years, more and more research has found that large earthquakes in subduction zones are often preceded by foreshocks and slow earthquakes."

Supported by the National Science Foundation, the research was published in the Journal of Geophysical Research: Solid Earth. Chao, who is also a member of Northwestern's Center for Optimization and Statistical Learning, served as the paper's first author. Suzan van der Lee, a professor of earth and planetary sciences in Northwestern's Weinberg College of Arts and Sciences, also contributed to the work.

Chao and his colleagues began their work several years ago by turning to a region within Taiwan, home to approximately 100 seismic stations that have continuously recorded ground motion for years. It was there the team noticed deep tremors, a type of slow earthquake that typically recurs in days- or weeks-long cycles.

"Deep tremor is very sensitive to small stress changes," Chao said. "So, we decided to use them as stress meters to monitor local variations in stress build-up and release before and after large earthquakes."

To detect and monitor this deep tremor activity, Chao's team developed a sophisticated set of algorithms and applied it to data from 10 seismic stations in Taiwan. They discovered that deep tremor started to change its behavior about two months before the occurrence of a 6.4-magnitude earthquake in March 2010 in southern Taiwan. The tremor's duration, for example, increased by two-fold before this event and continued to increase afterwards.

Although deep tremor was first reported in 2002, scientists have not found many cases in which behavior changed before large earthquakes. "After the 6.4-magnitude earthquake occurred, we noticed a potential to study deep tremor near the event," Chao said. "We identified the increase in tremor duration three weeks before the earthquake, but we initially could not draw conclusions because tremor rates increase all the time and for different reasons.

But three years after the 6.4-magnitude, Chao and his colleagues noticed that their observations of tremor activity coincided with nearby a GPS recording, which indicated a flip in the direction of ground motion near tremor sources.

By combining data from earth observatories, such as GPS and seismic stations, with statistics and a series of algorithms, the team showed that changes in deep tremor patterns could signal an impending earthquake nearby. To further test the finding, Chao examined four additional earthquakes and discovered that similar precursory patterns did exist. He and Van der Lee hope that this work will inspire more data-driven research in the seismology field.

"Much more data analysis of these tiny but fascinating tremor signals is necessary," he said, "before mid- to short-term earthquake forecasting become reliable."

http://bit.ly/2z5Xzmp

Liverwort genes and land plant evolution

Genome analysis of early plant lineage sheds light on how plants learned to thrive on land

Though it's found around the world, it's easy to overlook the common liverwort - the plant can fit in the palm of one's hand and appears to be comprised of flat, overlapping leaves. Despite their unprepossessing appearance, these plants without roots or vascular tissues for nutrient transport are living links to the transition from the algae that found its way out of the ocean to the established multitude of land plants.

As reported in the October 5, 2017 issue of Cell, an international team including researchers at the U.S. Department of Energy Joint Genome Institute (DOE JGI), a DOE Office of Science User Facility, analyzed the genome sequence of the common liverwort (Marchantia polymorpha) to identify genes and gene families that were deemed crucial to plant evolution and have been conserved over millions of years and across plant lineages. The work was led by researchers at Monash University in Australia, and at Kyoto University and Kindai University in Japan.

"Early plants like the liverwort are what set the world up for land plants. Without them, we wouldn't have plants more than two feet from the ocean and freshwater," said DOE JGI Plant Program head Jeremy Schmutz. "In going back to liverworts, we find genes shared with grasses that are candidate genes for crops for biofuel generation. Land plants began with same parts present in Marchantia today so the changes are all due to factors such as evolution, polyploidy, gene exchange and rounds of selection. We want to know what genes do and we do this by translating function across genomes using conserved sequences. Smaller genomes with less complexity - such as those in a basal or early plant model like liverwort - give us the ability to identify ancestral genes for a gene or gene family. We identify gene function in a plant and determine how this gene works, and then we identify other genes by understanding the evolutionary history of gene or gene family across the history of plants."

The genome sequencing and annotation was done through the DOE JGI's Community Science Program, and allows for genomic comparisons with other early plant lineages sequenced and analyzed by the DOE JGI: the spikemoss Selaginella moellendorffi and the moss Physcomitrella patens. One of the most important biochemical pathways concerns production of the hormone auxin, which is critical for regulating plant growth and development. The team identified a minimal but complete pathway for auxin biosynthesis in the liverwort. Another finding suggests that the genes encoding enzymes producing "sunscreen" that allowed early plants to tolerate ultraviolet light may have been transferred from ancient soil microbes.

One of the team's most important findings concern plant cell wall development. The variety of genes encoding enzymes for plant cell wall development found in Marchantia emphasizes the importance of plant cell walls for the transition to land plants. The team identified early lignin biosynthesis genes similar to those in Physcomitrella. While they identified genes involved in plasmodesmata formation (plasmodesmata are membrane channels involved in nutrient and signal molecule transfers) a pathway that is involved in cell division, they also found that liverworts retain the vestiges of cell division pathways predating land plant-specific pathway.

Another important finding involves water retention and distribution. Early plants had to develop strategies for dealing with drought and desiccation, and many of these same strategies are still employed by modern plants. Abscisic acid is a plant stress hormone that regulates when a plant goes dormant when water is in short supply. The team found homologous genes for abscisic acid biosynthesis, and were also able to identify when specific receptors became critical to land plant families.

Schmutz pointed out that through the Community Science Program, the DOE JGI's exploration of plant evolutionary history is expanding,

leading to the development of a comparative genomics framework, including those from early plant lineages like the liverwort, that benefits the plant research community at large. "The more we accumulate this information in early plant lineages, the easier it is to transfer plant function across plant phylogeny and compare plant families to see the radiation of these genes. We'll be focusing quite a bit more on the basal lineages of plants to get at the evolutionary history and position of genes. If we can understand the origin of these genes then we can understand historical function. Having multiple species allows us to do more and show more than what we can with just one genome."

By learning the original functions of genes, elucidated from the genomes of earlier, simpler, plants and cells, scientists can more easily solve for the functions of related genes seen in more complex plants that may help address DOE missions in bioenergy and environmental processes.

Collaborators on this project included researchers at: HudsonAlpha Institute for Biotechnology; Kobe University (Japan); National Institute of Genetics (Japan); Gregor Mendel Institute (Germany); Nara Institute of Science and Technology (Japan); University of Osnabruck (Germany); Universidad Veracruzana, INBIOTECA (Mexico); University of Cambridge (United Kingdom); CINVESTAV-IPN (Mexico); University of Oxford (United Kingdom); University of Tennessee-Knoxville; Uppsala University (Sweden); Vienna Biocenter Core Facilities (Austria); Institut de Recherche pour le Developpement (France) and, University of Zurich (Switzerland).

http://bit.ly/2y5dymO

The high price of the nocebo effect

People receiving an inert treatment believed they experienced more severe adverse side effects when the dummy drug was labeled as expensive, scientists report.

The researchers say brain regions responsible for higher-order cognition can influence primal pain sensing at the spinal level.

To study the neurological causes for the so-called nocebo effect (where people in clinical trials sometimes report negative side effects even though they received inactive substances), Alexandra Tinnermann and colleagues developed a new functional magnetic resonance imaging (fMRI) method for simultaneous activity measurements in the entire central pain system throughout the cortex, brainstem, and spinal cord.

For the nocebo treatment, the scientists enrolled 49 people in a trial for a supposed anti-itch cream that, in reality, contained no active ingredients.

All participants were told that increased pain sensitivity was a potential side effect for the inert cream, but some were informed that they were receiving an expensive ointment and others were led to believe that the lotion was cheap (the scientists even created two different packages for the balms, indicating high or low price).

People treated with the "expensive" cream reported greater sensitivity on a heat-tolerance test, and the nocebo effects became more pronounced over time.

The researchers identified portions of the spinal cord that became activated during nocebo effect pain, and determined that altered sensations due to perceived price were associated with differences in two brain regions - the periaqueductal gray and the rostral anterior cingulate cortex.

A related Perspective by Luana Colloca gives additional examples where patients' expectations alter placebo (positive) or nocebo effects, advocating for more research into the physiology underlying these phenomena for better clinical trial design.

http://bit.ly/2y7mBRM

Did Teddy Evans fatally undermine Scott of the Antarctic?

Research detective reveals how Scott's second-in-command may have been responsible for death of his leader and four men.

Sydney: The tragic death of Scott of the Antarctic and four companions on the return of his scientific expedition to the South Pole in 1912, has long been blamed on poor planning by Scott.

But the discovery of new documents by University of New South Wales researcher Prof Chris Turney revealed today in the journal *Polar Record* show how the actions of another expedition member brought about their deaths and why it has been covered-up for over a century.

This is an image of Scott and his team who all died on the return from the South Pole. **National Library**

Through patient detective work, Prof Turney found documents that reveal how the second in command, Lieutenant Edward (Teddy) Evans, later the 1st Baron Mountevans, crucially undermined Scott - stealing rations from food depots and failing to pass on orders to a dog sled team that would have brought Scott home safely.

"The new documents suggest at the very least appalling leadership on the part of Evans or at worst, deliberate sabotage, resulting in the death of Scott and his four companions," said Prof Turney.

"The documents also show how public records were altered in later recounts of the expedition and why a Committee of Inquiry into the expedition was rapidly shut down almost before it began."

Early on multiple members of Scott's expedition developed doubts about Lieutenant Teddy Evans' role as second in command. Scott himself described Evans in letters as "not at all fitted to be second-in-command," and promised to "take some steps concerning this".

It is likely one of the reasons that Scott sent Evans back to base before he pushed on to the South Pole with four companions. But on the return journey from the Pole, Scott's expedition found rations carefully planted on the journey out had disappeared.

In addition, the updated orders Scott gave to Evans to send a dog team out to meet the returning expedition were seemingly never delivered. Instead Scott and his team were left to die alone and starving in a blizzard.

The documents uncovered by Prof Turney reveal how Evans had a history of taking more than his share of supplies and how public statements were changed to deflect blame from Evans' role in the missing rations after Scott's death.

It even uncovers why the President of the Royal Geographical Society, Lord Curzon, decided not to hold a public committee of inquiry.

"For too long Scott has been held responsible for the death of himself and the men of his party who made the fateful expedition to the South Pole," said Prof Turney.

"These new documents tell a very different story about how Scott's planning for the expedition was undermined, reveal that his orders were fatally ignored and why the man who arguably contributed the most to his death was never held accountable for his actions."

Paper: *Why didn't they ask Evans?*

Chris Turney is a Professor of Earth Science and Climate Change at the University of New South Wales. Chris is the author of 'Iced In: Ten Days Trapped on the Edge of Antarctica" published by Citadel in North America and 'Shackled' by Penguin Australia.

http://nyti.ms/2fXFLl8

Bronze Arm Found in Famous Shipwreck Points to More Treasure Below

Marine archaeologists announced new findings from their most recent excavation of the roughly 2,000-year-old Antikythera wreck.

By NICHOLAS ST. FLEUR OCT. 5, 2017

A bronze statue's orphaned arm. A corroded disc adorned with a bull. Preserved wooden planks. These are among the latest treasures that date back to the dawn of the Roman Empire, discovered amid the ruins of the Antikythera shipwreck, a sunken bounty off the coast of a tiny island in Greece.

Marine archaeologists working on a project called Return to Antikythera announced these findings on Wednesday from their most recent excavation of the roughly 2,000-year-old wreck, which was first discovered 115 years ago. They said the haul hints at the

existence of at least seven more bronze sculptures still buried beneath the seafloor. Bronze sculptures from that era are rare because they were often melted down to make swords, shields and other items. Only about 50 intact examples have survived, so if the team can salvage the submerged statues, it would be a remarkable recovery of ancient artifacts.

"Say you discovered there are another seven Leonardo paintings that no one knew existed and the prospect of finding them is dangling before your eyes," said Kenneth Lapatin a curator of antiquities at the J. Paul Getty Museum in Los Angeles who was not involved in the project. "That's what this is like for classical archaeologists and those who study ancient Greek and Roman art."

For more than a century the wreck has yielded a trove of antiquities, from bronze and marble statues of Olympian gods and heroes to the mysterious Antikythera mechanism, a hand-held device for tracking planetary movements and predicting eclipses that is often called the "first computer." Last year the team also recovered human skeletal remains at the site from which they have retrieved DNA.

A corroded bronze hand from the Antikythera shipwreck in southern Greece. **Petros Giannakouris/Greek Culture Ministry, via Associated Press**

During their most recent dives in September, the team used a custom built high-tech metal detector to uncover items hidden in the sand. Alexander Sotiriou, one of the project's divers, stumbled upon the bronze arm buried more than a foot and a half below the sediment at a depth of about 160 feet below the sea surface.

"We knew from the very first moment that this was a significant finding," Mr. Sotiriou said. He spent most of his hour's worth of air trying to pry the heavy object from beneath a boulder. Other divers with the project took over and retrieved the green, encrusted limb that extended from shoulder to middle finger tip.

"It's missing a couple of fingers but it's still a magnificent finding. You can see the beauty of this arm," he said. "You see the muscles, you see the tendons, you see the fingers. You see all the details that you can admire on bare skin."

Because the limbs appeared to have been fragments of statues, rather than individual parts being transported, the researchers believe that the rest of their bodies are waiting to be found.

A Disc for a 'First Computer?'

During its most recent dives, the team also uncovered a small, bronze disc with four knobs. Each tab on the trinket had a hole in it which may have been used to screw the object into something to act as a cover. It was just as corroded as the arm.

Researchers are studying whether a small, bronze disc they found is a missing part of the Antikythera mechanism. **Brett Seymour/EUA/ARGO**

When Brendan Foley, co-director for the project and an archaeologist at Lund University in Sweden, found the item he couldn't believe his luck. He thought it may have been a missing piece to the Antikythera mechanism — perhaps the rarest needle in their underwater haystack.

"This thing emerges and I said 'Holy cow! Come over here guys. Doesn't this look like part of the mechanism?'" he said. "And we all started laughing because it couldn't possibly be. But it sure looks convincing."

They sent it to a laboratory in Athens for X-rays and found that beneath its green and black decay there was a decorative bull. They will perform more experiments to find out what it is. Although they have not ruled out whether it could be a part of the Antikythera

mechanism they said that it could just as easily be an adornment of the ship or a vase.

"If it is from the Antikythera mechanism it is a very, very perfect find," said Angeliki G. Simosi, director of the Greek Ephorate of Underwater Antiquities in Athens. "All of the world will speak about it."

The green and black corrosion on the bronze disc recovered from the Antikythera shipwreck, left, conceals a decorative bull that can be revealed under X-ray, right. **Brett Seymour/EUA/ARGO**

The Story from the Depths

The ship that carried the treasures of Antikythera was something like an ancient supertanker or luxury liner that carried grain and artwork for trading in the Mediterranean, including marble and bronze statues being shipped to the richest of the rich, according to Dr. Foley. The site thus provides a peek not just into the lives of the elite, but also into the blooming global and urban society at the beginning of the Roman Empire.

"We're looking at the biggest ancient ship ever investigated by underwater archaeologists," said Dr. Foley.

Measuring an estimated 160-feet long, the ship was like the Titanic of its time. It met its iceberg in the form of a violent storm that smashed it against the island's cliff, scientists believe. The ship then had a turbulent trip to the bottom of the ocean where it most likely rolled several times, flinging its treasure, and goods across the seafloor. In the two millenniums since, earthquakes and landslides have rocked its remains, further breaking and burying its trove of Hellenistic and Classical pottery and artwork.

But in their latest dives, the team recovered wooden planks and pieces of the ship's frame, which can help nail down its country of origin, which have recently come into question.

http://bit.ly/2ya5n82

New NASA study shows moon once had an atmosphere

New study shows that an atmosphere was produced 3 to 4 billion years ago around the ancient Moon, as volcanic eruptions spewed gases faster than they could escape to space

A new study shows that an atmosphere was produced around the ancient Moon, 3 to 4 billion years ago, when intense volcanic eruptions spewed gases above the surface faster than they could escape to space. The study, supported by NASA's Solar System Exploration Research Virtual Institute, was published in Earth and Planetary Science Letters.

When one looks up at the Moon, dark surfaces of volcanic basalt can be easily seen to fill large impact basins. Those seas of basalt, known as maria, erupted while the interior of the Moon was still hot and generating magmatic plumes that sometimes breached the lunar surface and flowed for hundreds of kilometers. Analyses of Apollo samples indicate those magmas carried gas components, such as carbon monoxide, the ingredients for water, sulfur, and other volatile species.

In new work, Dr. Debra H. Needham, Research Scientist of NASA Marshall Space Flight Center, and Dr. David A. Kring, Universities Space Research Association (USRA) Senior Staff Scientist, at the Lunar and Planetary Institute (LPI), calculated the amounts of gases that rose from the erupting lavas as they flowed over the surface and showed that those gases accumulated around the Moon to form a transient atmosphere. The atmosphere was thickest during the peak in volcanic activity about 3.5 billion years ago and, when created, would have persisted for about 70 million years before being lost to space.

The two largest pulses of gases were produced when lava seas filled the Serenitatis and Imbrium basins about 3.8 and 3.5 billion years ago, respectively. The margins of those lava seas were explored by astronauts of the Apollo 15 and 17 missions, who collected samples

that not only provided the ages of the eruptions, but also contained evidence of the gases produced from the erupting lunar lavas.

NASA's Needham says, "The total amount of H2O released during the emplacement of the mare basalts is nearly twice the volume of water in Lake Tahoe. Although much of this vapor would have been lost to space, a significant fraction may have made its way to the lunar poles. This means some of the lunar polar volatiles we see at the lunar poles may have originated inside the Moon."

David Kring notes, "This work dramatically changes our view of the Moon from an airless rocky body to one that used to be surrounded by an atmosphere more prevalent than that surrounding Mars today." When the Moon had that atmosphere, it was nearly 3 times closer to Earth than it is today and would have appeared nearly 3 times larger in the sky.

This new picture of the Moon has important implications for future exploration. The analysis of Needham and Kring quantifies a source of volatiles that may have been trapped from the atmosphere into cold, permanently shadowed regions near the lunar poles and, thus, may provide a source of ice suitable for a sustained lunar exploration program. Volatiles trapped in icy deposits could provide air and fuel for astronauts conducting lunar surface operations and, potentially, for missions beyond the Moon.

Over the past decade, the search for volatiles within the Moon and on the surface of the Moon has intensified. Those volatiles may hold clues about the material that accreted to form the Earth and Moon and, thus, our planetary origins. The volatiles may also provide the in-situ resources needed for sustained lunar surface activities that may follow the development of NASA's new Orion crew vehicle and a Gateway structure that may orbit the Moon. In addition, robotic assets, like NASA's Resource Prospector, are being developed to explore the nature and distribution of volatile deposits that might be suitable for scientific analysis and recovery. Based on the new results of Needham and Kring, those assets may be recovering ice that is partially composed of volatiles erupted from volcanic fissures over 3 billion years ago.

Debra H. Needham et al. ***Lunar volcanism produced a transient atmosphere around the ancient Moon****, Earth and Planetary Science Letters (2017). DOI: 10.1016/j.epsl.2017.09.002*

The new research was initiated from the LPI-Johnson Space Center's Center for Lunar Science and Exploration, led by Kring and supported by NASA's Solar System Exploration Research Virtual Institute. Needham is a former postdoctoral researcher at the LPI.

http://nyti.ms/2hXSlVw

In a First, Gene Therapy Halts a Fatal Brain Disease

For the first time, doctors have used gene therapy to stave off a fatal degenerative brain disease, an achievement that some experts had thought impossible.

By GINA KOLATA OCT. 5, 2017

The key to making the therapy work? One of medicine's greatest villains: HIV.

The patients were children who had inherited a mutated gene causing a rare disorder, adrenoleukodystrophy, or ALD. Nerve cells in the brain die, and in a few short years, children lose the ability to walk or talk. They become unable to eat without a feeding tube, to see, hear or think. They usually die within five years of diagnosis.

The disease strikes about one in 20,000 boys; symptoms first occur at an average age of 7. The only treatment is a bone-marrow transplant — if a compatible donor can be found — or a transplant with cord blood, if it was saved at birth. But such transplants are an onerous and dangerous therapy, with a mortality rate as high as 20 percent. Some who survive are left with lifelong disabilities.

Now a new study, published online in the New England Journal of Medicine, indicates that gene therapy can hold off ALD without side effects, but only if it is begun when the only signs of deterioration are changes in brain scans.

The study involved 17 boys (the disease strikes males almost exclusively), ages 4 to 13. All got gene therapy. Two years later, 15 were functioning normally without obvious symptoms.

"To me, it seems to be working," said Dr. Jim Wilson, director of the gene therapy program at the University of Pennsylvania's Perelman School of Medicine, who was not involved in the new study.

One of the remaining two boys died; his disease progressed so rapidly that gene therapy could not stop it. The other withdrew from the study in order to have a bone-marrow transplant. He died of complications from the procedure.The study opens new avenues for using gene therapy to treat brain diseases, said Dr. Theodore Friedmann, a gene therapy pioneer at the University of California San Diego School of Medicine.

"Many think the central nervous system is intractable and unapproachable," he said. This study proves them wrong.

The research began with a determined mother, Amber Salzman, who was an executive with a Ph.D. in mathematics at GlaxoSmithKline. In 2000, her nephew was diagnosed with ALD, a disease she had heard of only in the movie, "Lorenzo's Oil."

He was "this wonderful sweet brilliant kid," Dr. Salzman said. "All of a sudden he loses his abilities. He crumbles in front of your eyes."

She had her one-year-old son tested and found that he had the mutated gene, as did another nephew. She looked into Lorenzo's oil, a difficult dietary regimen featuring a specially designed oil. Statisticians at her company told her studies of it did not show any effect.

Dr. Salzman met with Dr. Tachi Yamada, who was head of research and development at Glaxo. "I said, 'It will be a few years before the bomb goes off in my son and other nephew. What do we do?'"

Dr. Yamada told her that her best bet was gene therapy, but it had never been tried against a disease like ALD.

Indeed, gene therapy had recently fallen out of favor after 18-year-old Jesse Gelsinger died during an experimental treatment. Then, in 2003, four of nine children who got gene therapy for an immunodeficiency disease developed leukemia.

Dr. Salzman, with assistance from her sister, Rachel, and from other scientists, was undeterred. She corralled researchers worldwide, asking why a different sort of virus couldn't be used to slip a good ALD gene into the boys' cells. The best choice, it turned out, was a disabled form of HIV, which can insert genes into human cells more safely than other viral carriers.

Scientists were understandably wary. Disabled AIDS viruses had not been used in human gene therapy. But "I don't take no for an answer," Dr. Salzman said. "I probably come just shy of stalking people."

***From left, Brian, Paul and Brandon Rojas. While Brian shows no sign of ALD, Brandon, now 10, no longer speaks, walks or eats. He has a feeding tube*. Misha Friedman for The New York Times**

The result of her lobbying was a tiny study in France in which researchers used a disabled form of HIV to deliver a normal form of the ALD gene. The investigators reported that the treatment seemed to stop brain degeneration in two boys. Yet the idea behind the treatment seems almost preposterous: Take bone marrow stem cells from a boy with the ALD gene mutation. Insert a good gene into those cells and then infuse them back into the bone marrow.

Wait about a year while stem cells with the good genes multiply in the bone marrow. Eventually, they drift up into the brain, where they slowly turn into glial cells — support cells that surround neurons and help insulate them. The proper gene in the glial cells takes over, stopping the brain deterioration that would otherwise occur.

That unlikely process also explains why bone marrow transplants work, said David A. Williams, chief scientific officer at Boston Children's Hospital and a principal investigator for the study. New bone marrow cells, from a healthy donor, supply good ALD genes to cells in the recipient that eventually become glial cells.

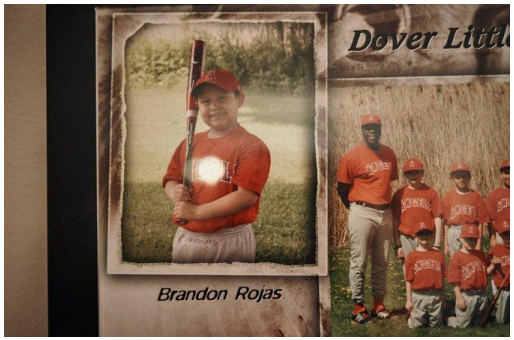
Either therapy must be administered early, before symptoms are apparent. In the year it takes for the treatment to become effective, the

brains of children who are already showing symptoms can deteriorate to the point of no return.

The success of the small pilot study was enough to inspire the founding of a company, Bluebird Bio, which sponsored the bigger study in hopes of marketing gene therapy for ALD.

The company has now expanded that study to include an additional eight boys, and in separate research is following boys who had bone marrow transplants to compare outcomes.

For Paul Rojas of Dover Plains, N.Y., whose son was in the study, gene therapy has been a lifesaver. He never heard of the disease until his son Brandon, who was 7, started drooling, losing his ability to concentrate and listing to one side when he walked.



Brandon was 7 when he was found to have ALD. "Brian misses playing with his brother," his father said. "Brandon was his idol." **Misha Friedman for The New York Times**

The diagnosis was a shock. And since Brandon was showing symptoms, it was too late for a bone-marrow transplant.

Brandon's doctors, Mr. Rojas said, sat across from him and his wife, Liliana, in a small conference room and gave them the bad news: "This is a disease that has no cure."

He had his 4-year-old, Brian, tested. He had the mutated gene, too.

The Rojases could not find a compatible donor for a bone-marrow transplant. But then they learned about the gene therapy trial and got Brian enrolled. He is now 7, with no sign of the disease.

But his older brother Brandon, now 10, no longer speaks, walks or eats. He has a feeding tube. "Brian misses playing with his brother," Mr. Rojas said. "Brandon was his idol."

For Dr. Salzman, the results of the new gene therapy study have come too late. She had to get treatment for her son before he developed symptoms. He had a cord blood transplant, which was successful. Her nephew also had one, but suffered complications and must use a wheelchair.

The results of the new study also give rise to a concern that is becoming a regular feature of gene therapy work and other new biotech therapies: How much will this treatment cost?

Bluebird Bio is not saying – companies generally do not announce prices until their drugs are approved.

Dr. David A. Williams, chief scientific officer at Boston Children's Hospital and a principal investigator of the new study, expects the price to be similar to the hundreds of thousands of dollars it costs for a bone-marrow transplant. But the new treatment "is a curative therapy," he said.

Dr. Friedmann is not assuaged by such arguments. The research enabling these products to come to market often begins with studies already paid for by grants from the federal government or from private foundations. The expected prices, he said, are "absolutely crazy."

http://bit.ly/2xsKbva

Little-known drug keeps climbers' minds sharp at high altitude

A so-called "smart drug" intended to boost cognitive performance also seems to protect the brain from altitude sickness, according to a military study that tested it at 4000 metres.

By Helen Thomson

An increasing number of people visit high-altitude sites nowadays, for work, sport, religious pilgrimages and military tasks. But even the fittest among us suffer in thin air: the lower oxygen content at altitude can lead to cognitive effects, including memory loss and attention difficulties. There is little you can do to prevent these symptoms other than acclimatise – but this takes time and doesn't always work. A drug called oxiracetam might be the answer.

Up and down

ShengLi Hu at the Third Military Medical University, Chongqing, China, and her colleagues took men from the military up to 4000

metres above sea level. All of the men lived in towns around 1800 metres above sea level. During the study, they spent eight days at this altitude, before climbing for three days to reach 4000 metres, where they stayed for up to a month.

Twenty participants took 800mg of oxiracetam three times per day for the first 15 days of the study, while another 20 men received no intervention. The men performed tests of attention and memory at the start and end of the study and 20 days in, by which time they had been at 4000 metres for nine days. While all participants experienced a drop in cognitive ability at 4000 metres, those who took oxiracetam showed a much smaller decline than the control group.

Using a technique that measures the brain's response to sounds, the team found that those who took the drug also showed less of a decline in the speed at which they could process sensory information.

Going with the flow

Blood flow measurements indicated that at high altitudes, certain parts of the cerebral circulatory system contracted and dilated in a way that promoted blood flow to the brain stem. This isn't surprising, since the brain stem plays a critical role in the maintenance of basic vital signs.

The team also found that the brain stem received blood at the expense of brain areas responsible for more advanced cognitive functions. But in people who took oxiracetam, more arteries dilated, so blood flow throughout the brain was increased. This may be how the drug seems to lessen cognitive problems associated with low oxygen. It is yet to be seen whether diverting the blood in this way could have any negative effects in the long run.

"The results are striking and imply that oxiracetam may be beneficial for helping to mitigate cognitive deficits caused by altitude," says Timothy Hales at the University of Dundee, UK.

Despite a wealth of people admitting to taking numerous kinds of smart drugs to improve their memory or focus, there is little research on oxiracetam in healthy people. In a single study in older adults with dementia, the drug appeared to help improve performance in some memory-associated tasks.

Oxiracetam is not licensed for medical use in the UK, but the drug is known to be a mild stimulant, says Hales. "Coca leaves have been used by native Andeans for centuries to overcome altitude sickness and this is attributed to their modest cocaine content. So perhaps it is not surprising that benefit can be derived from another, albeit mild, stimulant."

Journal reference: Brain and Behaviour, DOI: 10.1002/brb3.762

http://bit.ly/2wHOsH0

Madagascar in panic amid raging "double plague" outbreak; dozens dead

All public gatherings banned, schools closed as people swarm pharmacies.

Beth Mole - 10/7/2017, 3:40 AM

An unusually deadly seasonal outbreak of plague has gripped the island nation of Madagascar. As of Friday, 258 have been sickened and 36 have died just since August, according to Madagascar's Ministry of Public Health.

To try to stifle the spread, the government has forbidden public gatherings, including sporting events, and schools have closed for insecticide treatments that kill plague-spreading fleas. People have swarmed pharmacies, desperately seeking face masks and any antibiotics they can get. The World Health Organization on Friday announced that it has released $1.5 million in emergency funds and delivered nearly 1.2 million antibiotic doses to help combat the outbreak.

Plague, caused by the bacterium *Yersinia pestis*, is endemic to Madagascar and pops up all year-round. But outbreaks can erupt between September to November, with seasonal shifts in rat and flea populations. Rats, which harbor the bacteria, tend to see their populations plump and peak around harvest times in July and August. A boom in the flea population, which transmits the disease, follows in

tandem. But as crops are harvested and the weather cools, the rat population shrinks, and the surging, hungry batch of fleas turns to humans.

Distribution of plague as of 2016. **WHO**

The island has been battling the disease since it arrived there on steamboats from India in 1898. (The disease still appears in many countries around the world, including the US, but most epidemics occur in African countries.) Madagascar got a handle on its seasonal outbreaks during the 1950s with the help of antibiotics, insecticides, and better hygiene campaigns. But it lost its grip in the 1990s when it started seeing increases in case counts. In recent years, the country has tallied between 275 and 675 cases annually (PDF).

But this year is different. The disease is spreading not just in rural, agricultural areas; it's also spreading in cities. As of September 30, the disease had taken hold in 10 cities across the island, including the capital, Antananarivo.

"WHO is concerned that plague could spread further because it is already present in several cities and this is the start of the epidemic season, which usually runs from September to April," Dr. Charlotte Ndiaye, WHO representative in Madagascar, said in a recent statement.

Twice the fear

It's also spreading in two different ways—by fleas and by people—which some have dubbed a "double plague." Usually, plague infections arise as bubonic plague, spread by flea bites. In this case—the Black Death scenario—*Y. pestis* moves from the site of a flea bite on a human to the lymphatic system, taking up residence and inflaming a lymph node. This causes a painful swelling called a bubo, where the infection gets its name. If it's left untreated, the infection can spread to the blood, causing septicaemic plague, or the lungs, causing pneumonic plague.

Pneumonic plague is the most severe form. It can become a life-threatening situation in just 24 hours and can begin to spread from person to person in droplets, coughed or sneezed.

Most of the people infected in the current outbreak in Madagascar have the pneumonic form.

Authorities suspect that the outbreak kicked off when a 31-year-old man from the coastal city of Tamatave visited the Ankazobe District in the Central Highlands. On August 27, during his visit, he developed what he thought were malaria symptoms. Four days later, he was showing respiratory symptoms while taking a shared, public taxi on the way home. He died during the journey, and his body was prepared for burial—without safety precautions—in the Moramanga District Hospital, which was along the way. Health officials linked his case to 31 others, four of which resulted in death.

Officials caught on to the outbreak on September 11, and cases have piled up since then. People all over the island are spooked by the deadly and fast-spreading pneumonic version of the disease. Lines of people have been appearing at local pharmacies before dawn. They hope to get a face-mask and/or antibiotics, which are now in short supply and expensive.

Johannes Herinjatovo, a 50-year-old resident of Antananarivo, told the Agence France-Presse on Wednesday that he and his wife were alarmed by the current outbreak. "I'd already visited six [pharmacies]

this morning and at each one they told me that they didn't have any more masks," he said. He again left empty-handed.

Local health authorities have been trying to calm residents, telling them that face masks aren't necessary and that the plague can be treated.

"Plague is curable if detected in time. Our teams are working to ensure that everyone at risk has access to protection and treatment. The faster we move, the more lives we save," WHO's Dr. Ndiaye said.

http://nyti.ms/2ySnFrT

In Hong Kong, Folk Remedies Are Sickening Patients

Illegal products are damaging to people's health and can kill are still here

By RACHEL NUWER OCT. 6, 2017

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Every few weeks, Dr. Tony Wing Lai Mak, a pathologist at Princess Margaret Hospital in Hong Kong, receives blood and urine samples from yet another patient hospitalized after taking a traditional Chinese medical or health supplement.

A Chinese medicine shop in Mongkok, Hong Kong. Adulterants in traditional supplements in Hong Kong commonly send people to the hospital, pathologists reported. **Jean-Pierre Lescourret/Lonely Planet Images, via Getty Images**

His toxicology lab finds the same culprits over and over: adulterants hidden in the dose.

Although the Hong Kong Department of Health regularly issues warnings about the medicines, "we're still seeing this all the time," Dr. Mak said. "These are illegal products that are damaging to people's health and can even kill. Yet somehow, they're still here."

The frequency and serious nature of the cases inspired Dr. Mak and his colleagues to compile a decade's worth of observations, which they recently published in the British Journal of Clinical Pharmacology. From 2005 to 2015, they reported, 404 people ranging in age from 1 month to 90 were treated at the hospital after taking tainted supplements.

Their sample, they note, comprises only those patients who took proprietary products processed into pills or other finished doses — not the considerable number who consumed whole, unprocessed plant or animal materials.

After testing 487 products handed over by sick patients, Dr. Mak and his colleagues discovered 1,234 hidden ingredients, including both approved and banned Western drugs, drug analogues and animal thyroid tissue.

Sibutramine, an appetite suppressant taken off the market after it was linked to cardiovascular problems, was the most commonly identified adulterant, found in 155 products.

Health supplements containing undeclared ingredients are illegal in Hong Kong, Dr. Mak said, but residents may purchase them in unscrupulous local shops, on the internet, or while visiting mainland China or abroad.

It is impossible to say how prevalent these contaminated supplements are in Hong Kong, Dr. Mak said. He only tests samples from patients whose adverse reactions are severe enough to require medical attention.

Many more may not seek help, or may not experience any side effects at all. "In China, we have so many products around and we take them all the time," Dr. Mak said. "I do not know the denominator here."

Chinese medicinal remedies are gaining popularity worldwide thanks to a perception that they are "natural and safe," Dr. Mak said. A study of 2,600 proprietary Chinese medicine products in Taiwan found that a quarter were contaminated with synthetic drugs.

In the United States, the Food and Drug Administration has identified more than 800 adulterated dietary supplements on the market.