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The secret to tripling the number of grains in sorghum and perhaps other staple crops

A simple genetic modification can triple the grain number of sorghum

Cold Spring Harbor, NY -- A simple genetic modification can triple the grain number of sorghum, a drought-tolerant plant that is an important source of food, animal feed, and biofuel in many parts of the world. In new research reported today in Nature Communications, scientists at Cold Spring Harbor Laboratory (CSHL) have figured out how that genetic change boosts the plant's yield: by lowering the level of a key hormone, generating more flowers and more seeds. Their discovery points toward a strategy for significantly increasing the yield of other grain crops.

Sorghum grains are produced in clusters of flowers that develop from an elaborately branched structure at the top of the plant called a panicle. Each panicle can produce hundreds of flowers. There are two types of flowers. In the plant one finds in the wild (left), only one of these, the sessile spikelet (SS), is fertile. The other type, pedicellate spikelets (PS), do not make seeds. In a modified version of the plant (right) both sessile and pedicellate spikelets produce seeds, tripling each plants grain number. **Ware Lab, CSHL**

Doreen Ware, Ph.D., a CSHL Adjunct Associate Professor and research scientist with USDA's Agricultural Research Service (ARS), led the research, together with ARS colleague Zhanguo Xin, Ph.D. Their study was focused on high-yield strains of sorghum that were generated several years ago by Dr. Xin. An unknown genetic mutation introduced by chemical mutagenesis - a method used for many decades by breeders and researchers to induce genetic variations in plants - resulted in an increase in the number of grains, i.e., seeds contained within fruits, that each plant produced.

Like many cereal crops, sorghum's grains are produced in clusters of flowers that develop from an elaborately branched structure at the top of the plant called a panicle. Each panicle can produce hundreds of flowers.

There are two types of flowers, and usually only one of these, known as the sessile spikelet (SS), is fertile. The other flower type, called pedicellate spikelets (PS), do not make seeds. In the modified plants Dr. Xin produced, however, both sessile and pedicellate spikelets produced seeds, tripling each plant's grain number.

Ware and her team wanted to understand what caused this dramatic change. By completely sequencing the genomes of the modified plants, they found that the key mutations affected a gene that regulates hormone production. Plants carrying the mutation produce abnormally low levels of a development-regulating hormone called jasmonic acid, particularly during flower development.

Through subsequent experiments, the team learned that jasmonic acid prevents pedicellate spikelets from producing seeds. "So when the plant hormone is low, we get seeds set on every single one of the flowers. But when the plant hormone is high, we have a reduced number of fertile flowers, ending up in a reduced number of seeds," explains Dr. Yinping Jiao of the Ware lab, co-first author on the new paper.

Now that the team has uncovered the biological changes that triple sorghum's grain production, they hope to apply the same strategy to increase grain production in related plants that are vital in the global food supply, such as rice, corn, and wheat. The knowledge will help guide crop improvement through traditional breeding practices as well as approaches that take advantage of genome editing technologies, Ware says.

Funding: United Sorghum Checkoff program; U.S. Department of Agriculture Agricultural Research Service; National Research Foundation of Korea

Citation: Jiao J et al, "MSD1 regulates pedicellate spikelet fertility in sorghum through the jasmonic acid pathway," appears in Nature Communications on February xx, 2018.

http://bit.ly/2CmIvWr

Researchers find low magnesium levels make vitamin D ineffective

Study in The Journal of the American Osteopathic Association suggests up to 50 percent of US population is magnesium deficient

CHICAGO - There is a caveat to the push for increased Vitamin D: Don't forget magnesium. A review published in The Journal of the American Osteopathic Association found Vitamin D can't be metabolized without sufficient magnesium levels, meaning Vitamin D remains stored and inactive for as many as 50 percent of Americans.

"People are taking Vitamin D supplements but don't realize how it gets metabolized. Without magnesium, Vitamin D is not really useful or safe," says study co-author Mohammed S. Razzaque, MBBS, PhD, a professor of pathology at Lake Erie College of Osteopathic Medicine.

Razzaque explains that consumption of Vitamin D supplements can increase a person's calcium and phosphate levels even if they remain Vitamin D deficient. The problem is people may suffer from vascular calcification if their magnesium levels aren't high enough to prevent the complication.

Patients with optimum magnesium levels require less Vitamin D supplementation to achieve sufficient Vitamin D levels. Magnesium also reduces osteoporosis, helping to mitigate the risk of bone fracture that can be attributed to low levels of Vitamin D, Razzaque noted.

Deficiency in either of these nutrients is reported to be associated with various disorders, including skeletal deformities, cardiovascular diseases, and metabolic syndrome.

While the recommended daily allowance for magnesium is 420 mg for males and 320 mg for females, the standard diet in the United States contains only about 50 percent of that amount. As much as half of the total population is estimated to be consuming a magnesium-deficient diet.

Researchers say the magnesium consumption from natural foods has decreased in the past few decades, owing to industrialized agriculture and changes in dietary habits. Magnesium status is low in populations who consume processed foods that are high in refined grains, fat, phosphate, and sugar.

"By consuming an optimal amount of magnesium, one may be able to lower the risks of Vitamin D deficiency, and reduce the dependency on Vitamin D supplements," says Razzaque.

Magnesium is the fourth most abundant mineral in the human body after calcium, potassium, and sodium. Foods high in magnesium include almonds, bananas, beans, broccoli, brown rice, cashews, egg yolk, fish oil, flaxseed, green vegetables, milk, mushrooms, other nuts, oatmeal, pumpkin seeds, sesame seeds, soybeans, sunflower seeds, sweet corn, tofu, and whole grains.

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New method extracts information on psychiatric symptoms from electronic health records

Two reports published in Biological Psychiatry demonstrate an approach to use electronic health records to investigate the biological basis of neuropsychiatric symptoms

Philadelphia - Researchers at Massachusetts General Hospital and Harvard Medical School have developed a new method to extract valuable symptom information from doctors' notes, allowing them to capture the complexity of psychiatric disorders that is missed by traditional sources of clinical data. The study, published in Biological Psychiatry, was led by co-senior authors Tianxi Cai, Sc.D., and Roy H. Perlis, M.D. A second study published in *Biological Psychiatry*, also led by Dr. Perlis, applied the new method in a proof-of-concept study to identify genes associated with psychiatric symptoms.

"Many efforts to use clinical documentation in electronic health records for research aim to identify individual symptoms, like the presence or absence of psychosis," said Thomas McCoy Jr., M.D., co-first author with Sheng Yu, Ph.D. But this approach misses the complex overlap of symptoms between different mental disorders. "My co-authors and I developed a method that instead captures symptom dimensions, or sets

of symptoms, informed by the National Institute of Mental Health Research Domain Criteria," continued Dr. McCoy.

The method extracts the relevant symptoms from the wealth of information in the detailed narrative notes taken by clinicians in patients' electronic health records. Dr. McCoy and colleagues used the method to characterize 3,619 adults with psychiatric hospitalizations across a range of disorders, including schizophrenia, anxiety, major depressive disorder, and posttraumatic stress disorder.

Characterizing the patients based on symptom dimensions could predict the length of hospital stay and time to hospital readmission better than the use of more structured data alone, such as health billing information, that is based on the categorization of disorders. The symptom dimensions were also associated with scoring of notes by expert clinicians and with neurocognitive testing, validating the results.

The idea of symptom domains rather than disease categories also extends to the neurobiology of mental illness. "The recognition that the genetic basis of psychiatric illness crosses traditional boundaries has encouraged efforts to understand psychopathology according to dimensions, rather than simply presence or absence of symptoms," said Dr. McCoy.

In the second study, Dr. McCoy and colleagues demonstrated the application of this new method to examine the association between symptom dimensions and common genetic variation in psychiatric disease. They compared the information on the symptom dimensions extracted from the narrative hospital discharge notes of 4,687 adults with the patients' genomic information. The researchers identified four areas of interest, or loci, in the genome, highlighting two genes which have not previously been identified with existing methods.

"The ability to combine large DNA data sets with meaningful psychiatric information from the electronic health record is an important step in facilitating large scale medical genetics research in psychiatry," said John Krystal, M.D., Editor of *Biological Psychiatry*.

The authors suggest that the method offers a new approach to understand brain function in mental illness. Other researchers can apply the method to different sets of patients with hospital-linked genomic records, and identification of the same loci would strengthen the support for their role in psychiatric symptoms.

"We are making the scoring software freely available and hope this work will enable transdiagnostic dimensional phenotypes to be used in efforts to achieve precision psychiatry," said Dr. McCoy.

Notes for editors *The articles are "High throughput phenotyping for dimensional psychopathology in electronic health records," by Thomas H. McCoy Jr, Sheng Yu, Kamber L. Hart, Victor M. Castro, Hannah E. Brown, James N. Rosenquist, Alysa E. Doyle, Pieter J. Vuijk, Tianxi Cai, and Roy H. Perlis (https://doi.org/10.1016/j.biopsych.2018.01.011) and "Genome-wide association study of dimensional psychopathology using electronic health records" by Thomas H. McCoy Jr, Victor M. Castro, Kamber L. Hart, Amelia M. Pellegrini, Sheng Yu, Tianxi Cai, and Roy H. Perlis (https://doi.org/10.1016/j.biopsych.2017.12.004). They appear in* Biological Psychiatry, *published by Elsevier.*

http://bit.ly/2GMR6zz

The giant wave that marks the beginning of the end -- the neurobiology of dying

For the first time, researchers have been able to study irreversible brain damage from oxygen deprivation in humans

The human brain is highly sensitive to oxygen deprivation. Extensive and irreversible damage occurs within approximately 10 minutes of cardiac (and hence circulatory) arrest. For the first time, researchers from Charité - Universitätsmedizin Berlin and the University of Cincinnati have been able to study these events in humans. The results from this research, which has been published in Annals of Neurology*, may inform future treatment strategies of cardiac arrest and stroke.

Oxygen deprivation results in brain injury. For years, researchers have been studying the underlying processes in animals: within 20 to 40 seconds, the brain enters an 'energy-saving mode' - it becomes electrically inactive, and all interneuronal communication ceases. Within a few minutes, the brain's fuel reserves have become depleted that maintain the uneven distribution of ions between the inside and outside of nerve cells, and the ion gradients start to break down. This

breakdown takes the form of a massive wave of electrochemical energy release in the form of heat, which is known as 'spreading depolarization'. More vividly described as a 'brain tsunami', this energy loss spreads through the cortex and other areas of the brain, triggering pathophysiological cascades which gradually poison the nerve cells. Importantly, this wave remains reversible up to a certain point in time: nerve cells will recover fully if circulation is restored before this point is reached. However, if circulation remains disrupted, the cells will die. Until now, recordings of electrical brain activity obtained from human subjects have been of limited applicability, and experts have been divided as to the transferability of results from animal-based research.

It is usually impossible to take the relevant measurements in the minutes immediately following a stroke or cardiac arrest. Under the leadership of Prof. Dr. Jens Dreier of Charité's Center for Stroke Research, and working with Prof. Jed Hartings of the Mayfield Clinic in Cincinnati, researchers have now been able to study such cases for the first time. Their research was facilitated by a very specific setup. Specialist neuromonitoring techniques, which enable the early detection and subsequent treatment of clinical complications, are becoming an increasingly common feature of modern neurocritical care. In particular, electrocorticography and invasive methods of monitoring oxygen are becoming increasingly significant. In contrast to conventional electroencephalography, electrocorticography goes beyond the process of recording epileptic seizure activity, enabling clinicians to record spreading depolarization with never-before-seen precision. Over the past few years, a number of international clinical studies have been able to confirm that, in many severe cases of acute brain injury, spreading depolarizations develop as soon as the patient's condition worsens. When this happens, treatment must target the underlying causes of this phenomenon, in order to limit its occurrence. As part of their observational study, the researchers used state-of-the-art neuromonitoring technology. Scientific analysis of both monitoring data and each patient's clinical course showed that the event known as 'terminal spreading depolarization' also occurs in humans, beginning within minutes of circulatory arrest. "We were able to show that terminal spreading depolarization is similar in humans and animals. Unfortunately, the research community has been ignoring this essential process of central nervous system injury for decades, all because of the mistaken assumption that it does not occur in humans," explains Prof. Dreier. The reasons for this have been primarily methodological in nature. Reestablishing circulation as rapidly as possible has, until now, been the sole aim of treatment in stroke and cardiac arrest patients. "Knowledge of the processes involved in spreading depolarization is fundamental to the development of additional treatment strategies aimed at prolonging the survival of nerve cells when brain perfusion is disrupted," explains Prof. Dreier. He adds: "This of course follows from the tenet espoused by Max Planck that insight must precede application; our insights can give us hope for the future."

Dreier JP, Major S, Foreman B, Winkler MKL, Kang EJ, Milakara D, Lemale CL, DiNapoli V, Hinzman JM, Woitzik J, Andaluz N, Carlson A, Hartings JA. Terminal spreading depolarization and electric silence in death of human cortex. Ann Neurol. *2018 Jan 13. doi: 10.1002/ana.25147. PMID: 29331091.*

http://bit.ly/2CnO1Iq

Mom's immune system shapes baby's brain

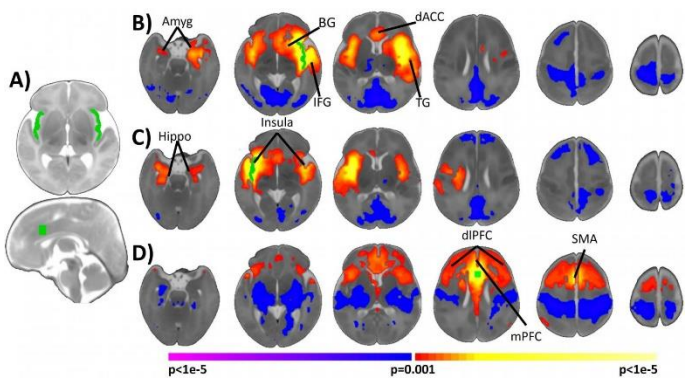
The state of a woman's immune system during pregnancy may shape the connectivity of her child's brain

The state of a woman's immune system during pregnancy may shape the connectivity of her child's brain, suggests a study of teenage mothers published in JNeurosci.

The research emphasizes the influence of maternal health on a child's susceptibility to psychiatric disorders later in life.

Marisa Spann, Bradley Peterson and colleagues studied adolescents (ages 14 to 19) pregnant with their first child to examine the relationship between two proteins released by the mothers' immune systems during the third trimester of pregnancy and the development in the infants of a brain network involved in disorders such as autism, schizophrenia and attention-deficit/hyperactivity disorder.

The researchers found that higher maternal levels of these proteins were associated with greater connectivity of the infants' brain regions in this network and with higher cognitive ability at 14 months of age.



This is neonatal salience network connectivity. A) Regions of interest used for seed connectivity. The right and left insula and dACC seeds are shown in green. B) Left and C) right insula connectivity. The insula is functionally connected primarily to the contralateral insula, bilateral amygdala (Amyg), ipsilateral hippocampus (Hippo), ipsilateral basal ganglia (BG), ipsilateral IFG, ipsilateral temporal gyrus (TG), and the dACC. D) Dorsal ACC connectivity. The dACC connectivity is primarily to dlPFC, mPFC, SMA, and bilateral anterior insula.
Spann et al., JNeurosci (2018)

Activation of the maternal immune system was also associated with lower fetal heart rate at the end of gestation, which may indicate delayed development of the autonomic nervous system.

These results suggest that the final weeks of pregnancy have an important influence on a child's brain development.

Article: Maternal immune activation during the third trimester is associated with neonatal functional connectivity of the salience network and fetal to toddler behavior
DOI: https://doi.org/10.1523/JEUROSCI.2272-17.2018
Corresponding author: Bradley Peterson (Children's Hospital Los Angeles, CA, USA), bpeterson@chla.usc.edu

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Discovery reveals way to stop inflammation in Alzheimer's, arthritis, more

Doctors could target electrical switch in immune system to battle many conditions, including deadly sepsis

A new discovery about the immune system may allow doctors to treat harmful inflammation that damages the brain in neurodegenerative diseases such as Alzheimer's. It might also let doctors save patients from the potentially deadly inflammation of sepsis, a full-body infection that kills a quarter-million Americans every year.

The finding "opens up a whole new research area to look at neuroinflammation in the context of Alzheimer's and Parkinson's," said lead researcher Bimal Desai, PhD, of the University of Virginia School of Medicine. "But the clinical impact will be in many, many different areas."

Neurological Treatments

Traditional treatments for neurological inflammation, such as in Alzheimer's and Parkinson's disease, are largely ineffective because biological drugs are blocked by what is known as the blood-brain barrier. That barrier protects the brain from dangers such as bacteria or toxins in the blood, but it also makes it very difficult to get drugs into the brain. "A lot of the drugs we use right now to treat inflammation, [known as] biologicals, don't work in the brain because they can't get through," explained Desai, of UVA's Department of Pharmacology and UVA's Carter Immunology Center.

His new finding, involving important immune cells known as macrophages (and microglia), could offer a way around that. He and his team have identified a specific electrical switch, known as an ion channel, within macrophages that controls the flow of calcium into the cells. Without calcium, the cells can't cause inflammation. By targeting this switch with tiny molecules, researchers could deny the macrophages calcium and prevent inflammation - even in the brain.

A Better Way to Battle Inflammation

That could let researchers develop a new and better way to stop inflammation. "Small molecules are perhaps more affordable as treatments and can hit things like this ion channel switch, TRPM7," said researcher Michael Schappe, a graduate student in Desai's lab. "We could use that to address inflammation in a bunch of contexts, but particularly in instances like neuroinflammation, where [current] treatments are particularly ineffective."

Desai noted that drug companies are already at work on drugs that could target this type of switch. And that could be good news for patients with many inflammatory diseases. "Right now, you have conditions like arthritis or IBD [inflammatory bowel disease], where inflammation plays a huge role. They do have very good drugs for them, but these drugs are extremely expensive and cannot be taken orally by the patients. They can cost as much as $20,000 a year," he said. "The reason for that is that they're biologicals. They're protein molecules that are very difficult to make and distribute. But having identified an ion channel as a target in this context allows you to use small molecules, which are ridiculously cheap compared to biologicals and can be taken orally by the patients."

The discovery of the new drug target, the researchers noted, was made possible by something very unusual about UVA. To learn more, visit the Making of Medicine blog at https://makingofmedicine.virginia.edu/2018/02/26/the-switch-that-could-shut-down-inflammation-even-in-the-brain/

Findings Published *The researchers have published their findings in the scientific journal Immunity. The study's authors were Schappe, Kalina Szteyn, Marta E. Stremska, Suresh K. Mendu, Taylor K. Downs, Philip V. Seegren, Michelle A. Mahoney, Sumeet Dixit, Julia K. Krupa, Eric J. Stipes, Jason S. Rogers, Samantha E. Adamson, Norbert Leitinger and Desai.*

The research was supported by the National Institutes of Health, grants GM108989 and 5T32GM007055-41.

http://bit.ly/2EUuQHx

Researchers use human neural stem cell grafts to repair spinal cord injuries in monkeys

Findings represent major and essential step toward future human clinical trials

Led by researchers at University of California San Diego School of Medicine, a diverse team of neuroscientists and surgeons successfully grafted human neural progenitor cells into rhesus monkeys with spinal cord injuries. The grafts not only survived, but grew hundreds of thousands of human axons and synapses, resulting in improved forelimb function in the monkeys.

The findings, published online in the February 26 issue of *Nature Medicine*, represent a significant step in translating similar, earlier work in rodents closer to human clinical trials and a potential remedy for paralyzing spinal cord injuries in people.

"For more than three decades, spinal cord injury research has slowly moved toward the elusive goal of abundant, long-distance regeneration of injured axons, which is fundamental to any real restoration of physical function," said Mark Tuszynski, MD, PhD, professor of neuroscience and director of the UC San Diego Translational Neuroscience Institute.

"While there was real progress in research using small animal models, there were also enormous uncertainties that we felt could only be addressed by progressing to models more like humans before we conduct trials with people," Tuszynski said.

"We discovered, for example, that the grafting methods used with rodents didn't work in larger, non-human primates. There were critical issues of scale, immunosuppression, timing and other features of methodology that had to be altered or invented. Had we attempted human transplantation without prior large animal testing, there would have been substantial risk of clinical trial failure, not because neural stem cells failed to reach their biological potential but because of things we did not know in terms of grafting and supporting the grafted cells."

Gregoire Courtine, PhD, a professor and investigator at the Center for Neuroprosthetics and at the Brain Mind Institute, both part of the Swiss Federal Institute of Technology (EPFL) in Geneva, also conducts research seeking to restore function after spinal cord injury. He underscored the importance of the new findings.

"Dr. Tuszynski and his collaborators overcame a number of methodological difficulties specific to primates to obtain this breakthrough," he said. "Direct translation of their work to humans would have failed, and yet too many studies are bypassing vital translational work in primate models that is necessary before human clinical trials."

Successfully growing and proliferating functional grafted stem cells in spinal cord injuries is hindered by a multitude of innate, biological challenges. For example, the region surrounding the injury site -- the so-called extracellular matrix -- inhibits growth in the same way that a superficial scar never resembles the original tissue in form or function. The injury site is abundant with inhibitory myelin proteins (used to make the insulating sheath around many nerve fibers) but lacks growth-promoting factors, such as neurotrophins, that would encourage regeneration of nerve cells' axons and synapses.

Previous work by Tuszynski and others have found solutions or work-arounds for many of these obstacles, reporting notable progress using rodent models. The new work involves the use of human spinal cord-derived neural progenitor cells (NPCs) -- stem cells destined to become nerve cells in the central nervous system (CNS) -- in rhesus monkeys, whose biology and physiology is much more similar to humans. Because the NPCs were derived from an 8-week-old human embryonic spinal cord, they possessed active growth programs that supported robust axon extension and appeared to be insensitive to inhibitors present in the adult CNS.

Two weeks after the initial injury (a period intended to represent the time required for an injured person to medically stabilize undergoing neural stem cell therapy), researchers grafted 20 million NPCs into the injury lesions in the monkeys, supported by a cocktail of growth factors and immune suppression drugs.

The work was done at the California National Primate Research Center at UC Davis. Most of the investigators are from UC campuses. "This highly complex translational project shows the value of collaborative research across UC campuses with unique facilities," said co-author Michael Beattie, PhD, professor and director of research at the Brain and Spinal Injury Center at UC San Francisco.

Over the next nine months, the grafts grew, expressing key neural markers and sending hundreds of thousands of axons -- the fibers through which nerve cells conduct signals to other nerve cells -- through the injury site to undamaged cells and tissue on the other side. Several months into the study, researchers noted that the monkeys began to display partial recovery of movement in their affected forelimbs.

Notably, the team documented regeneration of corticospinal axons, which are essential for voluntary movement in humans, into the lesion sites -- the first such known documentation in a primate model.

Courtine at EPFL, who was not involved in the study, said the findings challenge decades of work on the mechanisms of regeneration failure and "definitely represent a landmark in regeneration medicine." Nonetheless, he noted that the degree of functional improvement remained limited. "It is not surprising given that the functional integration of new cells and connections into the operation of the nervous system would require time and specific rehabilitation procedures," he said.

"It's possible that given a longer period of observation, greater recovery may have occurred," said the study's first author, Ephron S. Rosenzweig, PhD, an assistant adjunct professor in Tuszynski's lab. "Axon regeneration, synapse formation, myelination -- these all take time, and are critical for neural function. Grafts, and the new circuitry they were part of, were still maturing at the end of our observations, so it seems possible that recovery might have continued."

Tuszynski said work remains to be done before initiating human clinical trials, including production of a candidate neural stem cell line from humans that meets requirements of the Food and Drug Administration, and additional studies of safety. His group also continues to explore ways to further enhance the growth, distance and functionality of the regenerated cells.

"We seem to have overcome some major barriers, including the inhibitory nature of adult myelin against axon growth," he said. "Our work has taught us that stem cells will take a long time to mature after transplantation to an injury site, and that patience will be required when moving to humans. Still, the growth we observe from these cells is remarkable -- and unlike anything I thought possible even ten years ago.

There is clearly significant potential here that we hope will benefit humans with spinal cord injury."

Co-authors include: Hiromi Kumamaru, Janet L. Weber and Justine J. Liang, UC San Diego; John H. Brock and Paul Lu, UC San Diego and Veterans Affairs San Diego Healthcare System; Ernesto A. Salegio, Rod Moseanko and Stephanie Hawbecker, UC Davis; Ken Kadoya, UC San Diego and Hokkaido University, Japan; J. Russell Huie and Jacqueline C. Bresnahan, UC San Francisco; Leif A. Havton, UCLA; Yvette S. Nout-Lomas, Colorado State University; Adam R. Ferguson, UC San Francisco and San Francisco Veterans Affairs Medical Center.

http://bit.ly/2FbuknQ

Researchers sequence complete genomes of extinct and living elephants

One of the most comprehensive evolutionary pictures to date of elephants, mammoths, and mastodons-spanning millions of years

An international team of researchers has produced one of the most comprehensive evolutionary pictures to date by looking at one of the world's most iconic animal families - namely elephants, and their relatives mammoths and mastodons-spanning millions of years.

The team of scientists-which included researchers from McMaster, the Broad Institute of MIT and Harvard, Harvard Medical School, Uppsala University, and the University of Potsdam-meticulously sequenced 14 genomes from several species: both living and extinct species from Asia and Africa, two American mastodons, a 120,000-year-old straight-tusked elephant, and a Columbian mammoth.

The study, published in the *Proceedings of the National Academy of Science*, sheds light on what scientists call a very complicated history, characterized by widespread interbreeding. They caution, however, the behaviour has virtually stopped among living elephants, adding to growing fears about the future of the few species that remain on earth.

"Interbreeding may help explain why mammoths were so successful over such diverse environments and for such a long time, importantly this genomic data also tells us that biology is messy and that evolution doesn't happen in an organized, linear fashion," says evolutionary geneticist Hendrik Poinar, one of the senior authors on the paper and Director of the McMaster Ancient DNA Centre and principal investigator at the Michael G. DeGroote Institute for Infectious Research.

"The combined analysis of genome-wide data from all these ancient elephants and mastodons has raised the curtain on elephant population history, revealing complexity that we were simply not aware of before," he says.

A detailed DNA analysis of the ancient straight-tusked elephant, for example, showed that it was a hybrid with portions of its genetic makeup stemming from an ancient African elephant, the woolly mammoth and present-day forest elephants. "This is one of the oldest high-quality genomes that currently exists for any species," said Michael Hofreiter at the University of Potsdam in Germany, a co-senior author who led the work on the straight-tusked elephant.

Researchers also found further evidence of interbreeding among the Columbian and woolly mammoths, which was first reported by Poinar and his team in 2011. Despite their vastly different habitats and sizes, researchers believe the woolly mammoths, encountered Columbians mammoths at the boundary of glacial and in the more temperate ecotones of North America.

Strikingly, scientists found no genetic evidence of interbreeding among two of the world's three remaining species, the forest and savanna elephants, suggesting they have lived in near-complete isolation for the past 500,000 years, despite living in neighbouring habitats.

"There's been a simmering debate in the conservation communities about whether African savannah and forest elephants are two different species," said David Reich, another co-senior author at the Broad Institute who is also a professor at the Department of Genetics at Harvard Medical School (HMS) and a Howard Hughes Medical Institute Investigator. "Our data show that these two species have been isolated for long periods of time - making each worthy of independent conservation status."

Interbreeding among closely related mammals is fairly common, say researchers, who point to examples of brown and polar bears, Sumatran

and Bornean orangutans, and the Eurasian gold jackal and grey wolves. A species can be defined as a group of similar animals that can successfully breed and produce fertile offspring.

"This paper, the product of a grand initiative we started more than a decade ago, is far more than just the formal report of the elephant genome. It will be a reference point for understanding how diverse elephants are related to each other and it will be a model for how similar studies can be done in other species groups," said co-senior author Kerstin Lindblad-Toh, a senior associate member of the Broad Institute and Director of the Science for Life Laboratory at Uppsala University in Sweden.

"The findings were extremely surprising to us," says Eleftheria Palkopoulou, a post-doctoral scientist in at HMS. "The elephant population relationships could not be explained by simple splits, providing clues for understanding the evolution of these iconic species."

Researchers suggest that future work should explore whether the introduction of new genetic lineages into elephant populations-both living and ancient-played an important role in their evolution, allowing them to adapt to new habitats and fluctuating climates.

More information: *Eleftheria Palkopoulou el al., "A comprehensive genomic history of extinct and living elephants," PNAS (2018).* *www.pnas.org/cgi/doi/10.1073/pnas.1720554115*

http://bit.ly/2FCkp8S

Simple urine test could measure how much our body has aged

A promising new marker of aging could help predict the risk of developing age-related disease and even death

Researchers find that a substance indicating oxidative damage increases in urine as people get older. The study, published today in open-access journal in Frontiers in Aging Neuroscience, also describes a way to easily measure levels of this marker in human urine samples. The new marker potentially provides a method to measure how much our body has aged -- our biological rather than chronological age. This could help predict our risk of developing age-related disease, and even our risk of death.

While everyone born in the same year has the same chronological age, the bodies of different people age at different rates. This means that, although the risk of many diseases increases with age, the link between our age in years and our health and lifespan is relatively loose. Many people enjoy long lives, relatively free of disease, while others suffer chronic illness and premature death.

So, if our age in years isn't the most reliable indicator of aging in our bodies, what is?

Some researchers consider normal aging to be a disease, where our cells accumulate damage over time. The rate of this cellular damage can vary from person to person, and may be dictated by genetics, lifestyle and the environment we live in. This cellular damage may be a more accurate indication of our biological age than the number of years since we were born.

Finding a way to measure biological age could help to predict the risk of developing age-related disease and even death. We also need to be able to measure biological age to know whether treatments to slow aging - which may be possible in the future -- are effective.

One mechanism thought to underlie biological aging involves a molecule vital to our survival - oxygen - in what is called the free radical theory of aging.

"Oxygen by-products produced during normal metabolism can cause oxidative damage to biomolecules in cells, such as DNA and RNA," explains Jian-Ping Cai, a researcher involved in the study. "As we age, we suffer increasing oxidative damage, and so the levels of oxidative markers increase in our body."

One such marker, with the catchy name of 8-oxo-7,8-dihydroguanosine -- or 8-oxoGsn for short -- results from oxidation of a crucial molecule in our cells called RNA. In previous studies in animals, Cai and colleagues found that 8-oxoGsn levels increase in urine with age.

To see if this is true for humans as well, the researchers measured 8-oxoGsn in urine samples from 1,228 Chinese residents aged 2-90 years old, using a rapid analysis technique called ultra-high-performance liquid chromatography.

"We found an age-dependent increase in urinary 8-oxoGsn in participants 21 years old and older." said Cai. "Therefore, urinary 8-oxoGsn is promising as a new marker of aging."

Interestingly, levels of 8-oxoGsn were roughly the same between men and women, except in post-menopausal women, who showed higher levels. This may have been caused by the decrease in estrogen levels that happens during menopause, as estrogen is known to have anti-oxidant effects.

The team's rapid analysis technique could be useful for large-scale aging studies, as it can process urine samples from up to 10 participants per hour. "Urinary 8-oxoGsn may reflect the real condition of our bodies better than our chronological age, and may help us to predict the risk of age-related diseases," concludes Cai.

http://bit.ly/2HQ5zfF

Supercomputer model reveals how sticky tape makes graphene

Scientists at UCL have explained for the first time the mystery of why adhesive tape is so useful for graphene production.

The study, published in *Advanced Materials*, used supercomputers to model the process through which graphene sheets are exfoliated from graphite, the material in pencils.

Graphene is known for being the strongest material in the world, lightweight and with extraordinary electrical, thermal and optical properties. Unsurprisingly, it offers many benefits for commercial application.

There are various methods for exfoliating graphene, including the famous adhesive tape method developed by Nobel Prize winner Andre Geim. However little has been known until now about how the process of exfoliating graphene using sticky tape works.

Academics at UCL are now able to demonstrate how individual flakes of graphite can be exfoliated to make one atom thick layers. They also reveal that the process of peeling a layer of graphene demands 40% less energy than that of another common method called shearing. This is expected to have far reaching impacts for the commercial production of graphene.

"The sticky tape method works rather like peeling egg boxes apart with a vertical motion, it is easier than pulling one horizontally across another when they are neatly stacked," explained Professor Peter Coveney, Director of the Centre for Computational Science (UCL Chemistry).

"If shearing, then you get held up by this egg carton configuration. But if you peel, you can get them apart much more easily. The polymethyl methacrylate adhesive on traditional sticky tape is ideal for picking up the edge of the graphene sheet so it can be lifted and peeled," added Professor Coveney.

Graphite occurs naturally, its basic crystalline structure is stacks of flat sheets of strongly bonded carbon atoms in a honeycomb pattern. Graphite's many layers are bound together by weak interactions and can easily slide large distances over one another with little friction due to their superlubricity.

The scientists at UCL simulated an experiment conducted in 2015 at Lawrence Berkeley Laboratory in Berkeley, California, which used a special microscope with atomic resolution to see how graphene flakes move around on a graphite surface.

The supercomputer's results matched Berkeley's observations showing that there is less movement when the graphene atoms neatly line up with the atoms below. "Despite the vast amount of research carried out on graphene since its discovery, it is clear that until now our understanding of its behaviour on an atomic length scale was very poor," explains Ph.D. student Robert Sinclair (UCL Chemistry).

"The one reason above all others why the material is difficult to use is because it is hard to make. Even now, a dozen years after its discovery,

companies have to apply sticky tape methods to pull it apart, as the Laureates did to uncover it; hardly a hi-tech and industrially simple process to implement. We're now in a position to assist experimentalists to figure out how to prise it apart, or make it to order. That could have big cost implications for the emerging graphene industry," said Professor Coveney.

More information: *Robert C. Sinclair et al. Graphene-Graphene Interactions: Friction, Superlubricity, and Exfoliation, Advanced Materials (2018). DOI: 10.1002/adma.201705791*

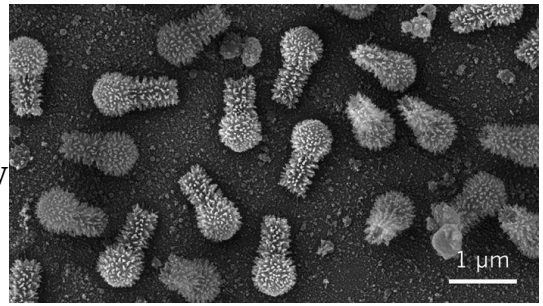
http://go.nature.com/2F9Adlz

Giant fuzzy virus found in soda lake

Newfound group boasts some of the longest individual viruses ever described.

Two giant viruses found in extreme environments have longer tails and more protein-making apparatus than any other virus known.

A team led by Didier Raoult and Bernard La Scola at Aix-Marseille University in France found one strain of virus in a highly alkaline 'soda' lake in Brazil and the other at a depth of 3,000 metres in the Atlantic Ocean off the coast of Brazil. Both strains can infect amoebae, and both belong to a new group that the team calls Tupanviruses. A covering of small fibres gives the viruses a fuzzy appearance.



A covering of small fibres gives this Tupanvirus from a Brazilian lake a furry appearance. **J. Abrahão et al./Nature Commun.**

The viruses contain genes for nearly all of the machinery that cells use to synthesize proteins. Viruses tend to borrow the protein-making machinery of their host cells, and there is no evidence yet that Tupanviruses use their own protein-making gear to encode proteins.

Nature Commun. (2018)

http://bit.ly/2GRSNMu

Wind and solar could meet most but not all US electricity needs

Generating 100 percent of electricity from solar and wind would require significant and costly energy infrastructure changes

Washington, DC--Wind and solar power could generate most but not all electricity in the United States, according to an analysis of 36 years of weather data by Carnegie's Ken Caldeira, and three Carnegie-affiliated energy experts: Matthew Shaner, Steven Davis (of University of California Irvine), and Nathan Lewis (of Caltech).

Right now, about 38 percent of carbon dioxide emissions come from electricity production, which must be reduced to combat climate change. The team found that as the amount of electricity produced by solar and wind increases, avoiding major blackouts becomes increasingly challenging. Policymakers and planners need to consider that wind and solar resources will have natural variability, the team said.

"Our team took a simplified approach aimed at understanding fundamental geophysical constraints on wind and solar power," explained lead author Shaner. "We looked at solar and wind power availability on an hourly basis across the U.S. and determined how much of current electricity demand could be met by varying amounts of solar panels, wind turbines, and energy storage, in addition to changes in the electricity grid."

According to the team's findings, solar power resources reached peak generating ability in June and July, and wind resources peak in March and April and slump during July and August. So, the resources have a complementary effect that would allow each to help alleviate the other's deficiencies. But this wouldn't be enough to overcome non-seasonal variation in solar and wind resources.

Their assessments showed that reliable electricity generation with 80 percent solar and wind would require a continent-scale transmission grid with at least 12 hours of storage to overcome ordinary day-to-day variation.

But to bump up to 100 percent of electricity coming from solar and wind power would require significantly greater and costlier energy infrastructure changes to overcome seasonal cycles and extreme weather events. It would be necessary to have either the capacity to store the generated electricity for several weeks--something not economically feasible today--or the ability to generate a surplus of electricity, much of which would be infrequently used. Likewise, a continent-scale transmission grid would also be required.

"Our work indicates that wind and solar would need to be supplemented by some kind of dispatchable power like natural gas or huge amounts of storage," Caldeira added. "The natural gas emits greenhouse gases and the storage is super expensive, so we need a search for better ways of supplying electricity when the sun is not shining, and the wind is not blowing."

http://bit.ly/2CqXsGP

Why are some mushrooms 'magic?'

Study offers evolutionary explanation, could pave way for neurological treatments

COLUMBUS, Ohio - Psychedelic mushrooms likely developed their "magical" properties to trip up fungi-munching insects, suggests new research.

The work helps explain a biological mystery and could open scientific doors to studies of novel treatments for neurological disease, said lead researcher Jason Slot, an assistant professor of fungal evolutionary genomics at The Ohio State University.

Mushrooms that contain the brain-altering compound psilocybin vary widely in terms of their biological lineage and, on the surface, don't appear to have a whole lot in common, he said.

From an evolutionary biology perspective, that is intriguing and points to a phenomenon in which genetic material hops from one species to another - a process called horizontal gene transfer, Slot said. When it happens in nature, it's typically in response to stressors or opportunities in the environment.

He and his co-authors examined three species of psychedelic mushrooms - and related fungi that don't cause hallucinations - and found a cluster of five genes that seem to explain what the psychedelic mushrooms have in common. "But our main question is, 'How did it evolve?'" Slot said. "What is the role of psilocybin in nature?"

Slot and his co-authors found an evolutionary clue to why the mushrooms gained the ability to send human users into a state of altered consciousness. The genes responsible for making psilocybin appear to have been exchanged in an environment with a lot of fungus-eating insects, namely animal manure.

Psilocybin allows fungi to interfere with a neurotransmitter in humans and also insects, which are probably their bigger foe. In flies, suppression of this neurotransmitter is known to decrease appetite.

"We speculate that mushrooms evolved to be hallucinogenic because it lowered the chances of the fungi getting eaten by insects," Slot said. The study appears online in the journal Evolution Letters.

"The psilocybin probably doesn't just poison predators or taste bad. These mushrooms are altering the insects' 'mind' - if they have minds - to meet their own needs."

And the reason that unrelated species have the same genetic protection probably comes down to the fact that they commonly grow in the same insect-rich mediums: animal feces and rotten wood.

This work could guide medical science by pointing researchers in the direction of other molecules that could be used to treat disorders of the brain, Slot said.

Psilocybin has been studied for the treatment of a variety of mental disorders, including treatment-resistant depression, addiction and end-of-life anxiety. A handful of researchers in the U.S. are looking at potential treatment applications, and much of the work is happening abroad. Strict drug laws have delayed those types of studies for decades, Slot said.

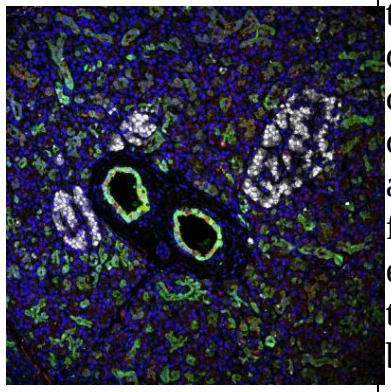
Other Ohio State researchers who worked on the study were Hannah Reynolds, Vinod Vijayakumar and Emile Gluck-Thaler. Hailee Korotkin and Patrick Matheny of the University of Tennessee also were on the research team.

http://bit.ly/2HVFwUt

Unique pancreatic stem cells have potential to regenerate beta cells, respond to glucose

Findings pave way for regenerative cell therapies in type 1 diabetes patients

Scientists from the Diabetes Research Institute at the University of Miami Miller School of Medicine have confirmed the existence of progenitor cells within the human pancreas that can be stimulated to develop into glucose-responsive beta cells. These significant findings, published in Cell Reports, open the door to developing regenerative cell therapies for those living with type 1 diabetes, addressing a major challenge that stands in the way of discovering a biological cure for the disease.



Diabetes Research Institute scientists have confirmed that the unique stem cells reside within large ducts of the human pancreas. Two such ducts (green), surrounded by three islets (white) are shown. **Diabetes Research Institute Foundation**

The notion that the pancreas harbors progenitor cells with the potential to regenerate islets has been hypothesized for decades, but not conclusively demonstrated. DRI scientists have now been able to identify the exact anatomic location of these stem cells and validate their proliferative potential and ability to turn into glucose-responsive beta cells.

"Our in-depth study of these pancreatic stem cells may help us tap into an endogenous cell supply 'bank' for beta cell regeneration purposes and, in the future, lead to therapeutic applications for people living with type 1 diabetes," said Juan Dominguez-Bendala, Ph.D., DRI director of pancreatic stem cell development for translational research and co-principal investigator of the study alongside Ricardo Pastori, Ph.D., director of molecular biology. "Together with our previous findings using BMP-7 to stimulate their growth, we believe that we may be able to induce these stem cells to become functional islets."

The DRI team previously reported that bone morphogenetic protein 7 (BMP-7), a naturally occurring growth factor already approved by the Food and Drug Administration (FDA) for clinical use, stimulates progenitor-like cells within cultured human non-endocrine pancreatic tissue. In the most recent study, the researchers went on to demonstrate that those stem cells that respond to BMP-7 reside within the pancreatic ductal and glandular network of the organ. Additionally, the cells are characterized by the expression of PDX1, a protein necessary for beta cell development, and ALK3, a cell surface receptor that has been associated with the regeneration of multiple tissues. Using "molecular fishing" techniques, they were able to selectively extract the cells that expressed PDX1 and ALK3, grow them in a dish and demonstrate that they can proliferate in the presence of BMP-7 and later differentiate into beta cells. Together, the combined study results may help move researchers closer to developing regenerative cell therapies for type 1, and potentially type 2, diabetes.

In type 1 diabetes, the insulin-producing cells of the pancreas have been mistakenly destroyed by the immune system, requiring patients to manage their blood sugar levels through a daily regimen of insulin therapy. In type 2 diabetes, patients are able to produce some insulin, but their beta cells may become dysfunctional over time. Islet transplantation has allowed some patients with type 1 diabetes to live without the need for insulin injections after receiving infusions of donor cells, however there are not enough cells to treat the millions of patients who can benefit. Thus far, research efforts have focused primarily on creating more pancreatic cells for transplant from sources like embryonic (hESc), pluripotent (hPSc) and adult stem cells, and porcine (pig) islets, among others. A more efficient and potentially safer solution could lie in regenerating a patient's own insulin-producing cells, sidestepping the need to transplant donor tissue altogether and eliminating other immune-related roadblocks.

"The ability to offer regenerative medicine strategies to restore insulin production in the native pancreas could one day replace the need for transplantation of the pancreas or insulin-producing cells. In type 1 diabetes, this would require abrogation of autoimmunity to avoid immune destruction of the newly formed insulin producing cells. For this reason our current efforts are converging on immune tolerance induction without the need for life long anti-rejection drugs," said Camillo Ricordi, M.D., director of the Diabetes Research Institute and Stacy Joy Goodman Professor of Surgery.

http://bit.ly/2FjfZ8W

Bonobo and chimpanzee gestures share many meanings

Chimpanzees and bonobos use gestures to initiate and change positions during grooming

If a bonobo and a chimpanzee were to meet face to face, they could probably understand each other's gestures. In an article publishing 27 February in the open access journal *PLOS Biology*, researchers from the Universities of St Andrews, York, and Kyoto have found that many of the gestures used by bonobos and chimpanzees share the same meanings.

The two great ape species are closely related, having separated about 1-2 million years ago, and we already know that they share many of the same gestures, but the degree of similarity between the meanings of the chimpanzee and bonobo gestures is a new discovery.

In the new study the researchers first define the meaning of each bonobo gesture by looking at the reaction that it elicits and whether the bonobo who gestured was "satisfied" with the reaction. If, for example, the first bonobo presents an arm in front of a second bonobo (video for "present (climb on)" at https://vimeo.com/214146154; videos for all gestures at http://greatapedictionary.ac.uk/video-resources/gesture-videos/), the second bonobo responds by climbing onto the first bonobo's back and the first bonobo then stops gesturing, the researchers infer that the first bonobo was satisfied, and therefore that the meaning of that single gesture is "climb on me". Taken over many observations, the researchers were able to systematically define the sets of meanings of 33 bonobo gesture types and compare them to gesture meanings already known for chimpanzees. It appears that many gesture meanings are shared by both species, and perhaps may have also been shared by our last common ancestor.

"The overlap in gesture meanings between bonobos and chimpanzees is quite substantial and may indicate that the gestures are biologically inherited", says lead author Kirsty Graham from the University of York. "In future, we hope to learn more about how gestures develop through the apes' lifetimes. We are also starting to examine whether humans share any of these great ape gestures and understand the gesture meanings, so watch this space."

Citation: *Graham KE, Hobaiter C, Ounsley J, Furuichi T, Byrne RW (2018) Bonobo and chimpanzee gestures overlap extensively in meaning. PLoS Biol 16(2): e2004825. https://doi.org/10.1371/journal.pbio.2004825*

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Competing Interests: *The authors have declared that no competing interests exist.*

http://bit.ly/2t66VzF

Saline use on the decline at Vanderbilt following landmark studies

Studies show increased survival and decreased kidney complications

Vanderbilt University Medical Center is encouraging its medical providers to stop using saline as intravenous fluid therapy for most patients, a change provoked by two companion landmark studies released today that are anticipated to improve survival and decrease kidney complications.

Saline, used in medicine for more than a century, contains high concentrations of sodium chloride, which is similar to table salt. Vanderbilt researchers found that patients do better if, instead, they are given balanced fluids that closely resemble the liquid part of blood.

"Our results suggest that using primarily balanced fluids should prevent death or severe kidney dysfunction for hundreds of Vanderbilt patients and tens of thousands of patients across the country each year," said study author Matthew Semler, MD, MSc, assistant professor of Medicine at Vanderbilt University School of Medicine.

"Because balanced fluids and saline are similar in cost, the finding of better patient outcomes with balanced fluids in two large trials has prompted a change in practice at Vanderbilt toward using primarily balanced fluids for intravenous fluid therapy."

The Vanderbilt research, published today in the New England Journal of Medicine, examined over 15,000 intensive care patients and over 13,000 emergency department patients who were assigned to receive saline or balanced fluids if they required intravenous fluid. In both studies, the incidence of serious kidney problems or death was about 1 percent lower in the balanced fluids group compared to the saline group.

"The difference, while small for individual patients, is significant on a population level. Each year in the United States, millions of patients receive intravenous fluids," said study author Wesley Self, MD, MPH, associate professor of Emergency Medicine. "When we say a 1 percent reduction that means thousands and thousands of patients would be better off," he said.

The authors estimate this change may lead to at least 100,000 fewer patients suffering death or kidney damage each year in the US.

"Doctors have been giving patients IV fluids for over a hundred years and saline has been the most common fluid patients have been getting," said study author Todd Rice, MD, MSc, associate professor of Medicine.

"With the number of patients treated at Vanderbilt every year, the use of balanced fluids in patients could result in hundreds or even thousands of fewer patients in our community dying or developing kidney failure. After these results became available, medical care at Vanderbilt changed so that doctors now preferentially use balanced fluids," he said.

http://bit.ly/2F7AUZn

Scientists posit microbes on Enceladus and Mars

Separate studies suggest plausible scenarios for archaean and bacterial communities on the red planet and the frozen moon.

Andrew Masterson reports.

At least some of the methane detected by the Cassini space probe around Saturn's moon Enceladus could have been produced by microbes, according to researchers.

The finding is contained in one of two recent papers that posit the existence of microbial life in space. The second concerns the potential for dormant bacteria on Mars.

In the Enceladus paper, published in the journal *Nature Communications*, a team led by systems biologist Simon Rittmann of Universität Wien in Austria focuses on a type of single-celled microorganism called archaea.

These microbes are not bacteria, but constitute an entirely different kingdom of life. They have a unique biochemistry that allows them (depending on the species) to exploit substances such as ammonia, metal ions and hydrogen gas as energy sources. Widespread in variety and distribution, archaea live everywhere from deep ocean hydrothermal vents to the human gut.

Rittmann and his colleagues suggest that such microbes (or analogues thereof) might also live on Enceladus – and that Cassini might have detected evidence of them.

The scientists look at a particular subclass of archaea known as methanogens, which use molecular hydrogen and carbon as energy sources, and release methane as a by-product of their metabolism. To test their hypothesis, the researchers grew three species of methanogenic microbes under conditions that mimicked the gas composition and atmospheric pressures thought to be present on Enceladus.

They found that one species, *Methanothermococcus okinawensis*, thrived in the tough conditions, continuing to produce methane even in

the presence of additional chemicals that stymied the other two contenders.

The scientists report that *M. okinawensis* achieved a very respectable carbon-dioxide-to-methane conversion rate of 72%. Other calculations found that a predicted type of crystal-forming mineralisation on Enceladus, called serpentinisation, might also result in enough molecular hydrogen to provide a substrate for methane production.

Therefore, Rittman and colleagues conclude, "some of the [methane] detected in the plume of Enceladus might, in principle, be produced by methanogens".

Meanwhile, over in South America, another group of researchers has been investigating microbial health and activity in the Atacama Desert in Chile. The desert in one of the driest places on Earth – known as a hyperarid zone – where rain falls as infrequently as once a decade.

A team led by Dirk Schulze-Makuch of the Centre of Astronomy and Astrophysics at Germany's Technical University Berlin set out to measure what, if any, bacterial life could survive in such an inhospitable environment.

The results, compiled over a couple of years, surprised them. In the desert sands they found DNA belonging to a wide range of bacterial species, particularly *Actinobacteria* and hyperarid specialists *Geodermatophilaceae*. They also found genetic material indicating the presence of diverse, if smaller, populations of archaea and fungi.

The next task was to run a separate analysis to discover whether the DNA collected was simply the remnants of long dead organisms or viable material indicating the presence of active or alive-but-dormant ones.

This analysis was conducted over three years, starting with samples taken in the wake of a rare rain event in 2015. The results showed high levels of intracellular DNA – considered a proxy for living microbes – immediately after the rainfall. The level then decreased sharply, in inverse proportion to the density of extracellular – dead – DNA over the subsequent two rain-free years.

The results, write Schulze-Makuch and colleagues in the journal *PNAS*, show that even in hyperarid environments microbes can survive for long periods – lying dormant and then becoming active following an increase in moisture.

Could the dry surface of Mars thus harbour stubbornly dormant microbes, awaiting only water in order to spring back to life? The scientists consider the scenario at least plausible.

"The insights gained from the hyperarid core of the Atacama Desert can serve as a working model for Mars, where environmental stresses are even harsher," they conclude.

"If life ever evolved on Mars, the results presented here suggest that it could have endured the transition from the early aquatic stage, through increasing aridity cycles, and perhaps even found a subsurface niche beneath today's severely hyperarid surface."

http://bbc.in/2FJnAvk

Some smear test abnormalities 'self-heal'

Early cell changes that can turn into cervical cancer may not need treatment and may get better on their own in 50% of cases, according to a new study.

By Michelle Roberts Health editor, BBC News online

The British Medical Journal research looked at the outcomes of more than 3,000 women and found half of the "moderate" lesions found on routine smear tests regressed spontaneously. The study authors stress it is still very important that women attend for cervical screening when invited. Regular screening saves lives.

What does a positive smear test mean?

Most women's smear test results will be normal, but for around one in 20, the test shows some abnormal changes in the cells of the cervix. Although most of these changes will not lead to cancer and the cells may return to normal, some lesions will need to be removed to prevent them turning cancerous.

Currently, doctors may treat "moderate" pre-cancerous lesions, classified as CIN2, but leave and monitor low grade CIN1 lesions. The

CIN grading reflects how deep the cell changes go into the surface of the cervix - the neck of the womb:

- ***CIN 1 - one-third of the thickness of the surface layer is affected***
- ***CIN 2 - two-thirds of the thickness of the surface layer is affected***
- ***CIN 3 - the full thickness of the surface layer is affected***

What did the study find?

The BMJ research, which looked at CIN2 lesions, suggests:

- ***More than half of all untreated cases will get better spontaneously within two years***
- ***Just under one-third will persist***
- ***Just under one in five will get worse***

For women under 30 only, the rates were 60%, 23% and 11%.

That would mean that in 1,000 women aged under 30 with a diagnosis of CIN2: 600 will have regression, 230 will persist and 110 will have a lesion that will get worse and could become cancer, although the researchers stress that the findings are not a perfect prediction and should be interpreted with caution.

What should women do?

Prof Maggie Cruickshank, an expert from the University of Aberdeen, advises in a linked editorial in the BMJ: "Knowing that the chance of regression is 50%-60%, still means taking a gamble that surveillance is simply delaying treatment and even a small risk of cancer (0.5% in this study) may still be unacceptable to some."

But she notes: "The effects of local excision, such as pain, bleeding, or menstrual disturbance, time off work, and the possibility of pregnancy complications, including preterm birth and mid-trimester miscarriage are also important considerations in decision-making."

Robert Music from Jo's Cervical Cancer Trust: "The findings of this study should be treated with caution, as indicated by the researchers. However, some women can experience psychological or physical side-effects following treatment for abnormal cells so if further evidence indicates monitoring over treatment is sufficient in some cases then this is positive.

"If you are currently waiting for or going through treatment, please do not let this deter you. Further and more rigorous research is needed to fully understand the implications of this study."

All women who are registered with a GP are invited for cervical screening:

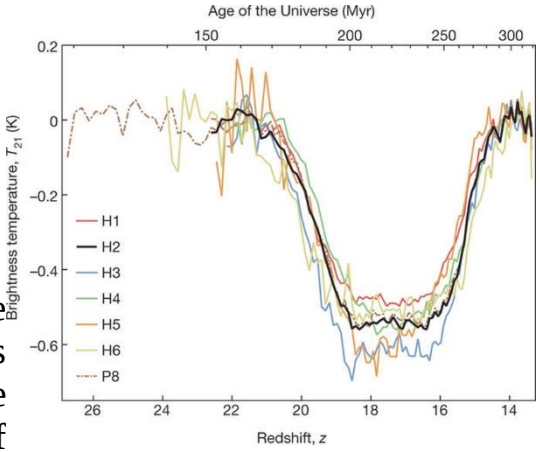
- ***aged 25 to 49 - every three years***
- ***aged 50 to 64 - every five years***
- ***over 65 - only women who haven't been screened since age 50 or those who have recently had abnormal tests***

http://bit.ly/2oAzMYe

Astronomers detect earliest evidence yet of hydrogen in the universe

Emitted just 180 million years after Big Bang, signal indicates universe was much colder than expected

CAMBRIDGE, MA -- In a study published today in the journal Nature, astronomers from MIT and Arizona State University report that a table-sized radio antenna in a remote region of western Australia has picked up faint signals of hydrogen gas from the primordial universe.



The scientists have traced the signals to just 180 million years after the Big Bang, making the detection the earliest evidence of hydrogen yet observed.

Figure 2: Best-fitting 21-cm absorption profiles for each hardware case.

They also determined that the gas was in a state that would have been possible only in the presence of the very first stars. These stars, blinking on for the first time in a universe that was previously devoid of light, emitted ultraviolet radiation that interacted with the surrounding hydrogen gas. As a result, hydrogen atoms across the universe began to

absorb background radiation - a pivotal change that the scientists were able to detect in the form of radio waves.

The findings provide evidence that the first stars may have started turning on around 180 million years after the Big Bang.

"This is the first real signal that stars are starting to form, and starting to affect the medium around them," says study co-author Alan Rogers, a scientist at MIT's Haystack Observatory. "What's happening in this period is that some of the radiation from the very first stars is starting to allow hydrogen to be seen. It's causing hydrogen to start absorbing the background radiation, so you start seeing it in silhouette, at particular radio frequencies."

Certain characteristics in the detected radio waves also suggest that hydrogen gas, and the universe as a whole, must have been twice as cold as scientists previously estimated, with a temperature of about 3 kelvins, or -454 degrees Fahrenheit. Rogers and his colleagues are unsure precisely why the early universe was so much colder, but some researchers have suggested that interactions with dark matter may have played some role.

"These results require some changes in our current understanding of the early evolution of the universe," says Colin Lonsdale, director of Haystack Observatory. "It would affect cosmological models and require theorists to put their thinking caps back on to figure out how that would happen."

Rogers' co-authors are lead author Judd Bowman of Arizona State University (ASU), along with Thomas Mozdzen, Nivedita Mahesh, and Raul Monsalve, from the University of Colorado.

Turning on, tuning in

The scientists detected the primordial hydrogen gas using EDGES (Experiment to Detect Global EoR Signature), a small ground-based radio antenna located in western Australia, and funded by the National Science Foundation.

The antennas and portions of the receiver were designed and constructed by Rogers and the Haystack Observatory team; Bowman, Monsalve, and the ASU team added an automated antenna reflection measurement system to the receiver, outfitted a control hut with the electronics, constructed the ground plane, and conducted the field work for the project. Australia's Commonwealth Scientific and Industrial Research Organization provided on-site infrastructure for the EDGES project.

The current version of EDGES is the result of years of design iteration and instrument calibration in order to reach the levels of precision necessary for successfully achieving an extremely difficult measurement.

The instrument was originally designed to pick up radio waves emitted from a time in the universe's history known as the Epoch of Reionization, or EoR. During this period, it's thought that the first luminous sources, such as stars, quasars, and galaxies, appeared in the universe, causing the previously neutral intergalactic medium, made mostly of hydrogen gas, to become ionized.

Prior to the appearance of the first stars, the universe was shrouded in darkness, and hydrogen, its most abundant element, was virtually invisible, embodying an energy state that was indistinguishable from the surrounding cosmic background radiation.

Scientists believe that when the first stars turned on, they provided ultraviolet radiation that caused changes to the hydrogen atoms' distribution of energy states. These changes induced hydrogen's single electron to spin in alignment or opposite to the spin of its proton, causing hydrogen as a whole to "decouple" from the background radiation. As a result, hydrogen gas began to either emit or absorb that radiation, at a characteristic wavelength of 21 centimeters, equivalent to a frequency of 1,420 megahertz. As the universe expanded over time, this radiation became "red-shifted" to lower frequencies. By the time this 21-centimeter radiation reached present-day Earth, it landed somewhere in the range of 100 megahertz.

Rogers and his colleagues have been using EDGES to try to detect hydrogen that existed during the very early evolution of the universe, in order to pinpoint when the first stars turned on.

"There is a great technical challenge to making this detection," says Peter Kurczynski, program director for Advanced Technologies and Instrumentation, in the Division of Astronomical Sciences at the National Science Foundation, which has provided funding for the project over the past several years. "Sources of noise can be a thousand times brighter than the signal they are looking for. It is like being in the middle of a hurricane and trying to hear the flap of a hummingbird's wing."

The instrument, about the size of a small table, sits in a remote region of western Australia where there are very little humanmade radio signals to interfere with incoming radio waves from the distant universe. The antenna detects radio waves from the entire sky, and the researchers had originally tuned it to listen in at a frequency range of 100 to 200 megahertz.

A switch hit

However, when the researchers looked within this range, they initially failed to pick up much of any signal. They realized that theoretical models had predicted that primordial hydrogen should give off emissions within this range if the gas was hotter than the surrounding medium. But what if the gas was in fact colder? Models predict that the hydrogen should then absorb radiation more strongly in the 50 to 100 megahertz frequency range.

"As soon as we switched our system to this lower range, we started seeing things that we felt might be a real signature," Rogers says.

Specifically, the researchers observed a flattened absorption profile, or a dip in the radio waves, at around 78 megahertz.

"We see this dip most strongly at about 78 megahertz, and that frequency corresponds to roughly 180 million years after the Big Bang," Rogers says. "In terms of a direct detection of a signal from the hydrogen gas itself, this has got to be the earliest."

The dip in radio waves was stronger and deeper than theoretical models predicted, suggesting that the hydrogen gas at the time was colder than previously thought. The radio waves' profile also matches theoretical predictions of what would be produced if hydrogen were indeed influenced by the first stars.

"The signature of this absorption feature is uniquely associated with the first stars," Lonsdale says. "Those stars are the most plausible source of radiation that would produce this signal."

"It is unlikely that we'll be able to see any earlier into the history of stars in our lifetimes," lead author Bowman of ASU says. "This project shows that a promising new technique can work and has paved the way for decades of new astrophysical discoveries."

The researchers say this new detection lifts the curtain on a previously obscure phase in the evolution of the universe.

"This is exciting because it is the first look into a particularly important period in the universe, when the first stars and galaxies were beginning to form," Lonsdale says. "This is the first time anybody's had any direct observational data from that epoch."

This research was supported by funding from the National Science Foundation.

http://bit.ly/2oJ8XQJ

New stem cell found in lung, may offer target for regenerative medicine

CHOP/Penn team: New type of cell multiplies after lung injury

Newly identified stem cells in the lung that multiply rapidly after a pulmonary injury may offer an opportunity for innovative future treatments that harness the body's ability to regenerate. Writing today in the journal Nature, scientists describe cells that could become a new tool to treat lung diseases across the lifespan, from premature infants to the elderly.

Researchers from Children's Hospital of Philadelphia (CHOP) and the Perelman School of Medicine at the University of Pennsylvania focused on the alveoli--tiny compartments in the lung in which gas exchange occurs, as oxygen is taken up by the blood and carbon dioxide is

removed. First in mouse models, then in humans, the study team identified a new cell lineage, which they called alveolar epithelial progenitor (AEP) cells.

"These cells sits quietly, but poised, in the lung until an injury activates them to proliferate and differentiate," said co-first author David B. Frank, MD, PhD, a pediatric cardiologist at CHOP. "If we can learn to manipulate the biological signals in this process, we may be able to regenerate lung tissue in patients."

Leading the research team was Edward E. Morrisey, PhD, director of the Penn Center for Pulmonary Biology and scientific director of Penn's Institute for Regenerative Medicine. Morrisey said "One of the most important places to better understand lung regeneration is the alveoli. To better understand these delicate structures, we have been mapping the different types of cells within the alveoli." He added that "understanding cell-cell interactions should help us discover new players and molecular pathways to target for future therapies."

The study team identified the new stem cells, first in mouse models, then in humans. They found that this cell system is evolutionarily conserved across separated species: AEPs share similar characteristics in both mice and humans. The underlying genes code for a similar set of proteins and respond to a similar set of signals--allowing researchers to investigate specific biological mechanisms in mice with relevance to how these cells function in humans. It also allowed them to perform experiments in organoid models--three-dimensional cell cultures that simulated specific ways that lungs function in living lower organisms.

Lung development in general, and alveoli in particular, are important to the evolution of life on earth, as one of the key steps allowing early animals to adapt to breathing oxygen on land. In our own early development, alveoli are also crucial in our transition from fluid respiration in the womb to preparing to breathe outside air at birth. In fact, if this normal development is short-circuited in premature births, infants with underdeveloped lungs may suffer a severe, even fatal disability, called bronchopulmonary dysplasia.

In the current study, the researchers studied how mice responded to lung injury caused by influenza virus. They discovered mechanisms by which alveolar cells are sensitive to Wnt signals, an important and powerful stem cell signaling pathway. Wnt signals, along with another set of signals called Fgf signals, act on the normally quiescent AEP cells in the lung to orchestrate their response to injury. Those AEP cells multiply rapidly and differentiate into alveolar cells, thereby regenerating lung tissue.

The researchers aim to translate their findings into eventual treatments for lung diseases in both children and adults. "As we have seen during this influenza season, lung damage from viruses and inflammation can be devastating," said Frank. "However, we now understand how the alveolar epithelial niche regenerates following injury. With this information, we may able to design pathway-specific modifiers or cell-based therapies to treat lung damage."

The AEP findings could lay the foundation for new treatments for children with BPD, adults with chronic obstructive pulmonary disease, or anyone with severe lung damage from influenza. Frank suggests the knowledge might even inform future tissue engineering treatments for premature babies or patients needing lung transplantation.

Given that respiration is intimately involved with the cardiovascular system, Frank also expects to pursue future research into tissue regeneration in the vascular system--the capillaries and arteries that supply the alveoli. As a pediatric cardiologist, he has a special focus on children with pulmonary hypertension, often a complication of congenital heart disease. He adds, "If we can eventually improve blood vessels along with healing damaged airways in our patients, we could significantly advance treatments for many of these children."

The National Institutes of Health supported this study (grants HL007586, HL007915, HD043245, HL007843, HL110942, HL087825, HL132999, HL129478, and HL134745).

William J. Zacharias et al, "Regeneration of the lung alveolus by an evolutionarily conserved epithelial progenitor," Nature, online Feb. 28, 2018. http://doi.org/10.1038/nature25786

http://bit.ly/2oL5X6h

Earth Was Vaporized 4.5 Billion Years Ago, and (Maybe) That's Why We Have a Moon

Once upon a time, about 4.5 billion years ago, the Earth was an unformed doughnut of molten rock called a synestia — and the moon was hidden in the filling.

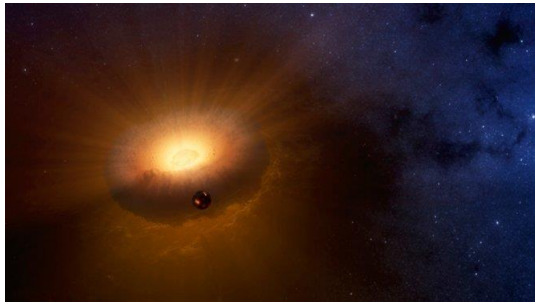
By Brandon Specktor, Senior Writer

That's one possible explanation for the moon's formation, anyway.

And according to a new paper published today (Feb. 28) in the Journal of Geophysical Research – Planets, it may be the best explanation scientists have so far.

"The new work explains features of the moon that are hard to resolve with current ideas," study author Sarah Stewart, a professor of Earth and planetary sciences at the University of California, Davis, said in a statement.

"The moon is chemically almost the same as the Earth, but with some differences. This is the first model that can match the pattern of the Moon's composition."



This artist's rendering shows the hot, molten moon emerging from a synestia, a giant spinning doughnut of vaporized rock that formed when planet-size objects collided. **Sarah Stewart/UC Davis based on NASA rendering**

The new lunar-creation model revolves around a hypothetical planetary object called a synestia, which Stewart and Simon Lock, a graduate student at Harvard University and co-author of the new study, first described in a paper published last year.

Named for the Greek words "syn," meaning together, and "Hestia," the goddess of structures and architecture, a synestia may form when two planet-size bodies collide in space, with the collision resulting in a cloud of superhot vapor.

If the two objects have great enough angular momentum (as most rotating planets do), the resulting storm of planetary debris could continue spinning fast enough to form a giant disc of molten vapor, indented in the center and puffing steadily outward in a giant doughnut shape many times wider than Saturn's rings.

As this giant, spinning space-doughnut gradually loses heat, it condenses into a solid again, combining bits of matter from both the original planet and the object it collided with.

According to Stewart and Lock's previous paper, Earth may have briefly become a synestia not long after its birth about 4.5 billion years ago, after being struck by a renegade Mars-size rock called Theia.

A popular theory of the moon's origin suggests that Earth took a glancing blow from Theia, throwing a spray of molten rock and metal into orbit that eventually condensed into the moon as we know it today.

If the moon formed inside an Earth-synestia, however, a slightly different story would have unfolded.

"Our model starts with a collision that forms a synestia," Lock said in a statement.

"The moon forms inside the vaporized Earth at temperatures of 4,000 to 6,000 degrees Fahrenheit [2,200 to 3300 degrees Celsius] and pressures of tens of atmospheres," or many times higher than the atmospheric pressure on modern-day Earth.

As the synestia first started to cool, vaporized rock at the outer edge of the system began condensing into droplets and falling inward in a "torrential rain."

As these droplets fell farther into the synestia's interior, they accumulated more and more vapor from the cloud around them, forming a series of "moonlets" and eventually the moon itself.

While the synestia continued to cool and condense, the moon eventually escaped the cloud entirely, but remained in Earth's orbit.

According to this model, the moon inherited its composition from the Earth but lost some of its more easily vaporized elements to the intense heat of the synestia.

This model adequately explains the moon's distinct composition as we understand it today, Stewart said.

One caveat to the new hypothesis: Synestias remain theoretical objects that have never been observed in the universe.

Astronomers may one day be able to spot them forming in alien solar systems, the researchers said — and if they do, they just might confirm an important story much closer to home.

http://bit.ly/2FcCQDp

Storm waves can move boulders we thought only tsunamis had the power to shift

Storms may be more powerful -- and more damaging -- than previously shown

Oxford - It's not just tsunamis that can change the landscape: storms shifted giant boulders four times the size of a house on the coast of Ireland in the winter of 2013-14, leading researchers to rethink the maximum energy storm waves can have - and the damage they can do.

In a new paper in Earth Science Reviews, researchers from Williams College in the US show that four years ago, storms moved huge boulders along the west coast of Ireland.

The same storms shifted smaller ones as high as 26 meters above high water and 222 meters inland. Many of the boulders moved were heavier than 100 tons, and the largest moved was 620 tons - the equivalent of six blue whales or four single-storey houses.

It was previously assumed that only tsunamis could move boulders of the size seen displaced in Ireland, but the new paper provides direct evidence that storm waves can do this kind of work.

According to the UN, about 40 percent of the world's population live in coastal areas (within 100 meters of the sea), so millions of people are at risk from storms.

Understanding how those waves behave, and how powerful they can be, is key for preparation.It is therefore important to know the upper limits of storm wave energy, even in areas where these kinds of extreme wave energies are not expected.

"The effect of the storms of winter 2013-14 was dramatic," said Dr. Rónadh Cox, Professor and Chair of Geosciences at Williams College and lead author of the study. "We had been studying these sites for a number of years, and realised that this was an opportunity to measure the coastal response to very large storm events."

In the summer after the storms, Prof. Cox and a team of seven undergraduate students from Williams College surveyed 100 sites in western Ireland, documenting with photos the displacement of 1,153 boulders.

They measured the dimensions and calculated the mass of each boulder. They knew where 374 of the boulders had come from, so for those they also documented the distance travelled. The largest boulder, at 237-239 m^3 was an estimated 620 tons; the second biggest, at 180-185 m^3, was about 475 tons.

These giant rocks were close to sea level (although above the high tide mark). At higher elevations, and at greater distances inland, smaller boulders moved upwards and inland.

Analysis of this information showed that the waves had most power at lower elevations and closer to the shore.

While this may not be surprising, the sheer energy of the waves and their ability to move such large boulders was - and this evidence proves that not only tsunami but also storm waves can move such large objects.

"These data will be useful to engineers and coastal scientists working in other locations," said Prof. Cox.

"Now that we know what storm waves are capable of, we have much more information for policy makers who are responsible for preparing coastal communities for the impact of high-energy storms."

The article is "Extraordinary boulder transport by storm waves (west of Ireland, winter 2013-2014), and criteria for analysing coastal boulder deposits," by Rónadh Cox, Kalle L. Jahn, Oona G. Watkins and Peter Cox. It appears in Earth Science Reviews, volume 177, (February 2018), published by Elsevier.

http://bit.ly/2oEy4Vw

An Even-Weirder-Than-Usual Tardigrade Just Turned Up in a Parking Lot

A new species of tardigrade was discovered in a parking lot in Japan.

By Stephanie Pappas, Live Science Contributor

A newfound species of tardigrade, or "water bear," with tendril-festooned eggs has been discovered in the parking lot of an apartment building in Japan.

The newfound tardigrade, *Macrobiotus shonaicus*, is the 168th species of this sturdy micro-animal ever discovered in Japan. Tardigrades are famous for their toughness: They can survive in extreme cold (down to minus 328 degrees Fahrenheit, or minus 200 Celsius), extreme heat (more than 300 degrees F, or 149 degrees C), and even the unrelenting radiation and vacuum of space, as one 2008 study reported.

They're bizarre and adorable at the same time, with eight legs on a rotund little body (they're usually far less than a millimeter in length) and circular mouths that make them look perpetually surprised.

Kazuharu Arakawa, a researcher who studies the molecular biology of tardigrades at Japan's Keio University, discovered the newfound species in a small sample of moss. He'd scraped the moss from the parking lot of his apartment in Tsuruoka City along the Sea of Japan.

"Most of [the] tardigrade species were described from mosses and lichens — thus any cushion of moss seems to be interesting for people working on tardigrades," Arakawa told Live Science in an email. But, he said, "it was quite surprising to find a new species around my apartment!"

Spaghetti eggs

Arakawa routinely samples moss he finds around town, he said, but the portion from his parking lot turned out to be special. The tardigrades he found there could survive and reproduce in a laboratory environment, which is very rare for these creatures, he said.

He sequenced the tiny animal's genome and only then realized that it matched no previously found tardigrade sequence. Arakawa looped in tardigrade expert Łukasz Michalczyk of Jagiellonian University in Poland, and the researchers determined that they had a newfound species on their hands.

The species ranges in length from 318 micrometers to 743 micrometers. It has the typical plump-caterpillar look of a tardigrade, and its O-shaped mouth is ringed by three rows of teeth.

It can live on algae, which is odd because other species in the *Macrobiotus* genus are carnivores that eat even tinier animals called rotifers, Arakawa said.

Perhaps the weirdest aspect of *M. shonaicus*, though, is its eggs. The spherical eggs are studded with miniscule, chalice-shaped protrusions, each of which is topped with a ring of delicate, noodle-like filaments. These features might help the egg attach to the surface where it is laid, Arakawa said.

Tardigrade family tree

The newfound species is part of a set of tardigrade species, known as the *hufelandi* group, that all have these cup-like egg decorations, Arakawa and his team reported today (Feb. 28) in the open-access journal PLOS One. *Macrobiotus hufelandi* was the first tardigrade species ever discovered, way back in 1834. That species was found in Italy and Germany originally, but it and its close relatives have now been found all over the globe, Arakawa said.

"This is the first report of a new species in this complex from East Asia," he said. More tardigrade-hunting is necessary to find out how tardigrades diversified and adapted over time, he said.

Also exciting is that *M. shonaicus* can thrive in the lab, Arakawa said. "It is an ideal model to study the sexual-reproduction machinery and behaviors of tardigrades," he said. "We are actually already submitting another paper describing their mating behaviors."

http://bit.ly/2F8mMDt

Heart attacks often follow dramatic changes in outdoor temperature

Findings suggest climate change may increase heart attack risk

WASHINGTON - Large day-to-day swings in temperature were associated with significantly more heart attacks in a study being presented at the American College of Cardiology's 67th Annual Scientific Session. Given that some climate models link extreme weather events with global warming, the new findings suggest climate change could, in turn, lead to an uptick in the occurrence of heart attacks, researchers said.

"Global warming is expected to cause extreme weather events, which may, in turn, result in large day-to-day fluctuations in temperature," said Hedvig Andersson, MD, a cardiology researcher at the University of Michigan and the study's lead author. "Our study suggests that such fluctuations in outdoor temperature could potentially lead to an increased number of heart attacks and affect global cardiac health in the future."

There is a large body of evidence showing that outdoor temperature affects the rate of heart attacks, with cold weather bringing the highest risk, but most previous studies have focused on overall daily temperatures. This new study is among the first to examine associations with sudden temperature changes.

"While the body has effective systems for responding to changes in temperature, it might be that more rapid and extreme fluctuations create more stress on those systems, which could contribute to health problems," Andersson said, noting that the underlying mechanism for this association remains unknown.

Along with an overall warming trend, climate change is projected to lead to more extreme events, such as heat waves and cold snaps, depending on where someone lives, the researchers explained.

The research is based on data from more than 30,000 patients treated at 45 Michigan hospitals between 2010-2016. All patients had received percutaneous coronary intervention, a procedure used to open clogged arteries, after being diagnosed with ST-elevated myocardial infarction, the most serious form of heart attack.

The researchers calculated the temperature fluctuation preceding each heart attack based on weather records for the hospital's ZIP code. Daily temperature fluctuation was defined as the difference between the highest and lowest temperature recorded on the day of the heart attack.

Overall, the results showed the risk of a heart attack increased by about 5 percent for every five-degree jump in temperature differential, in degrees Celsius (9 degrees Fahrenheit). Swings of more than 25 degrees Celsius (45 degrees Fahrenheit) were associated with a greater increase in heart attack rates compared to a smaller increase with temperature swings of 10 to 25 degrees Celsius (18-45 degrees Fahrenheit). The effect was more pronounced on days with a higher average temperature; in other words, a sudden temperature swing seemed to have a greater impact on warmer days.

At the far end of the spectrum, on a hot summer day, nearly twice as many heart attacks were predicted on days with a temperature fluctuation of 35-40 degrees Celsius (63-72 degrees Fahrenheit) than on days with no fluctuation.

"Generally, we think of heart attack risk factors as those that apply to individual patients and we have, consequently, identified lifestyle changes or medications to modify them. Population-level risk factors need a similar approach," said Hitinder Gurm, MD, professor of medicine and associate chief clinical officer at Michigan Medicine and the study's senior author. "Temperature fluctuations are common and [often] predictable. More research is needed to better understand the underlying mechanisms for how temperature fluctuations increase the risk of heart attacks, which would allow us to perhaps devise a successful prevention approach."

In their analysis, the researchers adjusted for precipitation totals, day of the week and seasonal trends to isolate the effects of daily temperature fluctuations from other potential environmental factors.

Gurm cautioned that the association does not necessarily prove that sudden temperature swings are the cause of the increase in heart attacks; other factors may have contributed to the results. He noted that it remains important to focus on modifiable cardiovascular risk factors such as smoking, high blood pressure and high cholesterol.

Andersson will present the study, "Daily Temperature Fluctuations and Myocardial Infarction: Implications of Global Warming on Cardiac Health," on Saturday, March 10 at 3:45 p.m. ET in Poster Hall A/B.

http://go.nature.com/2teYp1e

Colossal family tree reveals environment's influence on lifespan

Genetics explains only a small part of differences in how long a person lives, finds analysis that links 13 million people.

Erika Check Hayden

Did you forget your mother's birthday this year? Brace yourself: your family tree may now include the birthdays of 13 million people.

Computational biologist Yaniv Erlich of Columbia University in New York City and his colleagues have used crowdsourced data to make a family tree that links 13 million people. The ancestry chart, described today in *Science*[1], is believed to be the largest verified resource of its kind — spanning an average of 11 generations.

Erlich's team analysed the birth and death dates of the people in this tree, and calculated whether individuals were more likely to have died at similar ages if they were closely related. The group concludes that heredity explains only about 16% of the difference in lifespans for these individuals. Most of the differences were down to other factors, such as where and how people lived.

"This is a real tour de force," says genetic epidemiologist Braxton Mitchell of the University of Maryland School of Medicine in Baltimore. "This is a great example of using large, publicly available data sets to do interesting research."

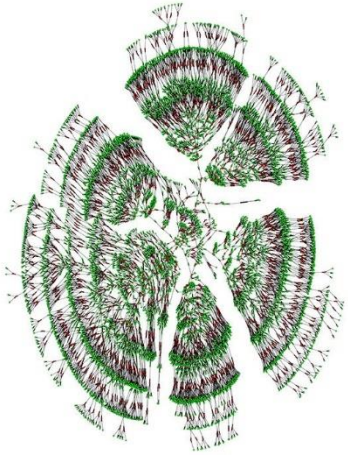
Live long and prosper

Scientists already suspected that environment has more influence than genes on how long people live. But Erlich estimates that genes have even less of a role than researchers had thought.

Some studies, such as one published by Mitchell's group in 2001[2], have estimated that genes determine about one-quarter of the variation in people's lifespan.

Erlich's finding proves the power of extremely large family trees, or genealogies, says Lisa Cannon-Albright, a geneticist at the University of Utah School of Medicine in Salt Lake City.

"These kinds of resources will be a powerful piece of future genetics research," she says.



This 6,000-person family tree was cleaned and organized using graph theory. Individuals are shown in green, spanning seven generations; marriages are depicited in red. **Columbia University**

Erlich says that "good" genes might extend a person's life by an average of five years. Some environmental factors make a much bigger impact on longevity; smoking, for instance, can subtract ten years.

Geneticists have long used family trees to study how genetics influence many traits, such as disease risk. But it can be costly and difficult to assemble databases of family records that contain vast numbers of people. Erlich's study is one of many under way that are now assembling digital records into very large family trees[3,4]; some have identified genes linked to illnesses such as cancer and Alzheimer's disease[5].

Data deluge

Erlich's study used data from an online genealogy tool, Geni.com. He is the chief scientific officer of MyHeritage, Geni's parent company, in Or Yehuda, Israel. The analysis drew on data on roughly 86 million people whose records were uploaded by Geni users. That's an order of

magnitude more participants than are included in the largest consumer genetic-testing database.

“The sheer number of participants is crazy,” says computational genomicist Atul Butte of the University of California, San Francisco. “You can only get data sets like this with crowdsourcing. It’s really impressive.”

Erlich’s team used the data to analyse the migration and marriage patterns of people listed on Geni. For instance, before 1750, the researchers found, most Americans and Europeans in the database married someone who lived at most 10 kilometres from their birthplace. By 1950, most Americans and Europeans had to travel at least 100 kilometres from their home towns to find a spouse..

In other words, your parents probably travelled farther than any of their ancestors to start your family. The least you can do is remember their birthdays.

http://bit.ly/2FQA7wY

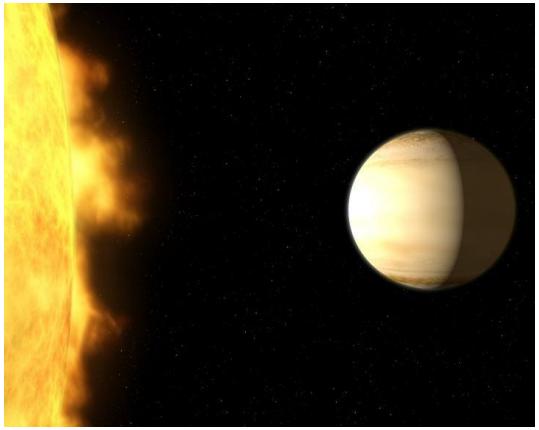
Hubble observes exoplanet atmosphere in more detail than ever before

Hints that formation processes of exoplanets can be very different from those of Solar System gas giants

An international team of scientists has used the NASA/ESA Hubble Space Telescope to study the atmosphere of the hot exoplanet WASP-39b. By combining this new data with older data they created the most complete study yet of an exoplanet atmosphere. The atmospheric composition of WASP-39b hints that the formation processes of exoplanets can be very different from those of our own Solar System giants.

Investigating exoplanet atmospheres can provide new insight into how and where planets form around a star. "We need to look outward to help us understand our own Solar System," explains lead investigator Hannah Wakeford from the University of Exeter in the UK and the Space Telescope Science Institute in the USA.

Therefore the British-American team combined the capabilities of the NASA/ESA Hubble Space Telescope with those of other ground- and space-based telescopes for a detailed study of the exoplanet WASP-39b. They have produced the most complete spectrum of an exoplanet's atmosphere possible with present-day technology [1].



A team of British and American astronomers used data from several telescopes on the ground and in space -- among them the NASA/ESA Hubble Space Telescope -- to study the atmosphere of the hot, bloated, Saturn-mass exoplanet WASP-39b, about 700 light-years from Earth. The analysis of the spectrum showed a large amount of water in the exoplanet's atmosphere -- three times more than in Saturn's atmosphere. **NASA, ESA, and G. Bacon (STScI)**

WASP-39b is orbiting a Sun-like star, about 700 light-years from Earth. The exoplanet is classified as a "Hot-Saturn", reflecting both its mass being similar to the planet Saturn in our own Solar System and its proximity to its parent star. This study found that the two planets, despite having a similar mass, are profoundly different in many ways. Not only is WASP-39b not known to have a ring system, it also has a puffy atmosphere that is free of high-altitude clouds. This characteristic allowed Hubble to peer deep into its atmosphere.

By dissecting starlight filtering through the planet's atmosphere [2] the team found clear evidence for atmospheric water vapour. In fact, WASP-39b has three times as much water as Saturn does. Although the researchers had predicted they would see water vapour, they were surprised by the amount that they found. This surprise, combined with the water abundance allowed to infer the presence of large amount of heavier elements in the atmosphere. This in turn suggests that the planet was bombarded by a lot of icy material which gathered in its atmosphere. This kind of bombardment would only be possible if

WASP-39b formed much further away from its host star than it is right now.

"WASP-39b shows exoplanets are full of surprises and can have very different compositions than those of our Solar System," says co-author David Sing from the University of Exeter, UK.

The analysis of the atmospheric composition and the current position of the planet indicate that WASP-39b most likely underwent an interesting inward migration, making an epic journey across its planetary system.

"Exoplanets are showing us that planet formation is more complicated and more confusing than we thought it was. And that's fantastic!", adds Wakeford.

Having made its incredible inward journey WASP-39b is now eight times closer to its parent star, WASP-39, than Mercury is to the Sun and it takes only four days to complete an orbit. The planet is also tidally locked, meaning it always shows the same side to its star. Wakeford and her team measured the temperature of WASP-39b to be a scorching 750 degrees Celsius. Although only one side of the planet faces its parent star, powerful winds transport heat from the bright side around the planet, keeping the dark side almost as hot.

"Hopefully this diversity we see in exoplanets will help us figure out all the different ways a planet can form and evolve," explains David Sing.

Looking ahead, the team wants to use the NASA/ESA/CSA James Webb Space Telescope -- scheduled to launch in 2019 -- to capture an even more complete spectrum of the atmosphere of WASP-39b. James Webb will be able to collect data about the planet's atmospheric carbon, which absorbs light of longer wavelengths than Hubble can see [3].

Wakeford concludes: "By calculating the amount of carbon and oxygen in the atmosphere, we can learn even more about where and how this planet formed."

[1] Data used to produce the full spectrum was also collected by NASA's Spitzer Space Telescope and ESO's Very Large Telescope. In addition older data from Hubble were used.

[2] When starlight passes through the atmosphere of an exoplanet, it interacts with the atoms and molecules in it. This leaves a weak fingerprint of the atmosphere in the spectrum of the star. Certain peaks and troughs in the resulting spectrum correspond to specific atoms and molecules, allowing scientists to see exactly what gases make up the atmosphere.

[3] Given the large amount of heavy elements in WASP-39b's atmosphere, Wakeford and her team predict that carbon dioxide will be the dominant form of carbon. This could be measured at a wavelength of 4.5 micrometres with James Webb's NIRSpec instrument. Such follow-up investigations would allow further constraints to be placed on the ratio of carbon to oxygen, and on the metallicity of WASP-39b's atmosphere.

More information

The Hubble Space Telescope is a project of international cooperation between ESA and NASA. The international team of astronomers in this study consists of H.R. Wakeford (University of Exeter, UK; Space Telescope Science Institute, USA), D.K. Sing (University of Exeter, UK), D. Deming (University of Maryland, USA), N.K. Lewis (Space Telescope Science Institute, USA), J. Goyal (University of Exeter, UK), T.J. Wilson (University of Exeter, UK), J. Barstow (University College London, UK), T. Kataria (NASA Jet Propulsion Laboratory, USA), B. Drummond (University of Exeter, UK), T.M. Evans (University of Exeter, UK), A.L. Carter (University of Exeter, UK), N. Nikolov (University of Exeter, UK), H.A. Knutson (California Institute of Technology, USA), G.E. Ballester (University of Arizona, USA), A.M. Mandell (NASA Goddard Space Flight Center, USA)

Image credit: NASA, ESA, G. Bacon and A. Feild (STScI), and H. Wakeford (STScI/Univ. of Exeter)

http://bit.ly/2CWxzdE

Calcium supplements may boost risk of abnormal bowel growths (polyps)

Possible risks must be weighed against the benefits of supplements

Calcium supplements, taken with or without vitamin D, may increase the risk of small growths in the large bowel (colon) called polyps, suggest results from a large US trial published online in the journal Gut.

The researchers say further studies are recommended to confirm these results - and any possible risks must be weighed against the benefits of supplementation. But given that calcium supplements are taken by millions of people around the world, the findings may have important implications for bowel cancer screening and prevention.

Polyps are small growths in the lower part of the large bowel. They are non-cancerous, but some could eventually turn into cancer if they are not removed.

Polyps come in different shapes and sizes, and this study specifically focused on the risk of serrated polyps, which are less common than conventional "adenomatous" polyps, but likely have the same risk of developing into cancer. Some studies have suggested that calcium and

vitamin D may protect against colon polyps, but results have been mixed.

So to investigate further, a team of US-based researchers set out to determine whether taking daily calcium and vitamin D supplements reduce the risk of serrated polyps.

They analysed findings from a large US trial involving over 2,000 patients aged between 45 and 75 who had a history of polyps and were due to have a follow-up test (colonoscopy) in 3 to 5 years.

Patients were excluded if they had a family history of bowel cancer, inflammatory bowel disease, or other serious health conditions - and several factors were taken into account at the start of the study, including sex, diet, weight (BMI), and use of anti-inflammatory drugs.

The remaining patients were randomly split into groups to receive either daily calcium supplements, daily vitamin D supplements, both or neither for 3 or 5 years (treatment phase) until their colonoscopy.

Effects 3 to 5 years after treatment ended (observational phase) were also recorded.

During the treatment phase, there was no effect of either calcium or vitamin D on cases of serrated polyps. However, during the later observational phase (6-10 years after treatment began), the researchers found increased risks of serrated polyps among patients taking calcium alone and among those taking a combination of calcium and vitamin D.

There was evidence that women and smokers were at higher risk when exposed to calcium supplements, but no association was found between vitamin D alone and the risk of serrated polyps.

The results also suggest an association with calcium supplements only, not dietary calcium.

Strengths of the study include its randomised design and large sample size, say the authors. However, they point out that findings are derived from a secondary analysis of a trial and it is possible that some results from these analyses were due to chance.

Further studies are recommended to confirm these results, say the authors, but if calcium and its combination with vitamin D are truly associated with an increased risk of serrated polyps, "this has important public health implications," they conclude.

In the meantime, they suggest that patients with a history of pre-cancerous serrated polyps, especially women and smokers, may wish to avoid vitamin D and calcium supplementation.

http://bit.ly/2CVit8x

Great mystery unravelled: Most viruses and bacteria fall from the sky

One billion viruses and over 20 million bacteria circulate in the Earth's atmosphere

An international research project led by the University of Granada has revealed for the first time that almost one billion viruses and more than twenty million bacteria circulate in the Earth's atmosphere and are deposited in high-mountain places every day.

The research findings, published recently in the ISME Journal: Multidisciplinary Journal of Microbial Ecology (part of the Nature group) help to explain why genetically identical viruses have been found in such distant locations and diverse environments of the planet. The University of British Columbia (Canada) and San Diego State University (United States) also participated in the project.

The mechanisms responsible for the dispersal of these microorganisms at the global scale are still practically unknown. However, this pioneering project marks the first time that researchers have quantified the amount of viruses and bacteria deposited in the high mountains of Sierra Nevada after- travelling thousands of kilometres in the Earth's atmosphere.

The research team was also able to determine that these viruses and bacteria are primarily transported from the Atlantic Ocean and the Sahara Desert.

Every day almost one billion viruses and more than 20 million bacteria are deposited on each square metre above the atmospheric boundary layer (above 2500-3000 metres) in the Sierra Nevada mountain range.

Interestingly, the deposition rates of viruses were found to be between 9 and 461 times higher than those of bacteria. Viruses and bacteria are normally deposited by means of atmospheric rain washout and gravity sedimentation. However, rain seems to be less efficient in the removal of viruses from the atmosphere than in the removal of bacteria. This seems to be related to the size of the particles to which viruses and bacteria respectively tend to adhere.

The main author of the paper, Dr. Isabel Reche, a Lecturer at the Department of Ecology (UGR), explains that: "We have discovered that most of the viruses are of marine origin and are usually transported attached to organic particles, which are smaller than the particles to which bacteria adhere."

Bacteria, meanwhile, tend to stick to mineral particles, especially those from the Sahara Desert. In short, bacteria and viruses, generally speaking, are deposited through rain events and dust intrusions.

"The small size of the particles to which viruses preferentially adhere and the low deposition efficiency associated with rain washout mean that viruses are able to stay in the atmosphere for longer periods and, consequently, they can be transported over greater distances", Dr. Reche points out.

According to the authors, this research helps explain why, for over twenty years, viruses that are genetically identical have been found in very distant parts of the planet and in highly disparate environments. The reason, according to their work, is that viruses travel through the Earth's atmosphere.

Professor Curtis A. Suttle, from the University of British Columbia (Canada) and Associate Professor Natalie Mladenov, from San Diego State University (United States) also participated in this research project.

Bibliographical reference:

Isabel Reche, Gaetano D'Orta, Natalie Mladenov, Danielle M. Winget & Curtis A. Suttle. Deposition rates of viruses and bacteria above the atmospheric boundary layer. The ISME Journal: Multidisciplinary Journal of Microbial Ecology (2018) doi:10.1038/s41396-017-0042-4

http://bit.ly/2I1YZTw

Here's how viruses inactivate the immune system, causing cancer

Describing how viruses use methylation of DNA promoter regions to inactivate the immune system, causing cancer.

It's no new news that viruses cause cancer. For example, human papillomavirus (HPV) causes almost all of the more than 500,000 annual worldwide cases of cervical cancer. This makes sense: By driving the proliferation of infected cells, viruses speed manufacture of more viruses, but excessive cellular proliferation is also a hallmark of cancer. Now a University of Colorado Cancer Center review published in the journal *Viruses* explores another strategy that viruses use to ensure their own survival, also with the unfortunate byproduct of promoting cancer, namely the viral ability to manipulate the human immune system. This new understanding may help to increase the effectiveness of immune-based therapies against cancer.

"Ultimately, the virus is suppressing the immune system for its own benefit, and promoting the formation and proliferation of cancer cells may be just a side effect of that," says Sharon Kuss-Duerkop, PhD, research instructor working in the lab of CU Cancer Center investigator Dohun Pyeon, PhD.

Interestingly, while viruses certainly have the ability to edit human DNA - most obviously by inserting their own genetic code into DNA so that the new viruses are built alongside DNA replication - the review article explains that viruses do not necessarily turn off the immune system by editing genes. Instead, viruses mute the immune system by epigenetic regulation - instead of changing the actual code of genes, viruses change the degree to which genes are expressed.

They do this by a process called DNA methylation, which, very basically, is a way to silt over parts of the human genome to keep it from being read. In this case, viruses cause methylation of parts of the genome known as DNA promoter regions. Think of these promoter regions like on-off switches for next-door genes - when a promoter

region is methylated, the switch is turned off and the gene it controls does not get read and expressed.

"You get lack of access by things that would be driving transcription," Kuss-Duerkop says. In other words, by methylating DNA promoter regions, viruses can turn off genes. But the virus itself doesn't do this - it's not as if viruses creep along a length of DNA spitting out methyl groups onto DNA promoters. Instead, in a Machiavellian twist, viruses recruit human proteins to methylate DNA and thus turn off important other bits of human DNA.

"Viruses encode particular proteins that can in some way modulate DNA methyltransferases," Kuss-Duerkop says, meaning that viruses can cause our own proteins to over-methylate our own DNA.

Of course, it makes sense that viruses would choose to turn off genes that the immune system needs to fight the virus, "like interferon-b, which is a highly anti-viral gene expressed in virtually all cell types; or genes that T cells need to recognize virus-infected cells," Kuss-Duerkop says.

The result is an immune system less able to fight the virus, and, if the virus causes cancer, a "microenvironment" near the tumor in which the immune system is suppressed. In fact, we see this in many cancers - tumors may specifically cloak themselves from the immune system, and they may also suppress the immune system more globally near the places they grow.

Sitting opposite these cancer-causing viruses and their ability to undercut the immune system are doctors and researchers who would like to recruit the immune system to attack cancer. Again: viruses turn down the immune system against the cancers they cause, and doctors would like to turn up the immune system against these same cancers.

And, in fact, these doctors and researchers are finding incredible success with this strategy; for example, PD-1 inhibitors remove this "cloak" that cancers use to hide from the immune system, and CAR-T cell therapies use specially engineered T-cells to seek cancer-specific proteins and destroy the cancer cells to which they are attached.

But challenges to immune-based therapies against cancer remain. Not least among which is the fact that while some patients respond to these therapies, others do not. The answer to increasing the effectiveness of immune therapies, or perhaps at least to choosing which patients are most likely to benefit from immune therapies, may lie in understanding the ways viruses (and cancers themselves) have evolved to evade the immune system.

Maybe if virus-related cancers have methylated DNA promoter regions of immune-related genes, the answer to increasing the effectiveness of immune-based therapies against cancer is to demethylate these genes.

"You don't want to just turn down methylation globally, which would result in over-activation of all genes in the cell, but demethylating some of these gene promoter regions selectively could revive an immune system muted by cancer-causing viruses," Kuss-Duerkop says.

"Ultimately viruses are causing these tumors to form and are further manipulating the immune system to allow tumors to keep growing," Kuss-Duerkop says. "But these same mechanisms may be key in combating tumors with immune-based therapies or in keeping cancer from developing in the first place."

http://bit.ly/2FddYIr

The 5 'New' Types of Diabetes, Explained

Researchers propose classifying diabetes as five types of disease, rather than two types

By Rachael Rettner, Senior Writer | March 2, 2018 06:19pm ET

Diabetes just got a little more complicated, or clearer, depending on your perspective. Researchers in Scandinavia have proposed classifying diabetes as five types of disease, rather than two types, according to a new study. But what are these different types, and why did the researchers make this decision?

Having diabetes means that a person's blood sugar (glucose) levels are too high. It's an increasingly common disease; about 30 million people in the U.S. have diabetes, according to the Centers for Disease Control and Prevention.

In people with type 1 diabetes, which most often appears in childhood, the body cannot make insulin — a hormone that helps glucose get into cells. This condition occurs because the body's immune system attacks the cells in the pancreas that make insulin.

In type 2 diabetes, the body does not make or use insulin well. Often, this condition begins with insulin resistance, which means cells aren't responding to insulin, even though the body is still making the hormone. The condition often occurs in middle-age or older adults and is thought to be related to lifestyle factors and obesity.

But in the new study, which was published yesterday (March 1) in the journal The Lancet Diabetes & Endocrinology, researchers found that diabetes patients in Sweden and Finland fell into five clusters. One of the clusters was similar to type 1 diabetes, while the other four clusters were "subtypes" of type 2. Three of the clusters were considered severe forms of the disease, while two clusters were considered mild forms.

Dr. Kathleen Wyne, an endocrinologist at The Ohio State University Wexner Medical Center, who was not involved with the study, said that the new classification could be very useful, but stressed that the researchers aren't suggesting getting rid of type 1 and type 2 diagnoses. Rather, they are suggesting that there are subtypes.

"This is not changing the diagnosis or the terminology for the diagnosis," Wyne said. "It's just providing a way to classify within the diagnosis" of type 1 and type 2, she said.

The clusters were:

Cluster 1: Called "severe autoimmune diabetes," this form is similar to type 1 diabetes. People in this cluster were relatively young when they were diagnosed, and they were not overweight. They had an immune system (autoimmune) disease that prevented them from producing inulin.

Cluster 2: Called "severe insulin-deficient diabetes," this form was similar to cluster 1 — people were relatively young at diagnosis and were not overweight. They were also not producing much insulin. But, crucially, their immune system was not the cause of their disease. People in this cluster "looked for all the world like [they had] type 1" diabetes, but they didn't have "autoantibodies" that indicate type 1, Wyne said. Researchers aren't sure why this happens, but people in this group may have a deficiency in the cells that produce insulin.

Cluster 3: Called "severe insulin-resistant diabetes," this form occurred in people who were overweight and had high insulin resistance, meaning their bodies were making insulin, but their cells were not responding to it.

Cluster 4: Called "mild obesity-related diabetes," this form occurred in people who had a milder form of the disease, without as many metabolic problems as those in cluster 3, and they tended to be obese.

Cluster 5: Called "mild age-related diabetes," this form was similar to cluster 4, but the people were older at their age of diagnosis. This was the most common form of diabetes, affecting about 40 percent of people in the study.

People in cluster 3 had the highest risk of kidney disease, a complication of diabetes, while people in cluster 2 had the highest risk of retinopathy, another complication of diabetes that can cause vision loss.

Clusters 2 and 3 are both severe forms of diabetes that were "masked within type 2 diabetes," the researchers said. People in these clusters may benefit from aggressive treatment to prevent diabetes complications, the authors said.

Improving diagnoses

Recognizing subtypes of diabetes, as the new paper suggests, might change the way doctors prescribe medications for diabetes, Wyne told Live Science.

"Right now, the algorithm for treating type 2 diabetes [is] pretty much a one-size-fits-all algorithm," Wyne said. Patients are often started on a drug called metformin, and other drugs are added if it doesn't work, she said. But recognizing subtypes might help doctors more specifically choose a first, second or third medication for their patients, she said.

The researchers noted that their study cannot confirm whether all five clusters of diabetes have different causes or whether people's classification might change over time, so future studies should look at these questions. Future research could also look at whether the clusters could be refined further by using other measures, such as genetic markers or blood pressure measurements, the researchers said.

http://bit.ly/2H2gpxW

Eating nuts may help colon cancer patients

Regularly eating tree nuts such as almonds and walnuts has been shown to be particularly beneficial for people with bowel cancer.

Sarah Wiedersehn, Australian Associated Press

A Yale Cancer Center study, published in the Journal of Clinical Oncology, found the regular consumption of all nuts significantly lowered the risk of disease recurrence and even death in patients with stage III colon cancer. Researchers followed 826 participants in a clinical trial for a median of six-and-a-half years after they were treated with surgery and chemotherapy.

The study found those who regularly consumed at least two, 28 gram servings of nuts each week demonstrated a 42 per cent improvement in disease-free survival and a 57 per cent improvement in overall survival.

"Further analysis of this cohort revealed that disease-free survival increased by 46 per cent among the subgroup of nut consumers who ate tree nuts rather than peanuts," said senior author Dr Charles Fuchs, director of Yale Cancer Center.

Tree nuts include almonds, walnuts, hazelnuts, cashews, and pecans, among others. Peanuts belong in the legume family of foods.

Lead researcher Temidayo Fadelu says the results highlight the importance of dietary and life-style factors in boosting survival.

"These findings are in keeping with several other observational studies that indicate that a slew of healthy behaviours, including increased physical activity, keeping a healthy weight, and lower intake of sugar and sweetened beverages, improve colon cancer outcomes," he said.

http://bit.ly/2CXDVJK

Deeper look at biopsy exposes mutation ready to ambush drug combination

Discovery of pre-existing, rare variation points to new approach to treatment, biopsies

HOUSTON - A powerful resistance mutation that appeared to emerge in melanoma after a patient received a targeted therapy combination, instead was lurking in the tumor all along, primed to thwart treatment before it began, researchers at The University of Texas MD Anderson Cancer Center report online at Cancer Discovery.

Researchers analyzed a series of biopsies taken before and during treatment to ferret out the pre-existing mutation and then developed a potential way to target its troublesome abilities.

The team, led by Lawrence Kwong, Ph.D., assistant professor of Translational Molecular Pathology, set out to find resistance mechanisms that arise against a combination of MEK and CDK4 inhibitors to treat melanoma that has a mutation in the NRAS gene.

The mutation, to a gene called PIK3CA, appeared initially to be an acquired resistance variation that arose after treatment. By re-analyzing the pretreatment biopsy, Kwong and colleagues were able to establish that it was rare but present from the start, hiding on one side of the tumor.

PIK3CA variant started rare, expanded rapidly

"Our study is the first to measure multiple regions in pre-treatment tumor biopsies at high resolution and then track the resistant mutation over years of treatment through six biopsies," Kwong said. "We are able to say that this mutation started out rare and then rapidly expanded as the MEK/CDK4 inhibitors killed off a large number of non-resistant cells."

This finding helps establish that such pre-existing mutations can lurk in a patient's tumor at 10 times the rarity than previously appreciated and still cause rapid drug resistance, raising the possibility that even more rare mutations exist in other patients, below the detection rate of current technology.

"Right now, when we detect a resistance mutation after treatment, we often don't know whether it came out of nowhere as a new mutation or was pre-existing but undetected in the original tumor," Kwong said.

Understanding the difference could guide treatment to make it more effective, earlier, Kwong notes, and identifying rare mutations that are geographically isolated on a tumor will require improving our approach

to analyzing biopsies. NRAS mutations occur in 15-20 percent of melanomas, and the MEK/CDK4 combination is often effective initially against these tumors, but resistance arises.

Initial response, then swift progression

A 59-year-old woman with stage III malignant melanoma was found to have an NRAS mutation in her tumor. She was enrolled in a clinical trial combining a MEK and a CDK4 inhibitor. After an initial partial response of a 39 percent reduction in tumor burden, resistance to the treatment arose swiftly and the disease progressed and spread.

Whole exome sequencing of the resistant tumor after treatment revealed a mutation to PIK3CA known to promote tumor growth. Since the mutation was detected only 16 days after treatment began, Kwong and colleagues decided to re-examine the pretreatment biopsy, which sampled a single region of the tumor and had not found a PI3KCA mutation.

By examining seven regions of the biopsy sample using an amplification method developed by co-author David Zhang, Ph.D., assistant professor of Bioengineering at Rice University, the team found PIK3CA mutations in three regions. The pre-existing mutation was both rare and geographically dispersed in the tumor, making it hard to detect by sampling a single region.

Their findings suggest multi-region sampling would expose pre-existing resistant cells, an approach that would not be cost-effective at present, Kwong said, but is likely to become more practical as technology develops.

The PIK3CA mutation could also be detected by isolating circulating cell-free DNA in the blood after resistance developed, making it a potential target for liquid biopsies that are under development.

S6 provides a common target

Simply adding a PIK3CA inhibitor to the MEK/CDK4 combination would likely be too toxic, so the team analyzed 300 proteins to find targets that might be present in more than one of the three pathways. They found a protein called S6 to be the only spot where all three of these cancer-promoting pathways meet. Treating mice with an S6 inhibitor re-sensitized them to treatment with the MEK/CDK4 combination, restoring the drugs' ability to shrink the PIK3CA mutation-bearing melanomas.

Kwong said an optimized human version of the S6 inhibitor in mice has not yet been developed, but their findings point to a possible target for human drug development.

"One of the main questions in cancer drug resistance is how often it comes from a pre-existing or a completely new mutation" said Gabriele Romano, Ph.D., a postdoctoral fellow in Translational Molecular Pathology and the study's first author. "Our study helps define some of the parameters and tools that will be needed to answer this tricky question."

Co-authors with Romano, Kwong and Zhang are Roger Liang, Mingguang Liu, M.D., Dzifa Duose, Ph.D., Fernando Carapeto, Ph.D., and Alexander Lazar, M.D., Ph.D., of Translational Molecular Pathology; Pei-Ling Chen, M.D., Ph.D., Whijae Roh, Ph.D., Jun Li, Ph.D., Jianhua Zhang, Ph.D., Andrew Futreal, Ph.D., and Jennifer Wargo, M.D., of Genomic Medicine; Jennifer McQuade, M.D., Michael Davies, M.D., Ph.D., and Rodabe Amaria, M.D., of Melanoma Medical Oncology; Merry Chen, M.D., of Neuro-Oncology: Ping Song, Ph.D., of Bioengineering at Rice University; and Jessica Teh, Ph.D., and Andrew Aplin, Ph.D., of Thomas Jefferson University, Philadelphia.

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http://bbc.in/2FRo7eS

Prostate test 'breakthrough' in NHS trial

The NHS plans to cut prostate cancer diagnosis times from six weeks to a matter of days, NHS England has said.

Currently a test for men with prostate cancer requires an MRI scan and a biopsy where a dozen samples are taken, requiring multiple hospital visits.

But a new "one-stop" service will be trialled in three west London hospitals which hopes to complete all the necessary tests in one day.

NHS England CEO Simon Stevens said the programme was "world-leading".

A new MRI scan, known as an mpMRI, provides higher quality imagery and provides up to 40% of patients with a a same day diagnosis.

For people who need a biopsy, ultrasound images with 3D MRI scans are used to target areas for taking tissue samples.

The NHS claims the technique virtually eliminates the threat of sepsis.

'Encouraging breakthrough'

The new technique is being trialled at Charing Cross Hospital, Epsom Hospital and Queen Mary's Hospital in Roehampton, where about 5,000 men will be tested over the next two years.

Imperial College London chairman of urology Professor Hashim Ahmed said: "Fast access to high-quality prostate MRI allows many men to avoid invasive biopsies as well as allowing precision biopsy in those men requiring it to find high risk tumours much earlier."

"What we are hoping to do is show the NHS that this can be done, that it can be done cost-effectively and that we can improve the outcomes for men in a much better way than we were doing."

Mr Stevens said: "This is an encouraging breakthrough in prostate cancer diagnosis that is genuinely world-leading.

"While still early days, the potential benefit to men with suspected cancer is significant."

However consultant radiologist Dr Anthony Chambers says there is nothing new about these tests.

He told the BBC: "The only new aspect is that they are rushing men through the process far too quickly."

"This leads to over investigation of men who have a common infection called prostatitis and has no compensating advantages to patients who do have cancer. It also diverts resources from more urgent conditions."

http://bit.ly/2FaxvsY

AI is helping seismologists detect earthquakes they'd otherwise miss

Using the same tools we use for voice detection, scientists are uncovering tiny earthquakes hidden in the data

By James Vincent@jjvincent Feb 14, 2018, 2:00pm EST

Oklahoma never used to be known for its earthquakes. Before 2009, the state had roughly two quakes of magnitude three and above each year. (Magnitude three is when things shake on the shelf, but before houses start getting damaged.) In 2015, this tally rocketed to more than 900, though it's calmed since, falling to 304 last year.

This sudden increase is thought to be caused by the disposal of wastewater by the state's booming fracking industry, and it's caught seismologists off-guard. As a historically quake-free area, Oklahoma doesn't have enough equipment to detect and locate all of these quakes, making it hard to investigate their root cause. "There are no major faults in Oklahoma so it's just not something we would expect," Thibaut Perol, a deep learning researcher who's worked on this problem, tells *The Verge*. "And to understand what's happening, we need a big, big catalogue of earthquakes."

The solution proposed by Perol and his colleagues from Harvard University's engineering and earth sciences departments is to use artificial intelligence to amplify the sensitivity of the state's earthquake detectors, otherwise known as seismographs. In a paper published today in the journal *Science Advances*, they show how effective this technique is — capable of detecting 17 times more earthquakes than older methods in a fraction of the time.

The method is similar to the voice detection software used by digital assistants like Alexa and Siri, explains Perol. It's all about uncovering the signal hidden in the noise. With Alexa, that means listening out for your voice commands while ignoring the background sound of your home. And for seismographs, it means cancelling out the normal geological rumblings of the Earth (what's known as "ambient seismic

noise") to spot the earthquakes that might be very small or far away. This way, scientists in Oklahoma can get more out of the data they already have.

To make this happen, Perol and his colleagues trained a convolutional neural network to recognize background noise, feeding it data from seismically quiet areas, like pre-fracking era Oklahoma and the geological dead-zone of Wisconsin. (The state has only really had one significant earthquake, and that was in 1947.) As with all neural networks, the software examines this input and learns to pick out common patterns. Once it knows what ambient rumblings sound like, it can remove these from the data, leaving behind the tiny earthquakes that had previously been hidden — like sea shells revealed by a retreating tide. As a bonus, the neural network is even able to identify the rough whereabouts of individual quakes by matching the patterns they created with historical data where a tremor's location was known.

"With this method we are able to detect earthquakes of magnitude zero or minus one, and these are signals you wouldn't be able to see with a human eye," says Perol.

William Yeck, a seismologist at the United States Geological Survey (USGS), praised the work as "compelling and novel." Speaking to *The Verge* by email, he noted that the neural network would best apply to "local earthquake monitoring efforts" — as in Oklahoma — "where there are high-seismicity rates." Yeck cautions, though, that earthquake detection is only ever going to be a part of the puzzle. "Estimations of earthquake sizes and accurate event locations are also necessary," says Yeck. "For the very small events that this technique detects, this will be challenging."

If this neural network can be used more widely in Oklahoma applied, says Perol, it'll help seismologists investigate the exact cause of the state's earthquakes. There's even some hope that it could *predict* earthquakes before they occur. This could be done by looking for patterns in the data; for example, finding times when a number of small earthquakes have happened in quick succession, triggering a bigger, potentially damaging quake.

The idea of using AI to predict — not just detect — earthquakes is an exciting one, but it's not something that the whole seismologist community is confident about. (You can watch the video below for more info.) In Oklahoma at least, prediction isn't as pressing as detection. But with the help of Perol and his colleagues' neural network, this important work could get a boost.

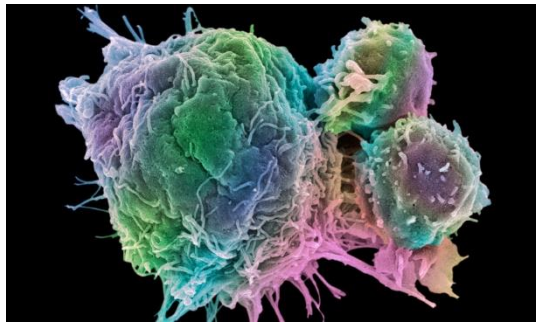
http://bit.ly/2F7AFl4

Cancer drugs shed light on rheumatism

Side-effects in immunotherapy for cancer patients have given scientists an ally in the battle against rheumatoid arthritis

Robin McKie

The human immune system is one of the most effective defence mechanisms known to nature. It can ward off myriad microbial invaders: bacteria, viruses and parasites. It is sometimes overwhelmed by disease, of course, but the billions of men and women who now live on Earth are a testament – at least in part – to the effectiveness of their immune defences.



Lymphocytes and a cancer cell. **Alamy Stock Photo**

However, on occasions they go too far. Instead of killing off invading organisms, our immune systems turn on our own tissue and attack it. Conditions such as type 1 diabetes, rheumatoid arthritis, and lupus are all triggered in this way, very often with deeply unpleasant consequences.

In the case of rheumatoid arthritis, immune cells – mainly lymphocytes and macrophages – start to attack the tissue that makes up joints, and these become painful, stiff and swollen. Around one-third of those who develop rheumatoid arthritis will have stopped working within two

years of its onset, so painful are its effects. And given that the disease affects more than 400,000 people in the UK, its financial impact is also high: estimates suggest it costs the economy between £3.8bn and £4.8bn a year.

Similar conditions include ankylosing spondylitis, which affects the joints in the spine, again causing pain, stiffness and restricted movement. Around 200,000 people in the UK are affected, at an estimated annual cost of up to £3.8bn to the economy. Meanwhile, juvenile idiopathic arthritis affects 12,000 children under 16, many of whom will suffer severe limitations in movement in their adult life.

Trying to understand exactly why a person's immune system turns on the body has proved to be tricky, a hindrance to developing cures. "In most cases of rheumatoid arthritis, for example, we can provide treatments that alleviate the worst symptoms, but patients will have to take these drugs for the rest of their lives," says immunologist Prof Adrian Hayday, of the Francis Crick Institute in London.

Recently, however, researchers, including Hayday, have found an unexpected ally in their battle against autoimmune disease: cancer. It is an unexpected link, but a promising one, as Hayday explains. "In the past five years, there has been a revolution in the way we treat some cancers – by using immunological techniques," he told the *Observer*. "These have had unprecedented positive results against metastatic melanomas and non-small-cell lung carcinoma. By giving patients drugs, we have been able to turn up their immune systems so they successfully mount attacks against these cancers. We have armed their immune systems and made them active."

It is one of the most important developments in the battle against cancer this century. But side-effects have recently emerged. "There are around 140 patients undergoing immunotherapy for their cancer at Guy's hospital in London, where I do my clinical research," says Hayday. "Our cancer drugs boost our patients' immune systems to help them kill off their tumours. But of course, that is the same sort of thing that happens in people with rheumatoid arthritis and diabetes: something triggers their immune systems so that they become overactive and souped-up.

"As a result, some of the cancer patients – happily, not too many – who are being treated with immunotherapies are beginning to develop rheumatoid arthritis and type I diabetes. By boosting their immune systems," Hayday said, "we have exacerbated any tendency for these people to have had these conditions and we are beginning to see the occasional case arising among our cancer patients."

The appearance of these conditions raises important issues for cancer patients. "We have to be very careful about ensuring quality of life for people once they have undergone cancer treatments, so obviously this is a concern," Hayday says.

However, there is also a more positive consequence of the discovery that cancer immunotherapies have the effect of triggering autoimmune diseases in some cases: "For the first time, we now have a chance to study rheumatoid arthritis at its earliest stages, and that is tremendously important."

At present, people are not diagnosed with the condition until symptoms have already made their lives so unpleasant they have gone to see their doctors. "By then the condition is well established, and that makes treating it difficult," said Hayday. "But if we have people in the ward who never had the disease but who, after we have given them drugs for their cancer, begin to develop rheumatoid arthritis or type 1 diabetes, then we can study and understand autoimmune diseases like these for the very first time."

As a result, research – backed by Cancer Research UK and Arthritis Research UK – has been launched with the aim of uncovering the roots of autoimmune disease from research on cancer patients. "You know that when you give a patient an immunotherapy drug for their cancer, if they are going to get an autoimmune disease, they are probably going to get it over the next few months," says Prof John Isaacs, of the Institute of Cellular Medicine, Newcastle. "So, we can monitor them – take regular blood samples and follow these patients very carefully – if

they are happy for that to happen. In this way, we can get a handle on the very first events that lead to them getting autoimmune cells. Can we see if something is happening to their B-cells or their T-cells that later leads them to get rheumatoid arthritis or another autoimmune condition, for example?"

The scientists involved stress that their work is only now beginning and warn that it will still take several years' research. Nevertheless, uncovering the first stages of an autoimmune disease emerging in a person's body should give researchers a crucial lead in ultimately developing treatments that will prevent or halt a range of conditions that currently cause a great deal of misery and require constant medication. "Autoimmune diseases are horrible afflictions," adds Isaacs. "Now, for the first time, we can think seriously of halting them in their tracks one day."

Our immune defences consist of a range of cells and proteins that detect invading micro-organisms and attack them. The first line of defence, however, consists of simple physical barriers like skin, which blocks invaders from entering your body. Once this defence is breached, they are attacked by a number of agents.

The key cells involved here are white blood cells (leukocytes), which seek out and destroy disease-causing organisms. There are many types. Neutrophils rush to the site of an infection and attack invading bacteria. Helper T-cells give instructions to other cells while killer T-cells punch holes in infected cells so that their contents ooze out. After this macrophages clean up the mess left behind.

Another important agent is the B-cell, which produces antibodies that lock on to sites on the surface of bacteria or viruses and immobilise them until macrophages consume them. These cells can live a long time and can respond quickly following a second exposure to the same infections.

Finally, suppressor T-cells act when an infection has been dealt with and the immune system needs to be calmed down – otherwise the killer cells may keep on attacking, as they do in autoimmune diseases. By slowing down the immune system, regulatory T-cells prevent damage to "good" cells.

http://bit.ly/2oQgBZB

New Plan Increases Cardiac Arrest Survival Rate

Development of a new plan of action called an ECPR alert

Carol Pearson

Mark Bradford walks through the park by his home every day, but one morning his heart stopped beating and he collapsed in sudden cardiac arrest. The next thing he remembered was waking up in the heart unit at the Ohio State University Wexner Medical Center.

With cardiac arrest, every second counts. The American Red Cross reports that more than 1,600 people suffer a cardiac arrest each day in the U.S.

Survival depends on many factors — how fast a person gets help and what caused the heart to stop.

Studies show that if a bystander starts cardio pulmonary resuscitation, or CPR, which is essentially pumping the chest rhythmically to get the heart started again, or if someone uses a defibrillator within a minute or two after a person's heart stops, the odds of surviving can be as high as 70 percent.

But if the heart quivers uncontrollably and can't pump blood, something called ventricular fibrillation, or if it goes wildly out of rhythm, it will stop beating and chances of survival are slim to none. In these situations, a patient's heart resists being shocked back to normal, and if it does begin beating again, chances are the patient will have permanent disabilities.

"Typically, if they [the patients] don't respond to getting shocked, these patients would die in the field because we didn't have any options to save them. Now, in certain situations, we have had patients survive and walk out of the hospital," Dr. Ernest Mazzaferri Jr. said. Mazzaferri is the medical director of The Ohio State University Richard M. Ross Heart Hospital, which is part of the Wexner Medical Center.

In the U.S., fire departments frequently are called upon to respond to emergencies. When the Columbus, Ohio Fire Department received a new device for CPR, fire fighters contacted the medical center, and the doctors and the fire fighters developed a new plan of action called an ECPR alert.

If a patient's heart resists being shocked back to normal, medics alert the hospital and put a mechanical CPR device on the patient in the ambulance. Meanwhile, a team at the hospital prepares the catheterization laboratory, or cath lab. The lab has diagnostic imaging equipment so doctors can see the heart's arteries and chambers.

Most patients who arrive at a hospital by ambulance go immediately to the emergency room. At Ohio State, patients who have suffered cardiac arrest go immediately to the cath lab. Dr. Ernest Mazzaferri said this protocol iscritically important "because the more time we wait, the more damage is done to the heart and the more damage is done to all of your organs including your brain."

At the cath lab, the patient is connected to an echmo machine that does the job of the heart and lungs. Dr. Bryan Whitson said this allows the heart and the lungs to rest while doctors work on the heart to try to get it restarted and beating well.

The doctors also try to fix what caused the heart to stop beating. Dr. K. Dean Boudoulas said the new protocol has increased survival rates from the deadliest types of cardiac arrest from zero to 40 percent.

"Patients have a chance to walk out of a hospital with neurological recovery, have a meaningful life, when essentially they would have been pronounced dead in the field."

Bradford was the first patient in Columbus, Ohio, to benefit from this procedure. "Without the protocol, I wouldn't be alive. I am very fortunate that they were trained in it, that they used it, that I was out in the park rather than in the house by myself."

The ECPR protocol has been tested only in a few small studies, and so far the limited data shows an increase to about a 40 percent chance of survival.

Mazzaferri said the doctors are hopeful the protocol will prove so successful that "perhaps some years from now, ECPR will be more routine and saving more lives across the U.S."

http://nyti.ms/2FfnOcu

A Painful Bruise Wouldn't Heal. It Took Several Hospital Visits to Discover Why.

Diagnosis

By LISA SANDERS, M.D. FEB. 28, 2018

The woman lay on the floor, too weak even to lift the phone to her ear. She could hear her sister calling her name through the phone's tinny speaker, but she couldn't reply. A rush of relief flooded over her when she heard her sister say to someone, "Call 911." And then there was darkness.

She had been sick for months at that point. She had seen many doctors. She had been given a variety of diagnoses, but no one could tell her — a usually vigorous woman of 39 — exactly what was wrong.

A Bruise That Won't Heal

It all seemed to start the previous autumn, when she dropped a can of paint on her foot. It gave her a big bruise. No surprise, but strangely, the bruise never went away. Instead, over the next several weeks, the purple discoloration and swelling snaked up her calf into her thigh and then over to her other leg. Now both limbs were painful and splashed with dark bruises.

Dr. Vivek Naranbhai, a doctor in his first year of training at Massachusetts General Hospital, was assigned to care for the patient once the ambulance brought her in. He opened her chart and saw that she'd been in the hospital twice recently. A couple of weeks before, she was in one closer to her home in the Boston suburbs. And just a few days earlier, she was seen at and discharged from this same hospital, Mass General. Each time, she had been worried about the huge bruises on her legs and the pain and numbness that traveled from foot to thigh when she walked.

During her visit to Mass General a few days earlier, doctors wanted her to see their physical therapists to help make walking easier until her bruising healed. But then something strange happened. As she waited in the E.R., her red-blood-cell count dropped, leaving her weak and pale; she was admitted for a transfusion and further evaluation. A CT scan of her swollen right leg revealed the reason for the drop: In her thigh, she now had a huge pool of blood that had leaked out of her vessels and into the muscle of her upper leg. She was bleeding internally. And no one knew why.

A Diagnostic Consensus

Like the patient herself, her doctors assumed all her symptoms were connected to the can she'd dropped on her foot. Why hadn't that injury healed? And why was the entire right leg — and some of the left — so painful? None of the tests conducted in her nearly two weeks in the hospital explained it. Eventually her first Mass General doctors concluded that she had an unusual disorder called complex regional pain syndrome (C.R.P.S.). This disorder, which usually affects a limb after some trauma, is thought to be caused by injury to the nervous system. That damage in turn causes pain, swelling and changes in skin color and temperature. No one knows why the body has this extreme overreaction. Treatment has to focus on reducing pain rather than on treating the disorder. Recovery takes months, even years. Having made this diagnosis, the doctors sent the patient home to follow up with specialists to treat the pain.

In the days after this second hospitalization, the patient worsened. She felt exhausted and cold all the time. One morning upon waking, she felt so weak and tired that she couldn't stand. She scooched herself along the floor toward the bathroom. Halfway there, she was so incapacitated that she lay down and called her sister. I think I'm dying, she told her. Her hand dropped weakly to the floor. Her sister asked for 911, and the E.M.T.s came and took her to the emergency room for the third time.

Loss of Blood

A blood test showed that she was bleeding internally again. She had less than half the blood she should have in her circulatory system. No wonder she was cold and tired and out of breath — these are classic signs of severe anemia. She was given more blood and then transported back again to Mass General.

As Naranbhai read through the records, he compiled a list of diseases that could bring this woman to the hospital three times over a month with severe pain and blood loss. It was a scary collection. At the top were cancers that could keep her from making blood. Next: diseases that interfered with her body's ability to form clots and stop bleeding. All were terrible possibilities.

Dr. Leigh Simmons, the internist supervising Naranbhai, usually waited to see patients until after the resident developed his own thoughts about the case. But it was late, and this patient sounded particularly sick, so Simmons and Naranbhai went to visit the patient together.

Seeing the Patient Anew

She was a small woman, quite thin and pale beneath a dark Mediterranean complexion. Her 15-year-old daughter stood holding her hand. Simmons introduced herself and then stepped back to let Naranbhai lead the investigation. Rather than focus his questions on her foot and leg, he cast a much wider net. Tell me everything that's going on, he asked. She'd had her period for nearly a month now, the woman said. That had never happened before. And, her daughter added, she had these weird dots on her legs. They just popped up a few weeks before. Naranbhai looked carefully at the mother's legs. They were covered with tiny freckle-size dots of blood trapped under the skin at the hair follicles.

Naranbhai looked at Dr. Simmons. Was she thinking what he was thinking? He looked back at the patient. Did her gums ever bleed when she brushed her teeth, he asked. All the time, she exclaimed.

Can I see? the young doctor asked. Her gums were swollen and beefy red. He felt as if they might start bleeding just by looking at them. He

looked up to Simmons, who smiled back encouragingly. He knew what she had. And so did Simmons.

Clues in the Diet

What kind of foods do you eat? he asked. Every morning she had two scrambled eggs. For lunch she had tuna on crackers. And for dinner she had more scrambled eggs and rice. Did she ever eat any fruits or vegetables — especially oranges or lemons? Never, she told him. They gave her wicked heartburn.

She had something known as gastroparesis, she explained. Her stomach and intestines didn't move food forward normally, and so food stayed in her stomach for hours. When food moves that slowly, you have to be careful that what you eat agrees with you.

No citrus for years. It was clear to Naranbhai that this modern woman had an ancient disease. She had scurvy — a disorder caused by a severe deficiency of vitamin C.

In the mid-18th century, a naval surgeon named James Lind proved that the juice of oranges and lemons would cure the bony aches, strange bleeding and sudden death of sailors afflicted with the illness, and the British Navy later mandated the use of lemon juice on all vessels. But it wasn't until the 20th century that researchers recognized that the cause of scurvy was the lack of a certain nutrient, which they named vitamin C. Without this organic chemical, new connective tissue, essential for the repair or replacement of damaged or dying cells, cannot be made, and that causes the bleeding, the bruising, the telltale little red dots and the terrible fatigue. Our bodies can't make vitamin C, and so we rely on the foods we eat to provide it. Avoiding these foods — as this woman did — can deplete the body's supply in just a few months.

The Miracle of Vitamin C

The doctors sent off a blood test to measure her vitamin C, and they started the woman on large doses of the required vitamin. The improvement was almost immediate: her gums stopped bleeding within days; her bruises started to turn yellow and fade. And she started to feel stronger and less fatigued.

That was two months ago. Now she feels great. She still can't eat oranges. But she takes her vitamin C tablets every single day.

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