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Arthritis on the rise

Study shows prevalence of painful disease has doubled since World War II, but also challenges the idea that arthritis is simply part of aging

The average American today is twice as likely to be diagnosed with knee osteoarthritis than in the years before World War II, Harvard scientists say, but that increase can't be blamed on the reasons most might think.

Based on the examination of more than 2,000 skeletons from cadaveric and archaeological collections across the U.S., the Harvard study is the first to definitively show that knee osteoarthritis prevalence has dramatically increased in recent decades. The research also upends the popular belief that knee osteoarthritis is a wear-and-tear disease that is widespread today simply because more people are living longer and are more commonly obese. The study is described in a paper published this week in the Proceedings of the National Academy of Sciences.

"Before this study, it was assumed without having been tested that the prevalence of knee osteoarthritis has changed over time," said Ian Wallace, the study's first author and a post-doctoral fellow in the lab of Daniel Lieberman, the Edwin M. Lerner II Professor of Biological Sciences and senior author of the study. "We were able to show, for the first time, that this pervasive cause of pain is actually twice as common today than even in the recent past. But the even bigger surprise is that it's not just because people are living longer or getting fatter, but for other reasons likely related to our modern environments."

Understanding the disease, Wallace and Lieberman said, is important not only because it is extremely prevalent today, affecting an estimated one-third of Americans over age 60, but also because it is responsible for more disability than almost any other musculoskeletal disorder.

"Understanding the origins of knee osteoarthritis is an urgent challenge because the disease is almost entirely untreatable apart from joint replacement, and once someone has knee osteoarthritis, it creates a vicious circle," Lieberman said. "People become less active, which can lead to a host of other problems, and their health ends up declining at a more rapid rate."

Wallace and Lieberman think that this study has the potential to shift the popular perception of knee osteoarthritis as an inevitable consequence of aging, and instead focus on efforts to prevent the disease - much like we now do with heart disease.

"There are a lot of well-understood risk factors for heart disease, so doctors can advise their patients to do certain things to decrease their chances of getting it," Lieberman said. "We think knee osteoarthritis belongs in the same category because it's evidently more preventable than commonly assumed. But to prevent the disease more work needs to be done to figure out its causes."

To do that, Wallace and Lieberman are currently addressing the question of the etiology of knee osteoarthritis from a variety of methodological approaches including studies of living human populations and animal models, but their first goal was to figure out how ancient the disease actually is, and whether it really is on the rise.

"There are famous examples in the fossil record of individuals, even Neanderthals, with osteoarthritis," Lieberman said. "But we thought, let's look at the data, because nobody had really done that in a comprehensive way before."

To find those data, Wallace undertook the daunting task of crisscrossing the country to examine thousands of skeletons spanning more than 6,000 years of human history to search for evidence of eburnation - a tell-tale sign of osteoarthritis.

"When your cartilage erodes away, and two bones that comprise a joint come into direct contact, they rub against each other causing a glass-like polish to develop," Wallace said. "That polish, called

eburnation, is so clear and obvious that we can use it to very accurately diagnose osteoarthritis in skeletal remains."

The data Wallace collected was combined with analyses from other contributors to the study, making this the largest sample ever studied of older-aged individuals from three broad time periods - prehistoric times, early industrial times (mainly the 1800s), and the modern post-industrial era.

"The most important comparison is between the early industrial and modern samples," Lieberman said. "Because we had data on each individual's age, sex, body weight, ethnicity, and in many cases, their occupation and cause of death, we were able to correct for a number of factors that we considered important covariates. So using careful statistical methods, we are able to say that if you were born after World War II you have approximately twice the likelihood of getting knee osteoarthritis at a given age or BMI than if you were born earlier."

Wallace and Lieberman are now working to identify what factors may be behind the increase, and said the evolutionary approach to the study is a critical part of that ongoing work.

"Epidemiology typically looks at large cohorts of individuals living today to search for associations between a disease and risk factors," Lieberman said. "That's a powerful and valuable method, but it has one critical imitation, which is that the world today is different in many ways from the world in the past, hiding important risk factors that are either no longer prevalent or have become ubiquitous. An evolutionary perspective opens new opportunities to test for associations we might not be able to study in populations like modern day America."

That perspective, Wallace and Lieberman said, allows researchers to zero in on specific things that changed pre- to post-World War II, and understand how they might contribute to the rise in knee osteoarthritis prevalence.

"This is an example of how evolutionary thinking can contribute to our understanding of what causes certain diseases," Wallace said. "We identified the post-war period as a critical time...and it's only with an evolutionary perspective that we gain that insight."

Ultimately, Wallace and Lieberman hope their study inspires new research to prevent knee osteoarthritis.

"Knee osteoarthritis is not a necessary consequence of old age. We should think of this as a partly preventable disease," Lieberman said. "Wouldn't it be great if people could live to be 60, 70 or 80 and never get knee osteoarthritis in the first place? Right now, our society is barely focusing on prevention in any way, shape or form, so we need to redirect more interest toward preventing this and other so-called diseases of aging."

This research was supported with funding from the Hintze Family Charitable Foundation and the American School of Prehistoric Research (Harvard University).

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Bacteria can feel their surroundings

Individual bacteria, too, can feel their external environment

For humans, our sense of touch is relayed to the brain via small electrical pulses. Now, University of Colorado Boulder scientists have found that individual bacteria, too, can feel their external environment in a similar way.

In a new study, CU Boulder researchers have demonstrated that E. coli bacteria cells get excited when poked, sending out voltage induced calcium ion signals -- the same way a vertebrate's sensory nervous system works. The results are believed to be the first documented observation of electrical excitability in individual bacteria cells.

The findings, which could advance fundamental bacteria research and may eventually aid drug development for infectious diseases, was published today in the journal Proceedings of the National Academy of Sciences.

"People typically think that [bacteria] are these little things, that all they are doing is trying to divide and create more energy," said Giancarlo Bruni, a doctoral candidate in CU Boulder's Department of Molecular, Cellular, and Developmental Biology and the lead author of the new research. "[But] we're not all that different."

Scientists have long known that bacteria respond to certain chemical cues. Feed them sugar, and their populations explode. Douse them in antibiotics and their cell walls rip apart. More recently, though, scientists have noticed that physical signals, too, seem to activate these microbes. For example, Salmonella become more efficient at infecting human cells when placed on a stiff surface as opposed to a soft one.

"What we think could be happening is that they're using these electrical signals to modify their lifestyle," said Joel Kralj, the senior author of the study and an assistant professor in MCDB and the BioFrontiers Institute.

To study how bacteria feel their surroundings, the team inserted special genes into E. coli bacteria that glow when calcium ions or electricity pulse through them. The cells were placed in a sticky substrate under a microscope. Left alone, the cells remained dim. But when the scientists pushed a pad against them, the bacteria lit up. The sparks of light indicated that proteins, ions and electricity were moving around in the bacteria.

The results indicate that bacteria and other creatures share a common tool for sensing their environment -- an electrical pathway with the same functionality as human sensory neurons. From an evolutionary perspective, this signaling trait could be billions of years old and used by some of the oldest organisms on Earth.

The study also sheds new light on bacterial activity with regard to infection. For example, when exposed to antibiotics, a few bacteria cells with unique electric signals usually survive. These survivors then go on to reproduce and share their drug-resistant capabilities with other bacteria, eventually rendering the antibiotic useless.

The CU Boulder researchers now plan to study how bacteria's electric pulses are used to sense when to infect human cells. In the future, they hope to test for small, masking molecules that can dull these signals when introduced. Such molecules could eventually translate into drugs that help treat bacterial infections and overcome antibiotic resistance.

"If we can block bacterial electrical activity, they may be less likely to infect, because now they don't know that they have landed on your soft delicious gut cell," said Kralj. "We could cut their hands off so they can no longer feel."

Additional co-authors of the new study include Andrew Weekley and Benjamin Dodd of MCDB and BioFrontiers. The National Institutes of Health and the Searle Scholars Program provided funding for the research.

http://bit.ly/2v6otra

Nearly 100 Hidden Volcanoes Detected Beneath Antarctic Ice

Scientists still don't know how many of these volcanoes are active

By Tia Ghose, Senior Writer | August 15, 2017 07:01am ET

Nearly 100 previously unknown volcanoes lurk beneath Antarctica, and scientists still don't know how many of these volcanoes are active.

A new remote survey has revealed 138 volcanoes on a portion of the continent known as the West Antarctic Rift System, a huge region that stretches 2,175 miles (3,500 kilometers) from the Ross Sea in the south to the Antarctic Peninsula in the northwest. Of these newfound structures, scientists had never heard of 91 of them before.

The volcanoes range from a modest 330 feet (100 meters) in height to an imposing 12,630 feet (3,850 m) tall. The findings were published earlier this month in the journal Geological Society Special Publications.

"Antarctica remains among the least studied areas of the globe, and as a young scientist, I was excited to learn about something new and not well-understood. After examining existing data on West Antarctica, I began discovering traces of volcanism. Naturally, I looked into it further, which led to this discovery of almost 100 volcanoes under the

ice sheet," said study co-author Max Van Wyk de Vries a geosciences student at the University of Edinburgh in Scotland.

Land of fire and ice

De Vries, who is currently an undergraduate student, was studying Antarctica when he learned from other sources that the coldest continent had a volcanic history. By using a combination of satellite data, ice-penetrating radar data and aerial surveys, de Vries was able to identify 91 spots where basaltic, or volcanic, rock was lurking beneath the ice. Known volcanoes in the same region carry this distinctive signature of volcanic activity, according to a statement.

The number of volcanoes in the region rivals that of the East African Rift Valley, one of the most volcanically dense regions of the world.

The scientists still don't know how many of these volcanoes are active, but active magmatism has roiled the continent in the past. However, as climate change warms the continent, thinning the ice, some of the now-dormant volcanoes could roar back to life, the scientists said in a statement. Past work has shown that Antarctica was more volcanically active during warmer periods of geologic history, according to the statement.

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Research review recommends eliminating widely ordered blood test for diagnosing heart attacks

Review is first publication from national consortium of academic medical centers working to eliminate unnecessary medical tests, treatments and procedures

Researchers at the Johns Hopkins University School of Medicine and the Mayo Clinic have compiled peer-reviewed evidence and crafted a guideline designed to help physicians and medical centers stop the use of a widely ordered blood test that adds no value in evaluating patients with suspected heart attack.

The investigators' report on the test, published Aug. 14 in JAMA Internal Medicine, points to a previous statement from the American College of Cardiology and five peer-reviewed studies concluding that creatine kinase-myocardial band (CK-MB) testing can no longer be considered an effective biomarker for detecting damaged heart muscle and can be safely eliminated from practice in this clinical setting.

The new report is the first in a series of peer-reviewed implementation guides co-authored by faculty from the High Value Practice Academic Alliance (HVPAA), a national coalition created by The Johns Hopkins University School of Medicine.

Faculty from more than 80 academic institutions, representing 15 medical specialties and subspecialties, have joined HVPAA and are working together to advance quality-driven value improvement.

"This article is the first in a series of collaborative multi-institutional publications designed to bridge knowledge to high value practice. We present multiple quality improvement initiatives that safely eliminated CK-MB to give providers reassurance about trusting troponin levels when managing patients with suspected acute coronary syndrome," says Jeffrey Trost, M.D., assistant professor of medicine at the Johns Hopkins University School of Medicine and the paper's corresponding author.

Heart disease remains the leading cause of death in men and women in the United States, and each year 735,000 Americans have heart attacks that damage the heart muscle, according to the U.S. Centers for Disease Control and Prevention. Of those, an estimated 120,000 die. About one in five heart attacks are "silent," yielding no symptoms, but symptoms such as chest tightness or pain, dizziness, nausea and fatigue are good reasons to seek immediate evaluation, according to the American Heart Association.

Among the diagnostic tools to detect heart attacks are blood tests that measure levels of various proteins released into the bloodstream when heart cells are injured. Two of these are cardiac troponin and CK-MB.

In 2000 the American College of Cardiology and the European Society of Cardiology identified cardiac troponin as the ideal biomarker due to its high sensitivity for detecting injury to the heart, and the 2014 American Heart Association/American College of

Cardiology guidelines concluded that CK-MB provides no additional diagnostic value for diagnosing heart attacks.

Despite these recommendations, Trost says, a 2013 survey conducted by the College of American Pathologists found that 77 percent of nearly 2,000 labs in the U.S. still use CK-MB as a cardiac damage biomarker.

The clinical and financial implications of institutions continuing CK-MB testing are significant, say the researchers, who estimate that all blood tests for diagnosing heart attacks add $416 million each year to the cost of care.

The research team also cites studies showing that in addition to its diagnostic value, troponin testing is a more definitive predictor of in-hospital mortality and severity of disease.

The new report, Trost says, is intended to highlight the need to phase out CK-MB and provide a blueprint for doing so based on the U.S. Health Resources & Services Administration's strategies for implementing any quality improvement initiative.

The four steps listed include:

1. Design and implement a hospitalwide education campaign.

2. Partner with clinical stakeholders (in cardiology, emergency medicine, internal medicine, laboratory/pathology) to remove CK-MB from standardized heart disease routine order sets.

3. Enlist information technology/laboratory medicine staff to create and integrate a best practice "alert" that appears on any computerized provider order entry system when clinicians order CK-MB.

4. Measure use of the test and patient care quality and safety outcomes before and after the intervention.

Additional guides being co-authored by HVPAA faculty from multiple institutions aim to reduce unnecessary transfusions, routine daily lab tests, antibiotics for asymptomatic bacteriuria, inappropriate Clostridium difficile testing and cardiac telemetry.

Visit the HVPAA website for more information or to register for the HVPAA inaugural national research and education symposium Oct. 8-9 in Baltimore.

http://bit.ly/2fQIEHl

Activated charcoal drug can protect microbiome from antibiotics

False-colour x-ray of the abdomen showing the large intestine (colon)

By Jessica Hamzelou

Antibiotics can save your life, but they can also mess up your microbiome. A special formulation of activated charcoal could help, protecting your body from the side effects of antibiotics, and perhaps even aiding the fight against antibiotic resistance.

The side effects of a course of antibiotics – such as stomach pains and diarrhoea – are familiar to many.

But by messing with the balance of microorganisms in a person's body, they may also cause longer term changes, potentially leading to obesity, allergies and eczema. And by killing too many of the good bacteria in your gut, they can make way for harmful and even drug-resistant bacteria, such as C. difficile, which is responsible for around 30,000 deaths a year in the US.

Jean de Gunzberg and his colleagues at Da Volterra, a biotech company based in Paris, think they have found a solution. Activated charcoal – a super-absorbent material – is routinely used to soak up excess drugs in the guts of people who have overdosed, and they have evidence that a modified version could do this for antibiotics.

Protective effect

To stop charcoal from simply soaking up an entire dose of oral antibiotics, the team coated tiny pieces of activated charcoal with a special covering. This breaks down by the time the charcoal reaches the large intestine – which hosts a rich ecosystem of beneficial bacteria – allowing it to mop up any antibiotics that make it this far and protect the bacteria.

The team tested its slow-release activated charcoal, named DAV132, in a clinical trial of 44 healthy volunteers.

A five-day course of the common antibiotic moxifloxacin was given to 28 people, half of whom also took DAV132 twice a day throughout the treatment, and for two extra days at the end. A further eight volunteers took DAV132 on its own, while eight people took nothing at all.

De Gunzberg's team found that DAV132 didn't affect how much of the antibiotic made it into a person's bloodstream, suggesting that it wouldn't stop the drug from killing off a bad infection.

However, the faeces of the people who took DAV132 with the antibiotic had only around 1 per cent of the level found in the faeces of those who took the antibiotic on its own, suggesting the charcoal mopped up the antibiotic in the large intestine.

The drug also seemed to protect gut bacteria. Around 250 species of bacteria reduced in number in the guts of those who took antibiotics alone. "Close to 90 per cent of those species were protected by our product," says de Gunzberg.

The team didn't look at whether DAV132 reduced the incidence of side effects from taking antibiotics, such as diarrhoea.

No side effects

"The results are promising," says Willem van Schaik at the University of Birmingham. "It's a really exciting approach to protect the microbiome from antibiotics."

So far, the team have seen no bad side effects from taking the charcoal. "The faeces become dark, but that's the only consequence," says de Gunzberg. But before their product becomes more widely available, the team want to see if it can stop resistant bacteria from developing. It's also possible that the charcoal might soak up important other compounds in the gut.

De Gunzberg plans to start testing the charcoal in people taking antibiotics to treat infections next year. In the meantime, people shouldn't give themselves regular activated charcoal, as this could simply stop their antibiotics from working.

Journal reference: bioRxiv, DOI: 10.1101/169813

http://bit.ly/2vNprui

Study identifies dinosaur 'missing link'

Bizarre dinosaur may be the 'missing link' between plant-eating dinosaurs and theropods

A bizarre dinosaur which looked like a raptor but was in fact a vegetarian may be the 'missing link' between plant-eating dinosaurs and theropods, the group that includes carnivores such as Tyrannosaurus rex and Velociraptor.

Researchers from the University of Cambridge and the Natural History Museum used a comprehensive dataset to analyse more than 450 anatomical characteristics of early dinosaurs and correctly place the creature, known as Chilesaurus, in the dinosaur family tree.

A blunt, rounded skull and short, leaf-shaped teeth gave away Chilesaurus as a strict plant-eater. **Gabriel Lío**

Their results, reported in the journal Biology Letters, suggest that Chilesaurus effectively fills a large gap between two of the major dinosaur groups, and shows how the divide between them may have happened.

Chilesaurus, which was discovered in southern Chile, was first described in 2015. It lived during the Late Jurassic period, about 150 million years ago, and has an odd collection of physical characteristics, which made it difficult to classify. For example, its head resembles that of a carnivore, but it has flat teeth for grinding up plant matter.

"Chilesaurus almost looks like it was stitched together from different animals, which is why it baffled everybody," said Matthew Baron, a PhD student in Cambridge's Department of Earth Sciences and the paper's joint first author.

Earlier research suggested that this peculiar dinosaur belonging to the group Theropoda, the 'lizard-hipped' group of dinosaurs that includes Tyrannosaurus, but the new study suggests that it was probably a very early member of a completely different group, called Ornithischia. This shuffling of the dinosaur family tree has major implications for understanding the origins of Ornithischia, the 'bird-hipped' group of dinosaurs that includes Stegosaurus, Triceratops and Iguanodon.

The bird-hipped dinosaurs have several common physical traits: the two most notable of these are an inverted, bird-like hip structure and a beak-like structure for eating. The inverted hips allowed for bigger, more complex digestive systems, which in turn allowed larger plant-eaters to evolve.

While Chilesaurus has a bird-like hip structure, and has flat teeth for grinding up plants, it does not possess the distinctive 'beak' of many other bird-hipped dinosaurs, which is what makes it such an important find.

"Before this, there were no transitional specimens - we didn't know what order these characteristics evolved in," said Baron. "This shows that in bird-hipped dinosaurs, the gut evolved first, and the jaws evolved later - it fills the gap quite nicely."

"Chilesaurus is one of the most puzzling and intriguing dinosaurs ever discovered," said co-author Professor Paul Barrett of the Natural History Museum. "Its weird mix of features places it in a key position in dinosaur evolution and helps to show how some of the really big splits between the major groups might have come about."

"There was a split in the dinosaur family tree, and the two branches took different evolutionary directions," said Baron. "This seems to have happened because of change in diet for Chilesaurus. It seems it became more advantageous for some of the meat eating dinosaurs to start eating plants, possibly even out of necessity."

Earlier this year, the same group of researchers argued that dinosaur family groupings need to be rearranged, re-defined and re-named. In a study published in Nature, the researchers suggested that bird-hipped dinosaurs and lizard-hipped dinosaurs such as Tyrannosaurus evolved from a common ancestor, potentially overturning more than a century of theory about the evolutionary history of dinosaurs.

Although their dataset has already thrown up some surprising results, the researchers say that as it currently analyses only early dinosaurs, there are probably many more surprises about dinosaur evolution to be found, once characteristics of later dinosaurs are added.

The research was funded by the Natural Environment Research Council (NERC).

http://bit.ly/2vIvphB

Evidence does not support the use of gabapentinoids for chronic low back pain

Demonstrates significant risk of adverse effects with no benefits on pain relief

Existing evidence on the use of gabapentinoids in chronic low back pain (CLBP) is limited, and demonstrates significant risk of adverse effects with no benefits on pain relief, according to a meta-analysis published in PLOS Medicine by Harsha Shanthanna from McMaster University, Canada, and colleagues.

Gabapentinoids, including pregabalin and gabapentin, are increasingly used for non-specific CLBP. In the new study, researchers analyzed findings from 8 randomized controlled trials that investigated the use of gabapentinoids in adult CLBP patients.

In 3 studies comparing gabapentin to placebo, gabapentin showed no significant improvement of pain; and in the 3 studies comparing pregabalin to other analgesics, pregabalin actually fared worse in pain relief. There were no deaths or hospitalizations reported in any included studies of the drugs, but commonly reported adverse events included dizziness, fatigue, confusion, and visual disturbances. Functional and emotional outcomes among patients taking gabapentinoids for CLBP showed no significant improvements.

"Despite their widespread use, our systematic review with meta-analysis found that there are very few randomized controlled trials that have attempted to assess the benefit of using gabapentin or pregabalin

in patients of chronic low back pain," the authors say. "The existing evidence does not support the use of gabapentinoids for predominant chronic low back pain, and calls for larger, high quality trials to more definitively inform this issue."

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http://bit.ly/2vIknsA

Study examines quality of evidence for drugs granted accelerated FDA approval

Efficacy was often confirmed in subsequent trials a minimum of 3 years after approval

Among drugs granted accelerated approval by the FDA in 2009-2013, efficacy was often confirmed in subsequent trials a minimum of 3 years after approval, and the use of nonrandomized studies and surrogate measures, instead of clinical outcomes, was common, according to a study published by JAMA.

Drugs treating serious or life-threatening conditions can receive U.S. Food and Drug Administration (FDA) accelerated approval based on showing an effect in surrogate measures, such as biomarkers, laboratory values, or other physical measures, that are only reasonably likely to predict clinical benefit.

Confirmatory trials are then required to determine whether these effects translate to clinical improvements.

Huseyin Naci, Ph.D., M.H.S., of the London School of Economics and Political Science, London, and colleagues compared the evidence on qualifying drugs before and after receiving accelerated approval, including the extent to which confirmatory studies were completed and determined whether the drugs demonstrated clinically meaningful benefits.

Characteristics of preapproval and confirmatory studies were compared in terms of study design features (randomization, blinding, comparator, primary end point).

The FDA granted accelerated approval to 22 drugs for 24 indications between 2009 and 2013; 14 of the 24 indications for these drugs entered the market on the basis of single-intervention-group studies that enrolled a median of 132 patients, which some investigators would consider a small number.

Half of required confirmatory studies were completed a minimum of three years after the approved drug was on the market.

The quality and quantity of postmarketing studies required by the FDA to confirm clinical benefit varied widely across indications.

There were few statistically detectable differences in the key design features of trials conducted before and after approval.

Nonrandomized studies were common in the accelerated approval pathway both before (60 percent) and after (44 percent) market entry.

Even though the majority of completed studies showed positive results in the postmarketing period, all completed confirmatory studies demonstrating drug benefit evaluated surrogate measures of disease activity rather than clinical outcomes.

Clinical benefit had not yet been confirmed for eight indications that had been initially approved five or more years prior.

The study notes some limitations, including that the adequacy of the confirmatory studies in addressing questions about the drugs that the FDA considered to be unresolved was not examined because such insights are not available from the FDA documents.

For more details and to read the full study, please visit the For The Media website. (doi:10.1001/jama.2017.9415)

Editor's Note: Please see the article for additional information, including other authors, author contributions and affiliations, financial disclosures, funding and support, etc.

http://bit.ly/2uNFUkW

Study gives first proof that the Earth has a natural thermostat

Enables the planet to recover from extremes of climate change

PARIS - New data provides the first proof that the Earth has a natural thermostat which enables the planet to recover from extremes of climate change - but the recovery timescales are significant. This work is presented today at the Goldschmidt conference in Paris, and has just been published in the peer-reviewed journal Geochemical Perspectives Letters*.

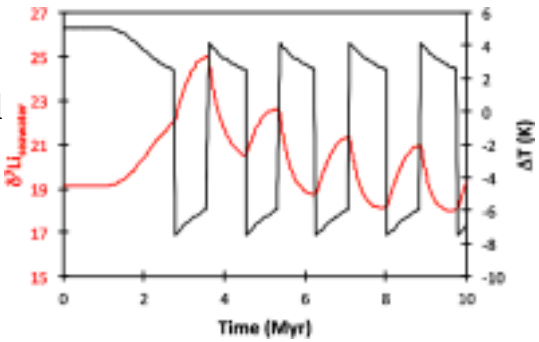
The idea of a natural temperature thermostat was first proposed in 1981, but until now no-one has been able to provide data to show that the recovery from the hot and cold temperature fluctuations were associated with a specific mechanism.

Now a group of British scientists has shown that recovery from global cooling events is associated with changes in the rate of weathering of rocks, which is the main mechanism of removing CO_2 from the atmosphere. In weathering, rocks are dissolved by rain and river water; the process removes CO_2 from the atmosphere, which is then transported to the seas by rivers to be locked up in carbon-rich rocks such as limestone. The more weathering, the more CO_2 is removed from the atmosphere.

The team had previously found evidence supporting the role of weathering in cooling the Earth in times of high temperature. This current work confirms that a slow-down of weathering takes place in cold periods, and so supports the concept of an "Earth thermostat".

The researchers were able to use the Lithium isotope ratios in rocks as a measure of weathering. They examined rocks from the period of the Hirnantian glaciation - around 445 million years ago - which correspond with the second greatest extinction of life in history, when around 85% of marine species were wiped out, due to the cooling and a dramatic drop in sea levels (estimated at around 80m) as water was locked into ice fields and glaciers.

The samples, which came from Anticosti Island (Quebec, Canada), and Dob's Linn (near Moffat, Scotland), show that global chemical weathering rate declined by a factor of four temporarily during the 5°C cooling that caused the glaciation, removing less CO_2, allowing the climate to recover from the cooling.



Effect of an oscillatory system from the feedbacks described in the text on the relative temperature and seawater δ7Li values.

Lead scientist, Dr Philip Pogge von Strandmann (University College London and Birkbeck, University of London) said:

"From looking at the relative abundance of lithium isotopes in ocean-derived rocks, we were able to confirm that chemical weathering is the driver of the Earth's natural thermostat. When there is a warmer climate, there is more weathering, and when it is cooler there is less weathering: this is what you would expect, given that chemical reactions go faster with increasing temperature. So more weathering removes CO_2 from the atmosphere and puts a break on global warming. However, when the temperature cools, the reverse is true, and less CO_2 is removed from the atmosphere in cold periods. This is the process that has allowed life to survive on Earth for around 4 billion years, and is what we are reporting in Paris".

Nevertheless, we need to be clear that the changes in temperature are gradual, and that recovery can take hundreds of thousands of years. Given the rapid increase in the rate of global warming at present, this kind of wait is not an option for us".

Commenting, Professor Jonathan Payne (Professor and Chair, Geological Sciences, Stanford University, CA, USA) said:

"The theory that chemical weathering provides a stabilizing feedback on Earth's climate goes back several decades, but observational confirmation of this hypothesis has been incomplete. In this study,

Pogge von Strandmann and colleagues add a critical new piece of confirmation by using lithium isotopes to demonstrate a reduction in the chemical weathering rate associated with climate cooling - exactly the behaviour predicted if rates of chemical weathering serve as a stabilizing feedback on climate. This study is illustrates beautifully how new isotope proxy systems are enabling critical new tests of hypotheses both old and new and, in this case, confirming a theory that helps to explain why the Earth has enabled life to flourish continuously for more than 3.5 billion years".

**This presentation is based on a paper published in the peer-reviewed journal Geochemical Perspectives Letters, June 2017 (see http://www.geochemicalperspectivesletters.org/article1726)*

http://bit.ly/2w6IHWa

Plant-produced polio vaccines could help eradicate age-old disease

Plants have been used to produce a new vaccine against poliovirus

Plants have been used to produce a new vaccine against poliovirus in what is hoped to be a major step towards global eradication of the disease.

A cross-cutting team of scientists, including Dr Johanna Marsian working in Professor George Lomonossoff's Lab at the John Innes Centre, Norwich, has produced the novel vaccine with a method that uses virus-like particles (VLPs) - non-pathogenic mimics of poliovirus which are grown in plants.

Genes that carry information to produce VLPs are infiltrated into the plant tissues. The host plant then reproduces large quantities of them using its own protein expression mechanisms.

Professor Lomonossoff, from the John Innes Centre said: "This is an incredible collaboration involving plant science, animal virology and structural biology. The question for us now is how to scale it up - we don't want to stop at a lab technique."

VLPs look like viruses but are non-infectious. They have been biologically engineered so they do not contain the nucleic acid that allows viruses to replicate. This means that they mimic the behaviour of the virus, stimulating the immune system to respond without causing an infection of poliomyelitis.

Laboratory tests demonstrated that the poliovirus mimics provided animals with immunity from the disease paving the way for human vaccines to be produced by plants on a major scale with the input of pharmaceutical industry collaborators.

The breakthrough was made by a consortium funded by the World Health Organisation (WHO) which is seeking to eradicate a disease that has been known since antiquity. The WHO is seeking alternative vaccines that avoid use of the live virus as part of an international drive to completely eradicate the virus worldwide.

A global scourge up to the middle of the last century, poliovirus has been reduced by 99 per cent since 1988 due to the Global Polio Eradication Initiative led by the WHO. Current polio vaccines, however, require the production of huge quantities of the virus. Using the live virus not only represents a risk of the virus escaping, the use of the live attenuated (weakened) virus, effectively maintains polio in the global population.

VLPs were expressed at the John Innes Centre using Hypertrans® transient plant expression system which had previously been developed there. This successful development not only holds promise for the production of vaccines for polio: it could become a frontline diagnostic resource in producing vaccines against other viral outbreaks.

"The beauty of this system of growing non-pathogenic virus mimics in plants, is that it boosts our ability to scale-up the production of vaccine candidates to combat emerging threats to human health," said Prof Lomonossoff.

In the past 20 years plants have become serious competitors to bacteria, insect cells, yeast or mammalian cells as production systems for pharmaceutical materials. They are cost-effective requiring simple nutrients, water, carbon-dioxide and sunlight for efficient growth and the transient expression system can be adjusted rapidly with low costs.

The work at the John Innes Centre furthered work of scientists at the University of Leeds, who first discovered a way of producing the virus-like particles (VLP) using the Hypertrans® expression system.

Despite successes of plant-based expression to produce VLPs of papilloma and hepatitis B viruses, poliovirus VLPs had previously proved too unstable to make practical vaccines using this technique. A problem is that the genetic material which causes replication of the virus and which is therefore absent from the VLPs, also has a role in holding the particles together.

However teams from The National Institute for Biological Standards and Control, and the University of Leeds identified mutations within protein coats which enabled the production of VLPs which are sufficiently stable to act as vaccines. Experiments at the University of Oxford showed that these were identical to native poliovirus retaining their shape when warmed, and which are effective in protecting animals against poliovirus.

The team used cryo-electron microscopy at Diamond Light Source's Electron Bio-Imaging Centre (eBIC) to obtain a clear look at the structure of the VLPs. They confirmed the structure and showed that the external features of the particles were identical to those of poliovirus.

Dave Stuart, Director of Life Sciences at Diamond and Professor of Structural Biology at University of Oxford said, "We were inspired by the successful synthetic vaccine for foot-and-mouth disease, also investigated at Diamond as part of UK research collaboration. By using Diamond's visualisation capabilities and the expertise of Oxford University in structural analysis and computer simulation, we were able to visualise something a billion times smaller than a pinhead and further enhance the design atom by atom of the empty shells. Through information gained at Diamond, we also verified that these have essentially the same structure as the native virus to ensure an appropriate immune response."

This collaboration means manufacturing the particles stabilised in plants on a large scale as precursors to vaccines is now much closer to becoming a reality. The results are outlined in the journal Nature communications: Plant-made Polio 3 stabilised VLPs - a candidate synthetic Polio vaccine. The collaboration includes the John Innes Centre, The National Institute for Biological Standards and Control, Oxford University, University of Leeds, Diamond Light Source, the Henry Wellcome Building for Genomic Medicine.

Background information: Poliovirus: the scourge of summers past

An ancient Egyptian stone engraving provides a clue that the poliovirus has been a disturbing blight on our lives since antiquity.

The 3,500-year-old engraving appears show a polio victim, a priest with a withered right leg.

An ancient Egyptian stone engraving appears to show a polio victim...a priest with a withered right leg **Getty Images**

From then the virus was widely feared up until the middle of the last century and the arrival of the first effective vaccines. Polio is now down to a few hundred cases a year world-wide, but these numbers remain steady as the virus is maintained in the environment by the use of the live attenuated vaccine.

"The poliovirus is a very nasty disease and certainly until the 1950s was a real scourge." said Professor George Lomonossoff of the John Innes Centre, based at Norwich Research Park. "It was known as the summer plague and here in Norwich the main source of it was bathing in the river Yare near Earlham Park."

"Most people had very mild symptoms but some people got paralytic polio and in worst cases couldn't breathe properly and had to be put in an iron lung in order to breathe."

Poliovirus is the causative agent of poliomyelitis which destroys motor neurons in the central nervous system causing paralysis or even death. Transmission is primarily by ingesting infected water.

The Global Polio Eradication Initiative led by the World Health Organisation has resulted in 99 per cent fewer cases in the past 30 years by using two highly effective vaccines: the live attenuated (weakened) vaccine developed by Albert Sabin and the formaldehyde-inactivated or killed virus developed by Jonas Salk.

Production of both vaccines, developed in the 1950s, requires propagation of large quantities of live poliovirus increasing the risk of accidental re-introductions.

Because of this risk, the WHO has intensified its search for cheap and viable alternatives, this breakthrough using the virus-like particles presents an exciting new option. Virus free vaccines will allow polio to be eradicated, they will prevent recurrences without the risks associated with the using the live virus vaccines.

1. Plant-made Polio 3 stabilized VLPs ¬- a candidate synthetic Polio vaccine (lead author Johanna Marisan) is published in Nature Communications (embargoed until 10:00am BST on 15th August). On publication the paper will be available at:
http://nature.com/articles/doi:10.1038/s41467-017-00090-w

http://bit.ly/2w78zRI

NIAID herpesvirus study in mice leads to discovery of potential broad-spectrum antiviral

Inhibiting enzyme complex suppresses viral infection

After herpesviruses infect a cell, their genomes are assembled into specialized protein structures called nucelosomes. Many cellular enzyme complexes can modulate these structures to either promote or inhibit the progression of infection. Scientists studying how one of these complexes (EZH2/1) regulated herpes simplex virus (HSV) infection unexpectedly found that inhibiting EZH2/1 suppressed viral infection. The research group, from the National Institute of Allergy and Infectious Diseases (NIAID) at the National Institutes of Health, then demonstrated that EZH2/1 inhibitors also enhanced the cellular antiviral response in cultured cells and in mice.

Once a person has been infected with a herpesvirus, the virus persists in a latent form, sometimes reactivating to cause recurrent disease. Two-thirds of the global population are infected with HSV-1, and at least 500 million are infected with HSV-2, according to the World Health Organization. These viruses cause a range of diseases and conditions from oral cold sores to genital lesions to serious eye infections that can lead to blindness. In infants who acquire the infection from their mothers, HSV can cause neurological and developmental problems. People infected with HSV also have an enhanced risk of acquiring or transmitting human immunodeficiency virus (HIV). Treatment usually involves antiviral drugs that interfere with viral replication, but new approaches to combat these infections are needed.

The NIAID group demonstrated that EZH2/1 inhibitors not only suppressed HSV infection, spread, and reactivation in mice, but also suppressed human cytomegalovirus, adenovirus, and Zika virus infections in cell culture using human primary fibroblast cell lines. These authors suggest that EZH2/1 inhibitors have considerable potential as broad-spectrum antivirals.

http://bit.ly/2fR2vpR

Precision medicine opens the door to scientific wellness preventive approaches to suicide

More precise way of diagnosing suicide risk, by developing blood tests that work in everybody

INDIANAPOLIS - Researchers have developed a more precise way of diagnosing suicide risk, by developing blood tests that work in everybody, as well as more personalized blood tests for different subtypes of suicidality that they have newly identified, and for different psychiatric high-risk groups.

The research team, led by scientists at the Indiana University School of Medicine, also showed how two apps, one based on a suicide risk checklist and the other on a scale for measuring feelings of anxiety and depression, work along with the blood tests to enhance the

precision of tests and to suggest lifestyle, psychotherapeutic and other interventions. Lastly, they identified a series of medications and natural substances that could be developed for preventing suicide.

"Our work provides a basis for precision medicine and scientific wellness preventive approaches," said Alexander B. Niculescu III, MD, PhD, professor of psychiatry and medical neuroscience at IU School of Medicine and attending psychiatrist and research and development investigator at the Richard L. Roudebush Veterans Affairs Medical Center.

The article, "Precision medicine for suicidality: from universality to subtypes and personalization," appears in the August 15 online edition of the Nature Publishing Group's leading journal in psychiatry, Molecular Psychiatry.

The research builds on earlier studies from the Niculescu group.

"Suicide strikes people in all walks of life. We believe such tragedies can be averted. This landmark larger study breaks new ground, as well as reproduces in larger numbers of individuals some of our earlier findings," said Dr. Niculescu.

There were multiple steps to the research, starting with serial blood tests taken from 66 people who had been diagnosed with psychiatric disorders, followed over time, and who had at least one instance in which they reported a significant change in their level of suicidal thinking from one testing visit to the next. The candidate gene expression biomarkers that best tracked suicidality in each individual and across individuals were then prioritized using the Niculescu group's Convergent Functional Genomics approach, based on all the prior evidence in the field.

Next, working with the Marion County (Indianapolis, Ind.) Coroner's Office, the researchers tested the validity of the biomarkers using blood samples drawn from 45 people who had committed suicide.

The biomarkers were then tested in another larger, completely independent group of individuals to determine how well they could predict which of them would report intense suicidal thoughts or would be hospitalized for suicide attempts.

The biomarkers identified by the research are RNA molecules whose levels in the blood changed in concert with changes in the levels of uicidal thoughts experienced by the patients. Among the findings reported in the current paper were:

- ***An algorithm that combines biomarkers with the apps that was 90 percent accurate in predicting high levels of suicidal thinking and 77 percent accurate in predicting future suicide-related hospitalizations in everybody, irrespective of gender and diagnosis.***
- ***A refined set of biomarkers that apply universally in predicting risk of suicide among both male and female patients with a variety of psychiatric illnesses, including new biomarkers never before linked to suicidal thoughts and behavior.***
- ***Four new subtypes of suicidality were identified (depressed, anxious, combined, and non-affective/psychotic), with different biomarkers being more effective in each subtype.***
- ***Biomarkers that were associated with specific diagnoses and genders, such as one, known as LHFP, that appears to be a very strong predictor for depressed men.***
- ***Two of the biomarkers, APOE and IL6, have broad evidence for involvement in suicidality and potential clinical utility as targets for drug therapies, as well as suggest a neurodegenerative and inflammatory component to the predisposition to suicide. APOE is responsible for proteins involved with managing cholesterol and fats, and some forms of the gene have been strongly implicated as risks for Alzheimer's disease. IL6 expresses proteins involved in the body's inflammation response.***
- ***Potential drug therapies and natural substances for preventing suicide, using the blood biomarker signatures and bioinformatics approaches. They included medications already in use to treat psychiatric illnesses and drugs approved for other uses, such as the diabetes medication metformin.***

Additional investigators contributing to the research were Helen Le-Niculescu, Daniel F. Levey, Peter L. Phalen, Helen L. Dainton, Kyle Roseberry, Elizabeth M. Niculescu, Joseph O. Niezer, Anantha Shekhar, George E. Sandusky, Vivek Venugopal and Michael Yard, of the Indiana University School of Medicine; Andrea Williams, Dawn L. Graham and Tammy J. Jones of the Roudebush VA Medical Center; Alfarena Ballew of the Marion County Coroner's

Office; Terri Gelbart, Sunil M. Kurian and Daniel R. Salomon of the Scripps Research Institute; and Nicholas J. Schork of the J. Craig Venter Institute.

The research was supported by a National Institutes of Health Directors' New Innovator Award (1DP2OD007363) and a VA Merit Award (2I01CX000139).

Additional information about Dr. Niculescu's work is available at his laboratory website: http://www.neurophenomics.info.

http://bit.ly/2w820hI

Deadly drug-resistant fungus sparks outbreaks in UK—and it's stalking US

It's unusually good at lurking in hospitals, resisting drugs, and killing vulnerable patients.

Beth Mole - 8/17/2017, 1:15 AM

More than 200 patients in more than 55 UK hospitals were discovered by healthcare workers to be infected or colonized by the multi-drug resistant fungus Candida auris, a globally emerging yeast pathogen that has experts nervous.

Three of the hospitals experienced large outbreaks, which as of Monday were all declared officially over by health authorities there. No deaths have been reported since the fungus was first detected in the country in 2013, but 27 affected patients have developed blood infections, which can be life-threatening. And about a quarter of the more than 200 cases were clinical infections.

Officials in the UK aimed to assuage fear of the fungus and assure patients that hospitals were safe. "Our enhanced surveillance shows a low risk to patients in healthcare settings. Most cases detected have not shown symptoms or developed an infection as a result of the fungus," Dr Colin Brown, of Public Health England's national infection service, told the BBC.

Yet, public health experts are uneasy about the rapid emergence and level of drug resistance the pathogen is showing. In a surveillance update in July, the US Centers for Disease Control and Prevention said that C. auris "presents a serious global health threat."

It was first identified in the ear of a patient in Japan in 2009. Since then, it has spread swiftly, showing up in more than a dozen countries, including the US, according to the CDC. So far, health officials have reported around 100 infections in nine US states and more than 100 other cases where the fungus was detected but wasn't causing an infection.

ungal foe

Though many people who pick up the fungus don't develop an infection or develop a mild one, the fungus can be deadly in patients with compromised immune systems or other underlying conditions. More than a third of people who develop an invasive infection die.

Those invasive infections are often hard to halt because C. auris is unusually resistant to anti-fungal dugs. For instance, every C. auris case in the UK has shown reduced susceptibility to the first line antifungal fluconazole, and many are resistant to multiple drugs. Some are resistant to all three main classes of antifungal drugs used to treat Candida infections, azoles, echinocandins, and polyenes.

C. auris is also oddly good at spreading among patients and lurking in environments, particularly healthcare settings. One of the three UK hospitals hit with an outbreak reported having trouble stamping it out over more than a year. Environmental sampling revealed the fungus was on "the floor around bed sites, trollies, radiators, windowsills, equipment monitors and key pads, and also one air sample." At least 50 patients were involved in the outbreak that began in April of 2015.

Healthcare officials have since adopted new protocols, including having healthcare workers wear more protective equipment and isolating all patients that are infected or colonized by the fungus. This month, Public Health England released new guidelines for managing the yeast's emergence.

http://bit.ly/2ibuyBn

Global megafauna study calls for conservation rethink

Introduced megafauna are "rewilding" modern ecosystems

August 15, 2017 by Jocelyn Airth

It's hard to imagine an Australia ruled by hippopotamus-sized wombats (Diprotodon) and three-metre-tall kangaroos (Procoptodon

golian). The continent lost all native megafauna to the Pleistocene extinctions, tens of thousands of years ago.

Remarkably, however, eight species of introduced megafauna now call Australia home and some of them are "rewilding" modern ecosystems, new research has found.

These include animals on the Red List of Threatened Species, compiled by the International Union for Conservation of Nature (IUCN), such as one of the largest populations of endangered wild horses (Equus ferus caballus) and the world's only population of wild dromedary camels (Camelus dromedarius).

Dr Arian Wallach and Dr Daniel Ramp from the UTS Centre for Compassionate Conversation, along with researchers from Arizona State University and Oregon State University, say the research challenges fundamental ideas surrounding "invasive" species and conservation.

The global study, published in Ecography, identified that of the world's 76 existing megafauna species, 22 have introduced populations. Of these introduced populations, almost half are either threatened or extinct in their native ranges. "The global decline of megafauna is being driven by habitat loss, changes in land use and overhunting. Despite this, some megafauna have found refuge in new habitats through introductions," says chief investigator Dr Wallach.

The team, led by Arizona State University's Erick Lundgren, has also found introduced megafauna can contribute unique ecological functions, some of which may have been lost since the late Pleistocene. "As large herbivores, these introduced species can consume plant matter indigestible to smaller herbivores, which may reduce fire frequency, accelerate nutrient cycling and shape plant communities," Lundgren says.

In North America's Sonoran Desert, wild donkeys are now digging groundwater wells more than a metre deep. These holes provide a much-needed water source for at least 30 species of mammals and birds, as well as germination nurseries for river vegetation. Critically endangered in its native range, the wild donkey has clearly found refuge and is contributing to ecosystems in its introduced range, says Lundgren.

Many existing populations of megafauna are either endangered or extinct. Conservation historically overlooks such populations, assuming anything "introduced" is "alien" or "invasive". Lundgren and his team, however, suggest such populations are critical buffers against extinction and may have a positive impact on their new homes. "What this study shows is that the world is much wilder than we often think," says Wallach.

"The question is whether we are willing to allow it to be."

http://bit.ly/2uOqkp9

Climate change will cut crop yields: study

Climate change will have a negative effect on key crops

Climate change will have a negative effect on key crops such as wheat, rice, and maize, according to a major scientific report out Tuesday that reviewed 70 prior studies on global warming and agriculture.

Experts analyzed previous research that used a variety of methods, from simulating how crops will react to temperature changes at the global and local scale, to statistical models based on historical weather and yield data, to artificial field warming experiments.

All these methods "suggest that increasing temperatures are likely to have a negative effect on the global yields of wheat, rice and maize," said the report in the Proceedings of the National Academy of Sciences, a peer-reviewed US journal. "Each degree Celsius increase in global mean temperature is estimated to reduce average global yields of wheat by six percent," said the report.

Rice yields would be cut by 3.2 percent, and maize by 7.4 percent for each degree of Celsius warming (almost two degrees Fahrenheit), it added. "Estimates of soybean yields did not change significantly."

These four crops are key to the survival of humanity, providing two-thirds of our caloric intake. Changing temperatures would likely cause yields to rise in some locations, said the report. But for the most part,

the overall trend planet-wide is downward, signaling that steps are needed to adapt to the warming climate and feed an ever-expanding world population.

Temperature increase reduces global yields of major crops in four independent estimates, Chuang Zhao, PNAS, DOI: 10.1073/pnas.1701762114 ,
http://www.pnas.org/content/early/2017/08/10/1701762114

http://bit.ly/2wVEB0N

The irresistible fragrance of dying vinegar flies

Bacterial pathogens cause infected flies to produce more sex pheromones and so expand their deadly reach

Markus Knaden and Bill Hansson, and their colleagues at the Department of Evolutionary Neuroethology, study ecologically relevant odors in the natural environment of insects, especially vinegar flies. In this new study they focused on a deadly smell: the odor of conspecifics which have a lethal bacterial infection.

"We had originally hoped to find a dedicated neuronal circuit in the flies which is specialized to detect and avoid sickness odors. Instead we observed that healthy flies were especially attracted to the smell of infected ones. When we realized that flies cannot avoid becoming infected, as sick flies produce particularly high amounts of pheromones, we were surprised but found that even more interesting," says Markus Knaden, one of the leaders of the study.

State-of-the-art analytical methods enabled the researchers to identify and quantify the odors of single flies. Vinegar flies which suffered from bacterial infection and their feces emitted dramatically increased amounts of the typical odors that attract other flies. The hypothesis that last-minute pheromone emission by sick insects would enhance their reproductive success turned out to be wrong, as mating assays demonstrated that sick flies were barely able to copulate.

Insect immunologist Nicolas Buchon from Cornell University and his team, who were also involved in the study, noticed that the increase in pheromone production matched the up-regulation of certain immune responses in the flies. Ian Keesey, the first author of the study, and his colleagues in Jena therefore tested mutant flies which lacked the ability to produce these responses and found that these flies emitted far fewer pheromones when they became infected in comparison to sick wild-type flies. Further analysis of the insects' metabolism convinced the researchers that ongoing bacterial growth and the subsequent damages caused by the pathogens are necessary to induce increases in pheromone production.

The scientists observed similar results when they conducted experiments with other fly species. Seven other Drosophila species as well as the yellow fever mosquito Aedes aegyptii conspecifics dramatically changed their olfactory profile after infection with the pathogen. Manipulation of social communication in insects by pathogenic bacteria seems to be a more general phenomenon in nature than thought.

Markus Knaden hopes that the new insights can one day contribute to useful applications: "A well-established method to combat insect-transmitted diseases and to control agricultural pest insects is the use of pheromone traps. By infecting insects with bacteria we could generally increase their pheromone emission. This could enable us to identify novel pheromones in species that have not been investigated so far."

Original Publication: Keesey, I. W., Koerte, S., Khallaf, M. A., Retzke, T., Guillou, A., Grosse-Wilde, E., Buchon, N., Knaden, M., Hansson, B. S. (2017). Pathogenic bacteria enhance dispersal through alteration of Drosophila social communication.
Nature Communications DOI: 10.1038/10.1038/s41467-017-00334-9
http://dx.doi.org/10.1038/10.1038/s41467-017-00334-9

http://go.nature.com/2wmEsp1

Budget cuts fuel frustration among Japan's academics

Funding trouble at flagship research centre reflects a broader malaise in the country's scientific priorities that must be addressed.

Japan's premier scientific research institution, RIKEN, turned 100 this year, and celebrated with a grand ceremony attended by the empress and emperor. But not everybody was in the mood to party. In the old days, RIKEN was known as a paradise for scientists because of its

generous funding. No longer: as Japan cuts off funds in the face of continuing financial uncertainty, the cracks are starting to show.

One scientist affected is Takaomi Saido, who researches Alzheimer's disease at RIKEN's Brain Science Institute (BSI) in Wako. At around the time of the centenary event in April, he was told that he would have 43% less money this year to support his work. Saido posted an angry response online, saying he wasn't given enough warning to find money to pay his staff and take care of his mice, which he says are sent to 250 laboratories around the world.

The problem is one of priorities, and is neatly demonstrated by a white paper published by Japan's science ministry last month. It is dominated by discussion of innovation, and how to foster greater interaction between businesses and academia to achieve it. One way is to drain funds from more-basic science; as a result, universities and research institutes, including RIKEN, are getting squeezed.

RIKEN's budget has been cut by more than 20% over the past 10 years. In response, the BSI has reduced its number of principal investigators from 61 to 41 over that period.

Japan's universities are in similar straits. Following reforms in 2004, their budgets have declined by 1% every year. The move was meant to make universities more responsive to strategic initiatives and more competitive, by aligning their research with industrial or military needs. But it has triggered other, less positive changes. The universities stopped hiring professors. New staff are brought in as contract employees, who flit from grant to grant to stay afloat.

The science ministry's white paper acknowledges that this has "given birth to a situation in which young researchers, facing unstable employment conditions and economic uncertainty, are forced to aim for results that can be accomplished in the short term and in which true originality and creativity are difficult to realize".

And it's not just the young ones. Thanks to greater administrative and grant-writing burdens, university researchers say they can put little more than one-third of their work time into research, compared with just under half in 2002.

As the economic and political headwinds increase, Japan's policymakers and administrators should do more to support scientific research through these unstable times. Universities need to make clear as early as possible what cuts are coming. RIKEN warned researchers that the incoming budget would be tight, but Saido says he heard nothing to suggest such a severe drop.

Institutions must also be more transparent. Other RIKEN researchers who shared Saido's frustration were afraid to talk about it openly because they felt so uncertain about their positions. A coming reorganization of RIKEN institutes is a major cause for concern. Scientists there don't know whether they will still have a job this time next year.

Japan rues the collapse of its ability to produce and publish important scientific findings, but it shouldn't be surprised: its publication record maps neatly onto its science and technology investment, both flat since 2000. Its scientists see the drop in global competitiveness measured by research papers (from fourth in the world in 2004 to tenth in the world in 2014) and look with envy at China and other nations that are increasing both their funding and their publication rates. Japan is rightly proud of its scientific past, but it must do more to safeguard its future.

http://bit.ly/2vIWSQ0

Researchers discover fundamental pathology behind ALS

Identifying the basic cellular malfunction underlying amyotrophic lateral sclerosis and a form of dementia opens the pathway to developing treatments to prevent the disease by preserving neurons

A team led by scientists at St. Jude Children's Research Hospital and Mayo Clinic has identified a basic biological mechanism that kills neurons in amyotrophic lateral sclerosis (ALS) and in a related genetic disorder, frontotemporal dementia (FTD), found in some ALS patients. ALS is popularly known as Lou Gehrig's disease.

The researchers were led by J. Paul Taylor, M.D., Ph.D., chair of the St. Jude Cell and Molecular Biology Department and a Howard Hughes Medical Institute investigator; and Rosa Rademakers, Ph.D., of the Mayo Clinic in Jacksonville, Florida. The findings appear today in the journal Neuron.

The disease-causing mutation identified is the first of its kind, Taylor said. Unlike in other genetic diseases, the mutation does not cripple an enzyme in a biological regulatory pathway. Rather, the mutation produces an abnormal version of a protein involved in a process called phase separation in cells.

Phase separation is a mechanism by which proteins assemble into organized assemblies, called membrane-less organelles, necessary for orderly cell functions. The researchers found that the ALS/FTD mutation produces an abnormal version of a protein called TIA1 that is a building block of such organelles. As a result, in ALS, the proteins within the organelles accumulate and kill neurons that control muscles. In FTD, the accumulation kills neurons in the brain. The researchers noted that abnormal phase separation may also underlie Alzheimer's disease.

There is currently no effective treatment for ALS/FTD. However, the researchers believe their finding offers a promising pathway for developing treatments to restore neurons' ability to disassemble the organelles when their cellular purpose has ended.

The TIA1 mutation was discovered when the scientists analyzed the genomes of a family affected with ALS/FTD. Tracing the effect of the mutation on TIA1 structure, the researchers found that it altered the properties of a highly mobile "tail" of the protein. This tail region governs the protein's ability to assemble with other TIA1 proteins. Taylor and his colleagues previously identified such unstructured protein regions, called prion-like domains, as the building blocks of cellular assemblies and as hotspots for disease-causing mutations.

In further studies, the researchers found that TIA1 mutations occurred frequently in ALS patients. The scientists also found that people carrying the mutation had the disease. When the investigators analyzed brain tissue from deceased ALS patients with the mutations, the scientists detected a buildup of TIA1-containing organelles called stress granules in the neurons. Such granules form when the cell experiences such stresses as heat, chemical exposure and aging. To survive, the cell sequesters in the granules' genetic material that codes for cell proteins not necessary for survival-critical processes.

The granules also contained a protein called TDP-43, another building block of stress granules, whose abnormality has been implicated in causing ALS. In test tube studies and experiments with cells, the researchers found that the TIA1 mutation causes the protein to become more "sticky," delaying the normal disassembly of stress granules, trapping TDP-43.

"This paper provides the first 'smoking gun,' showing that the disease-causing mutation changes the phase transition behavior of proteins," Taylor said. "And the change in the phase transition behavior changes the biology of the cell."

More broadly, he said, "These findings are part of an emerging theme that there is a whole spectrum of diseases that includes ALS, and some forms of dementia and myopathy, that are caused by disturbance in the behavior of these structures that perturbs cellular organization."

The findings offer a highly promising pathway to the first effective treatments for ALS/FTD, Taylor said. Current drugs, which are only minimally effective, seek to improve the function of already damaged neurons. However, the new findings suggest the possibility of treatments that would prevent neuronal damage by restoring the healthy balance of phase separation in the cells of people with ALS/FTD mutations.

"We know that these material properties are under tight regulation, so perhaps we don't have to target the disease-causing mutation itself," Taylor said. "Perhaps we can restore balance by targeting any of a large number of regulatory molecules in the cell. There are already therapeutic approaches in laboratory testing that seek to do just that."

In further studies, Taylor and his colleagues will seek to understand the basic process of phase transition. They will also map the regulatory machinery for stress granules, to seek potential therapeutic targets. He also noted that the same basic pathology of phase transition may also underlie other neurodegenerative diseases, including Alzheimer's disease, and he is aiding researchers in applying the same research approach as in ALS/FTD to Alzheimer's.

The paper's joint first authors are Ian Mackenzie of Vancouver Coastal Health and the University of British Colombia; Alexandra Nicholson of Mayo Clinic Jacksonville; and Mohona Sarkar of St. Jude. Other St. Jude co-authors were Jamshid Temirov, Hong Joo Kim and Tanja Mittag. Co-authors were also from Vancouver Coastal Health and the University of British Columbia, Mayo Clinics, Simon Fraser University, University of Texas, Sunnybrook Health Sciences Centre, Northwestern University, University of Toronto, University of Western Ontario, Drexel University, Thomas Jefferson University and the University of Pittsburgh.

The research was funded in part by Mayo Clinic for Individualized Medicine; the Arizona Alzheimer's Consortium; CREATE, the Canadian Institutes for Health Research; the National Institutes of Health (R35NS097974, R35NS076471, R35NS097273, P50AG016574, P50NS072187, P01NS084974, U01AG006576, U54NS092091, P30AG019610, R01AG031581, R01NS072248, R01NS075764); and ALSAC, the fundraising and awareness organization of St. Jude.

http://bit.ly/2xaZep0

New tool aims to make surgery safer by helping doctors see nerves

Nerve-illuminating tool outperforms visual inspection; could reduce surgery related injury and chronic pain

WASHINGTON -- During operations, it can be difficult for surgeons to avoid severing crucial nerves because they look so much like other tissue. A new noninvasive approach that uses polarized light to make nerves stand out from other tissue could help surgeons avoid accidentally injuring nerves or assist them in identifying nerves in need of repair.

Although nerve injuries are a known complication for many types of surgery, surgeries involving the hand and wrist come with a higher risk because of the dense networks of nerves in this area. There are a few techniques available to help doctors identify nerves, but they have various limitations such as not providing real-time information, requiring physical contact with the nerve or requiring the addition of a fluorescent dye.

"We have shown that nerves can be distinguished in human tissue by detecting the interaction of light with the structure of nerves without the need for fluorescent markers or physical interaction," said Kenneth Chin, a medical student at the Academic Medical Center (AMC), University of Amsterdam, Netherlands. "Using an intraoperative, noninvasive real-time method minimizes potential nerve damage, which can result in fewer negative consequences such as reduced function, loss of sensation or chronic pain."

Cousins, Kenneth and Patrick Chin, independently developed the idea to use an optical technique known as collimated polarized light imaging (CPLi) to identify nerves during surgery. They later joined a research group led by Thomas van Gulik, a surgeon at the Academic Medical Center, and brought along a working prototype which has been further developed into a practical system that can be deployed in the operating room.

In The Optical Society (OSA) journal Biomedical Optics Express, the researchers report that a surgeon using CPLi technology was able to correctly identify nerves in a human hand 100 percent of the time, compared to an accuracy rate of 77 percent for the surgeon who identified nerves using only a visual inspection.

Distinguishing nerve tissue

CPLi uses a polarized beam of light to illuminate the tissue. When this light passes through a nerve, the tissue's unique internal structure reflects the light in a way that is dependent on how the nerve fiber is oriented compared to the orientation of the polarization of the light. By rotating the light's polarization, the reflection appears to switch on and off, making the nerve tissue stand out from other tissue. For this application, it was important to use light that was collimated, meaning all the light waves were parallel to each other, to maximize the amount of light reflected by the tissue.

"We adapted the optics used for CPLi so that they could be incorporated in a surgical microscope, which can be placed above the surgical area," said Kenneth Chin. "The resulting system can be used in a wide range of surgical fields where superficial nerves need to be identified."

After testing their technique on animal tissue, the researchers used it to examine 13 tissue sites from the hand of a human cadaver. A surgeon looked for nerve tissue at these sites by eye under typical surgical illumination while a different surgeon used CPLi for an independent assessment. Histological evaluation was then used to verify the presence of nerve tissue at each site. The surgeon using visual inspection correctly identified nerve tissue in 10 of the 13 cases while the surgeon using CPLi correctly identified nerve tissue in all cases.

With patient consent, the researchers also used CPLi to successfully identify nerve tissue during a procedure to relieve pain in the wrist. They plan to do additional tests of the technique during live surgery to better understand how the optical reflection of nerves might vary among patients and under various surgical conditions.

"This technique could improve the effectiveness of surgical interventions by helping the surgeon identify nerves in the operative field," said van Gulik. "This leads to surgeons being more confident in their surgical procedure, which will lead to less accidental injury and more targeted surgical interventions."

Paper: K. W. T. K. Chin, A. F. Engelsman, P. T. K. Chin, S. L. Meijer, S. D. Strackee, R. J. Oostra, T. M. van Gulik, "Evaluation of collimated polarized light imaging for real-time intraoperative selective nerve identification in the human hand," Biomed. Opt. Express, Volume 8, Issue 9, 4122-4134(2017). DOI: 10.1364/BOE.8.004122.

http://bit.ly/2icFpeb

Scientists discover powerful potential pain reliever

New pain reliever that acts on a previously unknown pain pathway.

A team of scientists led by chemists Stephen Martin and James Sahn at The University of Texas at Austin have discovered what they say is a powerful pain reliever that acts on a previously unknown pain pathway. The synthetic compound, known as UKH-1114, is as effective at relieving neuropathic pain in injured mice as a drug widely used for pain relief called gabapentin, but it works at a much lower dose, with longer duration of action.

If the researchers can demonstrate that the drug is safe, effective and nonaddictive in humans -- a process that typically takes years -- the discovery could be instrumental in addressing one of today's biggest public health challenges: the opioid abuse epidemic.

Nearly a third of Americans suffer from chronic pain, yet the most effective pain relievers -- opioids -- are addictive and often require increased dosing to maintain efficacy. According to the National Institute on Drug Abuse, about 2 million people in the U.S. suffer from addiction to prescription opioid pain relievers. Alternatives to opioids have their own drawbacks -- for example, gabapentin (sold as Neurontin) can cause cognitive impairment in certain individuals.

"This opens the door to having a new treatment for neuropathic pain that is not an opioid," said Martin, a professor and the M. June and J. Virgil Waggoner Regents Chair in Chemistry. "And that has huge implications."

The pain drug they found binds to a receptor on cells throughout the central nervous system called the sigma 2 receptor. Although it was discovered 25 years ago, scientists still did not know what sigma 2 did until now.

Theodore Price, associate professor of neuroscience at The University of Texas at Dallas and a leading expert on chronic pain, tested UKH-1114 on mice with nerve damage and found that it alleviated pain as well as gabapentin did, but at a much lower dose (one-sixth as much) and was effective much longer (lasting for a couple of days, compared with 4 to 6 hours). This research is the first to demonstrate that the sigma 2 receptor may be a target for treating neuropathic pain.

Results are published in the Aug. 18 print edition of the journal ACS Chemical Neuroscience. An earlier paper, published online on May 28 in the journal Proceedings of the National Academy of Sciences,

described the molecular cloning and identification of the sigma 2 receptor.

The researchers have filed patent applications on the new compound.

Neuropathic pain, or chronic pain, is caused when nerves in the central nervous system are damaged. Among other things, it can result from chemotherapy, diabetes and injuries to the brain or spinal cord.

Much work remains to be done before UKH-1114 can enter the market. More studies are needed to demonstrate safety, efficacy and oral bioavailability. In the meantime, the scientists are working to understand, on a fundamental level, how activating the sigma 2 receptor relieves neuropathic pain. Still, Martin and Sahn are excited by the compelling results from the mouse model.

"We started out just working on fundamental chemistry in the lab," said Sahn, a research scientist in the Department of Chemistry. "But now we see the possibility that our discoveries could improve the quality of people's lives. That is very satisfying."

http://bbc.in/2v1FbIS

The algae that terraformed Earth

A planetary takeover by ocean-dwelling algae 650 million years ago was the kick that transformed life on Earth.

That's what geochemists argue in Nature this week, on the basis of invisibly small traces of biomolecules dug up from beneath the Australian desert. The molecules mark an explosion in the quantity of algae in the oceans. This in turn fuelled a change in the food web that allowed the first microscopic animals to evolve, the authors suggest.

"This is one the most profound ecological and evolutionary transitions in Earth's history," lead researcher Jochen Brocks told the BBC's Science in Action programme.

The events took place a hundred million years before the so-called Cambrian Explosion, an eruption of complex life recorded in fossils around the world that puzzled Darwin and always hinted at some kind of biological prehistory.

Scattered traces of those precursor multi-celled organisms have since been recognised, but the evolutionary driver that led to their rise has been much argued over.

Cambridge University palaeontologist Nick Butterfield has said the period "was arguably the most revolutionary in Earth history", and not just because of the rapid biological changes. There were violent swings in climate, too, that experts have long suspected are intertwined.

The context was a planet that previously had long had life-sustaining oceans and a benign climate. Yet, for over three billion years - since 3.8 billion years before present according to most estimates - all life was single-celled, mostly bacteria; little evolutionary innovation had happened.

Algae, more complex than bacteria but still single-celled, had themselves had been around for over a billion years (the "boring billion" some palaeontologists call it), but without making much of an ecological impact.

With their DNA packed away safely inside a nucleus (so-called eukaryotes, like all animals and plants today), they had an evolutionary advantage over bacteria they seemed unable to exploit.

That changed about 650 million years ago, according to the new study. There are no fossils of the algae. Instead, Brocks and his team at the Australian National University, have tracked down molecular remnants of their cell walls, molecules closely related to the cholesterol in our bodies, "the most stable thing of any organism - fat," Brocks quips.

After every other trace of the cells had decayed, these fat molecules remained and were absorbed into sediments, and over geological time became cemented into the bedrock of Australia. To be drilled up and analysed hundreds of millions of years later.

"The signals that we find show that the algal population went up by a factor of a hundred to a thousand and the diversity went right up in one big bang, and never went back again," Brocks says.

This ecological flip happened just after one of the greatest environmental catastrophes the planet has ever seen - the "Snowball Earth" period when ice extended from pole to pole, and even at the equator temperatures could have plunged to minus 60 degrees.

The episode ended after 50 million years, when the build-up of volcanic CO2 in the atmosphere created a supergreenhouse that melted the ice in a second cataclysm.

The connection, Brocks believes, is that glacial action ground up continental rocks, releasing the nutrient phosphate which was then washed into the oceans as the thaw progressed. Today's agricultural green revolution is dependent on phosphates dug up in giant mines around the world, and the pre-Cambrian biological revolution may have been powered the same way, the researchers believe.

"This rise in algae happens just around the time the first animals appeared on the scene," Brocks explains. "It was algae at the bottom of the food web that created this burst of energy and nutrients that allowed larger and more complex creatures to evolve."

Yale University's Noah Planavsky, whose study earlier this year [Nature link] revealed the phosphate nutrient outburst following the Snowball Earth, says the new revelations are "incredibly important".

"It gives the first evidence of ecosystems dominated by complex lifeforms - the eukaryotes," he told the BBC.

In a commentary also in Nature, Andrew Knoll of Harvard University, a world authority on pre-Cambrian life, says the new work makes "a substantial contribution" to revealing "the relationship between life and the surrounding physical environment" at a critical time in animal evolution. "Food source changes might have helped to pave the way for the animal radiation," he agrees, though adding "key questions remain".

Getting the data was painstaking work, says MIT's Roger Summons, who has previously collaborated with Brocks. The nanogram traces of pre-Cambrian oil measured in the study had to be picked out from a fog of contamination made by fossil fuels. "I applaud Jochen's insight and his tenacity," Summons wrote in an e-mail. "The results show how fastidious attention to detail ultimately pays off." However, he suggests the tale is not complete. Likewise, Cambridge University's Nick Butterfield, while accepting the data, disagrees with the interpretation.

In fact, he thinks that Brocks has got cause and effect back to front; the explosion of algae did not drive the rise of animals, he says.

"There's no evidence for animal evolution being constrained by a shortage of food," he argued in an e-mail. Instead, he says, it was the rise of animals - sponges to be precise - that cleared the ecological path for algae.

Brocks and Butterfield debated the interpretation in the corridors of the Goldschmidt geochemistry conference in Paris this week, as others looked on.Brocks remains unswayed - that the outburst of algae 650 million years ago "kicked off an escalating arms race" in which larger creatures, fuelled by their ocean-grazing, become prey to yet larger ones - until you end up with the complexity we see today.

http://bit.ly/2vPhDrP

Seeding the Gut Microbiome Prevents Sepsis in Infants

An oral mix of a pre- and probiotic can decrease deaths from the condition, according to the results of a large clinical trial conducted in rural India.

By Anna Azvolinsky | August 16, 2017

Pinaki Panigrahi, a professor at the University of Nebraska, and his colleagues treated 4,556 full-term newborns in villages in Odisha state in India, where there are high rates of infant death and infectious disease. They found that the synbiotic combination—which costs only $1 per treatment—reduced neonatal sepsis and death by 40 percent, from 9 percent in the placebo arm to 5.4 percent among babies given the experimental treatment.

“This is another report that underscores the importance of gut colonization on the maintenance of optimal immunologic function,” John Marshall, a surgeon at St. Michael’s Hospital in Toronto, Canada,

who studies sepsis and the immune system in adults at the University of Toronto, and who was also not involved in the work, tells *The Scientist*. "The [intervention] is simple, inexpensive, and looks very effective."

Sepsis is a clinical diagnosis of a systemic inflammatory response, due to an infection, that can damage vital organs and lead to death. In developing countries, sepsis remains a major source of morbidity and death in infants, yet the exact numbers are difficult to pin down, according to Panigrahi, because cultures are rarely taken, and the infants are instead diagnosed with a "possible severe bacterial infection" (pSBI).

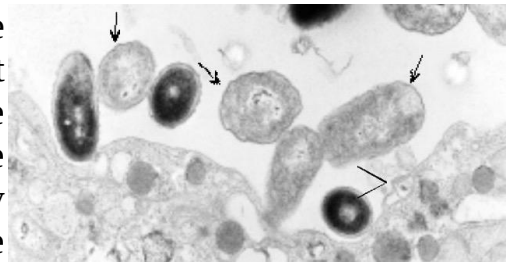
Following a pilot study that demonstrated persistent colonization of *L. plantarum* in the guts of infants given the synbiotic cocktail within the first three days of life, the researchers began the current larger trial, giving either a placebo or the synbiotic orally to two- to four-day-old healthy babies for a total of seven days. The rationale was to aid the colonization of the gut by non-pathogenic, commensal bacteria to set up an optimal immune system that better protects infants in the first few months of life.

The team followed the infants by tracking whether or not they were admitted to local hospitals for bacterial infections or other illnesses over a 60-day period. A total of 319 infants were hospitalized for pSBI and/or sepsis during the trial. Among the hospitalized infants who had a microbial infection, 27 were in the placebo arm and six in the treatment arm. The risk reduction among babies who took the probiotic was 82 percent and 75 percent for Gram-positive and Gram-negative bacterial infections, respectively.

Lower respiratory tract infections were also reduced by 34 percent, from 6.1 percent in the control arm to 4 percent in the experimental arm, an unexpected result, according to Panigrahi.

Lactobacillus plantarum ***(dark-stained cells) and*** **Escherichia coli** ***(arrows) compete to adhere to human colon mucosal cells, a first step in the pathogenesis of sepsis and immunomodulation.*** **Pinaki Panigrahi**

For both Marshall and Andi Shane, who studies pediatric infectious diseases at Emory University School of Medicine and who was not involved in the study, the decrease in respiratory infections suggests that the synbiotic may be altering the nature of the systemic immune response, bolstering immunity against infections other than those arising from the gut. The oral preparation was well tolerated, with only one gastrointestinal adverse episode reported.



The trial took more than 10 years to execute and complete. "Our critics said, 'You will never be able to do this trial because it is too complicated,' which is now a compliment for me," says Panigrahi.

"This is an amazing study because it used a large sample of mostly full-term infants to rigorously assess whether a particular probiotic/prebiotic combination could reduce the incidence of late-onset clinical sepsis in a part of the world where there is a very high disease burden from such infections," says Daniel Tancredi, a statistician in the department of pediatrics at the University of California, Davis who was not involved in the trial and who penned an accompanying perspective.

Two remaining questions, according to Shane, are whether premature infants may also benefit from the synbiotic and whether breastfeeding, together with the synbiotic, plays a role in infection prevention.

For Panigrahi, the ultimate goal is not just sepsis prevention but prevention of all kinds of diseases with probiotics, particularly in the context of the growing problem of antibiotic resistance and the rise in inflammatory disorders around the world.

The team would now like to test whether the same or other synbiotics may work as a preventive measure against infant sepsis, and acquisition of antibiotic-resistant bacteria, in other parts of the world.

"Neonatal sepsis is a condition with notable morbidity and mortality and is an area that we have not been as successful in combatting as we

have in other areas of child health," writes Shane in an email to *The Scientist.* "Studies such as this one with a rigorous and creative approach are beneficial and while it is important to understand mechanisms, clinical outcomes may be just as, if not more relevant."

P. Panigrahi et al., "A randomized synbiotic trial to prevent sepsis among infants in rural India," Nature, doi:10.1038/nature23480, 2017.

http://bit.ly/2wqXpXH

Lyme disease test distinguishes ticks from crossed wires

A method to accurately diagnose the common vector-borne disease could reduce symptoms being mistaken for other crippling conditions.

Andrew Masterson

A black-legged tick (Ixodes scapularis) of the sort that can carry Lyme disease.
Centres for Disease Control

Scientists in the US have developed a test to more accurately diagnose Lyme disease, a condition transmitted by black-legged ticks (*Ixodes scapularis*) infected by a bacterium called *Borrelia burgdorferi*.

The new test, described in a paper in *Science Translational Medicine*, is important because Lyme disease is the most common vector-borne illness in Europe and North America. In the US alone there are an estimated 300,000 cases each year. However, false-positive diagnoses are common because the symptoms closely resemble those of another tick-transmitted condition, Southern Tick-Associated Rash Illness (STARI).

It must be noted that the test, devised by a team led by John Belisle from Colorado State University, applies only to "classical" Lyme disease, a well-described condition that in the US is almost completely endemic to just 14 states, produces fever, rash, facial paralysis, and arthritis, and responds well to antibiotics.

Another alleged condition, dubbed "chronic" or "late stage" Lyme disease, is the centre of a multi-million dollar treatment industry in the US and elsewhere. However, evidence for the existence of the condition is strongly contested.

Recommended Cures deemed worse than misdiagnosed chronic Lyme disease

In a February editorial in *The American Journal of Medicine*, for instance, Yale University epidemiologist Eugene Shapiro described it as "persistent, unexplained subjective symptoms, with no documented history of Lyme disease and without credible laboratory evidence – past or present – of infection with *Borrelia burgdorferi*."

The test for standard Lyme disease developed by Belisle and colleagues distinguishes biomarkers arising from changes to metabolite levels. The changes differ between Lyme disease and STARI, enabling more reliable identification.

"The focus of our efforts is to develop a test that has a much greater sensitivity, and maintains that same level of specificity," Belisle says. "We don't want people to receive unnecessary treatment if they don't have Lyme disease, but we want to identify those who have the disease as quickly as possible."

People found not to have Lyme disease but STARI instead face a harder road back to health. The cause of the illness remains unknown, and treatment by antibiotics, while standard, is thought to be pointless.

The team is now working on adapting the test so it can be applied in community settings, rather than a laboratory.

http://bit.ly/2wqRu5d

This Is Why Taking Fish Medicine Is Truly a Bad Idea

Those who misuse aquatic antibiotics are playing a dangerous game with their health, doctors and veterinarians say

By Maya Wei-Haas smithsonian.com August 16, 2017

Earlier this month, a Tweet from author Rachel Sharp alerted the Internet to a disturbing trend: Some people were resorting to taking fish antibiotics to cure their ailments. Yes, *fish antibiotics*. Sharp's Tweet, which quickly went viral, included a screenshot of several thinly veiled Amazon reviews left by humans who were clearly using the aquatic pet medicine Moxifish on themselves.

Naturally, the Internet was appalled. But few stopped to ask: what's actually so wrong with taking fish antibiotics?

It's not quite as crazy as it sounds. Fish are given many of the same antibiotics as humans—amoxicillin, ciprofloxacin, penicillin and more—sometimes even in the same doses. These pills, which are intended to be dissolved in fish tanks and be absorbed through fishes' skin, can also look extremely similar to the human versions. And while a trip to the doctor can rack up hundreds of dollars for someone who doesn't have insurance, a bottle of 30 500mg capsules of Moxifish costs just $29.95 from the supplier, Fishceuticals.

But there are a few key reasons why taking your fish's drugs is a very bad, no good idea. Let's start at the top.

First, fish antibiotics are completely unregulated. Technically, they should fall under the purview of the Food and Drug Administration, which oversees both human and animal drugs. Those animals including companion animals (dogs, cats, horses) and food animals (cattle, pigs, chickens). Yet no ornamental fish antibiotics are approved by the FDA.

"The antibiotics available in pet stores or online for ornamental fish have not been approved, conditionally approved, or indexed by the FDA, so it is illegal to market them," the FDA said in a statement to *Smithsonian.com*. The statement continued:

If consumers are seeing these products in stores, they should be aware that these products have no assurance of purity, safety or effectiveness. The FDA does not have any information about the unapproved antibiotics sold in pet stores because they have not been evaluated for quality, safety, effectiveness, or purity. We strongly advise people to not substitute them for approved products that are intended for use in humans as prescribed by their health care provider.

Why aren't they regulated? According to some veterinarians, they're simply too small of a problem for the agency to bother with. Pet fish antibiotics make up a tiny fraction of the total amount of antibiotics used, says Samuel Young, a veterinarian and founder of the Uncommon Creatures Mobile Veterinary Services, which treats animals from fish to gila monsters to llamas. Thus, pet fish meds don't pose nearly the same risks as antibiotics used for food animals, which the FDA is currently working to regulate more tightly.

The FDA says that it does not have any data on how prevalent the fish antibiotics problem is. "We are currently looking into these products," representatives wrote in a statement. "FDA considers taking action based on its resources, the risk the product poses, and its public health priorities."

Lacking the stamp of FDA approval, fish meds instead often sport claims that they are pharmaceutical or "USP grade," a supposed quality benchmark set by an independent non-profit called the United States Pharmacopeia. The USP, however, is not a regulatory agency. Though it tests a small number of supplements through its "USP verified" program, it does not otherwise measure the purity or content of drugs for their purported contents.

"I think it's probably mostly B.S." Young says of these grades. "[Companies] are not able to guarantee—or even required to guarantee—what's actually in it, the purity of it, or the actual amount of it. It can be anything."

According to the FDA's website, the agency hopes to someday help make more of the medications given to "minor species," which include fish, legally available and therefore regulated. But for now, Young describes the field of fish medicine as being in its infancy. He likens the situation to the early days of the livestock industry, when farmers could purchase a range of medications without a prescription. "We're still figuring out what works for fish and what kind of diseases

we're treating," he says. But even if fish meds were labeled as human-grade medicines, using them to self-medicate would still be a bad idea.

When a doctor prescribes you antibiotics, the first step is to make sure you're dealing with a bacterial infection by running the proper tests. Antibiotics, which are intended to kill or slow the growth of bacteria that cause infection, are useless against a virus—and you don't want to use them if you don't have to, or it might lead to bacterial resistance.

***The fish antibiotic Fish Mox Forte contains amoxicillin, a type of penicillin. Penicillin comes with different risks and side effects than other classes of antibiotics, and has been known to breed bacterial resistance.* (http://www.fishmoxfishflex.com/)**

The next step is to find out what kind of bacteria you're up against. Even broad spectrum antibiotics work differently to target different kinds of infections. Moxifish, for instance, contains amoxicillin, a type of penicillin. When a fish absorbs this compound through their skin, it travels through the bloodstream until it latches onto a bacteria's rigid cell wall. There, it interferes with wall-building, leading to a build-up of pressure that eventually causes the the cell to burst. Unfortunately, many types of bacteria have grown resistant to penicillin: *Staphylococcus Aureus*, the bacteria commonly responsible for skin infections no longer responds to this class of antibiotics.

Other fish antibiotics, such as API's Erythromycin, are known as macrolides. These compounds destroy bacteria by targeting the protein-building structures of the cells. Without proteins—which act as messengers, structural supports, transporters, storage and more—the cell dies. Another antibiotic class called Quinolones, which include the fish drug Fish Flox, inhibit bacterial cells from copying their DNA, thus preventing the colonies from multiplying. Quinolone are used to treat a range of infections including urinary tract infections, but in recent years many bacteria have begun to develop resistance.

Matching the right antibiotic to the right illness is crucial. "Let's say the antibiotic is correct, that capsule contains the right amount of medicine, and it's a good quality medication and its able to be absorbed into the system," says Wilson E. Gwin, director of the Purdue Veterinary Teaching Hospital Pharmacy. "We don't really know if that's the right drug for what the person is trying to treat. If it's the wrong drug, they can do themselves even more harm."

Choosing the right med is also difficult. Learning the particulars of each antibiotic is "an exhausting part of medical school," says Daniel Morgan, a physician and epidemiologist at the University of Maryland. "It's a bit like learning verb tenses in a language."

So what if you skip the doctor, take a gamble and choose wrong? Well, each drug comes with its own set of potential side effects and allergic reactions. Taking amoxicillin while suffering a viral infection such as mono, for instance, can cause the body to erupt in rashes, says Morgan. Ciprofloxacin, previously a go-to for UTIs and sinus infections, has come under recent scrutiny for causing lasting damage to tendons, muscles, joints, nerves and the central nervous system. Many other antibiotic classes come with their own unpleasant effects.

And even choosing correctly doesn't guarantee success.

There's a reason that bacterial resistance is a major public health problem: Bacteria are hardy foes that adapt rapidly to the changing environment of you. Sometimes, when they divide, they end up with useful random mutations, which they can pass down to future bacterial generations in a matter of hours. Other times, they get genes that are transferred from already resistant bacteria. "As a result, each new progeny becomes a resistant one and a potential donor of resistance traits to new recipient bacteria," writes Stuart B. Levy, a microbiologist and drug resistance expert at Tufts University, in his book *The Antibiotic Paradox.*

Using these processes, the ingenious invaders eventually develop specific adaptations as they multiply that can tackle and even degrade the antibiotics. Some even take on genes that code for tiny "pumps," which actively eject antibiotics from the bacterial cell. "Bacteria are not there to be destroyed; they're not going to give up," Levy says.

Finally, antibiotics kill off both good and bad bacteria. That means that, to avoid unwanted side effects, it's crucial to take them for the proper amount of time. Ending an antibiotic regimen too soon—or taking one for too long—can both breed further bacterial resistance. Stop too soon and you risk relapse, potentially allowing the microbes causing the disease to proliferate and form resistance. But take antibiotics for too long, and you might be giving the bacteria greater amounts of time to develop ways to elude the meds, recent studies suggest.

In short, you don't want to mess around blindly with your bacteria.

... And yet, humans raiding the medicine cabinets of our finned friends is by no means a new trend. As Levy documents in his book, the practice stretches back to at least the 90's. While investigating antibiotics misuse, Levy describes a conversation with a pet store owner who admitted to taking the fish antibiotics for an infected finger—noting that the practice wasn't unusual among other pet store workers.

In 2002, Army physician Brandon J. Goff wrote a letter to the editor of the *New England Journal of Medicine* documenting an encounter with an unnamed Army Special Forces soldier who came to him with a sinus infection after self-medicating with fish antibiotics from a pet store. The soldier described this source of antibiotics as "common knowledge among all branches of the American Special Forces community," according to Goff.

In the years since, many pet stores have wised up to the trend and quietly removed these antibiotics from their shelves. PetSmart representatives told *Smithsonian.com* that the company had limited its selection to "fish medication in forms that could not easily be consumed by humans. This allows us to provide fish medication to the customers who need it for their aquariums while helping to prevent misuse." (The company did not say when they made the change and did not respond to a follow-up request.) In the last week, Amazon has also removed these antibiotics from their site last week in the wake of Sharp's Tweet; the company declined to comment about the move.

Unfortunately, fish antibiotics are still well within reach. A quick Google search for fish antibiotics pulls up a range of other sources, including Walmart and Thomas Labs. And many Youtube videos, blogs and websites provide guidance for humans seeking out information on taking fish medications for their own personal use. These often target Doomsday preppers—people who stockpile medical supplies and other necessities in case of a society-ending catastrophe—but reddit and other online forums show that the fad isn't limited to those preparing for the end of days.

Sure, some people using fish meds may get lucky, says Morgan. And others may experience few effects, good or ill. But if you are taking fish antibiotics, you're playing a dangerous game, and you're playing it with your health. "People will always find different ways to get at things that they think maybe helpful," says Morgan. "The issue is you need to balance potential harms and benefits … I would guess that there are people out there who have been harmed by doing it."

"We're not talking about a 50 cent or $200 fish—we're talking about a human life," adds Gwin. "You really are taking a chance. Is it worth it?"

http://bit.ly/2x0EzEI

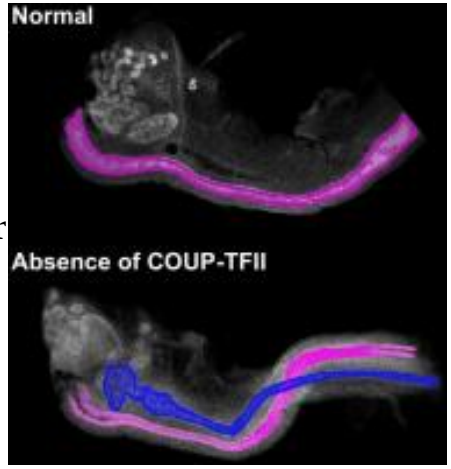
Female mouse embryos actively remove male reproductive systems

NIH researchers reveal novel insights into how sex-specific reproductive systems arise

A protein called COUP-TFII determines whether a mouse embryo develops a male reproductive tract, according to researchers at the National Institutes of Health and their colleagues at Baylor College of

Medicine, Houston. The discovery, which appeared August 18 in the journal Science, changes the long-standing belief that an embryo will automatically become female unless androgens, or male hormones, in the embryo make it male.

Humphrey Hung-Chang Yao, Ph.D., head of the Reproductive Developmental Biology Group at the National Institute of Environmental Health Sciences (NIEHS), part of NIH, studies how male and female mouse embryos acquire their sex-specific reproductive systems. He said all early-stage mammalian embryos, regardless of their sex, contain structures for both male and female reproductive tracts. For a mouse or human to end up with the reproductive tract of one sex after birth, the other tract has to disintegrate.



The normal female mouse embryo (top) contains only the female reproductive tract, highlighted in pink. The female mouse embryo without COUP-TFII (bottom) has both male, in blue, and female reproductive tracts. **NIEHS**

"I learned in graduate school that androgens are needed to maintain the male reproductive tract, but our work finds that maintenance of the male reproductive tract can be achieved without androgen," Yao said.

Since the 1950s, scientists have believed that androgens produced by embryonic testes, promote the survival of the male reproductive tract. The scientific consensus favored a female by default scenario, in which the absence of androgens in female embryos resulted in the breakdown of the male reproductive tract. However, Yao's work demonstrated that female embryos actively promote the elimination of the male tract through the action of COUP-TFII, challenging the female by default theory.

The evidence comes from a mouse model created by Yao and his group. The mice lack COUP-TFII in an embryonic structure that develops into distinct male and female reproductive ducts. To the surprise of Yao and his visiting fellow Fei Zhao, Ph.D., who is also lead author on the paper, female mouse embryos without COUP-TFII displayed both male and female ducts. Control females with COUP-TFII appropriately exhibited only the female duct.

Since Yao and his team did not find any evidence of androgen production in female mice without COUP-TFII, they concluded that the presence of the male reproductive tract in female embryos lacking COUP-TFII occurs without androgen.

The study suggests that COUP-TFII has to be present to block the growth of male reproductive tracts. Without COUP-TFII, the mice are born intersex, or having both male and female reproductive tracts.

"This work is just the beginning and many interesting questions remain unanswered," Zhao said. "We will continue to study how the embryo develops a functional reproductive system."

Yao's group plans to use mouse models to examine how birth defects of the reproductive system originate. These birth defects lead to disorders of sexual development (DSD), which include common defects, such as cryptorchidism, or undescended testicles, as well as the genetic disorders Klinefelter Syndrome and Turner Syndrome.

"Individuals with DSD may have developmental challenges due to the presence of intersex organ systems," said Kenneth Korach, Ph.D., head of the NIEHS Reproductive and Developmental Biology Laboratory. "With its highly novel approach and unexpected findings, Yao's research has important implications for understanding the potential causes of these conditions."

http://bit.ly/2fUnbgO

Noninvasive eye scan could detect key signs of Alzheimer's years before patients show symptoms

Findings offer new hope for early detection and disease monitoring

LOS ANGELES - Cedars-Sinai neuroscience investigators have found that Alzheimer's disease affects the retina -- the back of the eye -- similarly to the way it affects the brain. The study also revealed that an

investigational, noninvasive eye scan could detect the key signs of Alzheimer's disease years before patients experience symptoms.

Using a high-definition eye scan developed especially for the study, researchers detected the crucial warning signs of Alzheimer's disease: amyloid-beta deposits, a buildup of toxic proteins. The findings represent a major advancement toward identifying people at high risk for the debilitating condition years sooner.

The study, published today in JCI Insight, comes amid a sharp rise in the number of people affected by the disease. Today, more than 5 million Americans have Alzheimer's disease. That number is expected to triple by 2050, according to the Alzheimer's Association.

"The findings suggest that the retina may serve as a reliable source for Alzheimer's disease diagnosis," said the study's senior lead author, Maya Koronyo-Hamaoui, PhD, a principal investigator and associate professor in the departments of Neurosurgery and Biomedical Sciences at Cedars-Sinai. "One of the major advantages of analyzing the retina is the repeatability, which allows us to monitor patients and potentially the progression of their disease."

Yosef Koronyo, MSc, a research associate in the Department of Neurosurgery and first author on the study, said another key finding from the new study was the discovery of amyloid plaques in previously overlooked peripheral regions of the retina. He noted that the plaque amount in the retina correlated with plaque amount in specific areas of the brain.

"Now we know exactly where to look to find the signs of Alzheimer's disease as early as possible," said Koronyo.

Keith L. Black, MD, chair of Cedars-Sinai's Department of Neurosurgery and director of the Maxine Dunitz Neurosurgical Institute, who co-led the study, said the findings offer hope for early detection when intervention could be most effective.

"Our hope is that eventually the investigational eye scan will be used as a screening device to detect the disease early enough to intervene and change the course of the disorder with medications and lifestyle changes," said Black.

For decades, the only way to officially diagnose the debilitating condition was to survey and analyze a patient's brain after the patient died. In recent years, physicians have relied on positron emission tomography (PET) scans of the brains of living people to provide evidence of the disease but the technology is expensive and invasive, requiring the patient to be injected with radioactive tracers.

In an effort to find a more cost-effective and less invasive technique, the Cedars-Sinai research team collaborated with investigators at NeuroVision Imaging, Commonwealth Scientific and Industrial Research Organisation, University of Southern California, and UCLA to translate their noninvasive eye screening approach to humans.

The published results are based on a clinical trial conducted on 16 Alzheimer's disease patients who drank a solution that includes curcumin, a natural component of the spice turmeric. The curcumin causes amyloid plaque in the retina to "light up" and be detected by the scan. The patients were then compared to a group of younger, cognitively normal individuals.

Koronyo-Hamaoui and Koronyo also were key authors of the original results, published in the journal Neuroimage in 2011 and first presented at the Alzheimer's Association's International Conference in 2010.

Investigators who contributed to the study include David Biggs, Ernesto Barron, David S. Boyer, Joel A. Pearlman, William J. Au, Shawn J. Kile, Austin Blanco, Dieu-Trang Fuchs, Adeel Ashfaq, Sally Frautschy, Gregory M. Cole, Carol A. Miller, David R. Hinton and Steven R. Verdooner.

The study was funded by the National Institutes of Health/National Institute on Aging, The Marciano Family Foundation and The Saban Family Foundation.

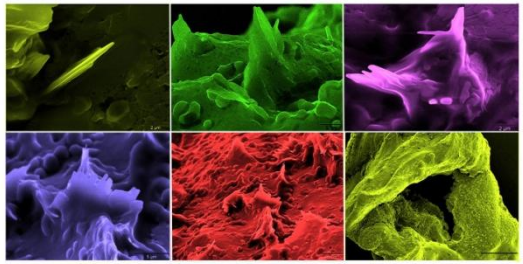
Disclosure: The optical imaging technology in humans was developed by Keith L. Black, MD, Steven Verdooner, Yosef Koronyo, and Maya Koronyo-Hamaoui, PhD. Cedars-Sinai licensed the technology to NeuroVision Imaging LLC, a company in which Black is chairman, founder and equity holder. Maya Koronyo-Hamaoui and Yosef Koronyo are founding members of NeuroVision Imaging. Cedars-Sinai has an equity interest in the company.

http://bit.ly/2fUoZXe

Cholesterol crystals are sure sign a heart attack may loom

89% of patients who suffered a heart attack had an excessive amount of cholesterol crystals

EAST LANSING, Mich. - A new Michigan State University study on 240 emergency room patients shows just how much of a role a person's cholesterol plays, when in a crystallized state, during a heart attack.



The protruding elements seen in the different slides are cholesterol crystals. Those elements are arising from within the artery wall, causing tearing and damage to the artery. The colors have been added for enhancement and imagery. **Michigan State University**

George Abela, lead author and chief cardiologist at MSU, analyzed the material that was obstructing the coronary arteries of patients who had suffered a heart attack and found that 89 percent of them had an excessive amount of these crystallized structures, referred to as cholesterol crystals. The research is now published online in the American Journal of Cardiology.

These crystals are released from plaque that can build up in the heart and is often made up of fat, calcium and other substances as well. When this material hardens over time in the arteries, it's known as atherosclerosis.

"In previous studies, we showed that when cholesterol goes from a liquid to a solid, or crystal state, it expands in volume like ice and water," Abela said. "This expansion inside the wall of the artery can tear it and block blood flow causing a heart attack or stroke."

After heart attack patients entered the emergency room, Abela and his team suctioned out this plaque. They were able to see that clusters of large crystals had formed and were able to break through the plaque and walls of the arteries and then released into the heart. This caused damage by blocking blood flow.

"We now know to what great extent these crystals are contributing to a heart attack," Abela said.

This latest research also reconfirms what Abela discovered in an earlier study that cholesterol crystals activated the production of inflammation molecules, known as Interleukin-1 beta, which aggravate, or inflame, coronary arteries.

"Now that we've shown how extensive cholesterol crystals are irritating and blocking off these arteries, treatments that dissolve these crystals may be used to reduce heart damage," Abela said.

Some of these treatments can include the use of statin drugs - often used to lower one's cholesterol - aspirin and solvents such as alcohol that can be injected in low doses into a vein during a heart attack. Using these options could allow doctors to improve patient outcomes and save more lives.

A recent clinical trial using an already FDA-approved antibody, known as canakinumab, has also shown to block the Interleukin-1 beta inflammation molecule and reduce the chances of a cardiac event.

"Saving heart muscle is the most important aspect of treating a heart attack," Abela said. "So, if we are able to provide patients with better, more targeted treatments, then this could help open up and calm down the aggravated artery and protect the heart muscle from injury."

Abela also added that by simply controlling one's cholesterol by eating a healthy diet, exercising and taking statin medications as needed, could be the best way to prevent these crystals from forming.

http://bit.ly/2wcfUQ5

Vitamin C may encourage blood cancer stem cells to die

Vitamin C may "tell" faulty stem cells in the bone marrow to mature and die normally, instead of multiplying to cause blood cancers.

This is the finding of a study led by researchers from Perlmutter Cancer Center at NYU Langone Health, and published online August 17 in the journal Cell.

Certain genetic changes are known to reduce the ability of an enzyme called TET2 to encourage stem cells to become mature blood cells,

which eventually die, in many patients with certain kinds of leukemia, say the authors. The new study found that vitamin C activated TET2 function in mice engineered to be deficient in the enzyme.

"We're excited by the prospect that high-dose vitamin C might become a safe treatment for blood diseases caused by TET2-deficient leukemia stem cells, most likely in combination with other targeted therapies," says corresponding study author Benjamin G. Neel, MD, PhD, professor in the Department of Medicine and director of the Perlmutter Cancer Center.

Changes in the genetic code (mutations) that reduce TET2 function are found in 10 percent of patients with acute myeloid leukemia (AML), 30 percent of those with a form of pre-leukemia called myelodysplastic syndrome, and in nearly 50 percent of patients with chronic myelomonocytic leukemia. Such cancers cause anemia, infection risk, and bleeding as abnormal stem cells multiply in the bone marrow until they interfere with blood cell production, with the number of cases increasing as the population ages.

Along with these diseases, new tests suggest that about 2.5 percent of all U.S. cancer patients - or about 42,500 new patients each year - may develop TET2 mutations, including some with lymphomas and solid tumors, say the authors.

Cell Death Switch

The study results revolve around the relationship between TET2 and cytosine, one of the four nucleic acid "letters" that comprise the DNA code in genes. Every cell type has the same genes, but each gets different instructions to turn on only those needed in a given cellular context.

These "epigenetic" regulatory mechanisms include DNA methylation, the attachment of a small molecule termed a methyl group to cytosine bases that shuts down the action of a gene containing them.

The back- and-forth attachment and removal of methyl groups also fine-tunes gene expression in stem cells, which can mature, specialize and multiply to become muscle, bone, nerve, or other cell types. This happens as the body first forms, but the bone marrow also keeps pools of stem cells on hand into adulthood, ready to become replacement cells as needed. In leukemia, signals that normally tell a blood stem cell to mature malfunction, leaving it to endlessly multiply and "self-renew" instead of producing normal white blood cells needed to fight infection.

The enzyme studied in this report, Tet methylcytosine dioxygenase 2 (TET2), enables a change in the molecular structure (oxidation) of methyl groups that is needed for them to be removed from cytosines. This "demethylation" turns on genes that direct stem cells to mature, and to start a count-down toward self-destruction as part of normal turnover. This serves as an anti-cancer safety mechanism, one that is disrupted in blood cancer patients with TET2 mutations, says Neel.

To determine the effect of mutations that reduce TET2 function in abnormal stem cells, the research team genetically engineered mice such that the scientists could switch the TET2 gene on or off.

Similar to the naturally occurring effects of TET2 mutations in mice or humans, using molecular biology techniques to turn off TET2 in mice caused abnormal stem cell behavior. Remarkably, these changes were reversed when TET2 expression was restored by a genetic trick.

Previous work had shown that vitamin C could stimulate the activity of TET2 and its relatives TET1 and TET3. Because only one of the two copies of the TET2 gene in each stem cell is usually affected in TET2-mutant blood diseases, the authors hypothesized that high doses of vitamin C, which can only be given intravenously, might reverse the effects of TET2 deficiency by turning up the action of the remaining functional gene.

Indeed, they found that vitamin C did the same thing as restoring TET2 function genetically. By promoting DNA demethylation, high-dose vitamin C treatment induced stem cells to mature, and also suppressed the growth of leukemia cancer stem cells from human patients implanted in mice.

"Interestingly, we also found that vitamin C treatment had an effect on leukemic stem cells that resembled damage to their DNA," says first study author Luisa Cimmino, PhD, an assistant professor in the Department of Pathology at NYU Langone Health. "For this reason, we decided to combine vitamin C with a PARP inhibitor, a drug type known to cause cancer cell death by blocking the repair of DNA damage, and already approved for treating certain patients with ovarian cancer."

Researchers found that the combination had an enhanced effect on leukemia stem cells, further shifting them from self-renewal back toward maturity and cell death. The results also suggest that vitamin C might drive leukemic stem cells without TET2 mutations toward death, says Cimmino, given that it turns up any TET2 activity normally in place.

"Our team is working to systematically identify genetic changes that contribute to risk for leukemia in significant groups of patients," says corresponding author Iannis Aifantis, PhD, professor and chair of the Department of Pathology at NYU Langone Health. "This study adds the targeting of abnormal TET2-driven DNA demethylation to our list of potential new treatment approaches."

Along with Neel, Aifantis and Cimmino, Igor Dogalev, Yubao Wang, Gaëlle Martin, Jingjing Wang, Victor Ng, Bo Xia, Matthew Witkowski, Marisa Mitchell-Flack, Isabella Grillo, Sofia Bakogianni, Delphine Ndiaye-Lobry, Maria Guillamot-Ruano, Robert Banh, Christopher Park, and Aristotelis Tsirigos in the Department of Pathology at NYU School of Medicine and Perlmutter Cancer Center, were study authors. Several authors were also part of the Center for Health Informatics and Bioinformatics at NYU School of Medicine. Also authors were Akihide Yoshimi and Omar Abdel-Wahab with the Human Oncology and Pathogenesis Program at Memorial Sloan-Kettering Cancer Center and Weill Cornell Medical College; Miguel Torres Martín, Maria Figueroa, and Mingjiang Xu at the University of Miami's Miller School of Medicine; and Ross Dickins with the Australian Center for Blood Diseases at Monash University in Australia.

The research was supported by the National Institutes of Health grants RO1 CA216421, R01 CA194923, R01 CA169784, R01 CA133379, R01CA149655, 5R01CA173636 and R01 CA49132, Leukemia & Lymphoma Society grants TRP#6340-11 and LLS#6373-13, New York State Department of Health grant CO030132, and a Feinberg Lymphoma pilot grant, as well as by The Chemotherapy Foundation, The V Foundation for Cancer Research, Alex's Lemonade Stand Foundation for Childhood Cancer, St. Baldrick's Cancer Research Foundation, and the Howard Hughes Medical Institute.

http://bit.ly/2x07aKv

Recently discovered brain chemical 'NPGL' controls appetite and body fat composition

Beneficial for our ancestors; potential cause of obesity pandemic

NPGL, a recently discovered protein involved in brain signalling, has been found to increase fat storage by the body - even when on a low-calorie diet.

In addition, NPGL was shown to increase appetite in response to high caloric food intake, suggesting that perhaps we shouldn't feel so guilty about gorging on junk food from time to time.

This latest discovery by Hiroshima University's Professor Kazuyoshi Ukena, along with collaborators from Japan and UC Berkeley, adds to our understanding of how the brain regulates energy usage and feeding habits - the control mechanisms of which are not yet fully understood.

For most of our evolutionary history, the brain did a seemingly good job of regulating body fat composition, accumulating fat essential for survival during times of famine. Unfortunately, in our modern age of extreme food abundance, overeating is a common occurrence - often leading to obesity.

With the brain still operating in evolutionary survival mode, this latest study, revealing NPGL as a brain chemical that regulates hunger and fat storage in mammals, has broad clinical and societal implications for the study and treatment of obesity and its associated diseases.

Professor Ukena, who first discovered NPGL in chickens - which he observed grew larger irrespective of diet, has also documented the protein in mice and humans. He carried out his latest study by observing how rats respond to increased exposure to the same brain chemical.

Initial observations found that NPGL was present in high concentrations in a specific part of the rat's hypothalamus, the brain's contrimage

ol center for appetite and metabolism, suggesting involvement in bodily energy regulation.

With this in mind, the researchers then carried out experiments on rats fed on two distinct diets for six weeks. One diet was highly caloric - high in fat and sugar. The other diet contained only sufficient calories required for healthy survival. A virus was then prepared that would cause NPGL secreting cells to increase production in the hypothalamus of both sets of rats.

In rats fed the high-calorie diet, body mass, and the proportion of the body composed of fatty tissue, both markedly increased. Interestingly, food intake greatly increased despite animals having an overabundance of calories. In regular-calorie fed rats in which NPGL production was induced, animals did not increase overall body mass and only moderately increased food consumption. However, body fat composition, as with the high calorie diet, increased significantly!

Conversely, when the rats on the high-calorie diet were exposed to an antibody that inhibited NPGL synthesis, the proportion of fatty tissues in the body decreased, further demonstrating a critical role for NPGL in regulating body fat composition. In these rats, food intake and overall body mass remained unchanged.

NPGL levels were also seen to increase and decrease proportionally with blood insulin levels, suggesting that this blood sugar/energy storing hormone harmonizes with the NPGL system to store fat during times of plenty and limit fat production when times are lean.

Taken together, these findings reveal an intricate neurochemical system where signals from the brain and other tissues combine to monitor the body's energetic status and adjust feeding and metabolism accordingly.

As dysregulated energy balance can result in obesity and lead to serious health problems such as diabetes and cardiovascular disease, it is vital that we gain an understanding of the mechanisms that regulate body fat makeup and appetite. This latest research into NPGL has greatly increased our understanding and should guide scientists in finding ways to assist the evolutionary-survivalist human body to adapt to a calorie-intense 21st century environment.

http://bbc.in/2vNEupp

Peanut allergy treatment 'lasts up to four years'

An oral treatment for peanut allergy is still effective four years after it was administered, a study has found.

By Katie Silver Health reporter, BBC News

Children were given a probiotic, with a peanut protein, daily for 18 months. When tested one month later, 80% could tolerate peanuts without any allergic symptoms and after four years, 70% of them were still able to eat peanuts without suffering any side-effects. Food allergies have risen dramatically in recent decades, with peanut allergy one of the most deadly.

Lead researcher Prof Mimi Tang, of Murdoch Childrens Research Institute in Melbourne, said half the children were consuming peanuts regularly while others were only eating them infrequently.

"The importance of this finding is that these children were able to eat peanuts like children who don't have peanut allergy and still maintain their tolerant state, protected against reactions to peanuts," she said.

Prof Tang said it was the first time a treatment for peanut allergy had been shown to be effective for this long.

The probiotic used is called *Lactobacillus rhamnosus,* which has been associated with preventing certain allergic symptoms.

When is it safe to eat peanuts?

- ***There is often confusion about when peanuts are safe as the guidelines used to advocate avoidance***
- ***Peanuts are now thought to be safe in pregnancy***
- ***If there is no family history of allergies or eczema then health officials say peanut butter and other ground or crushed nuts are OK after six months***
- ***If there is a heightened risk then parents should consult a doctor***
- ***This research suggests careful introduction of peanut may help such children, but parents should not do this on their own***
- ***No child under five should eat a whole nut***

The Australian research team now wants to assess whether the treatment has improved the children's quality of life, as some 250 million people worldwide are affected by food allergy - a number which has more than trebled in the last 20 years.

Peanut allergy, which is one of the most common causes of death from food allergy, has increased at the greatest rate.

Prof Tang said the findings, published in The Lancet Child & Adolescent Health, suggest "the exciting possibility that tolerance is a realistic target for treating food allergy".

She added: "This is a major step forward in identifying an effective treatment to address the food allergy problem in Western societies."

http://bit.ly/2xeQDBo

Oldest Antarctic ice ever found shows climate of 2.7 million years ago

And they didn't even have to drill deep.

Scott K. Johnson - 8/18/2017, 1:32 AM

Antarctic ice cores have recorded an impressive span of climatic history for us, covering the last 800,000 years. But scientists are greedy, always looking to go back *just a little further*. Climate records based on things like seafloor sediment cores already take us much further back, but ice cores can reveal unique details. Groups are currently searching for locations to drill new ice cores that might provide a contiguous record back to over the million-year mark.

But another group has been cheating, and this has allowed them to take a big leap past everyone else. Instead of looking at places where the ice at the bottom might be oldest, they've been looking at places where that oldest ice has been squeezed up to the surface against high points of bedrock. A few years ago, they published data from samples of ice that came back at right about 1 million years old. At a conference on Wednesday, the researchers revealed the fruits of their second attempt—ice as old as 2.7 million years, blowing away their previous record.

The ice is fairly squished up and convoluted, with sections of ice less than 800,000 years old showing up between sections of ice between 1 million and 2.7 million years old—the effort to determine its age requires careful dating based on isotopes of argon. But the researchers are able to measure greenhouse gas concentrations from trapped air bubbles and indicators of past ocean temperature.

One reason these samples are particularly interesting is that Earth's ice age rhythm changed around 1.2 million years ago. The 800,000-year ice core record shows a sequence of ice ages that were each about 100,000 years long. Prior to 1.2 million years ago, the cycle was a little shallower and faster, with ice ages lasting only 40,000 years due to some interaction between the regular cycles in Earth's orbit and our planet's response.

According to a report in *Science*, project member Ed Brook is hopeful that the next trip to Antarctica could yield *even older* ice that clears this latest find by a couple million years.

http://bit.ly/2x1QF0z

Mount Sinai identifies mechanism for resilience in people with high risk of bipolar disorder

Results suggest brain is able to adapt to biological risk of bipolar disorder

New York - Researchers from the Icahn School of Medicine at Mount Sinai have identified a brain mechanism in siblings of bipolar patients that makes them resilient to bipolar disorder. The results suggest that the brain is able to adapt to the biological risk for bipolar disorder and open new avenues in pursuing further research to enhance resilience in those at risk and currently affected.

The study will be published online on August 18th in the American Journal of Psychiatry.

Bipolar disorder, a brain disorder that causes unusual shifts in mood, energy, activity levels, and the ability to carry out day-to-day tasks, affects approximately 5.7 million Americans age 18 and older every year. The disease tends to run in families: siblings of patients with

bipolar disorder are 10 times more likely to develop the illness, compared with the general population. However, most people with a family history of bipolar disorder will not develop the illness.

To identify what makes people at risk for bipolar disorder resilient, investigators examined functional magnetic resonance imaging scans from 78 patients with bipolar disorder, 64 of their unaffected siblings, and a control group of 41 nonrelatives who did not have the disorder. While the siblings showed genetic evidence of abnormal connectivity in brain regions involved in sensation and movement which has been linked to bipolar disease in other studies, they compensated by having hyper-connectivity in the default mode network (DMN) of the brain. This hyper-connectivity was absent in the group with bipolar disorder. The DMN is a network of interacting brain regions known to have activity highly correlated with each other and distinct from other networks in the brain.

"Most of the risk factors for bipolar disorder, including genetic risk, early childhood adversity, and trauma, are not modifiable," said the study's senior author Sophia Frangou, MD, PhD, Professor of Psychiatry at the Icahn School of Medicine at Mount Sinai. "By contrast, this research shows that the brain can modify its connectivity to overcome biological adversity. This gives hope that we can harness this natural brain potential to develop preventive interventions."

Based on these results, the researchers are conducting a series of follow-up experiments to test whether it is possible to rewire at-risk patients' brains by simple computerized tasks that enhance brain connectivity. Initial results suggest that simple interventions may restore the functional architecture of the brain and reduce the severity of symptoms in patients.

This study was supported by grants from the National Institutes of Health; grant MH104284-01A1 Catherine T. MacArthur Foundation, the Alfred P. Sloan Foundation, the Army Research Laboratory and the Army Research Office through contracts W911NF-10-2-0022 and W911NF-14-1-0679, NIMH grant 2R01-DC-009209-11, National Institute of Child Health and Human Development grant 1R01HD086888-01, the Office of Naval Research, and grants BCS-1441502, BCS-1430087, and PHY-1554488 from the National Science Foundation.

http://bit.ly/2wkCAhA

Evolved masculine and feminine behaviour can be inherited from social environment – not just from genes

The different ways men and women behave, passed down from generation to generation, can be inherited from our social environment – not just from genes, experts have suggested.

Rather than the sexes acting differently because of genetic inheritance, the human environment and culture allow for the transfer of some gender-specific behaviour traits from generation to generation.

In an article in the journal Trends in Cognitive Sciences by Cordelia Fine, from the University of Melbourne, John Dupré, from University of Exeter and Daphna Joel from Tel-Aviv University show how new advances in evolutionary theory, and current models of how sex influences the brain, suggest that for some gender-related traits, the interactions between the genetic and hormonal components of sex with other factors create variability between individuals whereas environmental factors supply the stable conditions needed for the reproduction of the trait in each generation.

These two important shifts in scientific thinking point to the possibility that gender roles seen across different generations are sometimes best explained in terms of inherited socio-environmental conditions.

“Even in non-human mammals, adaptive traits that have reliably developed in offspring for thousands of years can disappear within a few generations, if the relevant environmental conditions change,” said Professor Dupré.

“Genetic inheritance continues to be critical for the capacity to quickly learn an adaptive behaviour, but environmental factors that are stable over generations remove any selective pressure for the development of parallel genetic mechanisms.”

The academics used recent thinking from evolution theory and recent findings from studies of the relations between sex and the brain for the article.

As part of another study Professor Joel and colleagues found that human brains are composed of unique mosaics of features, some more common in one sex and some more common in the other.

Professor Joel said: “Masculine and feminine behaviours cannot be explained by the existence of male and female brains, as has previously been suggested. Our research suggests that intergenerational inheritance of gender-specific traits may better be explained by highly stable features of the social environment.”

The article says non-genetic mechanisms may be particularly important in humans because our culture strongly encourages us to have male or female roles. The enormous human capacity to learn also allows for information to be passed from generation to generation.

Professor Fine said: “The conclusion is the need to question the pervasive assumption that it is always biological sex, via its direct action on the brain, that does the ‘heavy lifting’ when it comes to the gender traits we inherit and display.”

Sex-Linked Behavior: Evolution, Stability, and Variability is published in the journal Trends in Cognitive Sciences.

http://bit.ly/2uUM9n3

Seeking the secret ingredient in the original smallpox vaccine

Why does a vaccine originally developed using what was supposedly cowpox virus shows no trace of it?

Smallpox is an infectious disease caused by variola virus that has killed millions of people over the centuries. The disease is characterized by the growth of innumerable bumps that cover the entire body of the patient. The disease is fatal in 30% of cases, but this rate is much higher for hemorrhagic smallpox and flat-type smallpox.

Vaccination against smallpox throughout the 19th and 20th centuries was successful and contributed to the eradication of the disease in 1977, after a successful worldwide campaign (1967-1977) coordinated by the World Health Organization. The vaccine was developed by British physician Edward Jenner in 1796 and the virus circulating in the vaccine was named as vaccinia virus.

Cowpox virus, a cousin of variola virus, causes a mild smallpox-like disease in cows. The story goes that Jenner was told that milkers who acquired the "cow-version" of smallpox were immune to the human version of the disease. Thus, one day Jenner decided to perform a risky experiment. The researcher took pustular material from the lesion of a milker and used it to inoculate a young boy. If the hypothesis that previous cowpox infection protected humans from smallpox proved right, then the boy would not develop smallpox when later challenged with smallpox pustular material. Sure enough the young boy remained immune to smallpox and the experiment was a milestone in the history of the smallpox vaccine. Following this success, vaccination (from the Latin vacca meaning cow) was adopted worldwide as the main strategy to prevent smallpox.

According to this historical account, we could logically expect that the virus found in today's smallpox vaccine would be cowpox. But in fact this is not the case. Virtually all batches of modern smallpox vaccine contain no cowpox virus, but instead what is called vaccinia virus. Full-genome sequencing has revealed that the two viruses are quite different and that one could have not mutated into the other. How to explain, then, that a vaccine originally developed using what was supposedly cowpox virus shows no trace of it? Where and when did the mix-up occur?

It is known that natural cases of cowpox were quite rare in Jenner's time, which may have prompted him to perform the same experiments in humans using horsepox-infected pustular material. Did Jenner in fact play with horsepox virus as well as cowpox virus? If so, what was the role of horsepox virus in the development of the smallpox vaccine? And how to explain the observation that horsepox virus and the Brazilian smallpox vaccine bear great similarity ? The fact that vaccinia virus may cause horsepox in horses adds to the confusion.

These and many other questions surrounding the birth of what is considered the most successful vaccine ever developed are explored in a new study entitled "Revisiting Jenner's mysteries, the role of the Beaugency lymph in the evolutionary path of ancient smallpox vaccines" and conducted by Clarissa Damaso, a professor at the Instituto de Biofísica Carlos Chagas Filho at the Federal University of Rio de Janeiro, Brazil. The study, published on the 18th of August in The Lancet Infectious Diseases, is an in-depth investigation of the mysteries associated with the development of smallpox vaccine, and a rich account of how the vaccine lymph was spread worldwide. According to Damaso, "the intense mixing and exchange of several smallpox vaccine samples that occurred during the 19th century has resulted in an intricate and complex evolutionary relationship involving different types of viruses and lymphs that we are still trying to understand."

Combining the use of modern technology and access to historical records may eventually shed light on all the ingredients added to this mysterious recipe that has no doubt saved millions of people worldwide.

The study was supported by CNPq, Capes, and Faperj, in Brazil.

http://bit.ly/2v34RVr

Dengue Infection Impairs Immune Defense Against Zika

A memory B cell response to Zika virus in dengue-infected patients produced antibodies that were poorly neutralizing in vitro and instead enhanced infection.

By Catherine Offord | August 18, 2017

Previous exposure to dengue virus could dampen a patient's immune response to Zika, and potentially even aid infection, according to recent work carried out by US researchers. In a study published today (August 18) in *Science Immunology*, the team found that an early memory B cell response to Zika infection in patients who had already been exposed to dengue produced weak antibodies against Zika virus in vitro.

"It's an important paper," says Davide Robbiani, who studies cross-reactivity in antibodies for dengue and Zika virus at Rockefeller University, but was not involved in the current study. "It broadens our knowledge of the antibody responses to these viruses and informs how vaccines should be designed."

At the structural level, Zika virus shows substantial similarities to dengue, another mosquito-borne flavivirus that is endemic to many of the regions now at risk from Zika (see map), and research has shown that antibodies from dengue-infected patients are broadly cross-reactive with Zika virus in vitro.

See "Zika and Dengue Immunity: A Complex Relationship"

In particular, Zika shares substantial portions of the viral envelope protein, or E protein, with dengue's four serotypes (DENV1, 2, 3, and 4). This same protein is currently being explored for vaccine development.

CARLA SCHAFFER / AAAS

"Most Zika infections are occurring in people that have pre-existing dengue-specific antibodies, many of which, based on previous studies, you would think would cross-react with Zika," says Laura Walker, the associate director of antibody-discovery company Adimab. "What we

asked was, well, what is the immune response in donors that have these pre-existing antibodies?"

For the current study, Walker and colleagues recruited three recently infected Zika patients living in a region of Colombia where dengue virus is endemic. Preliminary blood tests for the presence of antibodies revealed that all three volunteers had previously been exposed to dengue. The team also took blood samples from a Zika-infected donor in the U.S. who showed no signs of previous dengue infection.

The researchers then measured B cell populations and isolated and characterized hundreds of antibodies from the blood samples of the four donors. They found that the US patient's blood showed evidence of a small B cell response and the presence of antibodies with low affinity for Zika—a typical feature of early immune reactions to a novel virus.

But the Colombian patients' blood showed a much larger B cell response, plus antibodies that were broadly cross-reactive with both Zika and dengue—a result likely attributable to a phenomenon, observed in other viruses such as influenza, known as original antigenic sin (OAS).

"Original antigenic sin refers to the propensity of the immune system to preferentially utilize immune memory," Walker explains. In this case, instead of producing novel and potentially more-specific antibodies for Zika virus, the immune system relies on memory B cells from previous dengue infections to launch an immediate immune response—albeit one that's potentially less effective against new infections.

See "Dengue Antibodies Enhance Zika Infection?"

In line with previous research, the team found that these cross-reactive antibodies were poorly neutralizing and in fact enhanced Zika infection in vitro. This latter result could be due to antibody-dependent enhancement (ADE) that has already been implicated in dengue and Zika infections in mouse models.

In this scenario, "when you have a dengue antibody that's bound to virus, but it's not neutralizing the virus . . . it can facilitate the interaction of the virus with the [target cell]," Walker explains. However, she adds, ADE has not yet been shown to play a role in Zika infection in humans.

See "Anti-Flavivirus Antibodies Enhance Zika Infection in Mice"

The study's findings help make the case that Zika vaccine development should focus on portions of the E protein that do not show substantial overlap with that of dengue virus, in order to avoid triggering the memory B cell response in dengue-exposed patients.

"If you give a vaccine [based on the full-length E protein] to donors that have been exposed to dengue . . . it's likely that their early immune response might be composed of mostly these antibodies that are poorly neutralizing," says Walker. "That's not good news in terms of protection." And because potential Zika vaccines are not generally being tested on dengue-exposed patients, "if there is going to be an issue, we might not even see it in clinical trials," she says.

"The data is very pertinent for the vaccine efforts for Zika," says Jean Lim, a virologist at the Icahn School of Medicine at Mount Sinai in New York City who recently demonstrated ADE occurring in a mouse model of concurrent dengue and Zika infection. While ADE for Zika has yet to be shown in humans, she notes, the results suggest that although "a Zika vaccine may be safe in areas where dengue does not circulate currently, the efficacy of a vaccine administered in dengue-endemic regions would be vastly different."

Encouragingly, Walker's team found that when they followed up with the dengue-infected Zika patients five months later, only about 50 percent of the Zika-attacking antibodies were of the cross-reactive, poorly neutralizing variety. "The other 50 percent, to our surprise, were antibodies that were actually Zika-specific," Walker says. "They didn't recognize any of the serotypes of dengue, and most of them were potently neutralizing. . . . So the original antigenic sin antibodies didn't just take over."

Her group is now studying a class of these Zika-neutralizing antibodies that they were unable to identify in the current study. “We’re collaborating with a group doing structural studies trying to identify where these antibodies are binding,” says Walker. This work, she hopes, “could reveal new targets for rational vaccine design.”

T.F. Rogers et al., “Zika virus activates de novo and cross-reactive memory B cell responses in dengue-experienced donors,”* Science Immunology, *2:eaan6809, 2017.

http://bit.ly/2iqcaaq

Japan launches satellite for better GPS system

Japan on Saturday launched the third satellite in its effort to build a homegrown geolocation system aimed at improving the accuracy of car navigation systems and smartphone maps to mere centimetres.

An H-IIA rocket blasted off at about 2:30 pm (0530 GMT) from the Tanegashima space centre in southern Japan, according to the Japan Aerospace Exploration Agency (JAXA). The rocket successfully released the "Michibiki" No.3 satellite about 30 minutes after launch. The launch was initially scheduled last week but was postponed due to a technical glitch.

Satellite geolocation systems, initially designed for the US military, now power countless civilian applications, from car navigation to internet browsing on mobile phones. Japan relies on the US-operated Global Positioning System (GPS). Saturday's launch was part of a broader plan to build a domestic version with four satellites focusing on the country and wider region. The first satellite was put into orbit in 2010 and the second was launched in June. The fourth is to be launched by March 2018 to start up the service.

The Japan-built system will still need to operate in tandem with GPS. Though GPS is widely used in Japan, having supplementary satellites is important in a country where mountainous terrain and high buildings may interfere with its signals. Michibiki, meaning "guidance" in Japanese, will cover the Asia-Oceania region and is intended for civilian use. Japan plans to boost the number of its satellites in orbit to seven by around 2023.

http://bit.ly/2wtuC55

Sugars in human mother's milk are new class of antibacterial agents

Mother's milk, which consists of a complex and continually changing blend of proteins, fats and sugars, helps protect babies against bacterial infections.

In the past, scientists have concentrated their search for the source of its antibacterial properties on the proteins it contains. However, an interdisciplinary team of chemists and doctors at Vanderbilt University have discovered that some of the carbohydrates in human milk not only possess antibacterial properties of their own but also enhance the effectiveness of the antibacterial proteins also present.

"This is the first example of generalized, antimicrobial activity on the part of the carbohydrates in human milk," said Assistant Professor of Chemistry Steven Townsend, who directed the study. "One of the remarkable properties of these compounds is that they are clearly non-toxic, unlike most antibiotics."

The results were presented Aug. 20 at the annual meeting of the American Chemical Society in Washington DC by doctoral student Dorothy Ackerman and published in the ACS Infectious Diseases journal on Jun. 1 in a paper titled, "Human Milk Oligosaccharides Exhibit Antimicrobial and Anti-Biofilm Properties Against Group B. Streptococcus."

The basic motivation for the research was the growing problem of bacterial resistance to antibiotics, which the Center for Disease Control and Prevention estimates causes 23,000 deaths annually.

"We started to look for different methods to defeat infectious bacteria. For inspiration, we turned to one particular bacteria, Group B Strep. We wondered whether its common host, pregnant women, produces compounds that can either weaken or kill strep, which is a leading cause of infections in newborns worldwide," Townsend said.

Instead of searching for proteins in human milk with antimicrobial properties, Townsend and his colleagues turned their attention to the sugars, which are considerably more difficult to study.

"For most of the last century, biochemists have argued that proteins are most important and sugars are an afterthought. Most people have bought into that argument, even though there's no data to support it," Townsend said. "Far less is known about the function of sugars and, as a trained glycoprotein chemist, I wanted to explore their role."

To do so, the researchers collected human milk carbohydrates, also called oligosaccharides, from a number of different donor samples and profiled them with a mass spectrometry technique that can identify thousands of large biomolecules simultaneously. Then they added the compounds to strep cultures and observed the result under the microscope. This showed that not only do some of these oligosaccharides kill the bacteria directly but some also physically break down the biofilms that the bacteria form to protect themselves.

In a pilot study, Townsend's lab collected five samples. They found that the sugars from one sample nearly killed an entire strep colony. In another sample, the sugars were moderately effective while the remaining three samples exhibited a lower level of activity. In a follow-up study, they are testing more than two dozen additional samples. So far, two broke down the bacterial biofilms and killed the bacteria, four broke down the biofilms but did not kill the bacteria and two killed the bacteria without breaking down the biofilms.

"Our results show that these sugars have a one-two punch," said Townsend. "First, they sensitize the target bacteria and then they kill them. Biologist sometimes call this 'synthetic lethality' and there is a major push to develop new antimicrobial drugs with this capability."

By dosing strep cultures with a mixture of milk sugars and antimicrobial peptides from human saliva, the researchers also showed that the sugars' ability to break down biofilms can also enhance the effectiveness of the other antimicrobial agents that breast milk contains.

In follow-up studies the team has also shown that the milk sugars' antimicrobial activity extends to a number of other infectious bacteria, including two of the six "ESKAPE" pathogens that are the leading cause of hospital infections worldwide.

Townsend is collaborating with colleagues in Vanderbilt's Mass Spectrometry Research Center to identify the specific types of carbohydrate molecules responsible for the antibacterial effects they have discovered.

Also contributing to the research were School of Medicine Fellow Ryan Doster, Associate Professor of Pediatrics Jörn-Hendrick Weitkamp, Associate Professor of Pathology, Microbiology & Immunology David Aronoff and Assistant Professor of Medicine Jennifer Gaddy.

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