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# Cannabis link to relieving intestinal inflammation explained

## *Endocannabinoids help control and prevent intestinal inflammation in mice*

WORCESTER, MA - Reports from cannabis users that the drug reduces the symptoms of inflammatory bowel disease (IBD) may finally be explained by new research from the University of Massachusetts Medical School and the University of Bath showing that endocannabinoids help control and prevent intestinal inflammation in mice.

This is the first-time scientists have reported a biological mechanism to explain why some marijuana users have reported beneficial effects from cannabis on intestine inflammation conditions such as ulcerative colitis and Crohn's disease. Researchers hope that their findings will lead to the development of drugs and treatments for gut disorders, which affect millions of people around the world and are caused when the body's immune defenses mistakenly attack the lining of the intestine.

The findings appear in the Journal of Clinical Investigation.

"There's been a lot of anecdotal evidence about the benefits of medical marijuana, but there hasn't been a lot of science to back it up," said Beth A. McCormick, PhD, vice chair and professor of microbiology & physiological systems at UMass Medical School. "For the first time, we have an understanding of the molecules involved in the process and how endocannabinoids and cannabinoids control inflammation. This gives clinical researchers a new drug target to explore to treat patients that suffer from inflammatory bowel diseases, and perhaps other diseases, as well."

The researchers discovered that gut inflammation is regulated by two important processes, which are constantly in flux and responding to changing conditions in the intestinal environment. The first process, identified in previous scientific research, promotes an aggressive immune response in the gut that destroys dangerous pathogens, but which can also damage the lining of the intestine when immune cells attack indiscriminately.

The second pathway, first described in this paper, turns off the inflammation response via special molecules transported across the epithelial cells lining the gut by the same process already known to remove toxins from these cells into the intestine cavity. Crucially, this response requires a naturally-produced molecule called an endocannabinoid, which is very similar to cannabinoid molecules found in cannabis.

If the endocannabinoid isn't present, inflammation isn't kept in balance and it can run unchecked, as the body's immune cells attack the intestinal lining. McCormick and colleagues believe that because cannabis use introduces cannabinoids into the body, these molecules could help relieve gut inflammation, as the naturally produced endocannabinoids normally would.

"We need to be clear that while this is a plausible explanation for why marijuana users have reported cannabis relieves symptoms of IBD, we have thus far only evaluated this in mice and have not proven this experimentally in humans. We hope, however, that these findings will help us develop new ways to treat bowel diseases in humans" said professor Randy Mrsny from the University of Bath Department of Pharmacy and Pharmacology.

***http://bit.ly/2vIn7WG***

# Amputees feel as though their prosthetic limb belongs to their own body

## *Scientists show that amputees can actually be convinced that the prosthetic hand belongs to their own body*

The famous idiom "seeing is believing" is not enough to help amputees with the use of their prosthetic limb. Many amputees opt out of prolonged use of their prosthetic limb because their missing

limb simply does not fit their prosthesis. In other words, their own perception of the missing limb, or the brain's representation of it, does not match-up with what they see of the prosthesis.

The underlying problem is twofold. Amputees still feel their missing limb, even if it is physically gone, and this ghost limb aka phantom limb is perceived as much smaller that the lost limb. Next, the commercially available prosthetic limb does not yet provide sensory feedback other than what the patient sees, meaning that the patient has no sense of touch from the prosthetic limb and must constantly watch it for correct use.

**Tricking the brain to embody the prosthetic limb**

Now, in a scientific collaboration led by EPFL (Ecole polytechnique fédérale de Lausanne), scientists show that amputees can actually be convinced that the prosthetic hand belongs to their own body. They do this by going beyond the "seeing is believing" idiom based on established research on how the brain identifies what belongs to its own body. Instead of using the sense of sight alone, they used an astute combination of two senses: sight and touch. The results are published today in the *Journal of Neurology, Neurosurgery & Psychiatry*.

"The brain regularly uses its senses to evaluate what belongs to the body and what is external to the body. We showed exactly how vision and touch can be combined to trick the amputee's brain into feeling what it sees, inducing embodiment of the prosthetic hand with an additional effect that the phantom limb grows into the prosthetic one," explains Giulio Rognini of EPFL's Laboratory of Cognitive Neuroprosthetics led by Olaf Blanke, in a collaboration with Silvestro Micera of EPFL and Scuola Superiore Sant'Anna in Italy. "The setup is portable and could one day be turned into a therapy to help patients embody their prosthetic limb permanently."

In two hand amputees, the scientists provided artificial tactile sensations at the tip of the index finger - of the phantom limb - by stimulating the patient's nerve in the stump. At the same time, the patient wore virtual reality goggles which showed the index finger of the prosthetic limb glowing in synchrony with the administered touch sensations. This combination of virtual reality with artificial tactile sensations takes the rubber-hand illusion to another level.

Both patients reported feeling as though the prosthetic hand belonged to their own body. Moreover, when asked to evaluate the position of their hands, both patients felt as though their phantom limb had extended into the prosthetic limb. Previous to the experiment, they both reported that the phantom hand was small and directly connected to the stump, as if the phantom limb had no forearm, a change in size referred to as "telescoping" in scientific jargon. In fact, their phantom limb extended during the experiment, and remained extended for up to 10 minutes afterwards.

The experiment simply requires the patient to passively observe two sensations on the fingertip, the visual glow and the artificial touch happening in synchrony, in order for embodiment and extension of the phantom limb to take place. This is the first time that the principles of multisensory integration, in particular how the brain integrates bodily multisensory information to create the coherent and compelling experience of having a body, have been tailored to provoke embodiment of the prosthetic hand and reduction of telescoping.

**Building upon results from a European-wide collaboration**

The study builds upon research that opened new avenues is prosthetics. In 2014, in a European collaboration led by EPFL, scientists overcame a major hurdle by giving an amputee the ability to feel - in real-time - with the help of their prosthetic hand. Information about touch coming from sensors at the prosthetic fingertips were directly processed and relayed into the nervous system via electrodes that were surgically wired to the stump's main nerves. The potential of this technology is still being explored, and

two years later in 2016, the scientists showed that the enhanced prosthetic technology could even help the same amputee detect differences in texture.

***http://bit.ly/2w8HxYh***

## Platelet-rich plasma does not promote stem cell-mediated cartilage repair

***New study has shown that it does not act by promoting stem cell proliferation or enhance the cartilage formation***

New Rochelle, NY - Platelet-rich plasma (PRP) is believed to provide pain relief and help improve joint function in degenerative joint disease, but a new study has shown that it does not act by promoting stem cell proliferation or enhance the cartilage formation capabilities of mesenchymal stem cells (MSCs). The effects of PRP treatment on cartilage formation and chondrogenesis in the presence of adult human MSCs derived from two different sources are reported in the study published in *Tissue Engineering, Part A*, peer-reviewed journal from Mary Ann Liebert, Inc., publishers. Click here to read the full-text article free on the *Tissue Engineering* website through September 13, 2018.

In the article entitled "Effect of Platelet-rich Plasma on Chondrogenesis of Adipose- and Bone Marrow-Derived Stem Cells," coauthors Jr-Jium Liou, Benjamin Rothrauff, Peter Alexander, and Rocky Tuan, University of Pittsburgh School of Medicine (PA), used MSCs derived from the fat pad of the knee and from the bone marrow. They showed that high concentrations of PRP treatment for long periods of time actually impaired cartilage formation, making it less likely for chondrocyte differentiation from the MSC to occur. This had important implications for the development of future strategies to repair cartilage damaged by injury or disease.

"This article presents a systematic study to elucidate the effects of PRP on the chondrogenic differentiation of adult human MSCs and its potential mechanism of action as a therapeutic adjunct for the treatment of joint diseases," says *Tissue Engineering* Co-Editor-in-Chief Antonios G. Mikos, PhD, Louis Calder Professor at Rice University, Houston, TX.

***http://bit.ly/2KPnljv***

## Blood test could detect kidney cancer up to 5 years earlier

***KIM-1 could indicate whether a person is more likely to develop kidney cancer over the following 5 years***

Scientists have discovered that a marker in the blood could help predict the risk that a person will develop kidney cancer, according to research* published in the journal *Clinical Cancer Research*.

Supported by Cancer Research UK, the IARC and the NIH, the work used samples taken as part of the EPIC** study to examine the blood of 190 people who went on to develop kidney cancer, compared to 190 controls who did not.

They found that measuring levels of a protein molecule in the blood, called KIM-1, could indicate whether a person was more likely to develop kidney cancer over the following 5 years.

The data also showed that the greater the concentration of KIM-1, the higher their risk*** of developing kidney cancer. In people with kidney cancer, KIM-1 levels were also found to be linked with poor survival, as those with the highest levels in their blood were less likely to survive.

In the future, the scientists think that testing for blood KIM-1 levels could be used alongside imaging to confirm suspicions of kidney cancer, or help to rule out the disease.

Dr David Muller, Cancer Research UK-funded co-first author based at Imperial College London, said: "This work is a big step forward; KIM-1 is the only blood biomarker shown prospectively to distinguish between people at high and low risk of kidney cancer. But there's a lot more work to do before we could envisage this in the

clinic. "The next steps are to look more closely at whether KIM-1 levels can help detect tumours that have a good prognosis, so those at an early stage, and to find out if it could be used as a tool to track whether a patient's treatment is working."

Kidney cancer is the 7th most common cancer in the UK and cases are on the rise. When diagnosed at its earliest stage, more than 8 in 10 people will survive their disease for 5 years or more. More than 4 in 10 cases in England are diagnosed at a late stage, however, and just 1 in 10 people survive kidney cancer when diagnosed at the latest stage.

Diagnosing the disease earlier therefore has the potential to boost survival, but the majority of early-stage tumours do not present symptoms and many cases are picked up incidentally during imaging for a range of other health conditions.

Professor Charles Swanton, Cancer Research UK's Chief Clinician, said: "The potential of blood tests for the detection and monitoring of cancers is becoming increasingly apparent, and this work offers further evidence that they could become powerful tools in the clinic. "There is a pressing need to shift kidney cancer diagnoses towards earlier stages, when treatment is more likely to be successful, and this promising research is progress towards that goal. This work is still in early stages, so prospective studies of larger populations are needed before this approach could be widely adopted."

Dr Rupal Bhatt, NIH-funded senior author based at Harvard Medical School, said: "It's now crucial to understand more about how KIM-1 could be incorporated into patients' treatment.

"We're excited about progressing this important work further and testing whether KIM-1 levels could help identify patients who may benefit from additional treatment after surgery, and therefore potentially improve their outlook."

* *Scelo et al. KIM-1 is a blood-based marker for early detection of kidney cancer: a prospective nested case-control study.*

***http://bit.ly/2OBvKct***

## Animal fat on ancient pottery reveals a nearly catastrophic period of human prehistory

***Animal fat on broken pottery from Çatalhöyük finally giving scientists a window into an ancient near miss with catastrophe***

**By Michael PriceAug. 13, 2018 , 3:05 PM**

A bit more than 8000 years ago, the world suddenly cooled, leading to much drier summers for much of the Northern Hemisphere. The impact on early farmers must have been extreme, yet archaeologists know little about how they endured. Now, the remains of animal fat on broken pottery from one of the world's oldest and most unusual protocities—known as Çatalhöyük—is finally giving scientists a window into these ancient peoples' close call with catastrophe.

"I think the authors have done an excellent job," says John Marston, an environmental archaeologist at Boston University who wasn't involved in the current study. "It shows the people of Çatalhöyük were incredibly resilient."

Today, Çatalhöyük is just a series of dusty, sun-baked ruins in central Turkey. But thousands of years ago it was a bustling prehistoric metropolis. From about 7500 B.C.E to 5700 B.C.E., early farmers grew wheat, barley, and peas, and raised sheep, goats, and cattle. At its height, some 10,000 people lived there. Among its more noteworthy features, Çatalhöyük's inhabitants were obsessed with plaster, lining their walls with it, using it as a canvas for artwork, and even coating the skulls of their dead to recreate the lifelike countenances of their loved ones.

Around 6200 B.C.E., climates cooled across the globe. Massive glacial lakes in North America emptied into the Atlantic Ocean, scientists believe, altering sea currents and weather patterns and triggering what's known simply as the 8.2-kiloyear event (referring to its occurrence 8200 years ago).

A team of researchers led by biochemists Mélanie Roffet-Salque and Richard Evershed of the University of Bristol in the United Kingdom and archaeologist Arkadiusz Marciniak at Adam Mickiewicz University in Poznań, Poland, wondered whether Çatalhöyük's farmers left behind any trace of the climate shift. Over the past few years, Marciniak had been digging up fragments of clay pottery (or potsherds) left buried in ancient trash piles, dating from about 8300 to 7900 years ago.

These clay pots were used to store meat, and researchers found relatively well preserved animal fat residue soaked into the porous, unglazed sherds. Extreme drought brought on by the 8.2-kiloyear event would have frizzled feed crops and grazing lands, and cooler winters would have increased animals' food requirements. The combined effect would have been leaner, thirstier livestock, and their fat may have recorded chemical echoes of that dietary stress, the researchers reasoned.

The team used a technique known as gas chromatography–mass spectrometry to identify elemental variants known as isotopes. When the researchers looked at the fat deposits' hydrogen isotopes, something interesting jumped out: In sherds dating to about 8200 years ago—and only those sherds—the ratio of the isotope deuterium, or heavy hydrogen, rose by about 9% in relation to other hydrogen isotopes from the samples. Previous research on the region's climate and plant chemistry has shown that lower precipitation rates correlate with higher ratios of heavy hydrogen, which the livestock would have consumed as they grazed during the drought.

The isotopic signature was thus likely caused by the 8.2-kiloyear event, the researchers report today in the *Proceedings of the National Academy of Sciences*, the first direct archaeological evidence of this phenomenon. By analyzing other fat-soaked pot sherds from sites around the world, the team adds, scientists will for the first time be able to accurately recreate climate conditions for other ancient societies.

"I think this could be a very useful tool indeed," says David Orton, a zooarchaeologist at the University of York in the United Kingdom. "[It's a] a big step forward."

Additional finds from Çatalhöyük reveal how the farmers adapted to the cooler, drier conditions. Animal bones from that time have a relatively high number of cut marks, suggesting they were butchering for every last edible bit. Cattle herds shrunk while goat herds rose, the authors note, perhaps because goats could better handle drought. Çatalhöyük's architecture changed, as well, with the site's iconic, large, communal dwellings giving way to smaller houses for individual families, reflecting a shift toward independent, self-sufficient households.

Although these changes underscore humans' historical resilience in the face of capricious conditions, they also show how even relatively minor climate shifts can fundamentally alter a society, Evershed says. Yet Orton cautions that Çatalhöyük's architecture had been gradually evolving for hundreds of years before the 8.2-kiloyear event, making it difficult to say how much of that was related to changing climate. "It seems that Çatalhöyük was already in a period of fairly rapid change well before the 8.2 event. So while the climatic shift probably fed into and perhaps accelerated these changes, it's certainly not the whole story."

***https://wb.md/2nAUiXB***

## Sulfonylureas: Just Stop

***Switching therapy from metformin to a sulfonylurea increases the risk for adverse outcomes in patients with type 2 diabetes***

**Charles P. Vega, MD**

Hello. I'm Dr Charles Vega, and I am a clinical professor of family medicine at the University of California at Irvine. Welcome to Medscape Morning Report, our 1-minute news story for primary care.

Switching therapy from metformin to a sulfonylurea increases the risk for adverse outcomes in patients with type 2 diabetes, according to a new study of 77,000 patients in the UK Clinical Practice Research Datalink.

Patients taking sulfonylureas as second-line therapy—replacing rather than adding on to metformin—had increased risks for myocardial infarction, all-cause mortality, and severe hypoglycemia compared with those on metformin monotherapy. This was true even when metformin-only patients had suboptimal glycemic control.

This class of drugs is also associated with weight gain, which may contribute to arrhythmias and cardiac ischemia.

Current guidelines downplay the use of sulfonylureas, although they remain the most common second-line agents for type 2 diabetes despite their consistent association with higher cardiovascular risk and the availability of newer classes of medications.

An editorial[1] reminded us that continuing metformin alone and accepting higher A1c targets is preferable to switching to sulfonylureas for both macrovascular outcomes and hypoglycemia.

***References***

*1. McGowan LD, Roumie CL. Sulfonylureas as second line treatment for type 2 diabetes. BMJ. 2018;362:k3041.*

***http://bit.ly/2nyqiLY***

## Passing Star May Have Shaped Early Outer Solar System

***A close flyby of a Sun-mass star several billion years ago could explain some unusual features observed in the outer Solar System.***

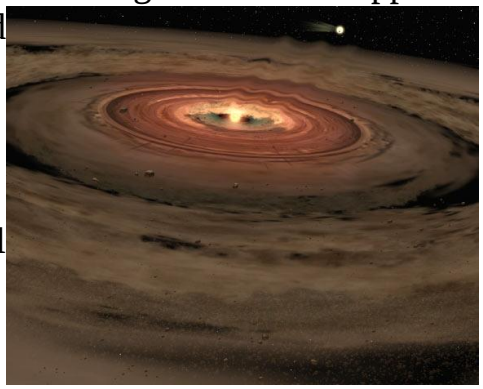
**Aug 13, 2018 by News Staff / Source**

"We've been looking for years at what flybys can do to other planetary systems never considering that we actually might live right in such a system," said lead author Dr. Susanne Pfalzner, of the Max-Planck-Institut für Radioastronomie.

Solar system planets formed from a gas-dust disk. However, there are some properties of our Solar System that are peculiar in this context.

"Due to the flatness of the disk one would expect that the planets orbit in a single plane unless something dramatic happened afterwards," Dr. Pfalzner and colleagues said.

"Looking at the Solar System right to the orbit of Neptune everything seems fine: most planets move on fairly circular orbits and their orbital inclinations vary only slightly. However, beyond Neptune things become very messy."



***An artist's concept of a Sun-mass star passing close to the early Solar System. Image credit: NASA / JPL-Caltech / Sci-News.com.***

"The biggest puzzle is the dwarf planet Sedna, which moves on an inclined, highly eccentric orbit and is so far outside, that it could not have been scattered by the planets there."

"Just outside Neptune's orbit another strange thing happens. The cumulative mass of all the objects dramatically drops by almost three orders of magnitude. This happens at approximately the same distance where everything becomes messy. It might be coincidental, but such conincidences are rare in Nature."

The team suggests that a neighboring star was 'approaching the Sun at an early stage, stealing most of the outer material from the Sun's protoplanetary disk and throwing what was left over into inclined and eccentric orbits.'

Using massive computer simulations, the astronomers checked what would happen when a star passes very close-by and perturbs the once larger disk. "It turned out that the best fit for the outer Solar System comes from a perturbing star which had the same mass as the Sun or

somewhat lighter (0.5-1 solar masses) and flew past at approximately 3 times the distance of Neptune," they said.

"However, the most surprising thing was that a flyby does not only explain the strange orbits of the objects of the outer Solar System, but also gives a natural explanation for several unexplained features of our Solar System, including the existence of two distinct populations of Kuiper Belt objects and the puzzling fact that Neptune has a higher mass than Uranus."

"It is important to keep exploring all the possible avenues for explaining the structure of the outer Solar System," said co-author Dr. Pedro Lacerda, of the Queen's University in Belfast.

"The data are increasing but still too sparse, so theories have a lot of wiggle room to develop."

"There is a certain danger that one theory crystallizes as truth, not because it explains the data better but because of other pressures. Our paper shows that a lot of what we currently know can be explained by something as simple as a stellar flyby."

The study was published in the *Astrophysical Journal*.

*Susanne Pfalzner* et al. *2018. Outer Solar System Possibly Shaped by a Stellar Fly-by.* ApJ *863, 45; doi: 10.3847/1538-4357/aad23c*

***https://bbc.in/2vMLi6d***

## Winged reptiles thrived before dinosaurs

***Palaeontologists have found a new species of pterosaur - the family of prehistoric flying reptiles that includes pterodactyl.***

**By Mary Halton Science reporter, BBC News**

It is about 210 millions years old, pre-dating its known relatives by 65 million years. Named *Caelestiventus hanseni*, the species' delicate bones were preserved in the remains of a desert oasis. The discovery suggests that these animals thrived around the world before the dinosaurs evolved.

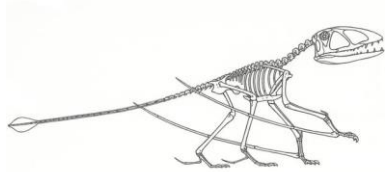
Pterosaurs are the oldest flying vertebrates; the first to crack the evolutionary puzzle of powered flight. As a result of this engineering, their delicate, bird-like skeletons are often found in quite a crushed state.

"Most of them are heavily distorted; literally like roadkill," says lead author Prof Brooks Britt, from Brigham Young University in Utah.

***A 3D printed model of the pterosaur skull discovered in Utah*** **Brigham Young University**

Finding the perfectly preserved skull of this early species provided researchers with a rare opportunity to study its structure.

"The bones are so delicate, you can't take them all the way out of the rock because they would just fall apart," explains Prof Britt. Instead, the team used a CT scanner to build a digital profile of the skull, and then printed a detailed 3D model.



***The pterosaur is a close relative of Dimorphodon, discovered by Mary Anning on Britain's Jurassic Coast*** **Science Photo Library**

This revealed a remarkably complex set of teeth, including sharp fangs protruding from the front of the mouth, and blade-like teeth along the lower jaw.

### Analysis

**Dr Steve Brusatte, University of Edinburgh**

***Finding a pterosaur in an ancient Triassic-aged sand dune is a hugely pleasant surprise.***

***What makes this discovery so remarkable is that very few pterosaurs are known from the entire Triassic Period, which means that we have few fossils that tell the story of how these strange winged reptiles evolved during the first 30 million years of their history.***

***It's a trifecta: a Triassic pterosaur from a new place, preserved in an immaculate way, and found in rocks from an environment that we didn't***

***think they lived in so early during their evolution. What this means is that pterosaurs were already geographically widespread and thriving in a variety of environments very early in their evolution.***

***They were not a fringe group restricted to a few habitats while their dinosaur cousins were rising up, but they were part of the fabric of the Triassic world, along with the earliest dinosaurs.***

***The new species is most closely related to an Early Jurassic-aged British pterosaur, which means that these primitive pterosaur groups not only were widespread, but they survived the great extinction at the end of the Triassic, when volcanoes welled up through the cracks of the fracturing supercontinent Pangaea and caused a runaway global warming event that may be similar to what we're experiencing today.***

The fossils come from a quarry in the Utah desert that was once a bustling oasis, about 210 million years ago.

"This one site we've pulled out 18,000 bones from an area the size of a good sized living room," says Prof Britt. "And there's only one pterosaur."

The specimen had not yet reached adulthood, but had a one-and-a-half metre wingspan. "It was probably the biggest of its day. Among its peers, we have no evidence that any rival came close to that," adds Prof Britt.

The pterosaur may have hunted small vertebrates living in the underbrush around the oasis, and there are signs that it had a throat pouch similar to some modern birds.

***Artist's impression of Caelestiventus hanseni*** **Michael Skrepnick**

Now, the team plan to do further research on the fossil, to better understand how it lived and what it ate.

The findings have been published in Nature Ecology & Evolution.

***http://bit.ly/2BdXaU5***

# Ancient Ceramic Cups Reveal Oldest Direct Evidence of Beer in Mesopotamia

## Researchers are working on resurrecting the recipe

**By Joshua Rapp Learn smithsonian.com**

Archaeologists have long known beer was important in the ancient world, but mainly from writings and drawings—finding actual archaeological evidence of the fermented beverage has been a major challenge.

But archaeologists have now employed a new technique to detect beer residues in nearly 2,500-year-old clay cups dug up in a site in northern Iraq.

“What Elsa [Perruchini] has demonstrated is the chemical signature of fermentation in the vessels that also contains the chemical signatures consistent with barley,” says Claudia Glatz, a senior lecturer in archaeology at the University of Glasgow and a coauthor of a study published recently in the *Journal of Archaeological Science*. “Putting those together is the interpretation that this is barley beer.”

The use of the technique will likely prove groundbreaking, giving archaeologists a chance to find beer at other excavations. But it is also helping Glatz and Perruchini, a PhD archaeology student at the university and the lead author of the study, understand more about the Babylonian Empire’s outer reaches during a period of cultural upheaval.

Archaeologists have long known beer has been around in Mesopotamia from iconography which showed beer drinking and references to the beverage in old accounting texts describing beer given as rations. Among the best known examples are those found in the Sumerian Hymn to Ninkasi dating to roughly 1800 BC. A beer recipe in the form of a poem, the text praises the beer goddess

Ninkasi for soaking malt in a jar and spreading mash on reed mats, among other things.

Further references to beer can be found in the *Epic of Gilgamesh* – a Mesopotamian poem considered the oldest surviving work of literature—in which Enkidu, a "wild man" who grew up in the forest, drinks seven jugs of beer and decides he likes civilization enough to become Gilgamesh's sidekick.

"[Beer] is a quintessential Mesopotamian food stuff," says Glatz. "Everyone drank it but it also has a social significance in ritual practices. It really defines Mesopotamian identities in many ways."

The earliest physical trace of beer dates back to the late fourth millennium BC in present day Iran at a site called Godin Tepe, where archaeologists found what is known as beerstone, a chemical byproduct related to the brewing process and visible to the eye, on ancient ceramic material.

But Perruchini got downright microscopic, examining the chemicals present in the residues clinging to the clay of old cups and jars. She and Glatz are involved with a larger archaeological project at the site, called Khani Masi, exploring the evidence of imperial expansion of the Babylonians into the Diyala River valley. The area, in present day Kurdistan in northern Iraq, is key because it formed a travel hub, connecting the lowlands where some of the world's first cities and imperial powers were formed with the resource-rich Zagros Mountains. "Those are very important long distance exchange routes that are leading through this area," Glatz says.

The excavated section of Khani Masi Perruchini and Glatz are working on dates from 1415 BC to 1290 BC, the late Bronze Age, according to the material evidence such as pottery and the evidence of burial practices excavated. Perruchini was interested in seeing how the people who lived in the area identified culturally, and what better way to get to the bottom of this than examining the food and drink they consumed?

Perruchini says that she first tried to use more traditional chemistry techniques to test the residues, but found the results had been contaminated. "During an excavation, usually people are touching everything, so it's going to leave residuals on it," she says.

One particularly troublesome contaminant comes from the sunscreen often used in sun-drenched digs. As Perruchini notes, some chemical compounds in sunscreen are similar to wine, which could be confusing archaeologists in some cases.

Perruchini decided to take the lab directly to the field, handling freshly excavated bowls or cups with gloves to get more reliable results before anyone else got their hands on them.

"This isn't something that is discussed a whole lot in the organic residue work in archaeology," Glatz says. "So Elsa's method is actually very important in gaining reliable archaeological results – that is not something that has happened so much in the past."

Perruchini then analyzed the distinct compounds of the residues using gas chromatography, a technique that separates the various compounds present in a mixture. Gas chromatography had not been used in archaeology to examine a collection of compounds to identify something like beer, and the method allowed her to get very specific in her analysis. The team could ignore any contemporary chemicals, while an analysis of soil samples taken from outside the clay vessels allowed them to rule out any soil contamination which could have affected the residues over the past two millennia and "only focus on archaeologically significant compounds." They then compared the remaining compounds with residues left from modern-day beer samples and found they matched.

"It's actually very affordable," Perruchini says about the process, adding that other archaeologists should be able to repeat her technique to identity beer or other residues in ancient remains.

"They were really able to get a gold mine of information out of these pots," says Mara Horowitz, an archaeology lecturer at Purchase

College at the State University of New York who was not involved in the recent work. “It looks like they have done what we’ve all been dreaming about doing.”

She adds that it’s a pity that so many cups already excavated can no longer be examined in this way, since they have likely already been contaminated by modern chemicals.

Augusta McMahon, a reader in Mesopotamian archaeology at the University of Cambridge, agrees that many archaeologists – herself included – haven’t been careful enough when handling old pots and other material evidence, other than keeping certain objects within the protocols required for radiocarbon dating. She added the study was “very exciting” and “good science.”

But both McMahon and Horowitz are also interested in the social aspect of the study and what it means.

According to iconography and excavations from sites older than Khani Masi, Mesopotamians usually drank beer from straws in a larger communal jar around the third millennium BC. But in the subsequent millennium, these larger beer jugs start to give way to individual vessels.

“We have this explosion of a very diverse range of drinking cups,” Glatz says, adding that archaeologists in the past assumed the “daintier vessels” were used for wine. But their chemical analysis shows they held beer.

Horowitz says that the shift to these cups gives archaeologists a sense of social processes, as well as marks of status and power depending on the degree of work that went into their design.

“Interactions at a site like Khani Masi can really give us a sense of what’s going on in a local scale,” she says.

Khani Masi was contemporary with the Kassite rule of the Babylonian empire in Mesopotamia and likely under Kassite control. The Kassites, who likely originated from the Zagros Mountains, assimilated many of the previous Mesopotamian cultural traditions and had diplomatic relations with other empires such as the Assyrians and the Egyptians.

“Khani Masi very much looks like another outpost if you like, or a settlement of Kassite origin in some ways,” Glatz says. But their analysis of the cups shows that while it may have sat near the edges of the empire, the locals drank beer similar to other Mesopotamians, indicating that cultural practices from the center of the empire had spread to the fringes.

Beer was important to the Mesopotamians because the malting process helps to preserve the grains for longer, while fermentation increased the grains’ nutritional value.

Or, in the words of McMahon, “It’s what most people drink because the water is not so good.”

Of course, the mild buzz was a draw, too – even the Hymn to Ninkasi notes the wonderful feeling and blissful mood of drinking beer.

Without a fridge handy, the stuff wouldn’t have lasted very long. “Mesopotamians would have been brewing beer constantly,” Glatz says.

The question on everyone’s minds, of course, is how the beer tasted. Perruchini and more of Glatz’s students are attempting to find out by brewing beer using techniques described in the Hymn to Ninkasi and ingredients which they think would lead to residues similar to those they’ve found at Khani Masi.

The trouble is, there were a number of types of beer described in old Mesopotamian texts, whether golden, red or dark ales, and Perruchini and her colleagues are uncertain of all the ingredients. Unlike other researchers who recently tried to reproduce 4,000-year old Hittite beer with tasty results, Perruchini says that they have not even tasted the stuff they brewed in their class yet.

“It smells so terrible,” she says.

http://bit.ly/2BcPRf9

# Can radar replace stethoscopes?

## *FAU researchers develop procedure for touch-free monitoring of heart sounds*

In conjunction with researchers at Brandenburg University of Technology (BTU) in Cottbus and the Department of Palliative Medicine at Universitätsklinikum Erlangen, electronic engineers at Friedrich-Alexander-Universität Erlangen-Nürnberg (FAU) have developed a procedure for reliably detecting and diagnosing heart sounds using radar. In future, mobile radar devices could replace conventional stethoscopes and permanent touch-free monitoring of patients' vital functions could be possible using stationary radar devices.

Along with a white coat, a stethoscope is the hallmark of doctors everywhere. Stethoscopes are used to diagnose the noises produced by the heart and lungs. Used in the conventional way, vibrations from the surface of the body are transmitted to a membrane in the chest-piece and then to the user's eardrum where they are perceived as sounds. Acoustic stethoscopes are comparatively inexpensive and have been used reliably for several decades, but they have one drawback. The diagnosis of heart murmurs, such as the assessment of heart valve function, is carried out subjectively and is directly dependent on the experience of the doctor conducting the examination.

**Radar can measure heart sounds**

In a joint project funded by the Federal Ministry of Education and Research, FAU researchers at the Institute of Electronics Engineering (LTE) have now developed a procedure that could eventually replace conventional phonocardiology. Using a six-port continuous wave radar system, they measured the vibrations on the skin caused by the heartbeat. 'In principle, we're using a similar method to detecting speed in road traffic,' explains Christoph Will, a doctoral candidate at LTE. 'During this process, a radar wave is aimed at the surface of an object and reflected. If the object moves, the phase of the reflecting wave changes. This is used to calculate the strength and frequency of the movement - of the chest in our case.' In contrast to radar systems for traffic monitoring, the biomedical radar system can detect changes in movement that measure a few micrometres, which is an important prerequisite to diagnosing even the smallest anomalies such as insufficiency, stenoses or heart valves that do not close properly.

**As reliable as established measuring methods**

Initial tests were very successful. The test patients were examined in various states of activity such as while resting and after sports and their heart sounds were detected. A direct comparison between the radar system and conventional standard instruments with a digital stethoscope and an electrocardiograph (ECG) showed a very high correlation. 'While diagnosing S1, which is the first heart sound, for example, we achieved a correlation of 92 percent with the ECG,' says Kilin Shi, who is also a doctoral candidate at LTE. 'The correlation was 83 percent in a direct comparison of the signal shapes with the digital stethoscope. That's absolutely reliable.' The researchers say that the slight deviations are caused by the fact that measurements using the radar system and the reference systems cannot be carried out simultaneously on exactly the same place on the body. In addition, the radar system measures a surface area and not a single spot like the stethoscope, which is also a reason for the varying measurement values.

**Touch-free and objective**

The FAU researchers are optimistic that mobile radar systems could replace conventional stethoscopes in diagnosing heart function in the near future. A significant advantage offered by radar is the fact that the values are recorded digitally and are thus not subjective allowing human error to be increasingly ruled out during the diagnosis of

anomalies or diseases. Using biomedical radar systems for automated prophylactic examinations for example in doctors' waiting rooms, at work, or at home, is also feasible.

The researchers are already working on another project for monitoring the vital functions of patients who are seriously ill using stationary radar systems around the clock and without disruptive cables. 'Touch-free and therefore stress-free measurement of vital parameters such as heart sounds has the potential to revolutionise clinical care and research, for example, in palliative medicine,' explains Prof. Dr. Christoph Ostgathe, Head of Palliative Medicine at Universitätsklinikum Erlangen at FAU and co-author of the study. 'For example, we could inform relatives of terminally ill patients more quickly at the beginning of the dying phase, as the radar system immediately detects any changes in patients' health. It would also be possible to detect any painful symptoms in patients who cannot communicate'.

***http://bit.ly/2nF4Uoq***

## Why do women get more migraines?

### *Estrogen and other sex hormones may be responsible for the higher prevalence of migraine in women*

Research published today reveals a potential mechanism for migraine causation which could explain why women get more migraines than men. The study, in *Frontiers in Molecular Biosciences*, suggests that sex hormones affect cells around the trigeminal nerve and connected blood vessels in the head, with estrogens -- at their highest levels in women of reproductive age -- being particularly important for sensitizing these cells to migraine triggers. The finding provides scientists with a promising new route to personalized treatments for migraine patients.

"We can observe significant differences in our experimental migraine model between males and females and are trying to understand the molecular correlates responsible for these differences," explains Professor Antonio Ferrer-Montiel from the Universitas Miguel Hernández, Spain. "Although this is a complex process, we believe that modulation of the trigeminovascular system by sex hormones plays an important role that has not been properly addressed."

Ferrer-Montiel and his team reviewed decades of literature on sex hormones, migraine sensitivity and cells' responses to migraine triggers to identify the role of specific hormones. Some (like testosterone) seem to protect against migraines, while others (like prolactin) appear to make migraines worse. They do this by making the cells' ion channels, which control the cells' reactions to outside stimuli, more or less vulnerable to migraine triggers.

Some hormones need much more research to determine their role. However, estrogen stands out as a key candidate for understanding migraine occurrence. It was first identified as a factor by the greater prevalence of migraine in menstruating women and the association of some types of migraine with period-related changes in hormone levels. The research team's evidence now suggests that estrogen and changes in estrogen levels sensitize cells around the trigeminal nerve to stimuli. That makes it easier to trigger a migraine attack.

However, Ferrer-Montiel cautions that their work is preliminary. The role of estrogen and other hormones in migraine is complex and much more research is needed to understand it. The authors emphasize the need for longitudinal studies focusing on the relationship between menstrual hormones and migraines. Their current work relies on in vitro and animal models, which aren't easy to translate to human migraine sufferers.

Nonetheless, Ferrer-Montiel and his colleagues see a promising future for migraine medication in their current findings. They intend to continue their research using pre-clinical, human-based models which better reflect real patients.

"If successful, we will contribute to better personalized medicine for migraine therapy," he says.

The research is part of a special article collection on cell membrane proteins as targets for drugs.

***http://bit.ly/2OF73Mu***

## Zombie gene protects against cancer -- in elephants

### *Dead gene reborn helps destroy cells with damaged DNA*

An estimated 17 percent of humans worldwide die from cancer, but less than five percent of captive elephants--who also live for about 70 years, and have about 100 times as many potentially cancerous cells as humans--die from the disease.

Three years ago, research teams from the University of Chicago and the University of Utah, working separately, began to unravel why. They knew that humans, like all other animals, have one copy of the master tumor suppressor gene p53. This gene enables humans and elephants to recognize unrepaired DNA damage, a precursor of cancer. Then it causes those damaged cells to die.

Unexpectedly, however, the researchers found that elephants have 20 copies of p53. This makes their cells significantly more sensitive to damaged DNA and quicker to engage in cellular suicide.

In the August 14, 2018 issue of the journal *Cell Reports*, the University of Chicago team describes a second element of this process: an anti-cancer gene that returned from the dead.

"Genes duplicate all the time," said Vincent Lynch, PhD, assistant professor of human genetics at the University of Chicago and the study's senior author. "Sometimes they make mistakes, producing non-functional versions known as pseudogenes. We often refer to these dismissively as dead genes."

While studying p53 in elephants, however, Lynch and colleagues found a former pseudogene called leukemia inhibitory factor 6 (LIF6) that had somehow evolved a new on-switch. LIF6, back from the dead, had become a valuable working gene. Its function, when activated by p53, is to respond to damaged DNA by killing the cell. The LIF6 gene makes a protein that goes, quite rapidly, to the mitochondria, the cell's main energy source. That protein pokes holes in the mitochondria, causing the cell to die.

"Hence, zombie," said Lynch. "This dead gene came back to life. When it gets turned on by damaged DNA, it kills that cell, quickly. This is beneficial, because it acts in response to genetic mistakes, errors made when the DNA is being repaired. Getting rid of that cell can prevent a subsequent cancer."

Elephants have eight LIF genes, but only LIF6 is known to be functional. Although it was only recently described, it appears to have been helping elephants and their relatives for a long time.

"We can use the tricks of evolution to try to figure out when this defunct gene became functional again," Lynch said. It seems to have emerged around the time when the fossil record indicates that the small groundhog-sized precursors of today's elephants began to grow bigger. This started about 25 to 30 million years ago. This supplementary method of suppressing cancer may have been a key element enabling enormous growth, which eventually led to modern elephants.

There are significant and lasting benefits to being huge. Small animals, for example--mice, squirrels, groundhogs--get eaten all the time, mostly by larger animals. But "if you are enormous, such as an elephant or a whale, nothing is going to mess with you," Lynch said. There are tradeoffs, however. Bigger animals have vastly more cells, and they tend to live longer, which means more time and opportunities to accumulate cancer-causing mutations. When those cells divide, their DNA makes copies of itself. But those copies don't match the original. Errors get introduced and the repair process can't catch up.

"Large, long-lived animals must have evolved robust mechanisms to either suppress or eliminate cancerous cells in order to live as long

as they do, and reach their adult sizes," said study co-author Juan Manuel Vazquez, a doctoral candidate in the Lynch laboratory.

These huge animals thus have higher odds of developing cancerous cells. This can also happen on a smaller scale. Taller humans, for example, have a slightly higher incidence of several cancer types than average sized people, and shorter people tend to be at a reduced risk for those cancers.

LIF6, the study authors suggest, was "reanimated sometime before the demands of maintaining a larger body existed." It helped enable the growth of animals that were the size of a 10-pound groundhog into majestic creatures that can weigh more than 15,000 pounds. It was "permissive for the origin of large bodies," the authors note, "but not sufficient."

Exactly how LIF6 induces apoptosis, however, remains unclear. This will be "the focus of continued studies," the authors wrote.

*The University of Chicago funded this study through a new lab startup account to Lynch. Additional authors were Michael Sulak and Sravanthi Chigurupati.*

***http://bit.ly/2ODUKQx***

## Byproducts of 'junk DNA' implicated in cancer spread

### *Emerging class of RNAs keep tumor-promoting genes turned on*

The more scientists explore so-called "junk" DNA, the less the label seems to fit.

Only an estimated two percent of the human genome encodes for functional proteins that carry out normal biological processes. The remaining approximately 98 percent--the "junk DNA"--has for many years been considered a useless artifact. Some junk DNA has been shown to be transcribed into RNA molecules that support cellular functions, including transfer RNAs (tRNAS) and microRNAs (miRNAs), while the remaining noncoding RNA has continued to be considered nonfunctional "junk" RNA.

Previous work by researchers at the University of California San Diego in Assistant Professor Shannon Lauberth's lab uncovered several thousand enhancer RNAs (eRNAs) that are robustly produced in colon cancer cells in response to chronic immune signaling. eRNAs are a recently identified class of noncoding RNAs and their identification has begged the interesting question of whether they are functional in the cell. Now, members of the Lauberth team have revealed that eRNAs play a significant role in cancer dissemination.

Publishing their results in Nature Structural and Molecular Biology, UC San Diego graduate student Homa Rahnamoun, Lauberth and their colleagues found that eRNAs have a direct role in the activation of genes that are important for tumor development. This eRNA role is facilitated by the ability of the eRNAs to directly interact with BRD4, a protein known as a cancer disseminator. BRD4 has been recognized as a promising target in cancer and several small molecules developed to act against BRD4 are under active clinical investigations.

"Our findings reveal that eRNAs are key regulators of cancer by acting to reinforce BRD4 binding and keep it anchored on DNA, which keeps the tumor-promoting genes turned on at high levels," said Lauberth. "Interestingly, when we deplete several of these eRNAs, we can significantly reduce the expression of the tumor-promoting genes that the eRNAs and BRD4 are co-regulating."

Now that we see that eRNAs impact BRD4 function, we have to rethink the way that we therapeutically target BRD4, Lauberth says. "Taken together, our findings are consistent with the emerging notion that eRNAs are functional molecules, rather than merely reflections of enhancer activation or simply transcriptional noise... So this is going to transform the way that we think about 'junk RNA' and the regulation of gene expression in the context of the human cell."

Future studies in the Lauberth lab will explore mechanisms of eRNA synthesis and function in gene regulation and the methods necessary to target eRNAs in order to halt their cancer-promoting mechanisms.

*On Aug. 1 the Lauberth lab was awarded a National Institute of General Medical Sciences (NIGMS) Maximizing Investigator's Research Awards for Early Stage Investigators (MIRA) to fund eRNA research for the next five years. MIRA grants aim to bring innovation and risk-taking back to basic medical research.*

*Coauthors of the research include Jihoon Lee, Zhengxi Sun and Hanbin Lu of UC San Diego's Section of Molecular Biology, Division of Biological Sciences; and Kristen Ramsey and Elizabeth Komives of UC San Diego's Department of Chemistry and Biochemistry, Division of Physical Sciences.*

*This research was supported by the UC San Diego Cellular and Molecular Genetics Training Program through an institutional grant from the National Institute of General Medicine (T32 GM007240); a research scholar award from the Sidney Kimmel Foundation for Cancer Research (857A6A), the American Cancer Society (ACS-IRG 70-002) and the University of California Cancer Research Coordinating Committee (CRN-17-420616).*

***http://bit.ly/2P6yfoa***

## Cancer-fighting drugs also help plants fight disease

***Cancer-fighting drugs used on humans can help plants fight disease as well.***

That discovery, by two Washington State University plant pathologists, could help scientists develop new pathways for plants to battle infection, as revealed in a paper in the journal Frontiers in Plant Science.

Lee Hadwiger and Kiwamu Tanaka from the WSU Department of Plant Pathology used anticancer drugs that change the DNA of cancer cells to slow or stop their growth when used in high levels on humans. But when the drugs are used in low levels in plants, they affect a cell's DNA by activating genes used to defend against pathogens.

The researchers applied a wide array of DNA-specific drugs, including actinomycin D, also known as dactinomycin, to pea tissue. There generally were two different results from those applications, with differing mechanisms of action.

First, the plants started producing higher levels of an antimicrobial substance called pisatin, a known marker that shows a plant's defense system is turning on.

Then, the scientists exposed the treated plants to fungal infections. The exposed plants stopped the infection within hours.

Hadwiger and Tanaka don't foresee using anticancer medications on crops, but this discovery helps build a deeper understanding of how the chemicals interact with plant DNA.

"We used these drugs as a tool to understand how plants defend themselves from pathogens," said Hadwiger. "We now understand how these defense genes can be activated and are using that knowledge to develop disease resistance against fungal infections and other pathogens."

**Unusual origins**

This research didn't start with the goal of seeing what happened when you applied anticancer drugs to plants. "We needed a tool to stop the growth process in the plants and knew actinomycin D did that," Hadwiger said.

"We thought we did something wrong because it didn't work at all." Then they used the drug in much smaller concentrations on the pea plants than what is used to fight cancer.

"We finally figured out what was going on with the different reactions based on high and low concentrations," Hadwiger said.

**Similar DNA**

Plant and animal genes are activated in similar ways, so the scientists assumed the drug would work the same on the plants as in humans. But DNA doesn't recognize a drug as anticancer medication, it's just something new altering its makeup.

The plants recognize the chemistry of whatever compound it interacts with. That's why the same compounds act in both plants and animals.

"Cells only recognize the chemistry shot at them," Hadwiger said. "We didn't expect anticancer drugs to help plants fight pathogens. But once we understood the interaction, it made sense."

Tanaka said that while nobody expects to apply chemotherapy drugs on crops, this discovery will have an impact.

"In basic research, when you actually understand the workings or mechanisms of something, you'll be able to apply it to real-world use," Tanaka said. "We think this will have important impacts for growers that will help better fight pathogens in the near future."

*To read more about Hadwiger's research, he has a free online book, http://openaccessbook.com/nonhost-resistance.html, that covers his lab's 50 years of research on disease resistance.*

***http://bit.ly/2BoY6Fl***

## News Clip Linked Coal to Climate Change — 106 Years Ago Today

***A newspaper clip published Aug. 14, 1912, predicts that coal consumption would produce enough carbon dioxide to warm the climate.***

**By Kimberly Hickok, Staff Writer | August 14, 2018 04:37pm ET**

A note published in a New Zealand paper 106 years ago today (Aug. 14) predicted the Earth's temperature would rise because of 7 billion tons of carbon dioxide produced by coal consumption.

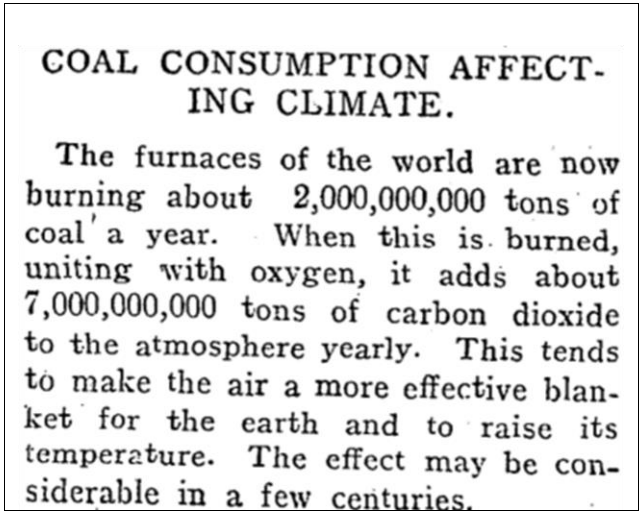
"The effect may be considerable in a few centuries," the article stated.

The clip was one of several one-paragraph stories in the "Science Notes and News" section of The Rodney and Otamatea Times, published Wednesday, Aug. 14, 1912. The paragraph seems to have been originally printed in the March 1912 issue of Popular Mechanics as the caption for an image of a large coal factory.

The image goes with a story titled *"Remarkable Weather of 1911: The Effect of the Combustion of Coal on the Climate — What Scientists Predict for the Future*," by Francis Molena.

In the article, Molena described how carbon dioxide in the air is associated with warmer temperatures, and "since burning coal produces carbon dioxide, it may be inquired whether the enormous use of that fuel in modern times may be an important factor in filling the atmosphere with this substance, and consequently indirectly raising the temperature of the Earth."

When Molena's story was published, scientists had already been predicting the effects of coal combustion on climate for the past few decades.



COAL CONSUMPTION AFFECTING CLIMATE.

The furnaces of the world are now burning about 2,000,000,000 tons of coal a year. When this is burned, uniting with oxygen, it adds about 7,000,000,000 tons of carbon dioxide to the atmosphere yearly. This tends to make the air a more effective blanket for the earth and to raise its temperature. The effect may be considerable in a few centuries.

***A newspaper clip published Aug. 14, 1912, predicts that coal consumption would produce enough carbon dioxide to warm the climate.*** **Fairfax Media/CC BY-NC-SA 3.0 NZ**

Researchers were studying the topic at least as early as 1882, as evidenced by H.A. Phillips' paper titled "Pollution of the Atmosphere," published that year in the journal Nature.

Jeff Nichols, a historian at the University of Illinois at Chicago, told Quartz that he's found many examples of newspaper articles published between 1883 and 1912 that make predictions about how rising carbon dioxide levels alter the climate.

The New York Times, The Philadelphia Inquirer, and The Kansas City Star all published articles about rising carbon dioxide levels affecting the climate more than a hundred years ago, Quartz reported.

Carbon dioxide continues to make up 65 percent of global greenhouse gas emissions, having increased by 90 percent between 1900 and 2010, according to estimates from the Environmental Protection Agency (EPA).

As of 2014, the top carbon dioxide-producing regions were China, the United States, the European Union, India, the Russian Federation and Japan, according to the EPA.

http://bit.ly/2MLSwOd

# Unpublished Egyptian texts reveal new insights into ancient medicine

***Texts contain new and exciting insights into Ancient Egypt***

**August 14, 2018 by Lise Brix, ScienceNordic**

The University of Copenhagen in Denmark is home to a unique collection of Ancient Egyptian papyrus manuscripts.

A large part of the collection has not yet been translated, leaving researchers in the dark about what they might contain.

***Instructions for a 3,500-year-old pregnancy test.*** **Carlsberg Papyrus Collection / University of Copenhagen**

"A large part of the texts are still unpublished. Texts about medicine, botany, astronomy, astrology, and other sciences practiced in Ancient Egypt," says Egyptologist Kim Ryholt, Head of the Carlsberg Papyrus Collection at the University of Copenhagen, Denmark.

An international team of researchers are now translating the previously unexplored texts, which according to one of the researchers, contain new and exciting insights into Ancient Egypt.

"It's totally unique for me to be able to work with unpublished material. It doesn't happen in many places around the world," says Ph.D. student Amber Jacob from the Institute for the Study of The Ancient World at New York University, USA. She is one of four Ph.D. students working on the unpublished manuscripts held in Copenhagen.

## The Egyptians knew about kidneys

Jacob's research focuses on the medical texts from the Tebtunis temple library, which existed long before the famous Library of Alexandria, up until 200 BCE.

In one of the texts, she has found evidence that Ancient Egyptians knew about the existence of kidneys.

"It's the oldest known medical text to discuss the kidneys. Until now, some researchers thought that the Egyptians didn't know about kidneys, but in this text we can clearly see that they did," says Jacob. The papyri also reveal insights into the Egyptian view on astrology.

***This little piece of papyrus is believed to contain a type of oracle question. The author has written two possible outcomes for a situation and asked the gods to indicate which one was the truth.*** **The Papyrus Carlsberg Collection/ University of Copenhagen**

"Today, astrology is seen as a pseudoscience, but in antiquity it was different. It was an important tool for predicting the future and it was considered a very central science," says Ryholt.

"For example, a king needed to check when was a good day to go to war," he says. Astrology was their way of avoiding going to war on a bad day, such as when the celestial bodies were aligned in a particular configuration.

## Egyptians' contribution to science

The unpublished manuscripts provide a unique insight to the history of science, says Ryholt. "When you hear about the history of science, the focus is often on the Greek and Roman material. But we have Egyptian material that goes much further back. One of our medical

texts was written 3,500 years ago when there was no written material on the European continent," he says.

Analysing this 3,500-year-old text is the job of Ph.D. student, Sofie Schiødt from the University of Copenhagen. One side of the manuscript describes unusual treatments for eye diseases, says Schiødt.

**Papyrus text discovered in Germany**

The other side, describes the Ancient Egyptian equivalent of a pregnancy test and scan.

"The text says that a pregnant woman should pee into a bag of barley and a bag of wheat. Depending on which bag sprouts first reveals the sex of her child. And if neither of the bags sprout then she wasn't pregnant," says Schiødt.

***Sofie Schiødt in front of a 3,500-year-old medical papyrus. Mikkel Andreas Beck***

Her research reveals that the ideas recorded in the Egyptian medical texts spread far beyond the African continent.

"Many of the ideas in the medical texts from Ancient Egypt appear again in later Greek and Roman texts. From here, they spread further to the medieval medical texts in the Middle East, and you can find traces all the way up to premodern medicine," she says.

The same pregnancy test used by Egyptians is referred to in a collection of German folklore from 1699.

"That really puts things into perspective, as it shows that the Egyptian ideas have left traces thousands of years later," says Schiødt.

**"Every single contribution is important"**

Translating the unpublished texts is important work, according to Egyptologist Hans-Werner Fischer-Elfert from the Department of Egyptology, University of Leipzig, Germany. "We still have a very fragmented knowledge of the natural sciences in Ancient Egypt. Therefore every singly contribution is important," he says.

"Today there are still a number of sources that theoretically were known by scientists but still sat dormant in various collections around the world without anyone looking at them in detail. Now the time has come to recognise them."

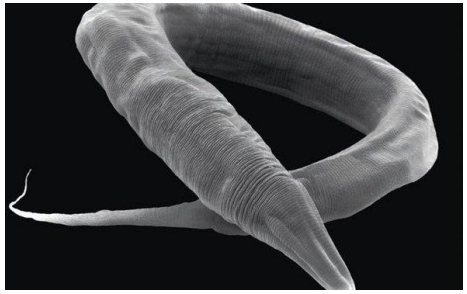
***http://bit.ly/2Ms5J1X***

## Tiny Worms Survive Forces 400,000 Times Stronger Than Gravity on Earth

***New findings give some weight to the idea that life was blasted here from another planet***

**By Katherine Kornei | Scientific American August 2018 Issue**

*Caenorhabditis elegans* would make an ace fighter pilot. That's because the roughly one-millimeter-long roundworm, a type of nematode that is widely used in biological studies, is remarkably adept at tolerating acceleration. Human pilots lose consciousness when they pull only 4 or 5 *g*'s (1 *g* is the force of gravity at Earth's surface), but *C. elegans* emerges unscathed from 400,000 *g*'s, new research shows.



**Credit: Steve Gschmeissner *Science Source***

This is an important benchmark; rocks have been theorized to experience similar forces when blasted off planet surfaces and into space by volcanic eruptions or asteroid impacts. Any hitchhiking creatures that survive could theoretically seed another planet with life, an idea known as ballistic panspermia.

Tiago Pereira and Tiago de Souza, both geneticists at the University of São Paulo in Brazil, spun hundreds of roundworms in a device called an ultracentrifuge.

After an hour, the researchers pulled them out, convinced that the animals would be dead. But they were “swimming freely as if nothing had happened,” Pereira says. More than 96 percent were still alive, and the survivors did not exhibit any adverse physical or behavioral changes. “Life tolerates much more stress than we typically think,” as Pereira puts it. His team's results were published online in May in the journal *Astrobiology*.



Still, this extreme test does not replicate the full brunt of an interplanetary journey, the researchers concede. For one thing, it took roughly five minutes for the ultracentrifuge to build up to these massive *g*-forces—whereas rocks blasted off a planet would reach them within a 1,000th of a second. Nor did the experiment replicate the harsh conditions of space.

“Other factors, such as temperature, vacuum and cosmic radiation, should also be tested,” says Cihan Erkut, a biochemist at the European Molecular Biology Laboratory in Heidelberg, Germany, who was not involved in the research. Pereira says his team's work is a starting point for other experiments to develop “an understanding of the limits of life.”

***https://go.nature.com/2PfkMe3***

## Dilemma over AI and drug patenting already under debate

***Problems foreseen over whether to designate the algorithm or its programmer as the inventor***

**Ross D. King & Patrick Courtney**

Initiatives are already under way to avoid ill-considered moves concerning the impact of artificial intelligence (AI) on drug patenting (see L. Heuer *Nature* **558**, 519; 2018).

Heuer mentions some of the issues. For example, he foresees problems over whether to designate the algorithm or its programmer as the inventor, and whether a drug discovered through machine-learning methods would be patentable.

In the United States, at least, some of these issues are currently clear. For example, US patent law states that “a person shall be entitled to a patent”, and an algorithm is not a person. It also states that “patentability shall not be negated by the manner in which the invention was made”. More generally, it is insufficient to assert that just because an AI could arrive at a particular solution, then that solution must be obvious.

However, a serious problem for pharmaceutical companies is that, according to US law, only people can make the inventive step in patents. In practice, it is likely that algorithms are making many of those steps, raising questions about the validity of these patents in the United States. We welcome efforts to arrive at a consensus over such dilemmas by the robotics research community, intellectual-property professionals, the European Commission and the European Patent Office.

*Nature* ***560***, *307 (2018) doi: 10.1038/d41586-018-05955-8*

***http://bit.ly/2MQ4bvC***

## World's oldest cheese found in Egyptian tomb

***Aging usually improves the flavor of cheese, but that's not why some very old cheese discovered in an Egyptian tomb is drawing attention.***

Instead, it's thought to be the most ancient solid cheese ever found, according to a study published in ACS' journal *Analytical Chemistry*.

The tomb of Ptahmes, mayor of Memphis in Egypt during the 13th century BC, was initially unearthed in 1885. After being lost under drifting sands, it was rediscovered in 2010, and archeologists found broken jars at the site a few years later.

One jar contained a solidified whitish mass, as well as canvas fabric that might have covered the jar or been used to preserve its contents.

Enrico Greco and colleagues wanted to analyze the whitish substance to determine its identity.

After dissolving the sample, the researchers purified its protein constituents and analyzed them with liquid chromatography and mass spectrometry. The peptides detected by these techniques show the sample was a dairy product made from cow milk and sheep or goat milk.

The characteristics of the canvas fabric, which indicate it was suitable for containing a solid rather than a liquid, and the absence of other specific markers, support the conclusion that the dairy product was a solid cheese.

Other peptides in the food sample suggest it was contaminated with *Brucella melitensis*, a bacterium that causes brucellosis. This potentially deadly disease spreads from animals to people, typically from eating unpasteurized dairy products.

If the team's preliminary analysis is confirmed, the sample would represent the earliest reported biomolecular evidence of the disease.

*The research was supported by the Italian Ministry of Education, University and Research, the University of Catania and Cairo University.*

*The abstract that accompanies this study is available here.*

***http://bit.ly/2nHr3CF***

## NIH-funded researchers reverse congenital blindness in mice

### *New technique generates rod photoreceptors that integrate into the retina and brain*

Researchers funded by the National Eye Institute (NEI) have reversed congenital blindness in mice by changing supportive cells in the retina called Müller glia into rod photoreceptors.

The findings advance efforts toward regenerative therapies for blinding diseases such as age-related macular degeneration and retinitis pigmentosa. A report of the findings appears online today in Nature. NEI is part of the National Institutes of Health.

"This is the first report of scientists reprogramming Müller glia to become functional rod photoreceptors in the mammalian retina," said Thomas N. Greenwell, Ph.D., NEI program director for retinal neuroscience. "Rods allow us to see in low light, but they may also help preserve cone photoreceptors, which are important for color vision and high visual acuity. Cones tend to die in later-stage eye diseases. If rods can be regenerated from inside the eye, this might be a strategy for treating diseases of the eye that affect photoreceptors."

Photoreceptors are light-sensitive cells in the retina in the back of the eye that signal the brain when activated. In mammals, including mice and humans, photoreceptors fail to regenerate on their own. Like most neurons, once mature they don't divide.

Scientists have long studied the regenerative potential of Müller glia because in other species, such as zebrafish, they divide in response to injury and can turn into photoreceptors and other retinal neurons. The zebrafish can thus regain vision after severe retinal injury. In the lab, however, scientists can coax mammalian Müller glia to behave more like they do in the fish. But it requires injuring the tissue.

"From a practical standpoint, if you're trying to regenerate the retina to restore a person's vision, it is counterproductive to injure it first to activate the Müller glia," said Bo Chen, Ph.D., associate professor of ophthalmology and director of the Ocular Stem Cell Program at the Icahn School of Medicine at Mount Sinai, New York.

"We wanted to see if we could program Müller glia to become rod photoreceptors in a living mouse without having to injure its retina," said Chen, the study's lead investigator.

In the first phase of a two-stage reprogramming process Chen's team spurred Müller glia in normal mice to divide by injecting their eyes with a gene to turn on a protein called beta-catenin. Weeks later, they injected the mice's eyes with factors that encouraged the newly divided cells to develop into rod photoreceptors.

The researchers used microscopy to visually track the newly formed cells. They found that the newly formed rod photoreceptors looked structurally no different from real photoreceptors.

In addition, synaptic structures that allow the rods to communicate with other types of neurons within the retina had also formed. To determine whether the Müller glia-derived rod photoreceptors were functional, they tested the treatment in mice with congenital blindness, which meant that they were born without functional rod photoreceptors.

In the treated mice that were born blind, Müller glia-derived rods developed just as effectively as they had in normal mice. Functionally, they confirmed that the newly formed rods were communicating with other types of retinal neurons across synapses. Furthermore, light responses recorded from retinal ganglion cells--neurons that carry signals from photoreceptors to the brain--and measurements of brain activity confirmed that the newly-formed rods were in fact integrating in the visual pathway circuitry, from the retina to the primary visual cortex in the brain.

Chen's lab is conducting behavioral studies to determine whether the mice have regained the ability to perform visual tasks such as a water maze task. Chen also plans to see if the technique works on cultured human retinal tissue.

*The study was funded in part by NEI grants R01 EY024986, R01EY021502.*

***Reference***

*Yao K, Qiu S, Wang YV, Park SJH, Mohns EJ, Mehta B, Liu X, Chang B, Zenisek D, Crair MC, Demb JB, and Chen B. 2018. Restoration of vision after de novo genesis of rod photoreceptors in mammalian retinas.* Nature *DOI: 10.1038/s41586-018-0425-3*

***http://bit.ly/2MtLdxX***

## Scientists discover chemical which can kill glioblastoma cells

***Aggressive brain tumour cells taken from patients self-destructed after being exposed to a chemical in laboratory tests, researchers have shown.***

The study could be the first step in tackling cancers like glioblastoma, which led to Dame Tessa Jowell's death earlier this year.

The research, led by the University of Leeds, found that the synthetic chemical, named KHS101, was able to cut the energy source of tumour cells from glioblastoma, leading to the death of the cells.

Published in Science Translational Medicine, the research represents an important step forward in tackling this disease, which is one of the deadliest cancers, with a five-year survival rate of less than¬ five per cent.

Over 2,000 people are diagnosed with glioblastoma in the UK every year, and it has recently been discussed in Parliament as a disease which urgently requires improvements in treatment options.

Funded initially by the Medical Research Council, the new study showed promising results which may lead to the development of a therapy to fight brain cancer in years to come.

Dr Heiko Wurdak, from the University of Leeds who led the international research team, said: "When we started this research we thought KHS101 might slow down the growth of glioblastoma, but we were surprised to find that the tumour cells basically self-destructed when exposed to it.

"This is the first step in a long process, but our findings pave the way for drug developers to start investigating the uses of this chemical, and we hope that one day it will be helping to extend people's lives in the clinic."

The study revealed that the chemical was disrupting the mitochondria and metabolism within the tumour cells, and shutting off the energy supply leading to their self-destruction.

To test whether KHS101 could cross the blood brain barrier in mammals, essential for it to be effective in stopping brain cancers, tumour cells were transferred from humans into mice. The blood brain barrier stops most molecules from entering the brain and severely limits treatment options.

The chemical successfully crossed the blood-brain barrier and significantly decreased tumour growth (by around 50 per cent) in mice treated with KHS101 compared with those given a placebo, leading to an increase in survival. Importantly, normal brain cells were unaffected by the chemical.

The team also reviewed how effective KHS101 would be against the different genetic profiles of cells within a tumour, and between tumours in different patients.

Genetic variation in tumours has complicated efforts to identify treatments in the past, but the team found that all tested variations of glioblastoma subtype cells responded to the treatment.

Professor Richard Gilbertson, Cancer Research UK's brain tumour expert who wasn't involved in the research, said: "Treatment for glioblastoma has remained essentially unchanged for decades, so there is a pressing need for preclinical research like this to identify and characterise potential new drugs.

"While the findings are encouraging, as an experimental chemical, further rigorous testing and refinement of KHS101 is required before trials in people can begin."

Further research into the properties of KHS101 may lead scientists to discover similar drugs which also disturb the energy sources causing self-destruction of tumour cells, and thus broaden the range of treatment options available in the fight against brain tumours.

*The interdisciplinary research group, led by the University of Leeds, included Leeds Teaching Hospitals Trust, Cancer Research UK Cambridge Institute, University of Huddersfield, California Institute for Biomedical Research and University of California, San Francisco.*

*The Medical Research Council, Cancer Research UK, Brain Tumour Research and Support across Yorkshire, Worldwide Cancer Research, the Brain Tumour Charity, the European Commission (FP7), and Engineering and Physical Sciences Research Council contributed to the funding of the study.*

***Notes to editors***

*The paper 'KHS101 disrupts energy metabolism in human glioblastoma cells and reduces tumor growth in mice' is published in* Science Translational Medicine *on 15 August.*

***http://bit.ly/2KZ2LNA***

# Funny bone: ASU survey finds 99 percent of science students appreciate instructor humor

## *Men and women find different humor subjects funny*

There's nothing like a good laugh to lighten a mood, especially when the atmosphere is serious -- like it can be in a science classroom.

Using humor in the classroom has been shown to positively impact student learning, but what if an instructor simply isn't funny? Or what effect does it have on students if a teacher tells an offensive joke?

In a first-of-its-kind study published today in the journal *PLOS ONE*, researchers from Arizona State University found that students appreciate when instructors tell jokes in science class, but that female and male students differ in what topics they find funny or offensive.

Researchers from the School of Life Sciences surveyed students from 25 college science courses about their perceptions of instructor humor. Of the 1,637 respondents, 99 percent say they appreciate instructor humor and believe it improves the classroom experience. Many students also say humor decreases stress, enhances the relationship between students and instructor, and helps them remember what is taught in class. Researchers were fascinated by the high number of students who valued humor.

"I went into [this study] thinking that maybe we shouldn't be joking in the classroom, but I left the study thinking that instructors should use humor as a way to better connect with students," said Sara Brownell, associate professor in the school and senior author of the paper. "But, as might seem obvious, we need to be careful with what we're joking about because we found the topics that instructors are joking about can have different effects on different students."

What if a science instructor tells a joke that's not funny?

The study found that even if teachers tell jokes that fall flat - jokes that students don't find funny - it did not change the students' attention to course content or their relationship with the instructor.

However, if a teacher tells a joke that is offensive and unfunny, more than 40 percent of students say it decreases their ability to pay attention to course content and negatively affects whether an instructor is seen as relatable. Although this can hurt all students, it may have a larger impact on women.

This study found that men and women in science classrooms differed on what topics they thought were funny or offensive. In the survey, science students were presented with hypothetical topics professors could joke about. Male students were more likely to find hypothetical jokes told by the instructor about gender, sexual orientation, religious identity and race funny, while women were more likely to find these same hypotheticals offensive. However, both men and women find three topics to be funny and not offensive: science, college and television.

"More and more studies are starting to paint a picture that the classroom environment is really important for student learning," said Brownell. "Science classrooms and the instructors teaching the science are typically described by students as boring, unapproachable and difficult. So, science instructors who try to be funny can create better learning environments, as long as they are not offensive."

What does this mean for instructors?

"They need to think twice about the type of humor they use," said Katelyn Cooper, lead author and postdoctoral researcher in Brownell's lab. "Is it a joke about cute animals? Probably OK. A pun about science? Probably OK."

**Student researchers**

One unusual aspect of this study is that it was carried out by 16 undergraduate and graduate students enrolled in a class that focused on biology education research. Advertised as a project-based course, the entire class worked on the research project during one semester. The students worked as investigators on the project -- formulating the initial research idea, collecting and analyzing data, and editing the final manuscript.

Taija Hendrix, an undergraduate student researcher at the time of the study, said by taking the course, she was able to see the entire process of research from the very beginning. Hendrix said the possibility of being published was exciting.

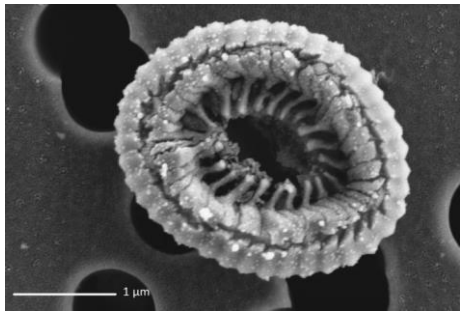
"This class brought together students from all across the School of Life Sciences, some of whom I probably wouldn't have worked with, but in this course, we were all able to work together towards a common goal," said Hendrix. "The instructors told us they wanted our research to be published. For me, this idea was incredible that something I did would be read not only by other students, but scientists. The idea of contributing to the scientific literature before officially being a scientist myself wasn't something I thought I would have the privilege to do. Because of this course I was able to."

Hendrix graduated in May of 2018 with her bachelor's in biological sciences. She is now teaching high school science classes in Avondale, Arizona, and plans on using plenty of humor to help

***http://bit.ly/2OznwBu***

## When viruses infect phytoplankton, it can change the clouds

***Viruses might be responsible for changes in cloud properties***




Microscopic plant-like organisms called phytoplankton are known to support the diversity of life in the ocean. Scientists in Israel now report that one species, *Emiliania huxleyi*, and a virus closely associated with it, might be responsible for changes in cloud properties as well.

***This photograph shows a scanning electron microscope image of an airborne coccolith captured in the laboratory system of this study.*** **Miri Trainic**

When infected, *E. huxleyi* releases its chalky shell into the air, where it acts as an aerosol reflecting sunlight and even affecting cloud creation and movement. The research appears August 15 in the journal iScience.

"Our aim is to better understand the effects that marine ecology can have on atmospheric properties like radiation and cloud formation," says first author Miri Trainic, an Earth scientist at the Weizmann Institute of Science. "This slim air-sea interface controls fluxes of energy, particles, and gases, so if we want to understand climate and climate change, we must understand how microscopic biological activity in the ocean alters this balance."

When the virus EhV infects *E. huxleyi* it forces the phytoplankton to emit bits of its shell into the air. When released, these shells, which are made of chalky calcium carbonate, become part of a class of marine emissions called sea spray aerosols (SSAs). "SSAs are particles emitted into the atmosphere when bubbles in the ocean burst," says Ilan Koren, an atmospheric scientist also at the Weizmann. "They cover 70% of the atmosphere and can serve as cloud condensation nuclei, be surfaces for chemical reactions, and significantly contribute to the Earth radiation budget (the balance of how much solar energy Earth absorbs and how much it emits back into space) because they are very reflective."

When observing a model system in the lab, the researchers found the volume of *E. huxleyi* SSA emissions to surpass anything they expected and the size of the particles themselves to be far larger than they had predicted. More numerous and larger particles will cumulatively be much more reflective than the researchers had anticipated and can strongly influence other cloud properties.

"Although *E. huxleyi* is extremely abundant, responsible for algal blooms covering thousands of kilometers, we didn't expect to measure such a large flux of SSAs emitted from them into the air. Plus, we expected no larger than a 1-micron diameter but measured 3 and 4 microns," says Trainic. "Before this work, we didn't know that such large particles would be so abundant in the marine-atmospheric size distribution."

The researchers were also surprised by the SSAs' complex structure and its effects on aerodynamics. "What we found was that we don't need to look at just the size of the SSA, but also its density," says Assaf Vardi (@vardilab), an environmental scientist at the Weizmann. "These ones are shaped like parachutes; they have an intricate structure of calcium carbonate with lots of space within it, which extends the particle's lifetime in the atmosphere."

From here, the researchers will venture to places like Norway to observe these blooms and their SSA emissions in the natural world. "This study focuses on one species and its virus, but in a broader context it can show that the state of the atmosphere actually depends on the daily interactions in the seawater," Trainic says. "Now we must do our best to further understand that relationship."

*This research was funded by Scott Jordan and Gina Valdez, the De Botton Center for Marine Science, and the Minerva Foundation.*

*iScience, Trainic, et al.: "Infection dynamics of a bloom-forming alga and its virus determine airborne coccolith emission from seawater" https://www.cell.com/iscience/fulltext/S2589-0042(18)30105-6*

***http://bit.ly/2BcQ42b***

## Chemicals Produced by Vegetables Such as Cabbage and Cauliflower Protect Mice from Colon Cancer

***Mice fed a diet rich in indole-3-carbinol (I3C) produced in vegetables of the Brassica genus were protected from gut inflammation & colon cancer***

A new study led by **Francis Crick Institute** researchers shows that mice fed on a diet rich in **indole-3-carbinol** (I3C) — a secondary plant metabolite produced in vegetables of the ***Brassica*** genus, including cabbage, cauliflower, and brussels sprouts — were protected from gut inflammation and colon cancer. The **findings** appear in the journal ***Immunity***.

"We studied genetically modified mice that cannot produce or activate a protein called the aryl hydrocarbon receptor (AhR) — which acts as an environmental sensor, passing signals to immune cells and epithelial cells in the gut lining to protect us from inflammatory responses to the trillions of gut bacteria — in their guts, and found that they readily developed gut inflammation which progressed to colon cancer," said study first author Dr. Amina Metidji, from the Francis Crick Institute.

***The new study offers evidence of how a phytochemical called indole-3-carbinol in the diet can prevent colon inflammation and cancer, by activating the aryl hydrocarbon receptor.*** **Jose Antonio Alba.**

"However, when we fed them a diet enriched with I3C, they did not develop inflammation or cancer. Interestingly, when mice whose cancer was already developing were switched to the I3C-enriched diet, they ended up with significantly fewer tumors which were also more benign."

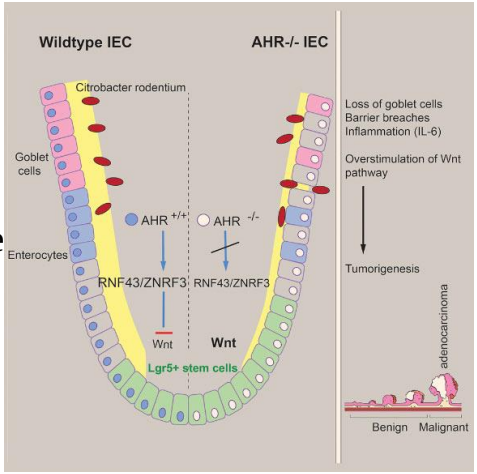
By studying both mice and mouse gut organoids ('mini guts' made from stem cells), Dr. Metidji and colleagues found that AhR is vital for repairing damaged epithelial cells. Without AhR, intestinal stem cells fail to differentiate into specialized epithelial cells that absorb nutrients or generate protective mucus. Instead, they divide uncontrollably which can ultimately lead to colon cancer.

"Seeing the profound effect of diet on gut inflammation and colon cancer was very striking," said study co-lead author Dr. Gitta Stockinger, also from the Francis Crick Institute.

"We often think of colon cancer as a disease promoted by a Western diet rich in fat and poor in vegetable content, and our results suggest a mechanism behind this observation. Many vegetables produce chemicals that keep AhR stimulated in the gut."

"We found that AhR-promoting chemicals in the diet can correct defects caused by insufficient AhR stimulation. This can restore epithelial cell differentiation, offering resistance to intestinal infections and preventing colon cancer."

"These findings are a cause for optimism; while we can't change the genetic factors that increase our risk of cancer, we can probably mitigate these risks by adopting an appropriate diet with plenty of vegetables."




***Metidji* et al *show that deletion of Ahr in intestinal epithelial cells results in a defective barrier and unrestricted proliferation of intestinal stem cells (ISCs), culminating in malignant transformation. Activation of AHR by dietary ligands guards the ISC niche and maintains intestinal barrier homeostasis.***
**Metidji *et al*, doi: 10.1016/j.immuni.2018.07.010.**

As well as correcting altered AhR dependent gene expression, dietary I3C also had a surprising effect on unmodified mice with normal AhR expression. While normal mice fed on standard or I3C-enriched food did not develop tumors during the study, those fed on a 'purified control diet' did.

"Normal mice on the purified control diet developed colon tumors within 10 weeks, whereas mice on the standard chow didn't develop any," said study co-lead author Dr. Chris Schiering, of Imperial College London. "This suggests that even without genetic risk factors, a diet devoid of vegetable matter can lead to colon cancer."

"This study in mice suggests that it's not just the fiber contained in vegetables like broccoli and cabbage that help reduce the risk of bowel cancer, but also molecules found in these vegetables too. This adds to the evidence that a healthy diet, rich in vegetables, is

important," said Cancer Research UK's Professor Tim Key, who was not involved in the study.

"Further studies will help find out whether the molecules in these vegetables have the same effect in people, but in the meantime there are already plenty of good reasons to eat more vegetables."

*Amina Metidji* et al. *The Environmental Sensor AHR Protects from Inflammatory Damage by Maintaining Intestinal Stem Cell Homeostasis and Barrier Integrity*. Immunity, *published online August 14,2018; doi: 10.1016/j.immuni.2018.07.010*

***https://bbc.in/2PeI2bI***

## Mystery Russian satellite's behaviour raises alarm in US

***A mysterious Russian satellite displaying "very abnormal behaviour" has raised alarm in the US, according to a State Department official.***

"We don't know for certain what it is and there is no way to verify it," said assistant secretary Yleem Poblete at a conference in Switzerland on 14 August. She voiced fears that it was impossible to say if the object may be a weapon.

Russia has dismissed the comments as "unfounded, slanderous accusations based on suspicions".

The satellite in question was launched in October last year.

"[The satellite's] behaviour on-orbit was inconsistent with anything seen before from on-orbit inspection or space situational awareness capabilities, including other Russian inspection satellite activities," Ms. Poblete told the conference on disarmament in Switzerland.

"Russian intentions with respect to this satellite are unclear and are obviously a very troubling development," she added, citing recent comments made by the commander of Russia's Space Forces, who said adopting "new prototypes of weapons" was a key objective for the force. Ms. Poblete said that the US had "serious concerns" that Russia was developing anti-satellite weapons.

Alexander Deyneko, a senior Russian diplomat, told the Reuters news agency that the comments were "the same unfounded, slanderous accusations based on suspicions, on suppositions and so on". He called on the US to contribute to a Russian-Chinese treaty that seeks to prevent an arms race in space.

**'Lasers or microwaves'**

Space weapons may be designed to cause damage in more subtle ways than traditional weapons like guns, which could cause a lot of debris in orbit, explained Alexandra Stickings, a research analyst at the Royal United Services Institute.

"[Such weapons may include] lasers or microwave frequencies that could just stop [a satellite] working for a time, either disable it permanently without destroying it or disrupt it via jamming," she said.

But it was difficult to know what technology is available because so much information on space-based capabilities is classified, she added.

She also said it would be very difficult to prove that any event causing interference in space was an intentional, hostile action by a specific nation state.

Ms. Poblete's comments were particularly interesting in light of President Donald Trump's decision to launch a sixth branch of the US armed forces named Space Force, added Ms. Stickings.

"The narrative coming from the US is, 'space was really peaceful, now look at what the Russians and Chinese are doing' - ignoring the fact that the US has developed its own capabilities."

A spokesman for the UK's Ministry of Defence said he could neither confirm nor deny any tracking of Russian satellites. "There are a range of threats and hazards to all space capabilities in what is an increasingly contested domain," he said. "These include the development of counter-space weapons by a number of nations.

"The UK is working closely with international allies, including the US, to re-enforce responsible and safe behaviours in space and to build knowledge, understanding and resilience."

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# Liver transplants 'may be unnecessary thanks to new drug treatment'

***A potential treatment for sudden liver failure could cut the need for transplants, say scientists at the University of Edinburgh.***

**By James Gallagher Health and science correspondent, BBC News**

The liver has an incredible natural ability to repair itself, but this can be lost in some injuries including severe drug overdoses.

The therapy is a cancer drug that restores this regenerative potential.

The work is at a very early stage, but the team say alternatives to transplant would have a huge impact on patients.

Around 200 people in the UK have sudden life-threatening liver failure each year.

## 'I needed a new liver'

Student nurse Kara Watt, 21, needed a liver transplant two years ago.

She was on placement at a care home when she started to feel sick and her face started to go yellow.

Tests identified a problem with her liver function which continued to get worse.

She ended up in intensive care in Edinburgh and was told she needed a new liver. It was "a horrible, horrible thing to hear", she said.

It is people like Kara whom scientists hope their work will ultimately help.

## Renewing regeneration

The team started by examining people's livers to see why they lose their ability to regenerate.

They discovered severe injuries rapidly triggered a process called senescence throughout the liver.

Senescence is when the body's cells become old, tired and stop working properly. It is part of ageing, but the researchers showed severe injuries were like "contagious old age" spreading through the organ.

The study, published in Science Translational Medicine, also found a chemical signal that seemed to be responsible.

The researchers then turned to mice and an experimental cancer therapy that could block the signal.

The animals were given a drug overdose that would normally lead to liver failure and death, but with the treatment they survived.

The researchers plan to test the drug on patients soon in the hope it could reduce the need for liver transplants.

## A normal life?

Dr Thomas Bird, one of the researchers at the University of Edinburgh, said: "The beauty of this clinically is even if you have massive injury, if the liver is regrown then you have a normal life after that.

"The most obvious thing to is to do now is clinical trials in patients with acute liver failure and see if we can prevent the need for transplant."

This could reduce pressures on the organ transplant list, but also make a difference to the lives of patients.

Kara is currently taking 13 tablets a day, mostly to prevent her body rejecting her new liver.

She said "If that treatment could help people it would be so beneficial."

The research group, which also includes the Beatson Institute in Glasgow, is also investigating whether senescence spreads beyond only the liver and could be part of the explanation for multiple organ failure.

Lindsay Keir, from the Wellcome Trust, said the study was "important".

She added: "The research so far suggests that a medication could be used to treat this condition, avoiding the need for a liver transplant which is a major operation and reducing the demand on the limited supply of livers available for transplant."

***http://bit.ly/2MlsaXq***

# That stinks! 1 American in 15 smells odors that aren't there

## *NIH study reveals prevalence of and risk factors for phantom odor perception*

Imagine the foul smell of an ash tray or burning hair. Now imagine if these kinds of smells were present in your life, but without a source. A new study finds that 1 in 15 Americans (or 6.5 percent) over the age of 40 experiences phantom odors. The study, published in *JAMA Otolaryngology-Head and Neck Surgery*, is the first in the U.S. to use nationally representative data to examine the prevalence of and risk factors for phantom odor perception. The study could inform future research aiming to unlock the mysteries of phantom odors.

The study was led by Kathleen Bainbridge, Ph.D., of the Epidemiology and Biostatistics Program at the National Institute on Deafness and Other Communication Disorders (NIDCD), part of the National Institutes of Health. Bainbridge and her team used data from 7,417 participants over 40 years of age from the 2011-2014 National Health and Nutrition Examination Survey (NHANES). The NHANES data were collected by the National Center for Health Statistics, which is part of the Centers for Disease Control and Prevention; data collection was partly funded by the NIDCD.

"Problems with the sense of smell are often overlooked, despite their importance. They can have a big impact on appetite, food preferences, and the ability to smell danger signals such as fire, gas leaks, and spoiled food," said Judith A. Cooper, Ph.D., acting director of the NIDCD.

Donald Leopold, M.D., one of the study's authors and clinical professor in the Department of Surgery at University of Vermont Medical Center, Burlington, adds that patients who perceive strong phantom odors often have a miserable quality of life, and sometimes cannot maintain a healthy weight.

Researchers used this NHANES survey question to determine whether participants had experienced phantom odor perception: "Do you sometimes smell an unpleasant, bad, or burning odor when nothing is there?" To explore the correlation between phantom odors and participant characteristics, the researchers looked at participants' age, sex, education level, race/ethnicity, socio-economic status, certain health habits, and general health status.

The ability to identify odors tends to decrease with age. Phantom odor perception, on the other hand, seems to improve with age. One previous study, using data from a community in Sweden, showed that 4.9 percent of people over the age of 60 experience phantom odors, with a higher prevalence in women than men. The present study found a similar prevalence in the over-60 age group, but in examining a broader age range, found an even higher prevalence in ages 40-60. The study also found that about twice as many women as men reported phantom odors, and that the female predominance was particularly striking for those under age 60.

Other risk factors for the onset of phantom odors include head injury, dry mouth, poor overall health, and low socio-economic status. Researchers hypothesized that people with lower socio-economic status may more commonly be exposed to environmental pollutants and toxins, or have health conditions that contribute to phantom odors, either directly or because of medications needed to treat their health conditions.

"The causes of phantom odor perception are not understood. The condition could be related to overactive odor sensing cells in the nasal cavity or perhaps a malfunction in the part of the brain that understands odor signals. A good first step in understanding any medical condition is a clear description of the phenomenon. From there, other researchers may form ideas about where to look further for possible causes and ultimately for ways to prevent or treat the condition," said Bainbridge.

http://bit.ly/2PhsFPR

# Cells agree: What doesn't kill you makes you stronger

## *Salk scientists show that cells adapt to brief stressors by boosting antioxidants and energy production longer term*

LA JOLLA -We've all heard the expression: "what doesn't kill you makes you stronger." Now, research led by a Salk Institute scientist suggests why, at a cellular level, this might be true. The team reports that brief exposures to stressors can be beneficial by prompting the cell to trigger sustained production of antioxidants, molecules that help get rid of toxic cellular buildup related to normal metabolism.

The research, which appeared in the journal *Cell Metabolism* on August 16, 2018, also revealed that short-term stress to cells leads to remodeling mitochondria, the powerhouses of the cell that deteriorate with age, so they generate fewer toxic byproducts. The findings could lead to new approaches to counter the cellular effects of aging, possibly even extending lifespan.

"The novelty of this study is that we've generated a model in which we can turn off antioxidant production in mitochondria but in a reversible way," says Salk Professor Gerald Shadel, the senior author of the paper. "So we were able to induce this stress for specific time windows and see how cells responded."

In the process of converting food into chemical energy, mitochondria produce a chemical called superoxide, which has a critical role in cells but is toxic if it builds up. For this reason, mitochondria also produce an enzyme--superoxide dismutase, or SOD--to convert superoxide to a less toxic form.

Shadel wanted to know how short-term cellular stress caused by mitochondrial superoxide very early in development might affect health later in life. So he led a team of researchers from the Yale School of Medicine and Appalachian State University in developing an approach to turn off the SOD enzyme for short periods of time in order to study how cells and animals responded to the cellular stress of toxic buildup.

In a group of genetically identical mice in utero, half with a molecular "off" switch for SOD experienced brief stress when the enzyme was deactivated. After the mice were born and continued to grow to adulthood, the two groups looked very similar. But liver samples taken when they were four weeks old told a strikingly different story: the mice whose SOD enzyme had been turned off briefly to trigger stress in mitochondria had--surprisingly--higher levels of antioxidants, more mitochondria and less superoxide buildup than the mice who had not experienced stress.

Additionally, cells grown in dishes, half which contained the SOD switch, showed the same results: those that experienced brief periods of stress turned out to be stress resistant and healthier from a cellular perspective.

When the team analyzed which genes were being activated in both the lab dishes and the liver samples of all the mice, they found unexpected molecular pathways at work in the SOD group that were reprogramming mitochondria to produce fewer toxic molecules while simultaneously increaseing the cells' antioxidant capacity.

The work suggests that short-term mitochondrial stress may lead to long-term adaptations (a concept called "mitohormesis") that could keep cells healthy longer, staving off aging and disease. Shadel next plans to study whether the mechanism elucidated here can delay the effects of aging in mammals.

Shadel, who holds the Audrey Geisel Chair in Biomedical Science, adds, "We are excited to test if the unique mitohormesis signaling pathways we will elucidate in this new mouse model can be targeted to prevent common age-related disease like cancer, Alzheimer's and heart disease."

*Other authors included Carly S. Cox, Sharen E. McKay, Marissa A. Holmbeck and Annie J. Tsay of Yale University; Brooke E. Christian of Appalachian State University; and Andrew C. Scortea and Laura E. Newman of Salk.*

http://bit.ly/2L0ws0x

# Scientists discover new method of diagnosing cancer with malaria protein

***New method of diagnosing a broad range of cancers at their early stages by using a malaria protein***

In a spectacular new study, researchers from the University of Copenhagen have discovered a method of diagnosing a broad range of cancers at their early stages by utilising a particular malaria protein, which sticks to cancer cells in blood samples. The researchers hope that this method can be used in cancer screenings in the near future.

Each year, cancer kills approximately nine million people worldwide, and early diagnosis is crucial to efficient treatment and survival. Now, researchers from the Faculty of Health and Medical Sciences at the University of Copenhagen have come up with a new method of diagnosing cancer in its early stages in humans by way of a malaria protein - VAR2CSA - which sticks to cancer cells. All the scientists need to determine whether or not a person has cancer is a blood sample.

"We have developed a method where we take a blood sample and with great sensitivity and specificity, we're able to retrieve the individual cancer cells from the blood. We catch the cancer cells in greater numbers than existing methods, which offers the opportunity to detect cancer earlier and thus improve outcome. You can use this method to diagnose broadly, as it's not dependent on cancer type. We have already detected various types of cancer cells in blood samples. And if there is a cancer cell in your blood, you have a tumour somewhere in your body," says Professor Ali Salanti from the Department of Immunology and Microbiology and joint author of the study, which has just been published in the scientific journal, Nature Communications.

Today, there are several ways of detecting cancer cells in blood. Most of them are based on a particular marker, which is found on the surface of tumour cells. However, not all tumour cells display this marker, which renders these methods unable to detect tumour cells spread to other organs such liver, lung and bones, as opposed to the method based on the malaria protein.

A few years ago, Ali Salanti and his fellow researchers discovered a new method of treating cancer with the protein VAR2CSA, which is produced by malaria parasites. And these discoveries have formed the basis of the research group's new method of diagnosis. Among other things, they have shown that the malaria protein sticks to a specific sugar molecule, which is found in more than 95 percent of all types of cancer cells. In other words, this new method of diagnosis can be used to detect practically all types of cancer.

**Circulating tumour cells**

A cancerous tumour consists of several different cancer cells, some of which spread by wandering through the tissue and into the blood. These cancer cells in the blood are called circulating tumour cells, and they can develop into metastases, which cause up to 90 percent of all cancer-related deaths. If cancer originating in the lungs spreads to the brain, it is called brain metastasis.

It is the circulating tumour cells that the researchers are able to retrieve from a blood sample by using the malaria protein. During the development of this new method, the researchers took ten cancer cells and added them to five millilitres of blood, and subsequently, they were able to retrieve nine out of ten cancer cells from the blood sample.

"We count the number of cancer cells and based on that we're able to make a prognosis. You can, for example, decide to change a given treatment if the number of circulating tumour cells does not change during the treatment the patient is currently undergoing. This method also enables us to retrieve live cancer cells, which we can then grow and use for testing treatments in order to determine which type of treatment the patient responds to," says Postdoc Mette Ørskov

Agerbæk, Department of Immunology and Microbiology and joint author of the study.

**Future screening programme**

The researchers have already come a long way in following up on their results in terms of a large clinical study where many more patients with cancer of the pancreas have been tested using this method.

"We found strikingly high numbers of circulating tumour cells in every single patient with pancreatic cancer, but none in the control group," says Professor Christopher Heeschen, School of Medical Sciences, UNSW, Sydney, Australia, and joint author of the study.

The researchers envision being able to use the method to screen people at high risk of developing cancer in the future.

However, they also expect that this method can be used as a biomarker indicating whether a patient with mostly vague symptoms indeed has cancer or not. This will enable doctors to determine the stage the disease is at.

"Today, it's difficult to determine which stage cancer is at. Our method has enabled us to detect cancer at stages one, two, three and four. Based on the number of circulating tumour cells we find in someone's blood, we'll be able to determine whether it's a relatively aggressive cancer or not so then to adjust the treatment accordingly," explains Professor Ali Salanti who adds that a much larger clinical study is needed before firm correlations to tumour staging can be made.

***https://bbc.in/2OHWqIv***

## NYU offers free tuition for all its medical students

***The New York University School of Medicine will provide free tuition for all present and future students, the university announced.***

Citing the risk of "overwhelming" debt, it says every student will qualify regardless of merit or financial need.

NYU said financial worries were driving graduates to more lucrative specialities, pushing doctors away from more general positions.

The scholarship covers annual tuition costs of up to $55,000 (£43,000).

A study produced by the Association of American Medical Colleges estimated that in 2017 75% of medical students graduated in debt.

The average debt level was $190,000 (£149,000).

The university has reportedly been working for more than a decade to accrue the necessary funds to pay for tuition, and hopes to raise a total of $600 million (£472m) to make the scholarships available permanently.

Students must still however cover the cost of living expenses and accommodation.

***I'll be paying my student loans until my son's in college," says Michael Nealis of the $64,000 debt he built up at university***

NYU School of Medicine made the surprise announcement at its annual White Coat Ceremony on Thursday - when new students receive a white lab coat as they begin their studies.

In their statement, the university said debt is "fundamentally reshaping the medical profession in ways that are adversely affecting healthcare".

Graduates move towards higher-paying areas of medicine over paediatrics, primary care or gynaecology due to their "staggering student loans".

Dr Robert Grossman said that "aspiring physicians and surgeons should not be prevented from pursuing a career in medicine because of the prospect of overwhelming financial debt".

NYU thanked more than 2,500 supporters who helped bring the scheme to fruition.

It says it is now the only top 10 US medical school to offer such help.

http://bit.ly/2PjEEN9

# Novel nanoparticle-based approach detects and treats oral plaque without drugs

***Practical nanotechnology-based method for detecting and treating the harmful bacteria that cause plaque***

When the good and bad bacteria in our mouth become imbalanced, the bad bacteria form a biofilm (aka plaque), which can cause cavities, and if left untreated over time, can lead to cardiovascular and other inflammatory diseases like diabetes and bacterial pneumonia.

A team of researchers from the University of Illinois has recently devised a practical nanotechnology-based method for detecting and treating the harmful bacteria that cause plaque and lead to tooth decay and other detrimental conditions.

Oral plaque is invisible to the eye so dentists currently visualize it with disclosing agents, which they administer to patients in the form of a dissolvable tablet or brush-on swab. While useful in helping patients see the extent of their plaque, these methods are unable to identify the difference between good and bad bacteria.

"Presently in the clinic, detection of dental plaque is highly subjective and only depends on the dentist's visual evaluation," said Bioengineering Associate Professor Dipanjan Pan, head of the research team. "We have demonstrated for the first time that early detection of dental plaque in the clinic is possible using the regular intraoral X-ray machine which can seek out harmful bacteria populations."

In order to accomplish this, Fatemeh Ostadhossein, a Bioengineering graduate student in Pan's group, developed a plaque detection probe that works in conjunction with common X-ray technology and which is capable of finding specific harmful bacteria known as Streptococcus mutans (S. mutans) in a complex biofilm network. Additionally, they also demonstrated that by tweaking the chemical composition of the probe, it can be used to target and destroy the S. mutans bacteria.

The probe is comprised of nanoparticles made of hafnium oxide ($HfO_2$), a non-toxic metal that is currently under clinical trial for internal use in humans. In their study, the team demonstrated the efficacy of the probe to identify biochemical markers present at the surface of the bacterial biofilm and simultaneously destroy S. mutans. They conducted their study on Sprague Dawley rats.

In practice, Pan envisions a dentist applying the probe on the patient's teeth and using the X-ray machine to accurately visualize the extent of the biofilm plaque. If the plaque is deemed severe, then the dentist would follow up with the administering of the therapeutic $HfO_2$ nanoparticles in the form of a dental paste.

In their study, the team compared the therapeutic ability of their nanoparticles with Chlorhexidine, a chemical currently used by dentists to eradicate biofilm. "Our $HfO_2$ nanoparticles are far more efficient at killing the bacteria and reducing the biofilm burden both in cell cultures of bacteria and in [infected] rats," said Ostadhossein, noting that their new technology is also much safer than conventional treatment.

The nanoparticles' therapeutic effect is due, said Pan, to their unique surface chemistry, which provides a latch and kill mechanism. "This mechanism sets our work apart from previously pursued nanoparticle-based approaches where the medicinal effect comes from anti-biotics encapsulated in the particles," said Pan, also a faculty member of the Carle Illinois College of Medicine and the Beckman Institute for Advanced Science and Technology. "This is good because our approach avoids anti-biotic resistance issues and it's safe and highly scalable, making it well-suited for eventual clinical translation."

In addition to Pan and Ostadhossein, other members of the research team include bioengineering post-doctoral researcher Santosh Misra,

visiting scholar Indu Tripathi, undergraduate Valeriya Kravchuk, visiting scholar Gururaja Vulugundam; and Veterinary Medicine clinical assistant professor Denae LoBato and adjunct assistant professor Laura Selmic.

*Their work is described in the paper, "Dual purpose hafnium oxide nanoparticles offer imaging Streptococcus mutans dental biofilm and fight it In vivo via a drug free approach," published online on July 30, 2018, in the journal Biomaterials. The research was funded by the University of Illinois at Urbana-Champaign Children's Discovery Institute and the American Heart Association.*

***http://bit.ly/2L1U3y2***

## Humans gave leprosy to armadillos – now they are giving it back to us

***Disease is growing in armadillos, and armadillo-to-human contact is spreading***

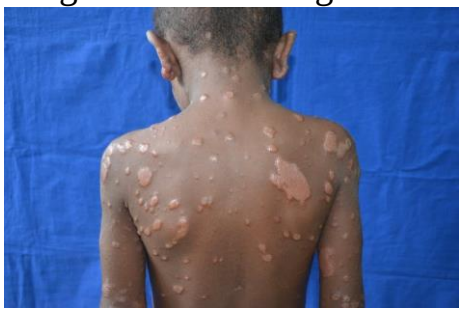
**John Stewart Spencer***

Leprosy is an ancient disease, the oldest disease known to be associated with humans, with evidence of characteristic bone pitting and deformities found in burial sites in India as far back as 2000 B.C. It's thus only natural that many might think the disease is a relic of the past. My recent studies in a Brazilian state where the disease is prevalent shows that leprosy is closer to us than we might think, however. The disease is growing in armadillos. And while these animals are not exactly the cuddly type to which humans are drawn, armadillo-to-human contact is spreading. And, when the species do interact, armadillos are giving leprosy back.

**An unsightly animal, a worse disease**

Leprosy, also called Hansen's disease, is caused by infection by the bacterium *Mycobacterium leprae*, causing skin lesions, nerve damage, disfigurement and disability, leading to social stigmatization common to people with this disease. It is is spread mainly by aerosol infection, or coughing and sneezing, from human to human.

Typically, infection requires living in close contact with an untreated infected individual. Symptoms develop slowly, as long as three to seven years after infection. It is rare in the United States, with an average of less than 200 cases diagnosed per year in the last 10 years, mostly in individuals who immigrated from foreign countries where the disease is prevalent. It is found mostly in tropical countries such as Brazil, India, Indonesia and other countries in Africa, southeast Asia and the Pacific Islands. There were 214,783 new cases worldwide in 2016.



***Severe leprosy case with many lesions in a year old child in Brazil.*** **Claudio Salgado, CC BY-SA**

Although drugs to treat and cure leprosy are cheap and available for free to anyone diagnosed with the disease, pockets of high incidence in dozens of countries have kept the numbers from declining much in the last few years. The root causes for the continued high prevalence rates remain poverty, poor sanitation and nutrition, and lack of health care availability to treat those diagnosed before nerve damage and disability occur.

**Enter the armadillos**

*Dasypus novemcinctus*, commonly known as the nine-banded armadillo in the U.S. or chicken-armadillo in Brazil, is the only species whose range includes North, Central and South America. These armadillos first extended their range from Mexico into Texas around the 1850's and then went north and east into the Gulf states of the southern U.S. In late 1940s, another group of armadillos escaped from captivity in central Florida and spread throughout Florida, eventually merging with the Texan armadillos in the early 1970s in the Florida Panhandle.

Around this time, Dr. Eleanor Storrs found that armadillos infected with *M. leprae* experimentally eventually came down with symptoms of leprosy, even having the same skin lesions and nerve damage found in human cases. Shortly after this, she and her team discovered that armadillos living in the wild in Texas and Louisiana were naturally infected by *M. leprae*. Analysis of archived serum samples for antibodies specific for the bacterium indicated that animals from this area had likely been infected since the 1960's. Exactly how the armadillos became infected by humans is not clear, but one theory is that they picked it up from contaminated soil by digging. Surveys of armadillos in the Gulf states found that up to 20 percent were infected with *M. leprae*.

At first, armadillos' susceptibility to leprosy was a boost to science and medicine. Because they were the only animal other than humans in which the bacteria could be isolated, armadillos allowed scientists to study leprosy and possible treatments.

Now, there are millions of armadillos in the southern U.S., and people interact with them in a variety of ways. The animals' leathery carapaces were fashioned into purses and boots; some were kept as pets in the home or brought to entertain people at petting zoos, children's schools and at armadillo races at county fairs. In certain areas, people hunted them to serve at barbecues.

All of this exposure eventually had consequences. In 2011, Dr. Richard Truman from the National Hansen's Disease Program in Baton Rouge, Louisiana, published a study showing that the strain infecting the majority of armadillos and native leprosy patients in Texas and Louisiana were identical, indicating that the disease was a zoonotic infection being transmitted to humans.

In 2015, another study from the same group found that a different strain type that existed only in central Florida was causing a second cluster of cases in armadillos and humans. Both of these reports caused a huge amount of media coverage, with people being somewhat surprised and alarmed that this ungainly and not very cuddly animal was transmitting the oldest and one of the most feared diseases to humans. Still, once the excitement died down, most people probably resumed their behaviors with these animals, ignoring the possible risks involved.

**What goes around, comes around: The same is true in Brazil**

Two things stand out about Brazil. Armadillos are native to South America; and leprosy, first brought to Brazil over 500 years ago by the European explorers and through the slave trade from West Africa, has been widespread there for hundreds of years. Knowing this, our research team wanted to know how much human contact there was with armadillos in Brazil and whether this could lead to leprosy transmission from these animals as had been shown in the southern U.S.

***A man in Ecuador in 2017 prepares an armadillo for lunch.***
**Fotos593/Shutterstock**

Our study focused on people living in a rural area in western Pará state in the Brazilian Amazon in the city of Belterra. People living there frequently ate armadillos as a source of protein. And there was a lot of interaction of people from this town with armadillos: 19 percent hunted the animals in the forests, and 65 percent cleaned the meat for cooking or ate armadillos at least once per year. The percentage of people with a positive antibody response to the bacterium (63 percent were positive, normal for this region) indicated that the majority of people had been infected by *M. leprae*. A surprising 62 percent of armadillos killed by hunters showed signs of infection with *M. leprae*, a rate three times higher than in Texas and Louisiana. Most importantly, a group of 27 individuals who ate armadillo meat most frequently had antibody levels 50 percent higher

than other groups, indicating that increased consumption almost doubled their risk for disease. The study concluded that similar to the southern states in the U.S., leprosy is being transmitted from armadillos to people in Brazil.

The broader message about this work is that wild animals harbor all kinds of diseases that can be transmitted to humans, particularly when there may be contact with blood or when eating the meat. Although leprosy remains a disease that few people in the U.S. worry about, people should take care with how they interact with armadillos.

***Associate Professor, leprosy researcher, Colorado State University***

***Disclosure statement***

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***https://nyti.ms/2L7I6a5***

## Vitamin D, the Sunshine Supplement, Has Shadowy Money Behind It

***The doctor most responsible for creating a billion-dollar juggernaut has received hundreds of thousands of dollars from the vitamin D industry.***

**By Liz Szabo**

Dr. Michael Holick's enthusiasm for vitamin D can be fairly described as extreme. The Boston University endocrinologist, who perhaps more than anyone else is responsible for creating a billion-dollar vitamin D sales and testing juggernaut, elevates his own levels of the stuff with supplements and fortified milk. When he bikes outdoors, he won't put sunscreen on his limbs. He has written book-length odes to vitamin D, and has warned in multiple scholarly articles about a "vitamin D deficiency pandemic" that explains disease and suboptimal health across the world.

His fixation is so intense that it extends to the dinosaurs. What if the real problem with that asteroid 65 million years ago wasn't a lack of food, but the weak bones that follow a lack of sunlight? "I sometimes wonder," Dr. Holick has written, "did the dinosaurs die of rickets and osteomalacia?"

Dr. Holick's role in drafting national vitamin D guidelines, and the embrace of his message by mainstream doctors and wellness gurus alike, have helped push supplement sales to $936 million in 2017. That's a ninefold increase over the previous decade. Lab tests for vitamin D deficiency have spiked, too: Doctors ordered more than 10 million for Medicare patients in 2016, up 547 percent since 2007, at a cost of $365 million.

But few of the Americans swept up in the vitamin D craze are likely aware that the industry has sent a lot of money Dr. Holick's way. A Kaiser Health News investigation for The New York Times found that he has used his prominent position in the medical community to promote practices that financially benefit corporations that have given him hundreds of thousands of dollars — including drug makers, the indoor tanning industry and one of the country's largest commercial labs.

In an interview, Dr. Holick acknowledged he has worked as a consultant to Quest Diagnostics, which performs vitamin D tests, since 1979. Dr. Holick, 72, said that industry funding "doesn't influence me in terms of talking about the health benefits of vitamin D."

There is no question that the hormone is important. Without enough of it, bones can become thin, brittle and misshapen, causing a condition called rickets in children and osteomalacia in adults. The issue is how much vitamin D is healthy, and what level constitutes deficiency.

Dr. Holick's crucial role in shaping that debate occurred in 2011. Late the previous year, the prestigious National Academy of Medicine (then known as the Institute of Medicine), a group of independent scientific experts, issued a comprehensive, 1,132-page report on vitamin D deficiency. It concluded that the vast majority of

Americans get plenty of the hormone naturally, and advised doctors to test only patients at high risk of certain disorders, such as osteoporosis.

A few months later, in June 2011, Dr. Holick oversaw the publication of a report that took a starkly different view. The paper, in the peer-reviewed Journal of Clinical Endocrinology & Metabolism, was on behalf of the Endocrine Society, the field's foremost professional group, whose guidelines are widely used by hospitals, physicians and commercial labs nationwide, including Quest. The society adopted Dr. Holick's position that "vitamin D deficiency is very common in all age groups" and advocated a huge expansion of vitamin D testing, targeting more than half the United States population, including those who are black, Hispanic or obese — groups that tend to have lower vitamin D levels than others.

The recommendations were a financial windfall for the vitamin D industry. By advocating such widespread testing, the Endocrine Society directed more business to Quest and other commercial labs. Vitamin D tests are now the fifth-most-common lab test covered by Medicare.

The guidelines benefited the vitamin D industry in another important way. Unlike the National Academy, which concluded that patients have sufficient vitamin D when their blood levels are at or above 20 nanograms per milliliter, the Endocrine Society said vitamin D levels need to be much higher — at least 30 nanograms per milliliter. Many commercial labs, including Quest and LabCorp, adopted the higher standard.

Yet there's no evidence that people with the higher level are any healthier than those with the lower level, said Dr. Clifford Rosen, a senior scientist at the Maine Medical Center Research Institute and co-author of the National Academy report. Using the Endocrine Society's higher standard creates the appearance of an epidemic, he said, because it labels 80 percent of Americans as having inadequate vitamin D. "We see people being tested all the time and being treated based on a lot of wishful thinking, that you can take a supplement to be healthier," Dr. Rosen said.

Patients with low vitamin D levels are often prescribed supplements and instructed to get checked again in a few months, said Dr. Alex Krist, a family physician and vice chairman of the United States Preventive Services Task Force, an expert panel that issues health advice. Many physicians then repeat the test once a year. For labs, "it's in their financial interest" to label patients with low vitamin D levels, Dr. Krist said.

In a 2010 book, "The Vitamin D Solution," Dr. Holick gave readers tips to encourage them to get their blood tested. For readers worried about potential out-of-pocket costs for vitamin D tests — they range from $40 to $225 — he listed the precise reimbursement codes that doctors should use when requesting insurance coverage. "If they use the wrong coding when submitting the claim to the insurance company, they won't get reimbursed and you will wind up having to pay for the test," Dr. Holick wrote.

Dr. Holick acknowledged financial ties with Quest and other companies in the financial disclosure statement published with the Endocrine Society guidelines. In an interview, he said that working for Quest for four decades — he is currently paid $1,000 a month — hasn't affected his medical advice. "I don't get any additional money if they sell one test or one billion," he said.


***Shire is among the pharmaceutical companies that have paid Dr. Michael Holick for consulting and other services.*** **Clodagh Kilcoyne/Reuters**

A Quest spokeswoman, Wendy Bost, said the company seeks the advice of a number of expert consultants. "We feel strongly that

being able to work with the top experts in the field, whether it's vitamin D or another area, translates to better quality and better information, both for our patients and physicians," Ms. Bost said.

Since 2011, Dr. Holick's advocacy has been embraced by the wellness-industrial complex. Gwyneth Paltrow's website, Goop, cites his writing. Dr. Mehmet Oz has described vitamin D as "the No. 1 thing you need more of," telling his audience that it can help them avoid heart disease, depression, weight gain, memory loss and cancer. And Oprah Winfrey's website tells readers that, "knowing your vitamin D levels might save your life." Mainstream doctors have also urged Americans to get more of the hormone, including Dr. Walter Willett, a widely respected professor at Harvard Medical School.

Today, seven years after the dueling academic findings, the leaders of the National Academy report are struggling to be heard above the clamor for more sunshine pills. "There isn't a 'pandemic,'" said A. Catharine Ross, a nutritional sciences professor at Penn State and chairwoman of the committee that wrote the report, in an interview. "There isn't a widespread problem."

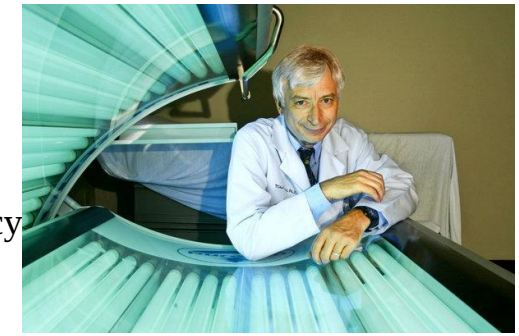
**Ties to Drugmakers and Tanning Salons**

In "The Vitamin D Solution," Dr. Holick describes his promotion of vitamin D as a lonely crusade. "Drug companies can sell fear," he writes, "but they can't sell sunlight, so there's no promotion of the sun's health benefits."

Yet Dr. Holick also has extensive financial ties to the pharmaceutical industry. He received nearly $163,000 from 2013 to 2017 from pharmaceutical companies for consulting and other services, according to Medicare's Open Payments database, which tracks payments from drug and device manufacturers. The companies paying him included Sanofi-Aventis, which markets vitamin D supplements; Shire, which makes drugs for hormonal disorders that are given with vitamin D; Amgen, which makes an osteoporosis treatment; and Roche Diagnostics and Quidel Corporation, which both make vitamin D tests.

The database includes only payments made since 2013, but Dr. Holick's record of being compensated by drug companies started before that. In his 2010 book, he describes visiting South Africa to give "talks for a pharmaceutical company," whose president and chief executive were in the audience.

Dr. Holick's ties to the tanning industry also have drawn scrutiny. Although Dr. Holick said he doesn't advocate tanning, he has described tanning beds as a "recommended source" of vitamin D "when used in moderation." Dr. Holick has acknowledged accepting research money from the UV Foundation — a nonprofit arm of the now-defunct Indoor Tanning Association — which gave $150,000 to Boston University from 2004 to 2006, earmarked for Dr. Holick's research. The International Agency for Research on Cancer classified tanning beds as carcinogenic in 2009.



***Dr. Holick in 2002. He has described tanning beds as a "recommended source" of vitamin D "when used in moderation." The devices were classified as carcinogenic in 2009.*** **Rick Friedman/Corbis, via Getty Images**

In 2004, the tanning-industry associations led Dr. Barbara Gilchrest, who then was head of Boston University's dermatology division, to ask Dr. Holick to resign from the department. He did so, but remains a professor at the medical school's department of endocrinology, diabetes, nutrition and weight management. In "The Vitamin D Solution," Dr. Holick wrote that he was "forced" to give up his position because of his "stalwart support of sensible sun exposure." He added, "Shame on me for challenging one of the dogmas of

dermatology." Although Dr. Holick's website lists him as a member of the American Academy of Dermatology, an academy spokeswoman, Amanda Jacobs, said he was not a current member.

Dr. Christopher McCartney, chairman of the Endocrine Society's clinical guidelines subcommittee, said the society has put in place stricter policies on conflict of interest since its vitamin D guidelines were released. The society's current policies would not allow the chairman of the guideline writing committee to have financial conflicts.

**A Miracle Pill Loses Its Luster**

Enthusiasm for vitamin D among medical experts has dimmed in recent years, as rigorous clinical trials have failed to confirm the benefits suggested by early, preliminary studies. A string of trials has found no evidence that vitamin D reduces the risk of cancer, heart disease or falls in the elderly. And most scientists say there isn't enough evidence to know if vitamin D can prevent chronic diseases that aren't related to bones.

Although the amount of vitamin D in a typical daily supplement is generally considered safe, it is possible to take too much. In 2015, an article in the American Journal of Medicine linked blood levels as low as 50 nanograms per milliliter with an increased risk of death. That's within the level considered healthy by the Endocrine Society, which defined vitamin D "sufficiency" as between 30 and 100 nanograms, Rosen said.

Some researchers say vitamin D may never have been the miracle pill that it appeared to be. Sick people who stay indoors tend to have low vitamin D levels; their poor health is likely the cause of their low vitamin D levels, not the other way around, said Dr. JoAnn Manson, chief of preventive medicine at Brigham and Women's Hospital in Boston. Only really rigorous studies, which randomly assign some patients to take vitamin D and others to take placebos, can provide definitive answers about vitamin D and health. Dr. Manson is leading one such study, involving 26,000 adults, expected to be published in November.

A number of insurers and health experts have begun to view widespread vitamin D testing as unnecessary and expensive. In 2014, the United States Preventive Services Task Force said there wasn't enough evidence to recommend for or against routine vitamin D screening. In April, the task force explicitly recommended that older adults outside of nursing homes avoid taking vitamin D supplements to prevent falls.

In 2015, Excellus BlueCross BlueShield of Rochester, N.Y. published an analysis highlighting the overuse of vitamin D tests. In 2014, the insurer spent $33 million on 641,000 vitamin D tests. "That's an astronomical amount of money," said Dr. Richard Lockwood, Excellus' vice president and chief medical officer for utilization management. More than 40 percent of Excellus patients tested had no medical reason to be screened.

In spite of Excellus' efforts to rein in the tests, vitamin D usage has remained high, Dr. Lockwood said. "It's very hard to change habits," he said, adding, "The medical community is not much different than the rest of the world, and we get into fads."

*Kaiser Health News is a nonprofit news service covering health issues. It is an editorially independent program of the Kaiser Family Foundation that is not affiliated with Kaiser Permanente.*