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Compounds derived from hops show promise for metabolic syndrome patients

A group of compounds derived from hops can likely improve cognitive and other functions in people with metabolic syndrome

CORVALLIS, Ore. - A group of compounds derived from hops can likely improve cognitive and other functions in people with metabolic syndrome, new research at Oregon State University and Oregon Health & Science University suggests. That's good news for the estimated 35 percent of the U.S. adult population that suffers from the syndrome.

A patient is considered to have metabolic syndrome if he or she has at least two of the following conditions: abdominal obesity, high blood pressure, high blood sugar, low levels of "good" cholesterol, and high levels of triglycerides.

A diet high in saturated fat results in chronic low-grade inflammation in the body that in turn leads to the development of metabolic syndrome, a serious condition associated with cognitive dysfunction and dementia as well as being a major risk factor for cardiovascular disease and type 2 diabetes. Led by corresponding authors Fred Stevens and Jacob Raber, the research focused on xanthohumol (XN), a prenylated flavonoid from hops, and two of its hydrogenated derivatives: DXN and TXN.

"We've studied xanthohumol for many years," said Stevens, professor of pharmaceutical sciences in the OSU College of Pharmacy and a principal investigator at Oregon State's Linus Pauling Institute. "We think what we have now is a big improvement."

Stevens explained that while earlier research had suggested XN could be an effective treatment for metabolic syndrome, the problem is that it transforms into 8-prenylnaringenin, or 8-PN, an estrogenic metabolite. Estrogens are the female sex hormones.

"We were always criticized about the potential side effects because 8-PN is one of the most potent phytoestrogens known in nature, and that's not good news," he said. "If someone took XN over longer periods of time, it could lead to estrogenic side effects, potentially." Those include endometriosis and breast cancer - most types of breast cancer are sensitive to estrogen, meaning that estrogen helps tumors grow.

"A double bond in the XN molecule is responsible for that 8-PN metabolism to be possible, so I thought if I could get rid of that double bond by hydrogenating the molecule, then that metabolite cannot be formed anymore," Stevens said. "I thought maybe this is the solution to the problem."

Stevens was right. Testing in a mouse model showed that XN and its hydrogenated derivatives, XN and TXN, improve glucose intolerance and insulin resistance, and sensitivity to leptin - a hormone that tells you to feel full when you've eaten enough and also helps regulate energy expenditure.

Best of all, the derivatives were even more effective than the original compound, without leading to that worrisome estrogenic metabolite or showing much affinity themselves for estrogen receptors. "TXN is especially potent in reducing insulin resistance in mice made obese by feeding a high-fat diet," said Cristobal Miranda, an associate professor at the Linus Pauling Institute who was involved in the research.

"Probably the bioavailability of the hydrogenated derivatives is better than for XN itself - that would explain why they work better," Stevens added. "Now we have compounds that still have the original beneficial effects but not the side effects. There are no adverse estrogenic effects, and the liver toxicity induced by the high-fat diet is mitigated. Our mouse study showed that XN, DXN and TXN are not hepatotoxic."

Testing mice in a water maze, researchers found XN and its derivatives ameliorated impairments in spatial learning and memory induced by the high-fat diet the mice had been fed.

"These findings could be important for people suffering from cognitive impairments associated with a high-fat diet and metabolic syndrome," said Raber, professor of behavioral neuroscience, neurology and radiation medicine at the OHSU School of Medicine.

Raber is also an affiliate scientist in the division of neuroscience at the Oregon National Primate Research Center.

"Our findings with rodents suggest that it may be possible to reduce or even prevent learning and memory impairments through a derivative of the same chemical compound found in beer," he said.

Results were recently published in Scientific Reports.

The Linus Pauling Institute, the OSU College of Pharmacy, Hopsteiner, Inc., the OSU Foundation Buhler-Wang Research Fund, and the National Institutes of Health supported this research, on which the University of Illinois also collaborated.

http://bit.ly/2FUxdpP

Neanderthals used fire to make tools

Neanderthals in Tuscany charred wooden tools with fire in order to shape them.

Kiona N. Smith - 2/6/2018, 5:00 AM

A collection of broken wooden tools unearthed in southern Italy offers new evidence that Neanderthals used fire to shape wooden tools as early as the Middle Paleocene, about 171,000 years ago. The find sheds important new light on the earliest use of fire, and it reveals how sophisticated Neanderthal technology was. The tools, called digging sticks, are still in use today.

***Enlarge* / *The handle of a digging stick from Pogetti Vecchi.* PNAS**

If you're a hunter-gatherer, the digging stick is your version of the Swiss Army knife for foraging: about a meter long, with one end rounded to offer a handle and the other tapered into a blunt almost-point. They're useful for digging up roots and tubers, hunting burrowing animals, or pounding and grinding herbs. And the Neanderthals of Middle Pleistocene Italy created and used digging sticks that would be perfectly familiar to modern members of the Australian Bindibu people, the Hadza people of Tanzania, and the San people of southern Africa.

Broken tools

Wood is a popular material for tools in modern hunter-gatherer societies, mostly because it's available and relatively easy to work with. Archaeologists assume early humans, including Neanderthals, must have used it as well.

"It could be supposed that simple wood or bone objects were the first artifacts created and used by early human ancestors, long before the earliest preserved artifacts, stone tools," said archaeologist Biancamaria Aranguren. But we don't have much actual evidence for how early humans used wood, because, unlike stone or bone, wood tends to decay after thousands of years in the ground.

That's what makes the new find so rare. Archaeologists unearthed pieces of several wooden digging sticks from a site in Tuscany called Poggetti Vecchi.

The site is a plain at the foot of a low hill, near some warm springs. One hundred and seventy-one thousand years ago, grasslands and marshes surrounded the shore of a lake here, according to lake sediments and pollen analysis. Those grasslands were home to large grazing mammals, including straight-tusked elephants known to science as *Palaeolaxodon antiquus*, the bones of which litter the site.

Artifacts here date to a period when Neanderthals roamed the hills of southern Italy. Archaeologists excavating the site in 2012 found 39 broken pieces of the sticks, along with an assortment of stone tools. Of the 39 fragments, only about four pointed tips and six rounded handles survived, along with 31 pieces of shafts. Four of the handles and all of the tips had been broken during the tools' lifetimes. And the digging sticks weren't well-preserved—microscopy showed that bacteria had eaten away at the cell walls of the wood, for instance. But poor preservation is better than no preservation, and the broken bits of wood had plenty to tell archaeologists.

Shaped by fire

Researchers noticed that one of the digging sticks had a 1mm-thick layer of black film on its shaft, and its surface was fractured in a square-like pattern reminiscent of charring. Chemical testing revealed that the wood had, in fact, been charred, and so had 11 of the other finds. This must have been deliberate, because they were all charred evenly, with

a thin film, and on the same part of the stick. That implies carefully controlled exposure to a flame.

Archaeologists say that the Neanderthals probably used fire to char the surface of the wood to make it easier to scrape off the bark and shape the ends. Boxwood is one of the strongest European hardwoods, which makes it perfect for a durable tool like a digging stick, but it's also hard to whittle into shape with stone tools. Fire would have softened an outer layer and made it easier to work. When Aranguren and her colleagues tried working some boxwood branches, they found that they couldn't shape the rounded handles and blunt points without charring the wood first.

Modern hunter-gatherers use the same method today, but we've never found evidence of the technique being used so early. Some archaeologists think that *Homo heidelbergensis*, an ancestor of Neanderthals, may have used a similar method to shape spears in a 300,000-year-old site in Germany. The German tips come to much sharper points than the digging sticks at Poggetti Vecchi, but there's no physical evidence for the use of flame.

That makes the Poggetti Vecchi digging sticks the earliest clear examples of wooden tools shaped with fire. They show that even early Neanderthals knew enough to choose the best wood for the tool—not just pick up whatever sticks happened to be lying around or easy to work with—and then utilize both fire and stone tools in order to produce a finished tool. It takes a lot of planning, specific knowledge, and painstaking, precise work to pull that off, which demonstrates the sophistication of Neanderthal tool-making abilities.

A look at prehistoric women's lives

And the Italian find also adds a chapter to the story of how humanity adopted and tamed fire. Archaeologists still aren't sure exactly when, or how, humans first learned to use and control fire and then to create it at their convenience.

"Most recent studies suppose during the Middle Pleistocene, a regular use of natural fire sources with perhaps the occasional development of fire-making technology," said Aranguren. If by 171,000 years ago, Neanderthals were using fire in very precise, complex ways, that's either an indication of how quickly our collective fire-handling skills advanced or a hint that fire use may be older than the first evidence we have for it so far.

The Poggetti Vecchi digging sticks may also be some of the earliest known tools used specifically by women. In most modern hunter-gatherer cultures, digging sticks are women's tools.

"Digging sticks are mostly used by women and regarded as women's personal property, in the same way that spears are regarded as men's personal property," wrote Aranguren and her colleagues. These artifacts may offer new insight into Neanderthal women's lives and work. And they're also an indication that a whole Neanderthal community, not just an all-male hunting party, may have spent time on the rich lakeside hunting grounds of Poggetti Vecchi.

PNAS, *2017. DOI: 10.1073/pnas.1716068115 (About DOIs).*

http://bit.ly/2nRJDaD

PSMA PET/CT clearly differentiates prostate cancer from benign tissue

Using nuclear medicine, German researchers have found a way to accurately differentiate cancerous tissue from healthy tissue in prostate cancer patients.

RESTON, Va. - The research is highlighted in the February issue of The Journal of Nuclear Medicine.

According to the American Cancer Society, one in nine men will be diagnosed with prostate cancer in his lifetime. Early diagnosis is key to successful treatment.

The new study demonstrates that the maximum standardized uptake value (SUV_{max}) on Gallium-68 prostate specific membrane antigen (^{68}Ga-PSMA) PET/CT scans correlates with PSMA-expression in primary prostate cancer. By this means, researchers were able to generate an SUV_{max} cutoff for the differentiation of cancerous and benign prostate tissue.

"To the best of our knowledge, this was the first study to generate a cutoff SUV_{max}, validated by immunohistochemistry, for separating prostate cancer from normal prostate tissue by ^{68}Ga-PSMA PET/CT images," explains Vikas Prasad, MD, PhD, of Charité Universitätsmedizin Berlin in Germany. "Our SUV_{max} cutoff can be used to confirm or rule out prostate cancer with a very high degree of sensitivity and specificity."

He points out, "Recent years have brought tremendous advances in image-based biopsy of the prostate. However, in many patients, histopathology may not yield correct diagnosis (e.g., if the tumor is missed during true-cut biopsy). This is especially true for multifocal prostate cancer, less aggressive tumors, and cases of prostatitis or prior prostate irradiation, where MRI alone may not give the correct localization and malignancy grade."

For the study, the data of 31 men (mean age of 67.2 years) who had undergone prostatectomies and preoperative PET scans were analyzed, with the SUV_{max} generated for suspicious areas and visually normal tissue. Both cancerous and benign prostate tissue samples (62 total) were stained with monoclonal anti-PSMA antibody. All the cancerous lesions could be confirmed histopathologically. The best cut-off value was determined to be 3.15 (sensitivity 97 percent, specificity 90 percent).

Prasad notes, "This validated cutoff of 3.15 for SUV_{max} enables the diagnosis of prostate cancer with a high sensitivity and specificity in both unifocal and multifocal disease." Looking ahead, he posits, "With advancement of image-registration/segmentation software and PET/MRI scanners, it is quite logical to predict that in the future PET images and SUV_{max} on a suspicious lesion in the prostate will be used for multimodal image-guided fusion biopsy."

Authors of "Immunohistochemical validation of PSMA-expression measured by ^{68}Ga-PSMA PET/CT in primary prostate cancer" include Nadine Woythal, Ruza Arsenic, Kurt Miller, Jan-Carlo Janssen, Kai Huang, Marcus R Makowski, Winfried Brenner and Vikas Prasad, Charité Universitätsmedizin Berlin, Berlin, Germany, and Carsten Kempkensteffen, Franziskus-Krankenhaus Berlin, Berlin, Germany.

http://bit.ly/2GVjiRH

TRAPPIST-1: Findings show exoplanets made of rock and water

Researchers start to unveil the secrets of this planetary system

In 2016, a team of researchers led by EU-funded astronomer Michael Gillon at the University of Liege, Belgium, discovered three temperate Earth-sized planets orbiting TRAPPIST-1, an ultra-cool dwarf star just 40 light years from Earth. A few months later, Gillon surprised the world with the discovery of a whole planetary system made of a total of seven planets around this star. A set of new studies reveals today the nature and composition of the planets, shedding light on their potential habitability.

Researchers start to unveil the secrets of this planetary system. **NASA/JPL-Caltech**

The four studies published today are essentially based on the intensive observations made by the terrestrial telescopes TRAPPIST and SPECULOOS and the space telescopes Hubble and Spitzer. Focusing on the mass, radii, and first atmospheric constraints of the exoplanets, the latest findings confirm the terrestrial and globally rocky nature of

the TRAPPIST-1 planets. They also suggest a high presence of water, up to five percent of their mass and about 250 times more than Earths Ocean. The closest planets to TRAPPIST-1 star could be surrounded by dense steamy atmospheres, much thicker than Earth's. The more distant ones may have water frozen on their surfaces.

However, "the best is yet to come", says Michael Gillon, co-author of the four publications. The next important step in studying the planets of TRAPPIST-1 will be the spectroscopic observation of their atmospheres using the new space telescope James Webb, which will be launched next year by NASA and the European Space Agency (ESA). "The James Webb will enable us to study in detail the atmospheres of these planets, notably to measure their composition and detect possible molecules of biological origin", explains Gillon.

Prof. Gillon's focus will also be on intensifying the search for planetary systems similar to that of TRAPPIST-1". As part of his ERC-funded research project SPECULOOS that led to the discovery of the TRAPPIST-1 system, the astronomer is currently setting up an observatory at the European Southern Observatory (ESO) of Paranal in Chile. "The TRAPPIST telescopes focus on about a hundred ultra-cold stars but the SPECULOOS telescopes will target about a thousand stars. Europe trusted me to make this possible. We are now on the good path to finding many interesting new planets and to learn much more about them".

http://bit.ly/2seELlA

Dye kills malaria parasites at speed not seen before

Research shows that the dye methylene blue is a safe antimalarial that kills malaria parasites at an unprecedented rate.

Within two days, patients are cured of the disease and no longer transmit the parasite if they are bitten again by a mosquito. This discovery was made by Radboud university medical center scientists and international colleagues during a research project conducted in Mali. The results will be published in The Lancet Infectious Diseases on February 6th.

The pressure is on when it comes to antimalarial medicines, as malaria parasites are increasingly resistant to the artemisinin-based combination therapies that are currently used. In addition, these medicines do very little to stop the spread of malaria, as the parasites remain in the blood for a long time, with the chance that other mosquitos are infected if they feed on the patient. The parasites split in the patient's red blood cells, forming male and female sex cells (gametocytes). If another mosquito bites the patient, it sucks up the sex cells and these are fertilized in the mosquito's stomach. The offspring then find their way to the mosquito's salivary glands, where the cycle starts again.

Effect after just 48 hours

The gametocytes can stay in a person's body for several weeks following treatment for malaria. In the new study in Mali, Radboudumc researchers added methylene blue to the artemisinin-based combination therapy. Methylene blue is a blue dye that is used in laboratories to distinguish dead cells from living cells. Adding the dye to the antimalaria medicine ensured that patients no longer infected other mosquitos, within as little as 48 hours. Patients who were not given methylene blue were able to infect other mosquitos for at least a week. Researcher Teun Bousema (Radboudumc) coordinated the study which was conducted together with the University of California (UCSF) and the Malaria Research and Training Center (MRTC). Bousema: "We noted that the male parasites disappeared from the bloodstream more quickly than the female parasites."

Blue urine

Encouraged by the promising results of laboratory experiments, Bousema's team has investigated for the first time the effect of methylene blue on the spread of malaria amongst humans. Bousema: "Methylene blue is very promising, because it can prevent the spread of malaria within such a short time following treatment. There are also indications that methylene blue also works well in species that are resistant to certain medicines." The dye is safe and was tolerated well

by patients. There is however just one awkward side effect: "I have used it myself, and it turns your urine bright blue. This is something that we need to solve, because it could stop people from using it."

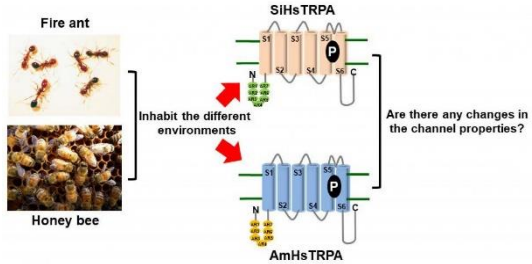
Malaria causes 430,000 deaths every year. Infection is caused by the bite of a malaria-carrying mosquito, and 90% of all deaths are in Africa, mostly amongst children. Malaria prevention focuses primarily on the use of mosquito nets, insecticides and medicine and, as a result, the number of deaths due to malaria has almost halved in the last ten years.

http://bit.ly/2EM27S5

Controlling fire ants with natural compounds

Compound found in cinnamon could be used to repel the invasive insect

New research published in eNeuro has identified natural, plant-derived compounds that repel fire ants. These compounds, including one found in cinnamon, work by activating a type of ion channel highly expressed in the antennae and leg of one of the world's most invasive insect species.



Fire ant and honey bee belong to Hymenoptera but they live under very different environment. The fire ant TRP channel has lost the chemical sensitivity compared to the honey bee version during evolution. Four of eight natural compounds activating the channel repel fire ants, suggesting that these could be used to develop the effective control methods **Tatsuhiko Kadowaki**

Native to South America, the red imported fire ant (*Solenopsis invicta*) has spread in recent decades across the world to countries such as the United States, Australia and China. Efforts to control the species, which can disrupt agricultural production and sting people with its venom, have been largely unsuccessful.

Tatsuhiko Kadowaki, Makoto Tominaga and colleagues investigated the fire ant transient receptor potential (TRP) channel and found that it functions as a sensor of harmful conditions in its environment. Comparing it to the well-studied honey bee TRP channel, the researchers demonstrate that although it is similarly activated by heat, only eight of the 24 compounds that activated the honey bee TRP channel activated the fire ant version. Since the genes encoding this channel in each species are derived from a common ancestor, this suggests that the fire ant TRP channel has evolved to be less sensitive to the compounds that activate the honey bee TRP channel.

Article: *The red imported fire ant, Solenopsis invicta HsTRPA functions as a nocisensor and uncovers the evolutionary plasticity of HsTRPA channels*
DOI: *https://doi.org/10.1523/ENEURO.0327-17.2018*
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http://bit.ly/2FUu09W

Half of all dementias start with damaged 'gatekeeper cells'

Once the cells are compromised, the brain's protective fort becomes leaky and allows blood toxins to trespass into the brain, damaging critical connections between brain areas, USC researchers say.

USC research sheds new light on how a breakdown in the brain's vascular system predates the accumulation of toxic plaques and tangles in the brain that bring about Alzheimer's disease. The research suggests an earlier target for preventing dementia and Alzheimer's.

Nearly 50 percent of all dementias, including Alzheimer's, begins with the breakdown of the smallest blood vessels in the brain and their protective "gatekeeper cells," according to a Keck School of Medicine of USC study.

That catastrophe causes a communications failure called small vessel disease. Many people with that disease also have white matter disease, the wearing away of fatty myelin that allows neurons to transfer messages within the brain network. In an animal model, researchers found that brain deterioration associated with dementia may start as early 40 in humans.

For more than 25 years, scientists have known that white matter disease impedes a person's ability to learn or remember new things, slows thinking and causes people to fall more often due to balance issues.

They identified a link between crippled small blood vessels in the brain and white matter disease but didn't know what started that process until now.

"Many scientists have focused their Alzheimer's disease research on the buildup of toxic amyloid and tau proteins in the brain, but this study and others from my lab show that the problem starts earlier -- with leaky blood vessels in the brain," said Berislav Zlokovic, senior author of the study and holder of the Mary Hayley and Selim Zilkha Chair in Alzheimer's Disease Research at the Keck School of Medicine.

"The collapse of pericytes -- gatekeeper cells that surround the brain's smallest blood vessels -- reduces myelin and white matter structure in the brain. Vascular dysfunctions, including blood flow reduction and blood-brain barrier breakdown, kick off white matter disease."

The role played by pericytes

The study, published in Nature Medicine on Feb. 5, explains that pericytes play a critical role in white matter health and disease via fibrinogen, a protein that circulates in blood. Fibrinogen develops blood clots so wounds can heal. When gatekeeper cells are compromised, an unhealthy amount of fibrinogen slinks into the brain and causes white matter and brain structures, including axons (nerve fibers) and oligodendrocytes (cells that produces myelin), to die.

Axel Montagne, first author of the study, said he and his colleagues are the first to show that fibrinogen is a key player in non-immune white matter degeneration. The protein enters the brain through a leaky blood-brain barrier.

"We demonstrated that controlling fibrinogen levels can, in a mouse model, reverse or slow white matter disease, the harbinger to dementia," said Montagne, an assistant professor of research in physiology and neuroscience at the Zilkha Neurogenetic Institute at the Keck School of Medicine.

Dementia affects 50 million people worldwide and costs the world an estimated $818 billion, according to the World Health Organization.

As a research institution devoted to promoting health across the life span, USC has more than 70 researchers dedicated to the prevention, treatment and potential cure of Alzheimer's disease and other dementias.

A new villain to target

The study found about 50 percent fewer gatekeeper cells and three times more fibrinogen proteins in watershed white matter areas in postmortem Alzheimer's brains of humans compared to healthy brains.

To understand what was happening, USC-led researchers studied mice lacking in pericytes and compared them with a control group.

Using a MRI technique the Zlokovic Lab developed, they noticed 50 percent increased vessel leakage in mice that were 36 to 48 weeks old, roughly the equivalent of 70-year-old humans. The animal model replicated what scientists observed in the postmortem brains of people. So they took a closer look.

The scientists also found reduced cerebral blood flow and increased accumulation of fibrinogen in the brains of mice deficient in gatekeeper cells. At 12 to 16 weeks old, the experimental mice had 10 times more fibrinogen in the corpus callosum compared to the control group. That region is the brain's central transit terminal that routes motor, sensory and cognitive information to their final destinations.

"Our observations suggest that once pericytes are damaged, blood flow in the brain reduces like a drain that is slowly getting clogged," said Angeliki Maria Nikolakopoulou, co-first author of the study and assistant professor of research in physiology and neuroscience at the Zilkha Neurogenetic Institute.

On the wheel

Researchers had the mice run on a wheel to test their subcortical brain region, the same area studied in postmortem humans. At first, the wheel had equally spaced rungs. After two weeks, scientists removed some of the rungs. When the experimental group was 12 to 16 weeks old, they reached a maximum speed that was about 50 percent slower than the control group. "The mice deficient in pericytes function slower because

there are structural changes in their white matter and a loss of connectivity among neurons," Zlokovic said.

The researchers used diffusion MRI techniques the Zlokovic Lab developed to see what was happening in the brain. They saw white matter changes in mice as early as 12 to 16 weeks old. Theoretically, that means white matter disease in humans could begin when they are just 40 years old, Montagne said.

"Pericytes are compromised early on," Montagne said. "Think of it as hair clogging a drain over time. Once the drain is clogged, cracks begin forming in the 'pipes' or brain's blood vessels. White matter frays and brain connections are disrupted. That's the beginnings of dementia."

Testing the poison

To confirm that fibrinogen proteins are toxic to the brain, researchers used an enzyme known to reduce fibrinogen in the blood and brain of mice. White matter volume in mice returned to 90 percent of their normal state, and white matter connections were back to 80 percent productivity, the study found.

"Our study provides proof that targeting fibrinogen and limiting these protein deposits in the brain can reverse or slow white matter disease," Zlokovic said. "It provides a target for treatment, but more research is needed. We must figure out the right approach.

"Perhaps focusing on strengthening the blood-brain barrier integrity may be an answer because you can't eliminate fibrinogen from blood in humans. This protein is necessary in the blood. It just happens to be toxic to the brain."

Angeliki Nikolakopoulou, Zhen Zhao, Abhay Sagare, Gabriel Si, Divna Lazic, Anita Ramanathan, Ariel Go, Erica Lawson, Yaoming Wang, Jobin Varkey, Ralf Langen and Russell Jacobs from the Zilkha Neurogenetic Institute, Samuel Barnes from the California Institute of Technology, Madelaine Daianu and Paul Thompson from the Imaging Genetics Center at the USC Mark and Mary Stevens Neuroimaging and Informatics Institute, William Mack from the Keck School of Medicine, Julie Schneider from Rush University Medical Center and Eric Mullins from the University of Cincinnati College of Medicine also contributed to this study.

The federal government funded this research with about $6 million in grants from the National Institutes of Health (NS100459, AG039452, NS034467, AG023084). The remainder was funded by the Foundation Leducq Transatlantic Networks of Excellence (no. 16 CVD 05 and ES024936).

http://bit.ly/2EOdqt0

Cloned crayfish conquers the world

A bizarre aquarium escapee has extra chromosomes, clones itself, and is spreading around the world.

Stephen Fleischfresser reports.

It may sound far-fetched, a but a real-life super-macromutant has been born, creating a new species with bizarre biology in the process. And it's hell-bent on cloning itself in a bid for world domination.

For real.

The monster from the home aquarium: a marbled crayfish clone. **Ranja Andriantsoa**

A team of scientists led by epigeneticist Frank Lyko of the German Cancer Research Centre in Heidelberg, Germany, is on the case of the remarkable story of the small freshwater crustacean known as the "marbled crayfish".

The start of this tale can all be traced back to an insect trade fair in Frankfurt, Germany, in 1995, where an American trader gave a German aquarium enthusiast a bag of unidentified crayfish. These multiplied rapidly, and the aquarist decided to distribute for other hobbyists. Soon, they spread through the German pet trade.

Somewhere in this string of events, the mutant marbled crayfish came into existence, almost certainly to parents who were genetically related to each other, and belonging to the species *Procambarus fallax*, the American slough crayfish, a popular aquarium pet. Their mutant prodigy was very different from its parents, so much so that Lyko determined it to be a whole new species, which he named *Procambarus virginalis*.

Most sexually reproducing organisms have two copies of each chromosome – the strings of DNA that contain all an individual's genetic information – one from each parent. *P. virginalis*, however, has

three – one from each parent plus an extra duplicate copy of one of the parental chromosomes, a condition called "autopolyploidy".

This triplicate structure gives the marbled crayfish some remarkable abilities. To begin with, it does not reproduce sexually. Instead, it has the capacity for parthenogenesis, which means that it can produce young from unfertilised eggs, something it can do at a much higher rate than other crayfish. Lyko's most recent paper, published in *Nature Ecology & Evolution*, further reveals that the parthenogenesis is "apomictic", meaning that the young are actually clones of the original individual mutant. All members of *P. virginalis* are genetically identical. These changes have made *P. virginalis* reproductively incompatible with *P. fallax*, part of the reason that Lyko determined them to be separate species. Like everything about the marbled crayfish, this too is fascinatingly different.

The evolutionary formation of species, certainly according to Darwin and many others, normally proceeds gradually, with the accumulation of mutations gently pushing populations away from each other to become separate species. With *P. virginalis*, Lyko and his team argue that speciation has occurred in a single large and sharp jump, from *P. fallax* to *P. virginalis* in one generation, a process known as saltational speciation. The marbled crayfish then is a macromutation, or what geneticist Richard Goldschmidt famously referred to in 1940 as a 'hopeful monster'.

If all this wasn't strange enough, this self-cloning super macromutant escaped the aquarium and leapt into the wild. Now spread around the world, it is endlessly cloning itself and taking up residence in habitat after habitat. Interestingly, Madagascar seems particularly hospitable, and *P. virginalis* is now emerging as a determined invasive species in its waterways. Lyko and his team have shown that the Madagascan population of has increased 100-fold in the past 10 years.

So, what about the future of this hopeful monster?

Despite its relentless spread, conventional wisdom suggests that the species will suffer at some point due to its incredibly restricted genepool. Such genetic bottlenecks normally reduce the robustness of a species. *P. virginalis* will be particularly vulnerable to environmental change. Lyko is philosophical: "The situation is what it is – obviously these animals are quite successful, even if they don't have any genetic variation," he says.

He adds that the fact they carry three, rather than two, copies of each chromosome might protect them from the slings and arrows of environmental change.

The future of Lyko's research is clearer. Given that all *P. virginalis* individuals are identical clones, any evolutionary adaptation can be observed very clearly and Lyko thinks this will take place epigenetically. Epigenetics is the study of the way in which various molecular mechanisms from the environment interact with and effect the way genes are expressed, and this is Lyko's primary interest.

P. virginalis, it transpires, might well help us to more clearly understand the role epigenetics play in evolution. "This is actually how I got drawn into the project," he says. "I'm an epigeneticist and we believe that marbled crayfish represent the perfect model for investigating the role of epigenetics in phenotypic adaptation and variation."

While there is still some controversy surrounding the idea that *Procambarus virginalis* is actually a new species (with some suggesting it is just a parthenogenetic lineage), the incredible story of the marbled crayfish is, no doubt, one to follow closely, as is the work of Lyko and his team.

http://go.nature.com/2nOssa4

Heaviest known element has electrons that break the mould

Oganesson nuclei are bathed in an electron haze.

Electrons generally orbit atomic nuclei in distinct shells, but calculations show that the outer electrons of oganesson, the heaviest element found so far, may instead orbit the nucleus as a gas.

Oganesson decays quickly, making it a challenge to probe experimentally. Instead, Peter Schwerdtfeger at Massey University

Auckland in New Zealand and his colleagues calculated the energy levels of electrons around oganesson nuclei. For greater accuracy, the researchers took into account what are known as 'relativistic effects' — the influence of the element's high nuclear charge, which is much greater than that of lighter elements.

The team found that in oganesson, the outermost electron orbits become indistinct, creating an outer layer that is almost an electron gas. Oganesson is classified as a noble gas, but the findings suggest that it may behave differently from other members of its group and may even be solid at room temperature.

http://bit.ly/2FWhnLl

Can over-the-counter pain meds influence thoughts and emotions?

Over-the-counter pain medicine such as Ibuprofen and acetaminophen may influence how people process information, experience hurt feelings, and react to emotionally evocative images, according to recent studies.

Los Angeles, CA - Examining these findings and how policymakers should respond, a new article is out today in Policy Insights from the Behavioral and Brain Sciences, a Federation of Associations in Behavioral & Brain Sciences (FABBS) journal published in partnership with SAGE Publishing.

Article authors Ratner et al. reviewed previous research suggesting that over-the-counter pain medicine may influence individuals':

Sensitivity to emotionally painful experiences: Compared to those who took placebos, women who took a dose of ibuprofen reported less hurt feelings from emotionally painful experiences, such as being excluded from a game or writing about a time when they were betrayed. Men showed the opposite pattern.

Ability to empathize with the pain of others: Compared to those taking placebos, individuals who took a dose of acetaminophen were less emotionally distressed while reading about a person experiencing physical or emotional pain and felt less regard for the person.

Ability to process information: Compared to those who took placebos, individuals who took a dose of acetaminophen made more errors of omission in a game where they were asked, at various times, either to perform or to not perform a task.

Reactions to emotional objects: Individuals who took a dose of acetaminophen rated pleasant and unpleasant photographs less extremely than those who took placebos.

Discomfort from parting with possessions: When asked to set a selling price on an object they owned, individuals who took a dose of acetaminophen set prices that were cheaper than the prices set by individuals who took placebos.

"In many ways, the reviewed findings are alarming," wrote Ratner et al. "Consumers assume that when they take an over-the-counter pain medication, it will relieve their physical symptoms, but they do not anticipate broader psychological effects."

The authors also wrote that while the medicine could have new potential for helping people deal with hurt feelings, more research is needed to examine the efficacy and determine if it would have negative effects for people who take it in combination with other medicines or who are depressed and have difficulty feeling pleasure.

While they emphasize that further studies are necessary before policymakers consider new regulations or policies, they recommend for policymakers to begin to think about potential public health risks and benefits in case preliminary studies are confirmed.

Find out more by reading the full article, "Can Over-the-Counter Pain Medications Influence Our Thoughts and Emotions?," by Ratner et al., in Policy Insights from the Behavioral and Brain Sciences. For an embargoed copy of the full text, please email tiffany.medina@sagepub.com.

http://bit.ly/2E9LJ0L

The recipe for life

UCSB researchers find that the amino acid arginine may have played a more important role in the chemical origins of life

Life as we know it originated roughly 3.5 to 4 billion years ago in the form of a prebiotic ("before life") soup of organic molecules that somehow began to replicate themselves and pass along a genetic

formula. Or so goes the thinking behind the RNA World, one of the most robust hypotheses of the origin of life.

Researchers at UC Santa Barbara have now found evidence that the amino acid arginine (or its prebiotic world equivalent) may have been a more important ingredient in this soup than previously thought.

"People tend to think of arginine as not being prebiotic," said Irene Chen, a biophysicist whose research focuses on the chemical origins of life. "They tend to think of the simpler amino acids as being plausible, such as glycine and alanine." Arginine, by contrast, is relatively more complex, and was therefore thought to have entered the game at a later stage.

Primordial Earth, according to the RNA World theory, had the conditions to host several types of biomolecules, including nucleic acids (which become genetic material), amino acids (which eventually link to form the proteins that are responsible for structure and function of cells) and lipids (which store energy and protect cells). Under what circumstances and how these biomolecules worked together is a source of ongoing investigation for researchers of the origins of life.

For their investigation, the UCSB scientists analyzed a dataset of in vitro evolved complexes of proteins and aptamers (short RNA and DNA molecules that bind to specific target proteins).

"We were looking at the interface for which properties favored binding," said Celia Blanco, a postdoctoral researcher in the Chen Lab, and lead author of a paper that appears in the journal Current Biology. In vitro evolution was an important factor when selecting these evolutionarily independent complexes, she pointed out, to avoid the confounding effects resulting from biological evolution and to closely mimic the conditions of a prebiotic world.

"There are so many constraints in biology," said Chen, who also is a medical doctor. "Biologically evolved protein-DNA or protein-RNA interactions have to work inside a cell; that's not exactly going to be the case for the origins of life."

What the researchers found was that arginine was a player in many of the chemical interactions between proteins and aptamers.

"Of course, we expected it to be very important for electrostatic interactions because it's positively charged," Chen said, "but it was also the dominant amino acid for hydrophobic interactions, stacking interactions and these other different modes of interacting that other amino acids are more known for." To a lesser degree, lysine (another positively charged amino acid) also played significant roles in these interactions.

Among other reasons, arginine may have been overlooked because it is a relatively more difficult amino acid to synthesize.

"Usually people base the consensus of what is prebiotic and what is not on experiments," Blanco said. "And using what people believe are prebiotic conditions, arginine and lysine seem to be difficult to either synthesize or detect." But just because something such as arginine hasn't been produced in the laboratory experiments conducted so far, Blanco continued, doesn't mean it wasn't there.

The researchers are careful to point out that although the amino acid we call arginine was found to be important in the aptamer-protein binding interactions they examined, billions of years ago the biomolecule may not necessarily have been today's arginine but perhaps a positively charged primordial equivalent.

This development sheds more light on what might have been the ideal conditions for the rise of life. There are a variety of hypotheses -- from comets to hydrothermal vents to other environments -- that may have been favorable for the eventual evolution of cells, as well as several landmark experiments that bolster the RNA World idea.

"If we had found that glycine was really important for RNA-protein interactions -- and glycine is everywhere -- then that would not have been helpful for determining plausible conditions," said Chen. "But finding that arginine was important constrains the type of scenarios that could have given rise to the genetic code."

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Bilingualism could offset brain changes in Alzheimer's

A Concordia study sheds light on how language history relates to brain plasticity

After more than a decade of research, this much we know: it's good for your brain to know another language.

A new Concordia study goes further, however, focusing specifically on the effects of knowing a second language for patients with Alzheimer's disease (AD) and mild cognitive impairment (MCI; a risk state for AD).

"Most of the previous research on brain structure was conducted with healthy younger or older adults," says Natalie Phillips, a professor in the Department of Psychology.

"Our new study contributes to the hypothesis that having two languages exercises specific brain regions and can increase cortical thickness and grey matter density. And it extends these findings by demonstrating that these structural differences can be seen in the brains of multilingual AD and MCI patients." Phillips's study, led by recent Concordia psychology grad Hilary D. Duncan (PhD 17), is soon to be published in Neuropsychologia (Jan, 2018).

New methods: Enter the MRI

Phillips and her team are the first to use high-resolution, whole-brain MRI data and sophisticated analysis techniques to measure cortical thickness and tissue density within specific brain areas.

Namely, they investigated language and cognition control areas in the frontal regions of the brain, and medial temporal lobe structures that are important for memory and are brain areas known to atrophy in MCI and AD patients. "Previous studies used CT scans, which are a much less sensitive measure," says Phillips, founding director of Concordia's Cognition, Aging and Psychophysiology (CAP) Lab.

The study looked at MRIs from participating patients from the Jewish General Hospital Memory Clinic in Montreal. Their sample included 34 monolingual MCI patients, 34 multilingual MCI patients, 13 monolingual AD patients and 13 multilingual AD patients.

Phillips believes their study is the first to assess the structure of MCI and AD patients' language and cognition control regions. It is also the first to demonstrate an association between those regions of the brain and memory function in these groups, and the first to control for immigration status in these groups.

"Our results contribute to research that indicates that speaking more than one language is one of a number of lifestyle factors that contributes to cognitive reserve," Phillips says. "They support the notion that multilingualism and its associated cognitive and sociocultural benefits are associated with brain plasticity."

What's next?

Phillips and her team are already building on their findings.

"Our study seems to suggest that multilingual people are able to compensate for AD-related tissue loss by accessing alternative networks or other brain regions for memory processing. We're actively investigating that hypothesis now."

http://bit.ly/2BPHplR

CDC Identifies Seoul Virus Outbreak Among Pet Rat Owners

These are the first known cases of individuals catching the virus from their pets in Canada or the U.S.

By Diana Kwon | February 6, 2018

A total of 31 pet supply stores, breeders, and homes across 11 US states have reported cases of Seoul virus infection, a rodent-borne hantavirus, in either humans or rats, according to a report published last week (February 2) by the Centers for Disease Control and Prevention (CDC). These are the first known instances of transmission from pet rats to their human owners in Canada or the U.S.

***A Norway rat (*Rattus norvegicus*)* ISTOCK, WHITEWAY

The CDC first identified cases of pet-rat-to-human transmission of Seoul virus in late 2016 when they were notified of local cases from health officials in Tennessee and Wisconsin. According to the report, one patient, who was hospitalized with influenza-like symptoms such as fever and a low white blood cell count, owned and operated an in-home rat-breeding facility (a rattery) with approximately 100 Norway rats (*Rattus norvegicus*)—the primary host of the virus.

This spurred a larger investigation, in which researchers identified the 31 US sites, which included ratteries, homes, and pet stores, with cases of Seoul virus infection. Six of those locations reported exchanging rats with Canadian ratteries. Investigators then tested blood samples from 183 people in the U.S. and Canada and found that 18 individuals had signs of a recent infection. Three people had been hospitalized with infection-related illness, but no deaths occurred.

Symptoms of Seoul virus infection range from mild influenza-like illness to hemorrhagic fever with renal syndrome, which can cause acute kidney failure and be fatal. According to the CDC, the virus is not known to spread between people.

“Pet rat owners should practice safe rodent handling to prevent Seoul virus infection,” the researchers write in the report.

http://bit.ly/2nQquxm

New study sheds light on Moon's slow retreat from frozen Earth

A study led by University of Colorado Boulder researchers provides new insight into the Moon's excessive equatorial bulge, a feature that solidified in place over four billion years ago as the Moon gradually distanced itself from the Earth.

The research sets parameters on how quickly the Moon could have receded from the Earth and suggests that the nascent planet's hydrosphere was either non-existent or still frozen at the time, indirectly supporting the theory of a fainter, weaker Sun that at the time radiated around 30 percent less energy than it does today.

"The Moon's fossil bulge may contain secrets of Earth's early evolution that were not recorded anywhere else," said Shijie Zhong, a professor in CU Boulder's Department of Physics and the co-lead author of the new research. "Our model captures two time-dependent processes and this is the first time that anyone has been able to put timescale constraints on early lunar recession."

Credit: CC0 Public Domain

The Moon currently recedes from the Earth at a rate of about 4 centimeters per year according to lunar laser ranging observations from the Apollo missions. The recession is believed to result from gravitational or tidal interaction between the Earth and Moon. The same process also causes Earth's rotation to slow down and the length of day to increase.

Scientists have theorized that tidal and rotational forces shaped the Moon after it separated from Earth, cooled and moved farther from the planet. The effects of these forces flattened the Moon slightly at its poles and solidified a permanent bulge in the lunar crust, creating the feature known as the fossil bulge. About 200 years ago, French mathematician and physicist Pierre-Simon Laplace determined that the Moon's equatorial bulge was 20 times too large for its one-revolution-per-month rotational rate.

The timing and necessary conditions of this fossil bulge formation have remained largely unknown given that no physical models have ever been formulated for this process. Using a first-of-its-kind dynamic model, Zhong and his colleagues determined that the process was not sudden but rather quite slow, lasting several hundred million years as the Moon moved away from the Earth during the Hadean era, or about 4 billion years ago.

But for that to have been the case, Earth's energy dissipation in response to tidal forces-which is largely controlled by the oceans for the present-day Earth-would have to have been greatly reduced at the time.

"Earth's hydrosphere, if it even existed at the Hadean time, may have been frozen all the way down, which would have all but eliminated tidal dissipation or friction," Zhong said, adding that a weaker, fainter young Sun could have made such conditions possible in theory.

The "snowball Earth" hypothesis has been suggested previously for the Neoproterozoic era approximately 600 million years ago based on geological record. Similar ideas have also addressed the possibility of a fainter young Sun, but direct observational evidence in the geological record is currently lacking, making it the subject of debate among scientists.

The researchers plan to continue optimizing their model and will attempt to fill in other knowledge gaps about the Moon and Earth's early days between 3.8 and 4.5 billion years ago.

The study was recently published online in *Geophysical Research Letters*, a journal of the American Geophysical Union.

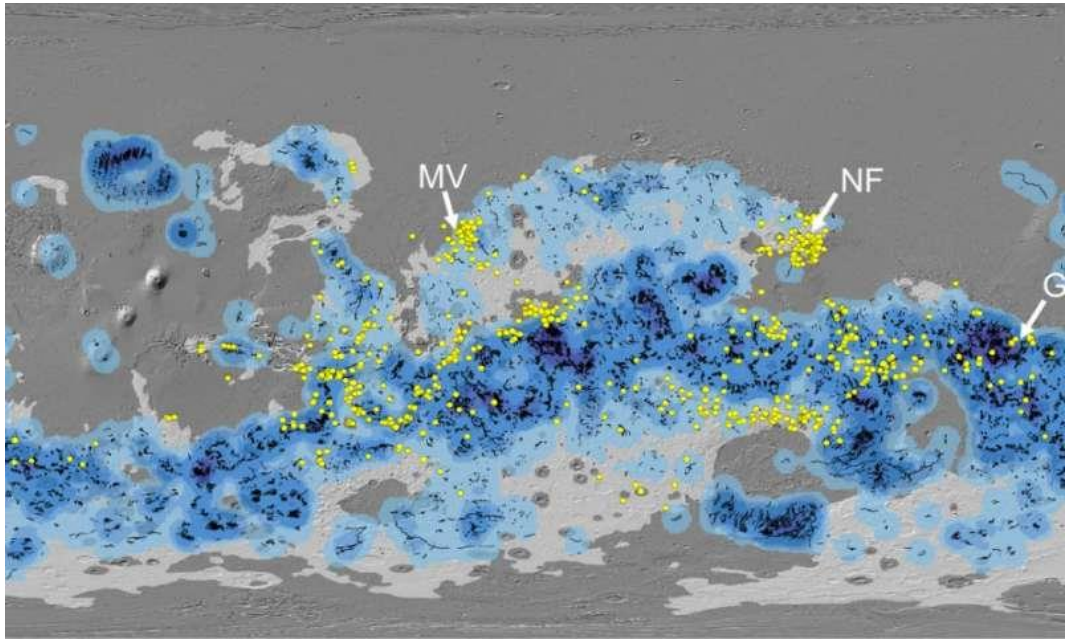
More information: *Chuan Qin et al, Formation of the Lunar Fossil Bulges and Its Implication for the Early Earth and Moon, Geophysical Research Letters (2018). DOI: 10.1002/2017GL076278*

http://bit.ly/2BQmdMt

New studies of clay formation provide clues about early Martian climate

New research published in Nature Astronomy seeks to understand how surface clay was formed on Mars despite its cold climate.

The climate on early Mars has presented an enigma for planetary scientists because surface features such as valley networks indicate abundant liquid water was present and the clay minerals found in most ancient surface rocks need even warmer temperatures to form, while atmospheric models generally support a cold climate on early Mars. This new study led by Janice Bishop of the SETI Institute and NASA's Ames Research Center in Silicon Valley has addressed this question by investigating the conditions needed for the formation of the ancient surface clays.

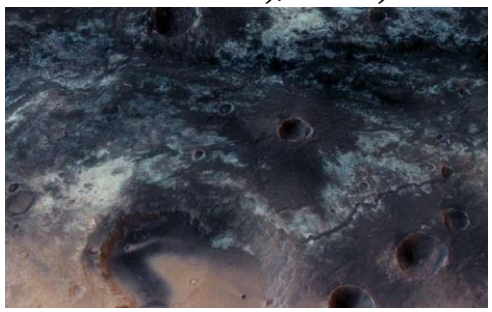


Ancient Noachian rocks on Mars are mapped in light gray with valley networks colored in blue tones and surface clays marked in yellow. Two locations with abundant smectite clays formed in surface environments include Mawrth Vallis (MV) and Nili Fossae (NF). The Mars Science Laboratory (MSL) rover is currently at Gale Crater (GC) where smectite clays have also been found. **SETI Institute**

Part of this early Martian climate puzzle comes down to how "warm" is warm. Currently Mars' temperature is below freezing, but we know it must once have been warm enough for liquid water to carve out features on the surface. However, cold water is not warm enough for surface clays to form. "We realized that in order to better constrain the early Martian climate, we needed to understand the formation conditions of Martian clays," said Bishop.

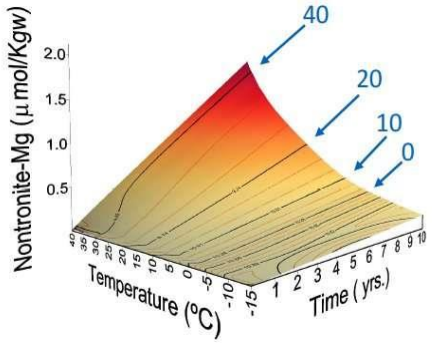
This study evaluated the types of clays present in ancient, altered rocks on Mars and separated these into 3 categories: 1) Mg-rich clays formed at high temperatures (100-400 °C) below surface (e.g. mixtures of saponite, serpentine, chlorite, talc, and carbonate), 2) clays

formed at warm temperatures (20-50 °C) in lakes, streams or rainy environments (dioctahedral Fe-rich or Al-rich smectites), and 3) poorly crystalline aluminosilicates such as allophane formed at cold temperatures (<20 °C). The authors used results from weathering in the field, clay synthesis experiments in the lab, and geochemical modeling of clay formation.



A view of light-toned phyllosilicates at Mawrth Vallis, Mars captured by the High Resolution Stereo Camera (HRSC) flown on Mars Express and provided by DLR and Free University in Berlin. This image illustrates water features cutting through the thick surface clay deposits. **SETI Institute**

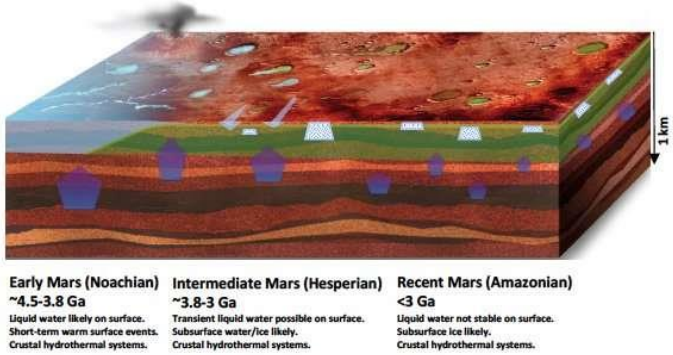
The authors postulate that short-term warm and wet environments, occurring sporadically in a generally cold early Mars, enabled the formation of the observed surface smectite occurrences on Mars. Further, there is a trade-off between temperature and time. Cooler temperatures (15-20 °C seasonal, diurnal Tmax) would require sustained periods of high water/rock ratio on Mars to produce the observed smectite outcrops. This could mean hundreds of millions of years at 5 °C global mean average temperature on Mars, which is unlikely given the current models of the atmosphere.



Geochemical modeling of nontronite formation shows that formation is almost nonexistent below 10 °C and still very slow up to 20 °C. Reaction proceeds significantly faster up to 40 °C and higher. **SETI Institute**

Surface smectite (nontronite, montmorillonite) beds may have formed quickly during short-term periods of warm temperatures (25-40 °C seasonal, diurnal Tmax). This could mean tens of thousands or millions of years at a global mean average temperature of 10-15 °C on Mars at intervals over hundreds of millions of years. These elevated temperatures could have been caused by volcanism, obliquity changes, or large impacts.

Understanding the climate on early Mars provides constraints for when liquid water was present on the surface and is essential for determining where on Mars to search for life. Clays are the most abundant hydrated mineral on Mars; thus, defining their formation conditions is a big step towards understanding the geochemical environment on Mars.



This diagram illustrates the timeline for water (blue) on the surface of Mars. Ancient Mars was likely cold with transient warming events that enabled formation of the surface clays (green) in warm water (20-40 °C). These surface clays have persisted through generally cold and dry climates since their formation, but are cut by fluvial events arising after formation of the clays that may have been warm enough to form liquid water but not warm enough to form additional clays. **SETI Institute**

More information: *Janice L. Bishop et al. Surface clay formation during short-term warmer and wetter conditions on a largely cold ancient Mars, Nature Astronomy (2018). DOI: 10.1038/s41550-017-0377-9*

http://bit.ly/2nVQkZi

Insane drug cocktails in India net drug makers millions and pose global threat

The drugs are made by international companies, but they're not approved anywhere.

Beth Mole - 2/6/2018, 10:10 PM

In August of 2016, doctors in Washoe County, Nevada, found that one of their patients couldn't shake a bad bacterial infection. The infection had likely taken hold years before while the local woman was on an extended visit to India. There, she had undergone multiple

hospitalizations and surgery for a leg injury and developed a bone infection. By the time she got back to Nevada, the infection had spread. The US doctors isolated her in a hospital room and threw all the antibiotics they could at the infection. It resisted all of them—26 in total, tests confirmed. In early September, the woman developed septic shock and died.

Though rare, the case highlights two important points: that drug-resistant bacteria don't stop at borders and that India is of particular concern in the fight against antibiotic-resistant infections.

While cases of drug-resistant bacterial infections are rising globally, recent data shows that India has among the highest rates of such infections in the world. The country is also the largest consumer of antibiotics per capita.

Now, new data paints a clearer picture as to why the country appears to be a breeding ground for drug resistant infections that threaten to spread within and beyond the country.

Drug companies—some international and even US-based—are selling millions of dubious and unapproved cocktails of antibiotics in India, all of which could spur the development of drug-resistant bacteria and imperil patients.

The finding, published Monday in the *British Journal of Clinical Pharmacology* by UK health experts, suggests that the country poses a risk to global health and undermines efforts to control drug resistance.

The study authors, led by Patricia McGettigan of Queen Mary University of London, recommend firm regulatory action within India to ban these unapproved drug cocktails. They also call for the multinational drug companies producing some of the antibiotic mixtures—such as Abbott, GlaxoSmithKline, Astra Zeneca, Pfizer, and Merck/MSD—to be accountable for their products.

Drug companies "should be required to justify the sale of products in India that do not have the approval of their own national regulators and, in multiple cases, not even the approval of the Indian regulator," they conclude.

Dodgy doses

For the study, Prof. McGettigan and her colleagues pulled antibiotic sales figures from a commercial database of Indian drug distribution called PharmaTrac. They looked at sales between October 2007 and November 2012. They then compared the inventory of drugs sold in India to the list of drugs approved by India's Central Drugs Standard Control Organization (CDSCO) as well as those approved by the US Food and Drug Administration (FDA) and the European Medical Agency (EMA).

The researchers found that drug companies sold 86 regular, so-called "single-dose antibiotics" and 118 "fixed-dose combination" antibiotics over the five-year period. The FDC drugs are formulations composed of two or more drugs at fixed ratios in a single dose. They can include two or more antibiotics or antibiotics and a different type of drug, such as an anti-protozoal drug. Such combo formulations are rare in the US and UK; drug companies sold just five of these in the US and UK during the same period.

Many of the 118 sold in India were "poorly considered," the authors note. Some combined antibiotics that needed to be taken at different intervals to work. For instance, one FDC paired an antibiotic that needs to be taken once a day with another that needs to be taken every eight hours to work effectively. Some combinations risked amplified side effects while others combined drugs that wouldn't be given to treat the same illness.

Of the 118 types of FDCs, 75 (64 percent) had no approval from either the CDSCO, FDA, or EMA. Nearly all of the single-dose antibiotics were approved, on the other hand. Still, FDCs overall made up 34 percent of antibiotics sold in India by 2012—roughly 872 million doses that year. And 42 percent of the FDCs sold contained antibiotics that the World Health Organization considered "highest-priority critically important" drugs, which should be used sparingly.

Twelve multinational companies were responsible for making 53 of the 118 types of FDCs. These included Abbott, Astra Zeneca, Baxter,

Bayer, Eli Lilly, GlaxoSmithKline (GSK), Merck/MSD, Novartis, Pfizer, Sanofi-Aventis, and Wyeth. Of the 53 FDCs, only four were approved by the FDA and/or the EMA, and 20 were not approved by even India's CDSCO. US-based Abbott, which has been criticized for its antibiotic sales in India before, sold 18 of those 20 unapproved combination drugs. In 2014, Abbott made $367 million from FDC profits in India, Reuters reported in 2015. At the time, a company spokesperson said that its manufacturing and marketing in India is "aligned with local regulations."

The authors noted that the Indian government has made attempts to ban the unapproved drugs. But the efforts have been held up in courts, and drug regulation is weak, generally.

"The use of unapproved, scrutinized antibiotic FDC formulations is likely to contribute to India's rising antimicrobial resistance," the authors conclude. "Until definitive action is taken to ban most systemic antibiotic FDCs from manufacture and sale, [antimicrobial resistance] initiatives in India are likely to be undermined and the global action plan impeded."

British Journal of Clinical Pharmacology, *2018. DOI: 10.1111/bcp.13503 (About DOIs).*

http://bit.ly/2EsnF8F

How solitary cockroaches gave rise to social termites—tales from two genomes

Termites are "social cockroaches."

February 6, 2018 by Coby Schal

They evolved from ancestral solitary cockroaches some 150 million years ago, at least 50 million years before bees, ants and wasps evolved similar intricate societies independently of termites. Termites live in complex societies characterized by division of labor of castes and close coordination of tasks among members of the colony. For example, the queen and king monopolize all reproduction within the colony, while workers and soldiers maintain and defend the colony. This separation of responsibilities within the colony requires clear recognition of who's who and mechanisms to suppress worker reproduction when a fertile queen is present, and stimulate new queens to develop when the resident queen dies. At the same time, termites have a relatively simple lifestyle – they eat wood and rarely venture in the open. These changes from the ancestral solitary cockroach should be reflected in the organization of the termite genes, the genome.

The German cockroach has a very different lifestyle from the termite. It is the quintessential omnivore, eating all foods, scavenging and even engaging in coprophagy – eating communal feces – to obtain symbiotic microorganisms and nutrients from members of its group.

A female German cockroach. A new paper compares cockroach and termite genomes to find clues to the evolution of sociality. **Matt Bertone**

This cockroach is a global indoor pest that has significant adverse effects on human health. Cockroaches produce potent allergens that can trigger allergies and asthma, especially in children living in cockroach-infested homes. They thrive in unsanitary conditions and therefore they not only transmit pathogens to people, but have evolved a broad range of immune mechanisms to prevent from being infected themselves. Finally, cockroaches have evolved many mechanisms to resist the broad array of offensive chemicals they encounter in their environment, including an expansive arsenal of insecticides we use in our efforts to eradicate them.

A paper in *Nature Ecology & Evolution* reports the sequencing, annotation and analysis of the genomes of the German cockroach, Blattella germanica, and the drywood termite, Cryptotermes secundus, within the context of the evolution of sociality in termites from solitary cockroaches.

The team, including NC State entomologist Coby Schal and principal research scholar Ayako Wada-Katsumata, compared these genomes and those of 15 other insect species so that the evolution of gene

families could be analyzed along the transition from non-social cockroaches to social termites.

Of particular interest in this paper are the chemosensory genes, which are used in chemical communication – smell and taste. The nocturnal and omnivorous lifestyle of cockroaches requires substantial investment in sensitive and discerning senses of smell and taste, and the genome of the cockroach reflects this. Four families of chemosensory proteins enable insects to distinguish diverse foods, locate and recognize mates and aggregation sites (pheromones), and avoid poisons and pathogens.

The German cockroach now holds the world record for the diversity of its chemosensory gene repertoire, and this resource will be invaluable for developing better lures and baits for pest control. The far more specialized but evolutionarily related termite experienced considerable losses of smell and taste genes, commensurate with the more specialized chemistry of its ecological habitat. Yet, the termite genome reveals signatures of chemosensory adaptations that persisted from cockroaches and likely shaped the evolution of social life in these "social cockroaches."

Expansions of many other gene families in the cockroach genome likely enabled adaptations and successful colonization of diverse habitats. The publically available genome sequence will enable researchers and the pest control industry to investigate the functions of many genes and target some with innovative and cockroach-specific pesticides. Among these are genes involved in the breakdown and clearance of insecticides. Expansions in these genes and their heightened expression allows B. germanica to develop resistance to a broad range of insecticides. Likewise, the cockroach can resist many different types of pathogens because it harbors expanded families of genes used in immune responses and defense against pathogens. The expanded repertoire of genes that encode digestive enzymes supports the success of the German cockroach as an extreme omnivore, capable of digesting a broad range of foods from Krispy Kreme donuts to leftover steak.

More information: *Mark C. Harrison et al. Hemimetabolous genomes reveal molecular basis of termite eusociality, Nature Ecology & Evolution (2018).* *DOI: 10.1038/s41559-017-0459-1*

http://bit.ly/2Bk358w

How old antibiotic compounds could become tomorrow's life-saving drugs

Looking back at previously discarded chemical compounds, to see if any could be developed for new antibiotics

As the fight against drug-resistant infections continues, University of Leeds scientists are looking back at previously discarded chemical compounds, to see if any could be developed for new antibiotics.

In the heyday of antibiotic development in the mid-20th century many different chemical compounds with antibacterial properties were examined, but only a small proportion were selected for development into drugs.

With modern-day diseases becoming increasingly resistant to existing drugs, biological scientists and chemists at Leeds are now re-examining these old compounds, applying advances in science and technology to test more precisely whether they could still hold the key to a future drug.

Dr Alex O'Neill, from the Antimicrobial Research Centre at the University, said: "We're showing the value of reviewing compounds previously put on the back of the shelf. Amongst the 3,000 or so antibiotics discovered to date, only a handful have been brought into clinical use. There may be a wealth of compounds out there with untapped potential.

"At the moment, the bugs are outsmarting the scientists, and we can't allow that to continue. By studying compounds which past research has shown already have antibacterial properties, there is scope for a potential fast-track through the challenging early stages of drug discovery. This approach could pave the way for life-saving new drugs." His work has been backed by the Medical Research Council, whose Head of Infections and Immunity described it as 'important'.

Potential for new drug

Dr O'Neill's latest research found that a compound identified in the 1940s could now be a realistic contender as the basis of a new antibiotic drug.

A family of compounds, known as the actinorhodins, was originally identified as having weak antibiotic properties, but was not taken forward for development into a drug.

However, Dr O'Neill said that at the time scientists did not fully differentiate the individual compounds within the family when they examined them, leading to a less than precise picture of their properties.

This prompted his team to divide the family and select a specific compound (y-ACT) for further evaluation, using an array of 21st century approaches, to assess its potential and to understand how it works against bacteria.

Serious contender

Dr O'Neill and colleague Professor Chris Rayner from the University's School of Chemistry have published their findings in the journal Scientific Reports, and believe the compound is worth serious consideration as the basis for a new drug to combat certain types of bacterial infections.

Dr O'Neill added: "y-ACT exhibits potent antibacterial activity against two important representatives of the ESKAPE class of pathogens, which are bacteria that have developed the ability to 'escape' the action of existing drugs.

"A major challenge in tackling the problem of antibiotic resistance is to discover new drugs - our study shows that potentially useful drug candidates can be 'discovered' from amongst the antibiotics we already know about."

"The weak activity previously published for the ACT family as a whole probably explains why this group was not further evaluated, and it is intriguing to think that other potentially useful antibiotic groups are languishing in obscurity in academic journals just needing expert review using modern processes and equipment."

Urgent need

Supporting Dr O'Neill's work, Dr Jonathan Pearce, Head of Infections and Immunity at the Medical Research Council, said: "There is an urgent need to discover new ways to fight AMR and the scientific community is leaving no stone unturned in its search for new antibiotics. This includes revisiting chemical compounds that were once shelved.

"Until recently, no new antibiotics had been discovered for 25 years. Dr O'Neill's research is important: it's providing another way of looking for potential antibiotics and could hold the key to uncovering options that were overlooked before but may be incredibly useful now."

Stopping E. coli

Also based in the School of Chemistry is Dr Michael Webb, whose research focuses on a compound, called pentyl pantothenamide, first assessed in the 1970s.

Then, it was found to be able to stop the growth of E.coli but not completely kill the bacteria, so was never taken into clinical use.

At the time, scientists did not understand how it was able to stop the growth, but Dr Webb and his team have proved it is driven by Vitamin B5, which is used to metabolise energy. Bacteria have to make B5 and a key part of the machinery they use to do so is called the PanDZ complex.

Pentyl pantothenamide targets the PanDZ complex, preventing E. coli from making Vitamin B5 and so starving it of the means to grow.

Dr Webb said: "The results of our latest study open up the possibility of designing new drugs that use the same means to attack E. coli, but in a more effective way."

Dr O'Neill concludes: "Our findings underscore the importance of revisiting unexploited antibiotics as a potential source of new antibiotic drug candidates. We now believe a comprehensive re-evaluation of such compounds is worthwhile, potentially offering new ways to protect against infections."

Notes to editors:

Dr O'Neill's study, Revisiting unexploited antibiotics in search of new antibacterial drug candidates: the case of γ-actinorhodin is published in the journal Scientific Reports. It was funded by the Medical Research Council, and members of the research team were supported

by the Saudi Arabian Government, King Abdulaziz University and the Engineering and Physical Sciences Research Council.

Dr Webb's study, Mechanism of regulation of pantothenate biosynthesis by the PanD-PanZ.AcCoA complex reveals an additional mode of action for the antimetabolite N-pentyl pantothenamide (N5-Pan) is published in Biochemistry. It was funded by Wellcome, and team members were supported by the University of Leeds, University of Hamburg and The German Federal Excellence Cluster.

**The ESKAPE class of pathogens are Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa and Enterobacter species.*

http://bit.ly/2skMZst

DNA shows the first modern Briton, known as 'Cheddar Man,' had dark skin and blue eyes

The first modern Briton had dark skin and blue eyes, London scientists said on Wednesday, following groundbreaking DNA analysis of the remains of a man who lived 10,000 years ago.

LONDON – Known as "Cheddar Man" after the area in southwest England where his skeleton was discovered in a cave in 1903, the ancient man has been brought to life through the first-ever full DNA analysis of his remains.

In a joint project between Britain's Natural History Museum and University College London, scientists drilled a 2-millimeter hole into the skull and extracted bone powder for analysis.

***A full facial reconstruction model made from a skull of a 10,000-year-old man, Britain's oldest complete skeleton, is displayed during a press preview at the National History Museum in London on Tuesday.* | AFP-JIJI**

Their findings transformed the way they had previously seen Cheddar Man, who had been portrayed as having brown eyes and light skin in an earlier model. "It is very surprising that a Brit 10,000 years ago could have that combination of very blue eyes but really dark skin," said the museum's Chris Stringer, who for the past decade has analyzed the bones of people found in the cave.

The findings suggest that lighter pigmentation being a feature of populations of northern Europe is more recent than previously thought. Cheddar Man's tribe migrated to Britain at the end of the last Ice Age, and his DNA has been linked to individuals discovered in modern-day Spain, Hungary and Luxembourg.

Selina Brace, a researcher of ancient DNA at the museum, said the cave environment in which Cheddar Man was found helped preserve his remains. "In the cave you have a really nice, cool, dry, constant environment, and that basically prevents the DNA from breaking down," she said.

A bust of Cheddar Man, complete with shoulder-length dark hair and short facial hair, was created using 3-D printing. It took close to three months to build the model, with its makers using a high-tech scanner that had been designed for the International Space Station.

Alfons Kennis, who made the bust with his brother Adrie, said the DNA findings were "revolutionary." "It's a story all about migrations throughout history," he told the British network Channel 4 in a documentary to be aired Feb. 18. "It maybe gets rid of the idea that you have to look a certain way to be from somewhere. We are all immigrants," he added.

http://bit.ly/2nVDxWI

Crop pesticide could fight hospital fungus

Compounds developed to protect farmers' crops could be used to fight the spread of a life-threatening fungal infection that is invading hospitals around the globe.

John von Radowitz, Press Association

Candida auris was first identified in Japan in 2009 and has since been reported in at least 15 countries.

The fungus is a less common cousin of the yeast organism that causes thrush. It enters the body through surgical wounds or via urinary catheters or drips and is carried on clothes, equipment and hands.

Because of its resistance to multiple drugs C. auris has proved difficult to control. The fungus can spread rapidly through hospitals and cause serious infections that may threaten life.

Scientists at the University of Sussex are now spearheading an urgent search for effective ways of combating the threat.

Promising early results suggest that one answer may be a family of compounds originally designed to protect cereal crops from resistant fungal infections. The drugs suppress an enzyme called alternative oxidase (AOX) that helps to make the organisms immune to fungicides.

Professor Tony Moore, who leads the University of Sussex team and has studied AOX for more than 40 years, said: "The fundamental problem here is the same whether it is as field of wheat or a human patient - fungi developing a resistance as they are exposed to ever-more potent traditional treatments.

"We have had a very encouraging start in tackling this infection and with assistance now there is the potential to create a simple compound that could prove to help manage this infection within 18 months." The research had the potential to "save lives around the world", he added.

C. auris outbreaks have been reported in the US, Japan, South Korea, South Africa, Kuwait, India, Pakistan, Venezuela and Columbia and the UK. The Centres for Disease Control and Prevention (CDC) in the US has described the fungus as a "serious global health threat".

Between 30 per cent and 60 per cent of people infected by C. auris have died, according to the CDC.

http://bit.ly/2EVJYBo

Spread of breast cancer linked to compound in asparagus and other foods

Using drugs or diet to reduce levels of asparagine may benefit patients, say researchers

Ian Sample Science editor

Breast cancer patients could be encouraged to cut asparagus and other foods from their diets in the future to reduce the risk of the disease spreading, scientists say.

Researchers are investigating whether a change in diet could help patients with breast tumours after studies in mice showed that asparagine, a compound first identified in asparagus but present in many other foods, drives the spread of the disease to other organs.

When scientists reduced asparagine in animals with breast cancer, they found that the number of secondary tumours in other tissues fell dramatically. The spread of malignant cells, often to the bones, lungs and brain, is the main cause of death among patients who are diagnosed with breast cancer.

“This is a very promising lead and one of the very few instances where there is a scientific rationale for a dietary modification influencing cancer,” said lead scientist Prof Greg Hannon, director of the Cancer Research UK Cancer Institute in Cambridge.

Asparagine is an amino acid that is made naturally in the body as a building block for proteins. But it is also found in the diet, and in high levels in certain meats, vegetables and dairy products.

The international team of cancer specialists from Britain, the US, and Canada studied mice with an aggressive form of breast cancer. The mice develop secondary tumours in a matter of weeks and tend to die from the disease within months.

Writing in the journal Nature, the researchers describe how they reduced the ability of breast cancer to spread in the animals by blocking asparagine with a drug called L-asparaginase. To a lesser extent, by putting the animals on a low-asparagine diet worked too.

Inspired by the results, the scientists examined records from human cancers and found that breast tumours that churned out the most asparagine were most likely to spread, leading patients to die sooner. The same was seen in cancers of the head, neck and kidney.

Asparagine appears to help cancer cells change into a form that easily spreads from the breast, through the bloodstream, to other organs where they grow into secondary tumours, Hannon said. While suppressing levels of asparagine reduced the spread of breast cancer around the body, it did nothing to prevent breast tumours forming in the first place.

If the findings hold in humans, breast cancer patients may be put on low asparagine diets while they have conventional treatments, such as chemotherapy, for the disease. But because asparagine is so ubiquitous in food, drugs that target the amino acid may be more effective. L-asparaginase breaks the amino acid down in the bloodstream, but more targeted drugs could block its production altogether.

“This is one case where we can show at a deep biochemical level how a change in diet can impact properties of cells that are relevant to the progression of lethal disease,” said Hannon. “But of course, until human studies are done, this isn’t a DIY method to prevent cancer.”

Prof Keqiang Ye, a cancer researcher at Emory University in Atlanta, said that lowering asparagine levels, either with drugs or dietary restriction, would help prevent cancer cells from spreading. But for patients, he said that drug treatments held more promise than changes to their diets.

“Asparagine is frequently found in various animal sources including beef, poultry, eggs, fish and seafood. It is also found in many vegetables including asparagus, potatoes, nuts, legumes and soy. Since these foods are so common, it seems that diet restriction may not be the ideal approach,” Ye said.

Baroness Delyth Morgan, chief executive of Breast Cancer Now, said: “This early discovery could offer a long-awaited new way to help stop breast cancer spreading – but we first need to understand the true role of this nutrient in patients. With nearly 11,500 women still dying from breast cancer each year in the UK, we urgently need to stop the disease spreading around the body, where it becomes incurable.

“On current evidence, we don’t recommend patients totally exclude any specific food group from their diet without speaking to their doctors. We’d also encourage all patients to follow a healthy and varied diet – rich in fruit, vegetables and pulses, and limited in processed meat and high fat or sugar foods – to help give them the best chance of survival.”

http://bit.ly/2EqfKMh

Large-group living boosts magpie intelligence

Growing up in a large social group makes Australian magpies more intelligent, new research shows.

Using four tasks to test intelligence, scientists from the University of Exeter and the University of Western Australia found wild Australian magpies from larger groups showed "elevated cognitive performance". The study also found more intelligent females produced more offspring. The research suggests that the demands of living in complex social groups may play a role in the evolution of intelligence.

"Australian magpies - from Western Australia, where we conducted our research - live in stable social groups," said Dr Alex Thornton, of the Centre for Ecology and Conservation on the University of Exeter's Penryn Campus in Cornwall.

"We showed that individuals living in larger groups in the wild show elevated cognitive performance, which in turn is linked to increased reproductive success.

"Repeated testing of juveniles at different ages showed that the link between group size and intelligence emerged in early life."

Researchers examined 14 wild groups of Australian magpies (Western Australian subspecies Cracticus tibicen dorsalis) in Perth, ranging in size from three to 12 birds.

Cognitive ability of each magpie was tested using four tasks, including one in which they had to learn to associate a particular colour with the presence of food, a memory task where food was hidden in the same place many times.

There was also a test of self-control, in which magpies had to stop themselves from pecking directly at the food through the transparent barrier and instead had to go round to the sides of the tube to get the food.

Lead researcher Dr Ben Ashton, from the University of Western Australia, said: "The challenges of living in complex social groups have long been thought to drive cognitive evolution.

"However, evidence to support this is contentious, and has recently been called into question." He added: "Our results suggest that the social environment plays a key role in the development of cognition.

"They also suggest that females who do well in cognitive tasks have more offspring, indicating there is the potential for natural selection to act on cognition. "Together, these results support the idea that the social environment plays an important role in cognitive evolution."

The paper, published in the journal Nature, is entitled: "Cognitive performance is linked to group size and affects fitness in Australian magpies."

http://bit.ly/2nYtG2J

Case for assisted dying 'stronger than ever' says The BMJ

Surveys suggest most UK doctors support legal assisted dying, and most people want it

A series of articles published by The BMJ today, explore the debate around assisted dying, in which, subject to safeguards, terminally ill people who are near to death, suffering, and of sound mind, could ask for drugs that they would take to end their lives.

They include a call for the BMA to poll its members or stop opposing assisted dying, personal accounts by a Dutch doctor who has helped terminally ill patients to die and a British patient who wants assisted dying, and a debate on the question: should doctor assisted dying be legal?

Jacky Davis, Consultant Radiologist at the Whittington Hospital in London, points to a recent survey showing that most UK doctors support legislation for assisted dying, while a 2015 poll showed that about 80% of the UK public support a change in the law. Yet the BMA, which represents UK doctors, has long been opposed to assisted dying, despite calls for it to adopt a neutral stance.

Davis, who is also a member of BMA Council, a board member of Dignity in Dying, and chair of Healthcare Professionals for Assisted Dying, argues that the current disconnect between BMA policy and the views of doctors and patients "undermines the BMA's credibility, and its continuing opposition excludes it from the public debate."

Assisted dying does not represent a leap into a dangerous unknown, she explains. Other jurisdictions, such as the US state of Oregon, have proved that it is possible to change the law, and doctors have shown that such laws can work hand in hand with excellent palliative care. "Ultimately legalisation for assisted dying will be a decision for UK society," she writes.

In a linked commentary, Bobbie Farsides, Professor of Clinical and Biomedical Ethics at the University of Sussex, argues that palliative care and assisted dying are not mutually exclusive.

An important debate is happening in wider society, she says. "Patients are more aware than ever of what is, and is not, possible for them as they approach the end of their lives, and practitioners need to be prepared and able to respond compassionately."

Rather than fighting against a possible future in which dying people could get medical help to die, she urges health professionals "to think about how they would negotiate such a future in the the best interests of their patients."

More than a quarter of Americans and Canadians now have the legal option of choosing a medically assisted death, since California and Canada legalised the procedure in 2016, explains journalist Bob Roehr. While rhetoric from opponents of assisted dying "creates the impression among the public that most doctors are opposed to assisted dying," he writes, data suggest otherwise - and once adopted, controversy tends to subside.

Sabine Netters, a consultant in medical oncology in The Netherlands, reflects on how it feels to help a terminally ill patient to die a dignified death. "The debate about assisted dying tends to focus on medical and legal aspects," she writes, "but little is said about the emotional impact on the professionals involved."

Sarah Jessiman, a patient living with terminal cancer, explains why she thinks doctors should support the campaign to legalise assisted dying in the UK. "I'm terrified of the sort of death I may have to face," she writes. "I would draw huge comfort from knowing that I could say "enough"

when I can no longer endure my illness, so I can die at home, supported by the people I love most."

She adds: "I don't want to go to Switzerland, and I don't want to attempt suicide. Why can't I die as I live -- in an open and honest way?"

Finally, two senior doctors debate the question: should doctor assisted dying be legal? Bernard Ribeiro, a retired surgeon and life peer, argues that assisting suicide would damage trust between doctors and patients and "is a matter for the courts, not for the consulting room."

But Terence English, a retired cardiac surgeon, says claims that assisted dying would undermine palliative care, or put society's most vulnerable people at increased risk of abuse, are not borne out by the evidence. He argues that safeguards in the proposed legislation "provide both safety for the majority and an option for that relatively small number of people who would wish for this degree of control over their final days."

"The BMJ supports the legalisation of assisted dying," says Dr Fiona Godlee, Editor in Chief. "The great majority of the British public are in favour and there is now good evidence that it works well in other parts of the world, as a continuation of care for patients who request it and are in sound mind. We believe that this should be a decision for Society and Parliament, and that medical organisations should adopt at least a neutral position to allow an open and informed public debate."

http://bit.ly/2BmbLes

Giant viruses may play an intriguing role in evolution of life on Earth

Biologist finds giant virus family and eukaryotes have similar set of genes

We all know viruses cause colds and flu this time of year, but you might be surprised to learn that a virus may have played a key role in the evolution of nearly all life forms on Earth.

In a new study, a University of Iowa biologist identified a virus family whose set of genes is similar to that of eukaryotes, an organism classification that includes all plants and animals.

The finding is important because it helps clarify how eukaryotes evolved after branching from prokaryotes some 2 billion years ago.

"It's exciting and significant to find a living family of giant viruses with eukaryote-specific genes in a form that predates the latest common ancestor of all eukaryotes," says Albert Erives, associate professor in the Department of Biology. "These viruses are like time machines that tell us more about how life on our planet came to be."

In the study, Erives analyzed the genome of a virus family called Marseilleviridae and found it shares a similar set of genes, called core histones, with eukaryotes. That places Marseilleviridae, and perhaps its viral relatives, somewhere along eukaryotes' evolutionary journey.

"We now know that eukaryotes are more closely related to viruses," says Erives, "and the reason is because they share core histones, which are fundamental to eukaryotes."

Core histones are packagers, like professional gift-wrappers. They're proteins that, in humans, coil DNA in the chromosomes so vital genetic information is compact and protected. Prokaryotes don't have core histones, so somehow, somewhere, eukaryotes picked them up.

Viruses like Marseilleviridae may have been the source. (An alternative and equally fascinating explanation is that an ancestor of the Marseilleviridae picked up this gene from a proto-eukaryotic organism, an intermediate between prokaryotes and eukaryotes.)

Erives discovered this possible origin somewhat fortuitously. For a class assignment, he asked students to investigate giant viruses. These super-sized viruses, first discovered in 2003 although believed to be in existence for billions of years, are the giants of the virus world: They're hundreds of times bigger and stocked with hundreds more genes than standard viruses. The one family of giant viruses not chosen by a student was Marseilleviridae, so Erives decided to take a look at it himself.

As he analyzed Marseilleviridae's genomes in data provided by the National Institutes of Health, Erives noticed the giant virus family encodes the eukaryotic core histones H2B-H2A and H3-H4. Unlike

eukaryotes, however, these Marseilleviridae core histones are primitively fused as dimer proteins. "So, when I saw this, it was wild," Erives says. "No one has ever seen a virus with histones."

Moreover, he realized Marseilleviridae "did not get these genes from any one eukaryotic lineage living, but rather from some ancestor who was proto-eukaryotic--that is, on its way to becoming a eukaryote. Until now, no 'organism' was known to have core histone genes besides eukaryotic cells," he says.

The discovery begs a larger question about the role giant viruses have played in the evolution of all life on Earth. Erives likens giant viruses to vines spreading out into the cellular tree of life--sampling here, borrowing there, and sharing genetic material among the branches of archaea, bacteria, and eukaryotes.

"Giant viruses have genes that no one has seen before," he says. "They're conserved. They've been using them for something, and for a very long time. Why not use them now to peer into the past?"

Erives is the sole author of the paper, published in the journal Epigenetics & Chromatin. The paper is titled, "Phylogenetic analysis of the core histone doublet and DNA topo II genes of Marseilleviridae: Evidence of proto-eukaryotic provenance."

There was no outside funding for the research.

http://bit.ly/2nWqP1R

Super wood could replace steel

New process could make wood as strong as titanium alloys but lighter & cheaper

COLLEGE PARK -- Engineers at the University of Maryland, College Park (UMD) have found a way to make wood more than 10 times stronger and tougher than before, creating a natural substance that is stronger than many titanium alloys.

"This new way to treat wood makes it 12 times stronger than natural wood and 10 times tougher," said Liangbing Hu of UMD's A. James Clark School of Engineering and the leader of the team that did the research, to be published on February 8, 2018 in the journal Nature.

"This could be a competitor to steel or even titanium alloys, it is so strong and durable. It's also comparable to carbon fiber, but much less expensive." Hu is an associate professor of materials science and engineering and a member of the Maryland Energy Innovation Institute.

"It is both strong and tough, which is a combination not usually found in nature," said Teng Li, the co-leader of the team and Samuel P. Langley Associate Professor of mechanical engineering at UMD's Clark School. His team measured the dense wood's mechanical properties. "It is as strong as steel, but six times lighter. It takes 10 times more energy to fracture than natural wood. It can even be bent and molded at the beginning of the process."

The team also tested the new wood material and natural wood by shooting bullet-like projectiles at it. The projectile blew straight through the natural wood. The fully treated wood stopped the projectile partway through.

"Soft woods like pine or balsa, which grow fast and are more environmentally friendly, could replace slower-growing but denser woods like teak in furniture or buildings," Hu said.

"The paper provides a highly promising route to the design of lightweight, high performance structural materials, with tremendous potential for a broad range of applications where high strength, large toughness and superior ballistic resistance are desired, " said Huajian Gao, a professor at Brown University who was not involved in the study. "It is particularly exciting to note that the method is versatile for various species of wood and fairly easy to implement."

"This kind of wood could be used in cars, airplanes, buildings - any application where steel is used," Hu said.

"The two-step process reported in this paper achieves exceptionally high strength, much beyond what [is] reported in the literature," said Zhigang Suo, a professor of mechanics and materials at Harvard University, also not involved with the study. "Given the abundance of wood, as well as other cellulose-rich plants, this paper inspires imagination."

"The most outstanding observation, in my view, is the existence of a limiting concentration of lignin, the glue between wood cells, to

maximize the mechanical performance of the densified wood. Too little or too much removal lower the strength compared to a maximum value achieved at intermediate or partial lignin removal. This reveals the subtle balance between hydrogen bonding and the adhesion imparted by such polyphenolic compound. Moreover, of outstanding interest, is the fact that that wood densification leads to both, increased strength and toughness, two properties that usually offset each other," said Orlando J. Rojas, a professor at Aalto University in Finland.

Hu's research has explored the capacities of wood's natural nanotechnology. They previously made a range of emerging technologies out of nanocellulose related materials:

(1) super clear paper for replacing plastic;
(2) photonic paper for improving solar cell efficiency by 30%;
(3) a battery and a supercapacitor out of wood;
(4) a battery from a leaf;
(5) transparent wood for energy efficient buildings;
(6) solar water desalination for drinking and specifically filtering out toxic dyes.

These wood-based emerging technologies are being commercialized through a UMD spinoff company, Inventwood LLC.

http://bit.ly/2H5ZsDJ

The 'Perfect Human Pathogen' Is Spreading at the Winter Olympics

A nasty stomach bug is spreading at the 2018 Winter Olympics, according to news reports.

By Sara G. Miller, Health Editor | February 9, 2018 12:40pm ET

As of yesterday (Feb. 8), 128 cases of norovirus — a highly contagious infection that causes vomiting and diarrhea — were confirmed at Olympic sites, according to the Korea Centers for Disease Control and Prevention.

In the U.S., there are 19 million to 21 million cases of norovirus each year, on average, the U.S. Centers for Disease Control and Prevention (CDC) says.

As Live Science has previously reported, the virus can spread very easily, in part, because its symptoms come on so quickly. That means that a person may start vomiting in places where they normally wouldn't, spreading virus particles around.

And norovirus particles can survive for days outside the body.

Indeed, some characteristics of norovirus have led one expert to deem it the "perfect human pathogen."

"These viruses possess essentially all of the attributes of an ideal infectious agent: highly contagious, rapidly and prolifically shed, constantly evolving, evoking limited immunity and only moderately virulent, allowing most of those infected to fully recover, thereby maintaining a large susceptible pool of hosts," Dr. Aron Hall, an epidemiologist on the viral gastroenteritis team at the CDC, wrote in a 2012 editorial published in The Journal of Infectious Diseases.

In other words, the virus spreads easily and rapidly. It constantly evolves to evade the body's immune system. And it doesn't kill people, instead getting them sick enough to spread the virus further and then recover to live another day as a potential host.

In the editorial, Hall noted several characteristics that make norovirus so formidable. First, it takes as few as 18 viral particles to make a person sick — a tiny amount, considering that a sick person can shed up to 5 billion viral particles in a single gram of feces, Hall wrote.

Next, in addition to being able to survive lengthy stints outside the human body, norovirus particles can withstand harsh conditions, Hall wrote, including freezing, some heating and many common chemical disinfectants. What's more, there are many ways that norovirus can spread, including by ingesting contaminated food or water, handling contaminated objects and ingesting aerosolized particles, he wrote.

Finally, because noroviruses rapidly evolve, people are unlikely to build up an immunity to the virus, meaning they can get infected once again, Hall wrote.

http://bit.ly/2BQrl2X

New tool helps physicians estimate survival for patients with cancers that have spread to bone

A simple three-factor tool can help doctors estimate survival time in patients with long bone metastases

A simple three-factor tool can help doctors estimate survival time in patients with long bone metastases (LBMs)--advanced cancer that has spread to the bones of the limbs, reports a study in the February 7, 2018, issue of *The Journal of Bone & Joint Surgery*. The journal is published in partnership with Wolters Kluwer. Reliable survival estimates in these cases can help prevent overtreatment and undertreatment.

"This study presents a model to easily stratify patients with symptomatic LBM according to their expected survival," write J.J. Willeumier, MD, of Leiden University Medical Center, the Netherlands, and colleagues from several European institutions. The researchers believe their model can help to select the most appropriate treatment for patients with symptomatic bone metastases.

Model Helps Match Treatment to Expected Survival

Physicians and surgeons are often called upon to estimate survival for patients with advanced cancer to help them maximize the remaining quality of life. Accurate survival estimates are important to avoid overtreatment (putting the patient through treatments that would ultimately not provide much benefit) and undertreatment (not offering treatments that would be beneficial). But data on which to base survival estimates are often sparse, especially for patients with LBMs.

To assess their "easy-to-use prognostic model," Dr. Willeumier and colleagues analyzed 1,520 patients treated for symptomatic LBMs at six Dutch hospitals between 2000 and 2013. The patients' average age was 65; the most common initial (primary) cancer sites were the breast and lung. The main symptoms requiring treatment were painful bone lesions and impending or actual pathologic fractures.

The authors previously identified three independent predictors of survival in patients with spinal metastases and applied them to these patients with LBM:

- ***Clinical profile of the primary tumor. Among the patients with LBM, the profile was "favorable" (longer survival) in those with primary breast cancer but "unfavorable" (shorter survival) in those with primary lung cancer.***
- ***Performance status. A standard score (Karnofsky Performance Scale) to assess the patient's ability to perform everyday tasks.***
- ***Presence of organ/brain metastases, in addition to LBMs.***

Depending on their individual combination of these factors, patients could be classified into groups with median survival times of 29.1 months, 10.5 months, 4.6 months, and 2.2 months. The authors created a simple-to-use flowchart for use in estimating survival. The model performed well in predicting the survival category for individual patients based on their actual survival. The model's performance was also validated when applied to a separate group of patients with symptomatic LBMs.

The new model can help physicians and patients with LBMs make decisions about the most appropriate treatment, the authors believe. For example, in patients with longer expected survival, more extensive surgery might avoid failure of the implant over time and preserve function. In contrast, for those expected to live only a few months, palliative therapy might be a more appropriate choice.

The authors have developed an online and mobile app that further facilitates use of the model. The English-language version of the "OPTIModel" app can be accessed at http://optimal-study.nl/nl_NL/tooleng/.

"The simplicity and clarity of the model facilitate and encourage its use in the routine care of patients with LBM, to provide the most appropriate treatment for each individual patient," Dr. Willeumier and coauthors add. They believe their survival estimation tool might become even more useful in the future, with continued advances in tumor classification and individualized cancer therapies.

Click here to read "An Easy-to-Use Prognostic Model for Survival Estimation for Patients with Symptomatic Long Bone Metastases." DOI: 10.2106/JBJS.16.01514

http://bit.ly/2Cd72sa

Drug shown to reverse brain deficits caused by alcohol

QUT researchers have identified a drug that could potentially help our brains reboot and reverse the damaging impacts of heavy alcohol consumption on regeneration of brain cells.

Queensland University of Technology (QUT) researchers have identified a drug that could potentially help our brains reboot and reverse the damaging impacts of heavy alcohol consumption on regeneration of brain cells.

Their studies in adult mice show that two weeks of daily treatment with the drug tandospirone reversed the effects of 15 weeks of binge-like alcohol consumption on neurogenesis - the ability of the brain to grow and replace neurons (brain cells). The findings have been published in *Scientific Reports*.

- ***This is the first time tandospirone has be shown to reverse the deficit in brain neurogenesis induced by heavy alcohol consumption***
- ***Tandospirone acts selectively on a serotonin receptor (5-HT1A)***
- ***The researchers also showed in mice that the drug was effective in stopping anxiety-like behaviours associated with alcohol withdrawal, and this was accompanied by a significant decrease in binge-like alcohol intake***

"This is a novel discovery that tandospirone can reverse the deficit in neurogenesis caused by alcohol," said study leader neuroscientist Professor Selena Bartlett from QUT's Institute of Health and Biomedical Innovation.

"We know that with heavy drinking you are inhibiting your ability to grow new neurons, brain cells. Alcohol is specifically very damaging for neurons.

"Other studies in mice have shown that tandospirone improves brain neurogenesis, but this is the first time it has been shown that it can totally reverse the neurogenic deficits induced by alcohol.

"This opens the way to look at if neurogenesis is associated with other substance-abuse deficits, such as in memory and learning, and whether this compound can reverse these."

Professor Bartlett, who is based at the Translational Research Institute, said the discovery by study co-authors QUT postdoctoral research fellows Dr Arnauld Belmer and Dr Omkar Patkar came about serendipitously after research started in a different direction.

"It was surprising, and exciting," Dr Belmer said.

"This drug is relatively new and available only in China and Japan. It is commonly used there and shown to be highly effective in treating general anxiety and well tolerated with limited adverse effects."

Professor Bartlett said researchers are constantly looking at new treatment strategies for alcohol abuse and addiction, which is characterised by extended periods of heavy alcohol use, binges and abstinence, and anxiety and depression which contribute to relapse.

"This is not just another drug that shows promise in helping to reduce binge drinking," she said.

"While it could possibly have that effect, it might be able to help reboot the brain and reverse the deficits the alcohol abuse causes - both the inhibition to the brain's ability to regenerate, and the behavioural consequences that come from what alcohol is doing to the brain, like increases in anxiety and depression."

The study by Professor Bartlett, Dr Belmer, Dr Patkar and Dr Vanessa Lanoue (Queensland Brain Institute) can be accessed here.

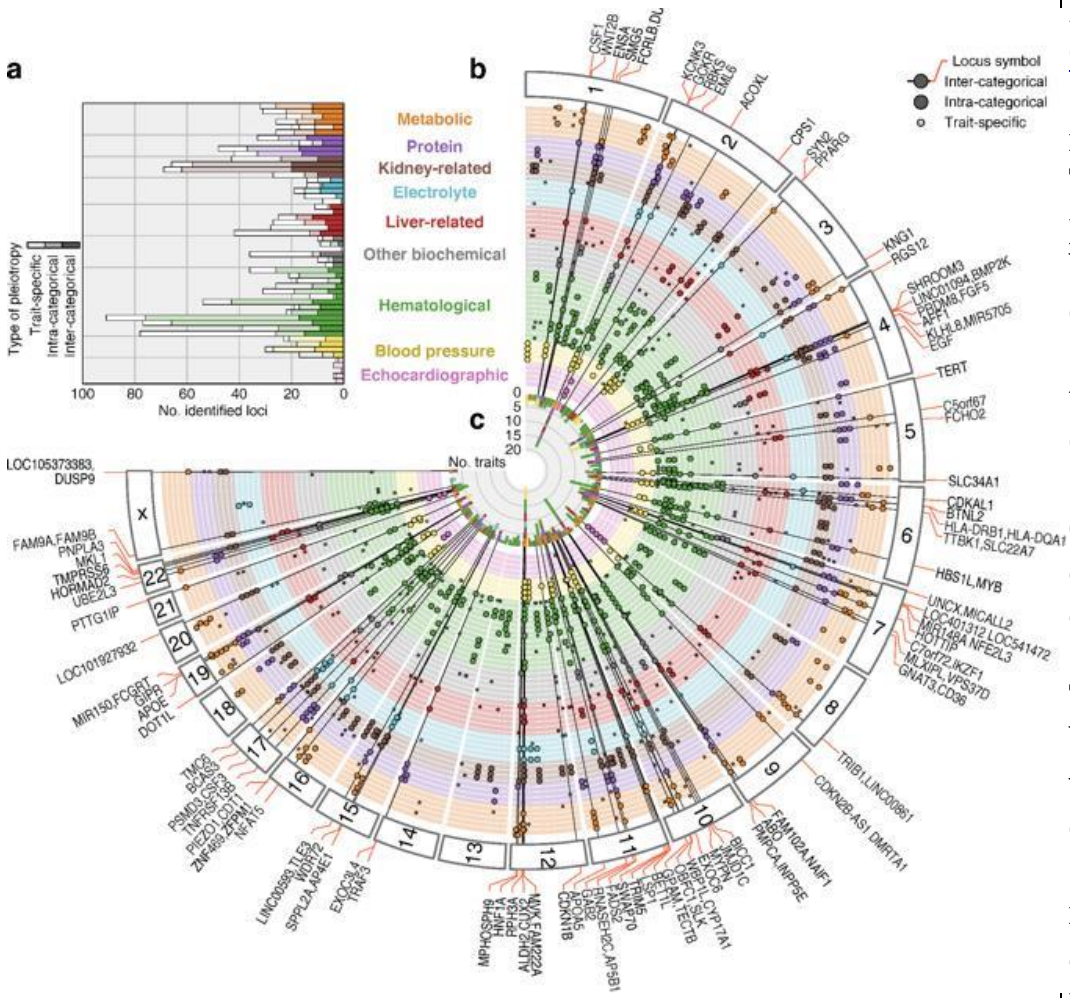
http://bit.ly/2EjqFVH

Study reveals genetic basis of quantitative traits and diseases in Japanese

Genome-wide association study reveals genetic basis of quantitative traits and complex biological links

Osaka - Genome-wide association studies (GWAS) are an emerging method for scientists to identify genes involved in human disease. GWAS searches the whole genome region for small variations, called single nucleotide polymorphisms (SNPs), which occur more frequently

in people with a particular disease than in people without. Each study can look at millions of SNPs at the same time. Researchers use data from this type of study to pinpoint genes that may contribute to a person's risk of developing a certain disease.



These are GWAS results of 58 quantitative traits for more than 160,000 Japanese subjects, **Osaka University**

Most existing GWAS have primarily examined European-ancestral subjects, and each separately focused on a few quantitative traits. To obtain a comprehensive landscape, additional studies in non-European populations are needed - and a team of Japanese researchers centered at Osaka University recently did just that.

"We conducted a large-scale GWAS using genetic information of more than 160,000 Japanese from the BioBank Japan Project," explains Masahiro Kanai, lead author of the study recently published in Nature Genetics. "We successfully identified 1,407 genetic variations in the genome sequence that affect 58 traits, including anthropometric, metabolic, kidney-related, hematological, and blood pressure."

The BioBank Japan Project, launched in 2003, enrolled 200,000 patients with 47 target diseases, making it one of the largest hospital based biobanks in the world. Without prior biological knowledge of cross-phenotype relationships, the team's findings demonstrated that genetics clinical measurements successfully recapture their relevance to diseases, and thus could contribute to elucidation of unknown etiology and pathogenesis.

"By incorporating the additional GWAS results of the 32 complex diseases and traits in Japanese, we further identified cellular tissues that affect diseases and clinical laboratory values by cross-cutting omics analysis (that integrates with epigenome information) obtained from 220 types of cellular tissues," co-senior author Yukinori Okada says.

The new findings also suggested there are complex interrelations between the clinical measurements and diseases, demonstrating the value of conducting GWAS for a variety of traits in a single large-scale cohort with detailed clinical information.

"Our study substantially expanded the knowledge of genetic relationships across clinical measurements and diseases," co-senior author Yoichiro Kamatani adds. "Our results not only shed light on numerous clinically meaningful genetic mutations, but also showed that the integration of genomic information and epigenome information makes it possible to clarify the molecular and cellular basis of diseased tissues."

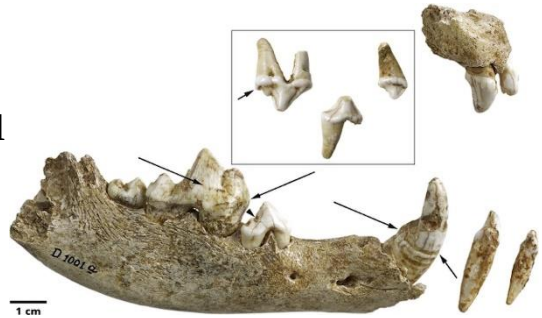
http://bit.ly/2nYU3W9

Humans Cared for Sick Puppies Long Ago, Ancient Burial Shows

Ancient people likely cared for a sick, domesticated pup for weeks on end before it died about 14,000 years ago during the Paleolithic era, a new study finds.

By Laura Geggel, Senior Writer | February 9, 2018 05:06pm ET

After it died, the dog was buried with the remains of another dog and an adult man and woman — making it not only the oldest burial of a domestic dog on record, but also the oldest known grave to contain both dogs and people, the researchers said.



The teeth and jaw from the younger dog in the grave: This pup likely had canine distemper. **Pütz Martin, Jürgen Vogel, Ralf Schmitz/LVR-LandesMuseum Bonn**

This discovery suggests that even though the dog was young, sick and likely untrained as a result, ancient people still had an emotional bond with it, the researchers wrote in the study. This may explain why the people buried the animal with two of their own, the researchers said.

The grave itself was found in 1914 in Oberkassel, a suburb of Bonn in western Germany. Until now, however, researchers thought the burial contained two humans and just one dog. But a new analysis of the canid bones and teeth revealed that two dogs were in fact buried there: an older dog and a younger dog, which likely had a serious case of morbillivirus, better known as canine distemper.

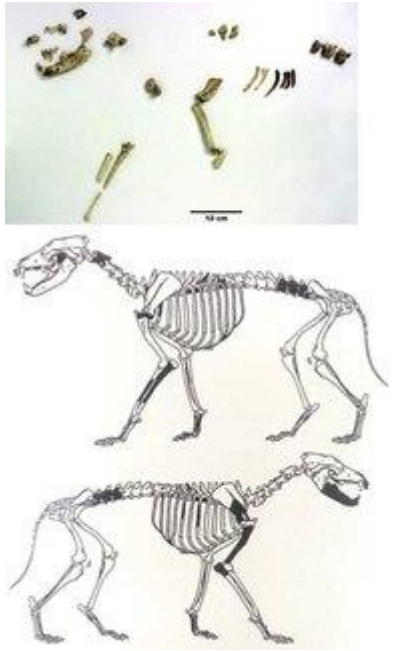
The younger dog was about 28 weeks old when it died, the study's lead researcher, Luc Janssens, a veterinarian and doctoral student of archaeology at Leiden University in the Netherlands, said in a statement. A dental analysis showed that the pup likely contracted the disease at around 3 to 4 months of age, and likely had two or even three periods of serious illness, each lasting up to six weeks, Janssens said.

Canine distemper is a serious illness that has three phases. During the first week, infected dogs can show signs of high fever, lack of appetite, dehydration, tiredness, diarrhea and vomiting, the researchers wrote in the study. Up to 90 percent of dogs with distemper die during the second phase, when they can develop a stuffy nose, laryngitis and pneumonia. In the third phase, dogs experience neurological problems, including seizures.

There is now a vaccine for canine distemper, but unvaccinated dogs, as well as tigers and Amur leopards, can still die from the virus.

Given the severity of the disease, the ancient pup would have likely died right away unless it received intensive human care, the researchers said. "This would have consisted of keeping the dog warm and clean [from] diarrhea, urine, vomit [and] saliva," as well as giving the pup water and possibly food, the researchers wrote in the study.

"While it was sick, the dog would not have been of any practical use as a working animal," Janssens said. "This, together with the fact that the dogs were buried with people, who[m] we may assume were their owners, suggests that there was a unique relationship of care between humans and dogs as long as 14,000 years ago."



The bone fragments from the dogs found in the grave at Bonn-Oberkassel. The highlights in the drawing show which bones were found. **Pütz Martin, Jürgen Vogel, Ralf Schmitz/LVR-LandesMuseum Bonn**

The humans buried with the dogs had medical problems of their own. The roughly 40-year-old man had two healed bones, one on his arm and the other by his clavicle. He and the roughly 25-year-old woman also had moderate-to-severe dental disease, the researchers noted.

The grave also contained several artifacts, including a bone pin, a sculpture of an elk made from elk antlers, the penis bone of a bear and a red-deer tooth.

Although this finding is the oldest known domestic dog burial, it's not the only ancient one. Other dog burials have been dated to about 11,600 years ago in the Near East, and archaeologists have found others dating to about 8,500 to 6,500 years ago in Scandinavia and about 8,000 years ago at the Koster Site in Illinois, the researchers said.

The study was published online Feb. 3 in the Journal of Archaeological Science.

http://nyti.ms/2EiburL

Two Prostate Cancer Drugs Delay Spread of the Disease by Two Years

Researchers have results from two independent clinical trials showing that two different drugs help prostate cancer patients

By PAM BELLUCK FEB. 8, 2018

They are among the most challenging prostate cancer patients to treat: about 150,000 men worldwide each year whose cancer is aggressive enough to defy standard hormonal therapy, but has not yet spread to the point where it can be seen on scans.

These patients enter a tense limbo which often ends too quickly with the cancer metastasizing to their bones, lymph nodes or other organs — sometimes causing intense pain.

Now, for the first time, researchers have results from two independent clinical trials showing that two different drugs help these patients — giving them about two more years before their cancer metastasizes. That means two additional years before pain and other symptoms spread and they need chemotherapy or other treatments.

“We’re going from rags to riches,” said Dr. Judd Moul, a professor of surgery and director of the Duke Prostate Center, who was not involved in either study. “Up until now, we haven’t had anything for these guys. We just had to tell them ‘We’ll keep an eye on it.’”

The studies, each involving more than 1,200 patients in countries around the world, were presented Thursday at the Genitourinary Cancers Symposium in San Francisco. They used very similar drugs — both androgen receptor inhibitors, which block testosterone from binding to prostate cancer cells and entering them.

The study of an experimental drug called apalutamide was published Thursday in the New England Journal of Medicine. The other study of a drug called enzalutamide, currently approved for treating prostate cancer that has already metastasized, has not yet been peer-reviewed for publication, the authors said.

Prostate cancer is the second most common cancer in men worldwide. The American Cancer Society estimates that in 2018, there will be about 164,690 new cases and about 29,430 deaths. Worldwide, there were 1.1 million new cases and about 307,000 deaths in 2012, according to the most recent data available from the World Health Organization.

The patients in both studies were men who had previously received some treatment for prostate cancer, such as surgery or radiation, but who later began to show rapid increases in their prostate-specific antigen or PSA, a protein associated with prostate cancer. They did not respond to the standard treatment to suppress testosterone, called androgen deprivation therapy.

Each year, about 30,000 to 50,000 American men and about 150,000 worldwide, fall into this category, called nonmetastatic castration-resistant prostate cancer. (The medical term for blocking male hormones is chemical castration.) Globally, about 200,000 of the four million men with prostate cancer are estimated to have this diagnosis, said Dr. Matthew Smith, director of the Genitourinary Malignancies Program at Massachusetts General Hospital’s Cancer Center, who co-led the apalutamide study with Dr. Eric Small, deputy director of the Helen Diller Family Comprehensive Cancer Center at University of California, San Francisco.

In the studies, two-thirds of the men took one of the androgen receptor inhibitors, while a third took a placebo. They all continued to receive androgen deprivation therapy.

In the study of men receiving apalutamide, it took, on average, 40.5 months for cancer to spread to the point where it could be detected by conventional scans. For men receiving the placebo, the cancer spread in 16.2 months, on average. In the enzalutamide study, metastasis took 36.6 months on average in men receiving that drug compared to 14.7 months with placebo.

"Delaying median time to metastases by over two years is a big deal," said Dr. Scott Eggener, a urologic oncologist and professor of surgery at University of Chicago, who was not involved in the studies. He said the studies were also important scientifically because they show that "maximally decreasing testosterone production and its ability to bind or enter cancer cells leads to meaningful clinical improvement for these men."

Still, he said, while the studies both show preliminary indications that the drugs might extend patients' survival, researchers will have to follow the patients longer to know.

Both studies were funded by the companies that make the drugs. Janssen Pharmaceutical Companies of Johnson & Johnson, the maker of apalutamide, has applied for approval from the Food and Drug Administration, which has put it under priority review, Dr. Smith said. The developers of enzalutamide, Pfizer and Astellas Pharma, have applied to the F.D.A. for approval to expand the use of the drug, marketed as Xtandi, to patients in this category, said Dr. Maha Hussain, deputy director of the Robert H. Lurie Comprehensive Cancer Center at Northwestern University's Feinberg School of Medicine. She co-led that study with Dr. Cora Sternberg, chief of medical oncology at San Camillo and Forlanini Hospitals in Rome.

Both drugs appear to be safe with relatively few serious side effects, experts said. Negative effects for some patients included fatigue, hypertension, rashes, fractures, falls, nausea, and mild cognitive and memory slippage.

Ron Scolamiero, 72, of Marshfield, Massachusetts, a patient of Dr. Smith's, began taking apalutamide in 2012 for an earlier phase of the clinical trial. He still takes a four-pill dose daily.

In the drug's initial formulation, side effects included hot flashes, diarrhea and nausea, but those diminished greatly after it was reformulated, said Mr. Scolamiero, who owns a financial services company. About 18 months ago, a tumor that developed at the site of his prostate had to be removed, but his cancer has not metastasized to other parts of his body.

"It's controlled my cancer," he said. "I'm so grateful."

Still, some experts said enthusiasm about the new drugs should be tempered by other changes occurring in the prostate cancer landscape.

"I don't want to say this is the best thing since sliced bread — it's not," said Dr. Oliver Sartor, medical director of Tulane Cancer Center. "You're taking a person with no symptoms and potentially giving them side effects, definitely giving them an expensive drug. And it is unclear if this is the optimal management of these patients."

The current list price of enzalutamide is more than $10,000 a month; a price hasn't been set for apalutamide, which is not yet on the market

Dr. Sartor and others noted that another androgen receptor inhibitor, abiraterone, which is used to treat cancer once it metastasizes and is also produced by Janssen, is likely to go off-patent soon and will become much cheaper because generic versions will be produced. Since abiraterone operates on the same biological pathway, experts expect that it will be tried for patients with cancer that hasn't metastasized and could end up working as well.

Increasingly sophisticated imaging techniques are allowing doctors to spot previously undetectable signs of metastasis. While some patients in these trials might have had cancer spread that was not detected by conventional scans, Dr. Smith said what matters is that they were early

in the cancer trajectory and the drug helped them stay in that early state longer.

The two new studies did not compare the drugs against each other, only against a placebo. “You can look at that as being a challenge for physicians,” said Dr. Ian Thompson, Jr., president of CHRISTUS Santa Rosa Hospital-Medical Center in San Antonio. “You can also look at that as being an advantage for the patient.”

Besides giving patients options, Dr. Hussain said, having both apalutamide and enzalutamide “opens up the door for more investigation to happen to even prevent this disease stage from happening in the first place.”

Gina Kolata contributed reporting.

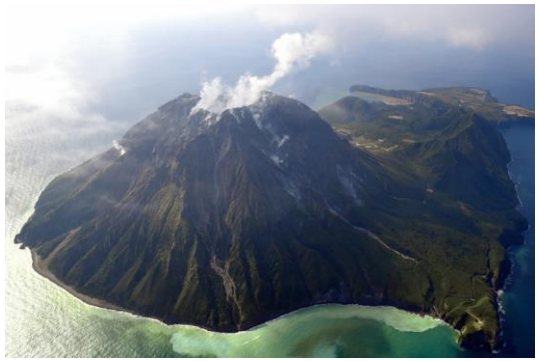
http://nyti.ms/2EWLVO1

At Site of Japanese Volcano’s Supereruption, an Immense Lava Dome Lurks

Scientists have discovered that a dome of lava lurks beneath the Kikai Caldera

By NICHOLAS ST. FLEUR

Some 7,300 years ago, a supereruption devastated the southern islands of what is now Japan, burying most of the archipelago in thick ash. Known as the Akahoya eruption, the blast was so powerful it caused the volcano’s magma chamber to collapse, leaving a 12-mile wide scar called Kikai Caldera, which is mostly underwater.



Satsuma Iojima Island in the East China Sea straddles the western edge of the Kikai Caldera, which sits on top of an immense lava dome, scientists say. **The Asahi Shimbun, via Getty Images**

Now in a study published Friday, scientists have discovered that a dome of lava lurks beneath the caldera. By studying its magma plumbing, volcanologists could gain insight into the entire caldera system, which could help them better predict when another eruption in the Japanese archipelago might occur.

“The most serious problem that we are worrying about is not an eruption of this lava dome, but the occurrence of the next supereruption,” said Yoshiyuki Tatsumi a volcanologist at Kobe University in Japan and lead author of the study that appeared in the journal Scientific Reports.

Dr. Tatsumi’s previous work has suggested that the chances of a supereruption happening in the Japanese archipelago in the next century are only about 1 percent. But if a volcano in this area erupts, it could eject nearly 10 cubic miles of magma, covering almost all of the country and its 120 million people in nearly eight inches of thick ash, he found.

He and his colleagues at the Kobe Ocean Bottom Exploration Center conducted three surveys of the caldera, during which they used remotely operated vehicles to observe the depression. On their trips they investigated the caldera using seismic analysis as well as geological and electromagnetic tests. They found the lava dome using an acoustic survey.

The dome — a trapped buildup of viscous lava — is estimated to have a volume of about eight cubic miles, a diameter of about six miles and a height of almost 2,000 feet. While other volcanic remnants, like the Yellowstone caldera and the Long Valley caldera, have also been brewing with activity, the paper noted that this dome has a much more immense volume of lava.

This site has experienced at least three supereruptions. One 140,000 years ago, another 95,000 years ago, and then the Akahoya eruption. The scientists are not sure when exactly the current dome began to form, whether it was immediately after the eruption or gradually in the thousands of years that followed. “The lava dome is chemically different from the supereruption, suggesting that a new magma supply system had been developed after 7,300 years ago,” said Dr. Tatsumi.

They did find that the lava dome was made of similar magma to what is seen in volcanoes on nearby islands. Dr. Tatsumi said it was

interesting to find a lava dome in the caldera because usually the period following the birth of a caldera is calm. But the finding shows considerable activity at the Kikai Caldera, similar to the preparation stage for the next supereruption.

Dr. Tatsumi said another survey in March will gather high-resolution images of the underground magma system.

Janine Krippner, a volcanologist at Concord University in West Virginia who was not involved in the study, pointed out that the team has not determined whether what it found is a single large dome or multiple smaller buildups of lava. She stressed that the finding does not mean there will be another large eruption anytime soon and that calderas have a spectrum of activity and hazards that require further research to understand.

“Calderas occur around the world and the more we know about the differences and similarities,” she said, “the more we can understand the hazards and how to prepare for potential eruptions in the future.”

http://bbc.in/2BkXU8i

First human eggs grown in laboratory

Human eggs have been grown in the laboratory for the first time, say researchers at the University of Edinburgh.

By James Gallagher Health and science correspondent, BBC News

The team say the technique could lead to new ways of preserving the fertility of children having cancer treatment. It is also an opportunity to explore how human eggs develop, much of which remains a mystery to science. Experts said it was an exciting breakthrough, but more work was needed before it could be used clinically.

Women are born with immature eggs in their ovaries that can develop fully only after puberty. It has taken decades of work, but scientists can now grow eggs to maturity outside of the ovary. It requires carefully controlling laboratory conditions including oxygen levels, hormones, proteins that simulate growth and the medium in which the eggs are cultured.

'Very exciting'

But while the scientists have shown it is possible, the approach published in the journal Molecular Human Reproduction still needs refinement. It is very inefficient with only 10% of eggs completing their journey to maturity. And the eggs have not been fertilised, so it is uncertain how viable they are.

Prof Evelyn Telfer, one of the researchers, told the BBC: "It's very exciting to obtain proof of principle that it's possible to reach this stage in human tissue. "But that has to be tempered by the whole lot of work needed to improve the culture conditions and test the quality of the oocytes [eggs]. "But apart from any clinical applications, this is a big breakthrough in improving understanding of human egg development."

The process is very tightly controlled and timed in the human body - some eggs will mature during the teenage years, others more than two decades later. An egg needs to lose half its genetic material during development, otherwise there would be too much DNA when it was fertilised by a sperm. This excess is cast off into a miniature cell called a polar body, but in the study the polar bodies were abnormally large.

"This is a concern," said Prof Telfer. But it is one she thinks can be addressed by improving the technology.

Work on mouse eggs, which was nailed 20 years ago, showed the technology could be used to produce live animals. Matching this achievement in human tissue could eventually be used to help children having cancer treatment.

Cancer option

Chemotherapy and radiotherapy risks making you sterile. Women can freeze matured eggs, or even embryos if they are fertilised with a partner's sperm, before starting treatment - but this is not possible for girls with childhood cancers.

At the moment they can have ovarian tissue frozen before treatment, which is then put back in to mature years later if the patient wants children of their own. But if there are any abnormalities in the frozen sample then doctors will think it is too risky. Being able to make eggs in the lab would be a safer option for those patients.

Mr Stuart Lavery, a consultant gynaecologist at Hammersmith Hospital, said: "This work represents a genuine step forward in our understanding. "Although still in small numbers and requiring optimisation, this preliminary work offers hope for patients."

It would be legal to fertilise one of the lab-made eggs to create an embryo for research purposes in the UK.But the team in Edinburgh do not have a licence to carry out the experiment. They are discussing whether to apply to the embryo authority for one, or collaborate with a centre that already has one.

Prof Azim Surani, the director of germline research at University of Cambridge's Gurdon Institute, said: "Molecular characterisation and chromosomal analysis is needed to show how these egg cells compare with normal eggs. "It might be of interest to test the developmental potential of these eggs in culture to blastocyst stage, by attempting IVF."

http://bit.ly/2soFccP

NIH scientists adapt new brain disease test for Parkinson's, dementia with Lewy bodies

Modified prion disease assay offers the possibility of improving early diagnosis of Parkinson's disease and dementia with Lewy bodies

National Institutes of Health scientists developing a rapid, practical test for the early diagnosis of prion diseases have modified the assay to offer the possibility of improving early diagnosis of Parkinson's disease and dementia with Lewy bodies. The group, led by NIH's National Institute of Allergy and Infectious Diseases (NIAID), tested 60 cerebral spinal fluid samples, including 12 from people with Parkinson's disease, 17 from people with dementia with Lewy bodies, and 31 controls, including 16 of whom had Alzheimer's disease. The test correctly excluded all the 31 controls and diagnosed both Parkinson's disease and dementia with Lewy bodies with 93 percent accuracy.

Importantly, test results were available within two days, compared to related assays that require up to 13 days. The group conducted the tests using Real-Time Quaking-Induced Conversion (RT-QuIC), an assay developed and refined over the past decade at NIAID's Rocky Mountain Laboratories. Scientists from the University of California San Diego, University of Verona in Italy, Indiana University School of Medicine, Indianapolis, and the Case Western Reserve University School of Medicine, Cleveland, collaborated on the project. The research findings were published in *Acta Neuropathologica Communications*.

Multiple neurological disorders, including Parkinson's disease and dementia with Lewy bodies, involve the abnormal clumping of a protein called alpha-synuclein into brain deposits called Lewy bodies. The pathological processes in these diseases resembles prion diseases in mammal brains. Like prion diseases, Parkinson's disease and dementia with Lewy bodies result in progressive deterioration of brain functions and, ultimately, death. Parkinson's disease is about 1,000 times more common than prion diseases, affecting up to 1 million people in the United States, with 60,000 new cases diagnosed each year. Lewy body dementia affects an estimated 1.4 million people in the United States, according to the Lewy Body Dementia Association.

Early and accurate diagnoses of these brain disorders is essential for developing treatments and identifying patients eligible for clinical trials. The diseases typically progress for years before symptoms appear, and once they do, distinguishing one disease from another can be difficult.

The NIAID group continues to adapt the RT-QuIC assay to detect additional types of neurological diseases with greater accuracy using the least invasive patient sample possible--whether that is blood, skin, nasal brushings, or other samples. The group also has trained many international colleagues to use and advance the test.

This research was supported in part by NIH funding awards ZIA AI001086-08, AGO5131, and PHS P30-AG010133.

***ARTICLE**: B Groveman et al. Rapid and ultra-sensitive quantitation of disease-associated a-synuclein seeds in brain and cerebrospinal fluid by aSyn RT-QuIC. Acta Neuropathologica Communications DOI: 10.1186/s40478-018-0508-2 (2018).*

***WHO**: Byron Caughey, Ph.D., a senior investigator in NIAID's Laboratory of Persistent Viral Diseases, is available to comment on this study.*

http://bit.ly/2o2hUo2

Blood test plus ultrasound boosts liver cancer detection by 40 percent

Combined ultrasound imaging and blood test for high AFPlevels improves early-stage liver cancer detection by up to 40 percent

DALLAS - Combining ultrasound imaging with a blood test for high alpha fetoprotein (AFP) levels improves detection of early-stage liver cancer by as much as 40 percent, researchers at UT Southwestern's Simmons Cancer Center found.

Earlier detection is important to improving survival of patients with liver cancer, a disease that is on the rise and the fastest increasing solid-tumor cancer in the U.S., according to the National Cancer Institute (NCI).

"If the cancer is found early, then we can perform curative therapies, allowing patients to live many years," said hepatologist Dr. G. Amit Singal, Associate Professor of Internal Medicine and Clinical Sciences with UT Southwestern Harold C. Simmons Comprehensive Cancer Center.

"Unfortunately, most liver cancer in the United States is discovered at later stages, when curative treatment is not possible and survival is much worse."

While the incidence of most cancers is decreasing in the U.S., the incidence of liver cancer has increased by 2.7 percent a year over the last 10 years, according to the NCI, which estimated about 40,700 new cases of liver cancer will be diagnosed in the U.S. in 2018.

Risk factors for liver cancer, also known as hepatocellular carcinoma or HCC, include hepatitis C infection, chronic heavy alcohol consumption, and nonalcoholic fatty liver disease related to diabetes and obesity.

Symptoms can include upper abdominal pain or swelling, loss of weight or appetite, white chalky stools, and general fatigue.

Liver cancer screening guidelines for patients with cirrhosis vary, with some guidelines calling for just imaging and other guidelines calling for both imaging and AFP measurement.

"Liver cancer screening in patients with chronic liver disease has traditionally been performed using an abdominal ultrasound. While ultrasound is readily available and noninvasive, it misses many cancers when they are small," said Dr. Amit Singal, who holds the David Bruton, Jr. Professorship in Clinical Cancer Research.

"Our study found that adding the blood biomarker alpha fetoprotein increased detection of early-stage hepatocellular carcinoma from 45 percent with ultrasound alone to 63 percent using the two tests in combination.

AFP is a plasma protein that is produced in abundance by the liver cells in the fetus. In adults, AFP levels are normally low, but liver cancer can cause AFP levels to rise.

The research, a meta-analysis of 32 previous studies, appears in the journal Gastroenterology.

Collaborators on the study included Dr. Jorge Marrero, Professor of Internal Medicine, and Dr. Adam Yopp, Associate Professor of Surgery, also members of the Simmons Cancer Center, one of just 49 NCI-designated Comprehensive Cancer Centers in the nation and the only NCI-designated Comprehensive Cancer Center in North Texas.

Simmons Cancer Center is among just 30 U.S. cancer research centers to be designated by the NCI as a National Clinical Trials Network Lead Academic Participating Site.

"Our results highlight the importance of continued development and validation of blood-based biomarkers for liver cancer early detection. Most important, our results support a change in clinical practice and the routine use of ultrasound and biomarkers together for liver cancer screening," said Dr. Singal, Dedman Family Scholar in Clinical Care at UT Southwestern, which is recognizing its 75th anniversary this year.

This work was supported by the National Cancer Institute and the Cancer Prevention Research Institute of Texas.

http://bit.ly/2BSe7CZ

A Boy Scrapes His Elbow. One Week Later, Docs Find a Sea Snail in the Wound.

A scraped elbow may not seem like an unusual injury, but for one 11-year-old boy in California, his health took an odd turn after he fell and hurt his left elbow while exploring a tide pool.

By Cari Nierenberg, Live Science Contributor

The boy's parents cleaned his wound after the incident, but noticed during the following week that the "blister" on his left elbow wasn't healing, but instead was gradually getting bigger, according to a report of the boy's case, which was published Feb. 7 in the journal BMJ Case Reports.

Checkered periwinkle sea snails (*Littorina scutulata*). Daniel L. Geiger/SNAP/Alamy

Concerned that their son might have a skin infection, his parents took him to see his pediatrician. After examining the boy's red and swollen elbow, his doctor diagnosed him with a skin abscess, or pus-filled infection, according to the case report. [27 Oddest Medical Cases]

The standard treatment for an abscess is to drain the wound, and the doctor did just that. But as the doctor cut into the boy's elbow, he noticed a small, dark-colored object inside of it.

The object turned out to be a tiny sea snail, snuggled firmly in its shell, according to the report. Even more surprisingly — though the doctor and patient didn't know it at the time — the snail was still alive.

Checkered periwinkle

So, what's a pediatrician to do when he finds a marine animal inside a skin abscess?

Lead author Dr. Albert Khait, an assistant professor of pediatrics at Loma Linda University in Loma Linda, California, who treated the boy, said he reached out to a mollusk expert at the Natural History Museum of Los Angeles County, who identified the snail as a checkered periwinkle marine snail (*Littorina scutulata*).

The egg of the checkered periwinkle, referred to as a micro snail, likely got into the boy's skin when he slipped and scraped his elbow on the wet rock while he was fetching a sea cucumber, which is another type of marine animal, Khait told Live Science. "This is a young snail, though it is bigger than something that can enter the skin unnoticed," he added.

A checkered periwinkle can have a dark, smooth shell, with a white checkerboard pattern, according to the Slater Museum of Natural History in Washington state. The small, pointy-shelled snails feed on algae found on rocks, and, unlike most marine organisms, spend much of their time out of the water.

"A unique visitor inside the human body"

One of the unique features of the checkered periwinkle is that it can seal its shell shut, which keeps water and moisture inside, and prevents the snail from drying out and suffocating, according to the case report.

"These characteristics made the checkered periwinkle a unique visitor inside the human body," the case report authors wrote.

What's more, sea snails can thrive in the ocean under extreme temperatures and pressure, Khait said. "This is probably why it was able to live in the abscess as well," he added.

Given the boy's interest in tide pools and marine life, he thought it was cool that his doctor found a sea snail in his elbow. He asked to keep the critter as a reminder of his adventure.

So, after Khait bandaged up the wound and prescribed a course of antibiotics, he placed the sea snail in a specimen jar and the boy took it home to show his friends.

A week later, when Khait called the family to see how the boy was doing, he found out that the wound had fully healed. He was also fascinated to learn that the boy said he saw the snail move on his first day home — meaning it was alive — but there was no movement after that.

After removing the snail, it was hard to tell just by looking at it whether it was still living, but since the snail had grown in size and the family reported it moving, this was the obvious conclusion, Khait said.

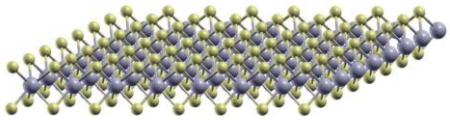
http://bit.ly/2spSPZn

Scientists identify hundreds of atomically-thin materials

Computer scan of existing databases spits out materials that are only atoms thick.

John Timmer - 2/12/2018, 12:00 AM

Graphene may seem like a modern wonder-material, but it's been with us for ages in the form of graphite. Graphene is a sheet of carbon atoms bonded to each other, just one atom thick; graphite is just an agglomeration of these sheets layered on top of each other.



***Enlarge** / Molybdenum disulfide, one of the 2D materials we knew about.* NC State

To study graphene, however, it took someone clever to devise a way of peeling single layers off from this agglomeration (the secret turned out to be a piece of tape).

Since then, we've identified a handful of additional chemicals that form sheets that are a few atoms thick. These have a variety of properties—some are semiconductors and have been combined with graphene to make electronic devices. To expand the range of device we can craft that build on the advantages of these atomically thin materials, a larger catalog of chemicals like this would be handy.

Now, a Lithuanian-Swiss team says it's done just that. The team has found materials just like graphite: a bulk material with atomically thin layers hidden inside.

The work relies heavily on other scientists having shared their data in open repositories. These include large databases that hold the structure of crystals for a huge number of chemicals. The Inorganic Crystal Structure Database, for example, held nearly 100,000 unique crystal structures when this research was performed; the Crystallography Open Database another 90,000. Each of these structures provides the details of how the atoms of a material are arranged in three-dimensional space. Almost all of these materials, however, are 3D, with a repeating pattern of atoms extending to the edges of the material in all directions.

Not your typical database search

The authors developed computer code that could search through the structures for something like graphite. Graphite has strong chemical bonds among the carbon atoms of each layer. But the layers are held together by a relatively weak electrostatic interaction called a van der Waals force. While the van der Waals forces are enough to hold the material together under most conditions, they're weak enough to allow individual layers to be peeled off the bulk graphite.

So the authors' new software searched for something similar: strong chemical bonds along one plane and a relatively weak non-chemical interaction in a perpendicular one. This narrowed things down dramatically, leaving the team with a bit over 5,500 chemicals to consider. The team then used other software to calculate the strength of the attraction between adjacent sheets in the material. If this attraction is too strong, a layer will probably break instead of flaking or peeling off. While this eliminated a number of chemicals from the authors' search, there were still over 1,800 left.

In many cases, the materials were structurally similar in terms of the locations of the atoms and the chemical bonds among them. For example, molybdenum disulfide is a well-studied example of an atomically thin material, but the authors identified 13 additional chemicals that form similar structures. Another structure, exemplified by cadmium di-indide, showed up in 64 different chemicals in total. While many of these sheets would end up being similar in behavior, the different atoms involved raise the possibility that some will end up being quite distinct. And a few of the structures had never been described before.

Tracking electrons

To figure out what sorts of materials we could add to our arsenal, the researchers calculated what the electrons would be doing in 258 of the less-complex chemicals. Most of them (166) turned out to be semiconductors, although the voltage difference between their ground and conducting states ranged from zero to 1.5 electronVolts. Another 92 materials were metallic. Another 56 are likely to have unusual magnetic properties, and a few others are likely to have behaviors that depend on an electron's spin, like a half-metal.

Now, it's not clear how many of these materials will actually be easy to make and then flake off into atomically-thin sheets. But even if only 10 percent of the original collection work out, that's still a big leap forward. The large number of distinct properties in this collection of materials raises the prospect of having the ability to choose one that's appropriate for specific applications.

In addition, it opens up possibility for the layering of these atomically thin materials. Because they're so thin, dropping one sheet on top of another will change the proprites of both, in part depending on how the atoms line up next to each other. Lots of different materials means lots of potential to tweak this alignment. So, while this paper distills down to a very elaborate database search, I'm excited to see what happens as researchers begin testing some of the materials it's identified.

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http://bit.ly/2BoJFPI

Instead of filling cavities, dentists may soon regenerate teeth

Researchers recently discovered certain drugs stimulate innate self-repair mechanisms

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For dentists, a cavity is a conundrum — in order to save the tooth they must further damage it. Currently, the primary way to treat a cavity is to excavate the decay and the surrounding area before filling the resulting crater with a durable surrogate material such as metal, plastic or glass cement.

But what if instead of drilling holes into teeth and patching them up with synthetic fillers, dentists could coax our pearly whites to regrow themselves? Recently, Paul Sharpe, a bioengineer at King's College London, and his colleagues discovered a new way to do exactly this in mice. Last year they published a study describing their innovative techniques in Scientific Reports. And since then they have made even more progress that edges this experimental procedure closer to human clinical trials. If the treatment eventually becomes part of the dentist's standard tool kit, scientists say it would easily be one of the field's most important advances in 50 years.

Our teeth get damaged all the time. Most of the injuries they endure are due to everyday wear and tear as well as the activity of microbes in the mouth. These organisms coat the surface of each tooth and feed on meal remnants. As they break down particles of food, some of these microbes produce and secrete acids as a by-product. And that acidity degrades enamel — the tooth's hard outer layer.

Like skin, teeth can usually repair minor mishaps themselves. When our teeth remain uncleaned for too long, however, acid can eat through the enamel and begin dissolving underlying layers of dense, bony tissue called dentin. When dentin is seriously injured, stem cells located in the tooth's soft, innermost layer — the dental pulp — morph into cells called odontoblasts, which secrete new tissue. (Stem cells are capable of becoming virtually any type of cell.) Yet when the injury is too large or deep, that fresh dentin is not sufficient to restore the tooth. The result is often a cavity.

Sharpe suspected he could dramatically boost teeth's natural healing ability by mobilizing stem cells in the dental pulp. Earlier research had demonstrated the Wnt signaling pathway — a particular cascade of molecules involved in cell-to-cell communication — is essential for tissue repair and stem cell development in many parts of the body such as the skin, intestines and brain. Sharpe wondered: Could this signaling

pathway also be important for self-repair processes in teeth? If so, maybe exposing damaged teeth to drugs that stimulate Wnt signaling would similarly encourage the activity of stem cells in the dental pulp — giving teeth the kind of regenerative superpowers usually seen only in plants, salamanders and starfish.

To test this idea, Sharpe and his fellow researchers drilled holes into the molars of mice, mimicking cavities. They then soaked tiny collagen sponges (which are made from the same protein found in dentin) in various drugs known to stimulate Wnt signaling, including tideglusib, a compound that has been investigated in clinical trials for its potential to treat Alzheimer's and other neurological disorders. The scientists then placed these drug-soaked sponges in the drilled mouse molars, sealed them up and left them for four to six weeks. The teeth treated with these drugs produced significantly more dentin than ones untreated or stuffed with an unsoaked sponge or typical dental fillers. In most cases the technique restored the rodents' pearly whites to their former intact state. "It was essentially a complete repair," Sharpe says. "You can barely see the joint where the old and new dentin meet. This could eventually be the first routine pharmaceutical treatment in dentistry."

David Mooney, a professor or bioengineering at Harvard University who has also investigated new ways to heal teeth but was not involved in the study, says he is "very impressed" by these findings. "This is not just scientifically important, but has significant practical advantages," he says. Adam Celiz, an assistant professor of bioengineering at Imperial College London who was also not involved in the recent research, says this is an important advance in the emerging field of regenerative dentistry. "The materials dentists use could soon be revolutionized," he says.

Any treatment that recruits the body's native stem cells or adds new stems cells to the body, however, poses a risk of uncontrolled tissue growth. Experimental and unregulated stem cell therapies have resulted in brain tumors, for example, as well as bones growing in eyelids. But in this case, Sharpe says, the amounts of drug used are so tiny that the risk of unwanted growth is minimal. Celiz agrees the danger is small but he says rigorous testing in lab animals and clinical trials should be done to rule out potential side effects.

Since publishing their initial study Sharpe and his colleagues have tested their regenerative technique on rats. (Because those rodents have larger teeth than mice, a drilled rat molar better approximates human tooth decay.) The treatment worked just as well on the rats as it had on the mice, Sharpe says, but the data has not yet been published. Now Sharpe's team is investigating a larger group of candidate drugs in order to determine whether another medication works better than those already tested, and to determine the optimal dose. They are also developing an alternative delivery system that is more amenable to modern dental practices: The chosen drug will be dissolved in a gel that is injected into a cavity and bathed with ultraviolet light to solidify it — a quick and easy procedure similar to one dentists already use to seal and repair teeth.

In order to formally introduce this treatment to modern dentistry, however, the researchers will need to perform clinical trials with human patients. Such work is at least several years away, Sharpe says. But some of the drugs he might consider are already approved for other uses in humans, which he hopes could expedite the process for eventual approval. "A lot of dental treatments are still in the dark ages," Sharpe says. "It's time to move on."