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The little lights now packing a deadly punch

Tech could transform water sanitisation techniques and offer access to clean drinking water to even remote developing regions

"The tech we are working on could transform water sanitisation techniques and offer access to clean drinking water to even remote developing regions via portable systems," says Christian Zollner from the University of California in Santa Barbara.

Mr Zollner has been working on light emitting diodes (LEDs), the long-lasting technology in modern lightbulbs. They are probably in the lightbulbs in your house, or the headlamps of your car.

Because they are tough and energy efficient, researchers are always trying to find new ways of using them.

Mr Zollner and his team have been working on LEDs that emit ultraviolet light, in particular UV-C light, which is deadly to bacteria and viruses, including the coronavirus.

His goal is to make those LEDs more powerful, robust and cheaper.

"Right now, UV LEDs are capable of a few milliwatts of power. Our aim is to make them 10 to 20 times more powerful.

"Our focus previously was mainly on using them for water sterilisation, but the Covid-19 pandemic has made us realise there is also a big market for sanitising surfaces and equipment. If there is another virus situation in say five or 10 years, this technology could be very useful."

At the moment his lights are powerful enough to cleanse a closed cabinet, but need to be 20 times more powerful to zap a whole room. The light can also damage human skin and eyes, so the commercial applications are limited.

But one firm has found a use. Californian firm LARQ makes what it says is the world's first self-cleaning water bottle.

Its solution to prevent exposure to UV-C light is to ensure the tiny UV LEDs in the lids of its bottles only come on when the bottles are screwed shut. Users must then push down on the lid to activate the technology, which the company claims eradicates more or less all bacteria and viruses in 60 seconds.

LEDs have come a long way since the first were produced in the 1960s. Back then, the only light the semiconductor devices could generate was an infrared light invisible to the human eye. Now, they cover the entire visible spectrum, as well as infrared and UV light and come in a dazzling array of forms.

It might look like an ordinary bottle, but it can zap viruses **LARQ**

Micro-LEDs that measure less than 1mm across are another of the latest variants. Designed for use in high-end screens, micro-LEDs promise blacker blacks, brighter blues.

Samsung has been showing off its massive screen made of micro-LEDs at consumer electronics shows. "Micro-LED display technology offers a huge improvement to standard LED panels due to its optimum brightness and image definition," says Damon Crowhurst, head of display at Samsung UK.

But the engineering involved is mind-boggling. The screens need millions of micro-LEDs, which means they are expensive - a 75-inch TV costs tens of thousands of pounds.

"Micro-LED screens cost about £1,000 per inch to make, so a 75-inch micro-LED television could easily cost the same as a new Porsche Cayenne," says Paul Gray, an analyst at global technology researcher Omdia. "You have to ask yourself how many people will be prepared to pay that to get better contrast when they watch TV."

The crushingly high cost of micro-LEDs is one reason a number of manufacturers currently prefer mini-LEDs, which though still tiny measure more than 1mm across.

Apple, for example, is rumoured to be developing six new products with mini-LED displays, including both iPads and MacBooks.

In the short term, small-screen devices such as smartwatches are expected to be the biggest growth area for micro-LEDs.

"Small screens are a much easier proposition, as a 1cm micro-LED screen can be made on a single silicon chip," Mr Gray says. "They are already being used in camera viewfinders. So for products such as smartwatches, we are looking at a much shorter timeframe."

Researchers are finding ever more exotic ways to make the perfect LED - more light with less power.

UK-based start-up Kubos Semiconductors is developing LEDs based on a form of Gallium Nitride (GaN) with a crystal structure that is cubic rather than hexagonal, an approach it believes could solve long-term problems creating more efficient micro-LEDs.

At the moment, green and amber LEDs are up to three times less efficient than blue and red ones. Known as the Green Gap, the phenomenon reduces the performance and increases the cost of lighting and displays. "This will be very important in applications such as mobile phones and smartwatches where displays need to run off a battery," says Kubos chief executive Caroline O'Brien.

Elsewhere, researchers are working to reduce LED production costs and environmental impact.

An EU-funded study is experimenting with using naturally occurring fluorescent protein structures to create bio-LEDs.

Based in Austria, Spain, and Italy, the multi-university project began in January and is due to run for four years.

"The goal is to find a cheaper and more environmentally friendly way of producing LEDs by avoiding the need for inorganic phosphates that have to be mined in specific locations," says Gustav Oberdorfer, who is leading research at Graz University of Technology in Austria.

"We hope our LEDs will be used commercially in devices within the next 10 years, and believe they could both lower the cost of LED devices and make them much more sustainable."

So next time you turn on a light, think of the humble LED, which has come a long way since the 1960s and has a bright future.

https://bit.ly/30cBYbK

First-of-Its-Kind Study Hints at How Psilocybin Works in The Brain to Dissolve Ego

No one really knows what these drugs actually do to our perception of self

Carly Cassella

The psychedelic experience can be rough on a person's ego. Those who experiment with magic mushrooms and LSD often describe a dissolution of the self, otherwise known as ego-death, ego-loss, or ego-disintegration.

For some, the experience is life-changing; for others, it's downright terrifying. Yet despite anecdote after anecdote of good trips and bad trips, no one really knows what these drugs actually do to our perception of self.

The human brain's cortex is where the roots of self awareness are thought to lie, and growing evidence has shown the neurotransmitter, glutamate, is elevated in this region when someone is tripping.

But up until now we've only had observational evidence. Now, for the first time, researchers have looked directly into how taking psilocybin affects glutamate activity in the brain. And the evidence suggests that our tripping experience, whether good or bad, might be linked to glutamate.

In a double-blind, placebo-controlled experiment, neuroscientists carefully analysed what happens to glutamate levels and a person's ego when taking psilocybin, the active ingredient in magic mushrooms.

Using magnetic resonance imaging (MRI) to monitor the brains of 60 healthy volunteers, the team found significant changes in activity in both the cortex and the hippocampus in those taking psilocybin.

Glutamate is the most common neurotransmitter in the brain, and it's known to be critical for fast signalling and information, especially in the cortex and hippocampus, the latter of which is thought to play a role in self esteem. It also looks like psychedelics have a way of tapping into this system.

Interestingly enough, in the new clinical study, these two regions of the brain had quite different glutamate responses to psilocybin. While the authors found higher levels of glutamate in the prefrontal cortex during a trip, they actually found lower levels of glutamate in the hippocampus.

What's more, this may have something to do with whether a person has a good experience with their ego or a bad one.

"Analyses indicated that region-dependent alterations in glutamate were also correlated with different dimensions of ego dissolution," the authors write.

"Whereas changes in [cortical] glutamate were found to be the strongest predictor of negatively experienced ego dissolution, changes in hippocampal glutamate were found to be the strongest predictor of positively experienced ego dissolution."

Practically, we still don't really understand how this activity in the brain is linked to our ego, or even if it is. Still, it's been suggested that psychedelics decouple regions of the brain, so factual or autobiographical information is momentarily separated from a sense of personal identity.

"Our data add to this hypothesis, suggesting that modulations of hippocampal glutamate in particular may be a key mediator in the decoupling underlying feelings of (positive) ego dissolution," the authors suggest.

After decades of limited research, drugs like psilocybin, LSD and DMT are now finally being considered for their therapeutic benefits. Understanding how these drugs work on a neurochemical basis could allow scientists to develop better treatments for those with mental health issues, such as depression and anxiety.

Although if we're going to be using these substances to treat mental health issues like anxiety, depression and addiction, we're going to need to also understand the way the drugs mess with our ego - hopefully without the bad trip to go along with it.

The study was published in *Neuropsychopharmacology*.

https://bit.ly/3qWnGlB

Gut Microbiome Composition Linked to Human Behavior

A study uncovers connections between the bacteria in our guts and our social lives.

Amy Schleunes

Researchers have shown that fecal transplants in mice can change the animals' temperaments. Several studies have also linked the human microbiome to psychiatric illnesses, including autism and depression. But to date, few experiments have considered the microbiome of the general population and whether variations in gut bacteria are associated with personality traits, says microbiome-gut-brain axis researcher Katerina Johnson of Oxford University.

In a recent study, Johnson analyzed gut microbiome data obtained from stool samples of 655 individuals, along with survey-based information about their personality and behavior, health and lifestyle, dietary habits, and sociodemographics. She found that people who have larger social networks are more likely to have greater gut microbiome diversity, which research indicates is associated with both gut health and general health. The analysis also showed that "sociable people tend to have a higher abundance of certain types of gut bacteria" that have been found to be less

abundant in people with autism, Johnson says. She adds that her analysis also identified bacteria found in lower abundances in sociable people that had previously been found to be highly abundant in autistic people.

She notes that further research is needed to directly investigate any effect that gut bacteria may have on human behavior, but ultimately, she says, these findings and follow-up research "might help with the development of new therapies for conditions like autism."

Gerard Clarke, a microbiome researcher at University College Cork in Ireland who was not involved in the study, tells *The Scientist* in an email that we can't definitively say whether "these very interesting associations manifest in biological or physiological terms of relevance to social behavior," but that the paper yields "a number of important clues as to who might be involved in the conversation between the gut and the brain."

The paper - *K.V.-A. Johnson, "Gut microbiome composition and diversity are related to human personality traits," J Hu Mic, 15:100069, 2020.*

https://bit.ly/372GtqQ

Mars Does Have a Magnetic Field of Sorts – And We've Finally Got Data to Map It

Unlike Earth, Mars doesn't have a global magnetic field to protect it from the rigours of space weather – but it does have spots of local, induced magnetism.

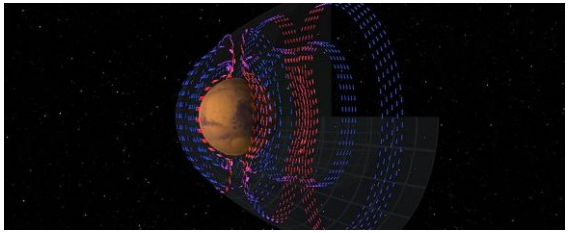
David Nield

Now, researchers have been able to create an incredible, detailed map of the electric currents that are responsible for shaping these magnetic fields. It gives scientists a much greater understanding of how Mars might have lost much of its atmosphere over the course of billions of years, as well as how interactions between the solar winds and Mars' magnetosphere are playing out today.

As you can see from the video embedded below, the team working with the Mars Atmosphere and Volatile Evolution (MAVEN) spacecraft have been able to produce some jaw-dropping visualisations from the captured magnetic readings. Previously hidden flows of energy are suddenly visible in full colour.

"These currents play a fundamental role in the atmospheric loss that transformed Mars from a world that could have supported life into an inhospitable desert," says planetary scientist Robin Ramstad, from the University of Colorado, Boulder.

"We are now currently working on using the currents to determine the precise amount of energy that is drawn from the solar wind and powers atmospheric escape."



NASA/Goddard/MAVEN/CU Boulder/SVS/Cindy Starr

The team analysed five years of data from MAVEN to come up with their maps, which show electrical currents creating a nested, double-loop structure around Mars, wrapping all the way around both the day and night side of the planet.

These currents interact with the incoming solar wind, causing it to envelop Mars and flow around it like spaghetti noodles around a basketball. The findings build on the discovery of the planet's unique magnetic tail, spotted by MAVEN three years ago.

What's also interesting for the researchers is the detail of the interplay between the solar winds and the electric currents, and how energy is transferred between the upper atmosphere, the magnetosphere, and the solar wind.

"Mars' atmosphere behaves a bit like a metal sphere closing an electric circuit," says Ramstad. "The currents flow in the upper atmosphere, with the strongest current layers persisting at 120-200 kilometres (75-124 miles) above the planet's surface."

"With a single elegant operation, the strength and paths of the currents pop out of this map of the magnetic field."

Besides making for some stunning visualisations, the map of electric currents that the researchers have put together should be able to tell us more about how the atmosphere of Mars continues to get stripped away, and how these interactions may have evolved over the course of the planet's history.

Scientists still have a lot of questions about what happened to Mars' once thick, busy atmosphere – and about how we might one day make it habitable again.

There's lots more to come from this data, and from MAVEN.

Understanding the behaviour of the magnetic field around the Red Planet has the potential to give us some big clues about why its atmosphere is now so different from our own – and indeed from Venus, which also has an induced magnetosphere.

"If you want to understand how the atmosphere of Mars and Venus are so different from the Earth's, and why they're different from each other despite both being non-magnetised, we need to understand their induced magnetospheres first," says Ramstad.

The research has been published in *Nature Astronomy*.

https://bit.ly/2AKMqwI

Here's how plants became meat eaters

Carnivorous plants are the 'most skillful green hunters on the planet.'

By Diane Lincoln - Live Science Contributor

About 70 million years ago, when dinosaurs roamed the Earth, a genetic anomaly allowed some plants to turn into meat eaters. This was done in part, with a stealthy trick: repurposing genes meant for their roots and leaves and using them instead to catch prey, a new study finds.

This step is one of three that some non-carnivorous plants took over tens of millions of years to allow them to turn into hungry carnivores, the researchers said.

The meat-eating shift gave these plants a number of advantages. In effect, "carnivorous plants have turned the tables by capturing and consuming nutrient-rich animal prey, enabling them to thrive in nutrient-poor soil," the researchers wrote in the study, published online May 14 in the journal Current Biology.

To investigate how carnivorous plants evolved, an international team of botanists and biologists led by Jörg Schultz, Associate Professor, at the University of Würzburg, Germany, compared the genomes and anatomy of three modern meat-eating plants.

Carnivorous plants like Venus flytraps have evolved to be skillful hunters.
Image: © Kuttelvaserova Stuchelova/Shutterstock

There are hundreds of carnivorous plant species, but the researchers chose to look at three related insect-eating plants, all members of the Droseraceae family. All three of these plants use motion to capture prey, the researchers said.

One plant is the familiar Venus flytrap (*Dionaea muscipula*), a native to the wetlands of the Carolinas that has influenced Pokémon characters, made appearances in various Saturday morning cartoons, and even inspired a Broadway play. The closely related aquatic waterwheel plant (*Aldrovanda vesiculosa*) occupies the waters of almost every continent. It has spindly underwater flaps that quickly tighten around unsuspecting marine animals. The third plant investigated, the beautiful but deadly sundew plant (*Drosera spatulata*), is common in Australia. Luring victims with sweetness, the sundew rolls up a sticky strip around its catch.

After analyzing these plants, the team discovered the three-step process toward carnivory. First, about 70 million years ago, an early non-carnivorous ancestor of the three modern plant carnivores underwent a whole-genome duplication, generating a second copy of its entire DNA, or genome. This duplication freed up one of the copies of leaf and root genes to diversify, allowing them to serve other functions. Some leaf genes developed into genes for traps, while carnivorous nutrition and absorption processes were guided by genes that otherwise would have served roots seeking nutrition from soil.

The second step in their journey to carnivory occurred once the plants began receiving new nutrients from prey. At that point, traditional leaves and roots were no longer as necessary. Many genes that were not involved in carnivorous nutrition began to disappear. For instance, seedlings of aquatic waterwheel plants acquire an early proto-root, but it fails to develop as they mature. This is the only remnant of what once was a root system. As a result of losing this gene and others, the three plants observed in this study are the gene-poorest plants to be sequenced to date, the researchers stated.

Two earlier studies by other groups of scientists in 2013 showed similar gene-poor findings in other carnivorous plants. They found that an aquatic bladderwort thriving on all continents but Antarctica and a corkscrew ground-covering plant native to Brazil both had very small genomes compared with non-carnivorous plants. These carnivores may also have undergone the same gene-shedding process, the researchers of the new study said.

In the third step of the transformation to carnivory, the plants underwent evolutionary changes specific to their environment. The roots and leaves evolved to be trap-specific, the researchers found. Genes for roots that were once used to seek out and absorb nutrients from soil were now commandeered to create enzymes needed to digest and absorb nutrients from prey. Genes once used in glands that secreted nectar to attract pollinating insects were summoned to traps, where they produce substances to attract prey.

Most plants with leaves and roots contain the material necessary to become carnivorous. Researchers wrote that the three-step process revealed by the new study shows how, over time, ancient "non-carnivorous plants evolved into the most skillful green hunters on the planet."

https://bit.ly/2UfXs3E

Up to 81% of COVID-19-Positive Patients are Asymptomatic: Study

The majority of COVID-19-positive patients may be asymptomatic.

In a paper published in the journal *Thorax*, a team of Australia researchers described the first instance of complete COVID-19 testing of all passengers and crew on an isolated cruise ship during the current pandemic: of the 217 passengers and crew on board, 128 tested positive for COVID-19 on reverse transcription-PCR; of the COVID-19-positive patients, only 24 (19%) were symptomatic.

Macquarie University's Dr. Alvin Ing, Dr. Christine Cocks of Sunshine Coast University Hospital, and Dr. Jeffery Peter Green from Royal Australian College of General Practitioners described events on an expedition cruise ship carrying 128 passengers and 95 crew members.

The ship departed from Ushuaia, Argentina, for a planned 21 day cruise of the Antarctic, taking a similar route to that of Ernest Shackleton in 1915-17. It set sail in mid-March after the World Health Organization had declared COVID-19 a global pandemic.

Passengers who, in the previous three weeks, had passed through countries where COVID-19 infection rates were already high, were not allowed to board. And everyone's temperature was taken before embarkation. Hand sanitizing stations were plentiful aboard ship, particularly in the dining room.

The first case of fever was reported on day 8, prompting the immediate adoption of infection control measures.

This included confining passengers to their cabins, stopping daily servicing, apart from the delivery of meals, and the wearing of personal protective equipment for any crew member in contact with sick passengers.

As Argentina had closed its borders, the ship sailed to Montevideo, Uruguay, arriving on day 13.

Eight passengers and crew eventually required medical evacuation to hospital at this point for respiratory failure.

On day 20, all the remaining 217 passengers and crew were swab tested for coronavirus; 128 (59%) tested positive.

Original and subsequent route of cruise ship. **Image credit: Ing et al, doi: 10.1136/thoraxjnl-2020-215091.**

"In 10 instances, two passengers sharing the same cabin didn't have the same test result, possibly because the current swab test returns a substantial number of false negative results," the researchers said.

Of those testing positive, 24 (19%) had symptoms, but 108 (81%) didn't.

The ship had no contact with other people for 28 days after its departure, so was the equivalent of a hermetically sealed environment. "The prevalence of COVID-19 infection on cruise ships is likely to be significantly underestimated," the scientists said. "We recommend that passengers should be monitored after disembarkation to ward off potential community spread of the virus." "And the potentially high rate of false negative results obtained with the current swab tests suggests that secondary testing is warranted."

A.J. Ing et al. COVID-19: in the footsteps of Ernest Shackleton. Thorax, published online May 27, 2020; doi: 10.1136/thoraxjnl-2020-215091

https://bit.ly/3eUqiFo

SARS-CoV-2 Spike Protein Shares Sequence with a Human Protein

Eight amino acids are identical to part of the human epithelial sodium channel, leading researchers to suspect the virus might interfere with the channel's function.

Abby Olena

Scientists determined earlier this year that there is a cleavage site in the SARS-CoV-2 spike protein for furin, a human protease, and that the spike protein is split into two subunits at that spot. This cleavage has been implicated in helping break the virus open so it can enter human cells.

In a paper published May 26 in *eLife*, researchers found that the spike protein's furin cleavage site is identical to a sequence in the human epithelial sodium channel, which likewise must be cut by furin in order to be activated.

The authors propose that the virus may be competing with the sodium channel for furin, and possibly disrupting its function, but that remains to be demonstrated.

"The paper's really nice because it gets at this common view that many viruses co-opt parts of human cells to help them survive," says David Perlin, who studies infectious diseases and is the chief scientific officer at Hackensack Meridian Health's Center for Discovery and Innovation in New Jersey. He was not involved in the study.

This discovery came about when researchers at nference, an artificial intelligence company, started looking to see whether are there any sequences of amino acids in SARS-CoV-2 proteins that seemed surprising or unusual.

One that stuck out, says Venky Soundararajan, nference's chief scientific officer, was a stretch of four amino acids present in the spike protein of 10,956 of 10,967 SARS-CoV-2 isolates from

around the world, but not in the protein's sequence in related coronaviruses, such as SARS-CoV or varieties that infect bats or pangolins.

Other groups had reported in February and April that this insertion forms a cleavage site for the human protease furin, which is thought to sever the two subunits of the spike protein to facilitate entry into human cells.

Soundararajan and colleagues strengthened this idea when they determined that the furin cleavage site is identical to a proven furin cleavage sequence in the alpha subunit of the human epithelial sodium channel, which plays a role in managing the balance of salt and fluid in many of the body's cells. This site is essential in the process of assembling the channel's subunits into a functional whole capable of regulating sodium levels in a cell.

Next, the researchers turned to a platform they developed, which uses a database of single-cell RNA expression data from 65 previously published human and mouse studies, to look into gene expression of the sodium channel and other human genes known to be involved in SARS-CoV-2 infections. They found that expression of the epithelial sodium channel's gene overlaps with that of the gene for furin and for the primary SARS-CoV-2 receptor, ACE2, in the cell types most affected by the virus.

The coupling of ACE2, the epithelial sodium channel, and furin in the epithelial cells of the nasal cavity, the respiratory tract, and the gut supports the idea that those regions are the initial hubs of infection in the human body, Soundararajan says.

Perlin warns against making assumptions about ACE2 abundance based on transcript levels. "We have to always be a little careful going from gene expression to what's assembled on the membrane," he says.

Based on this RNA co-expression, the authors hypothesize that during a SARS-CoV-2 infection, the viral spike protein might compete with the human sodium channel for furin cleavage.

If this competition disrupts the activation of the sodium channel, it could become dysregulated, which could interfere with its role in regulating fluid balance. This could explain why COVID-19 patients sometimes end up with large amounts of fluid in the lungs.

The study "is all computationally based with no wet experiments. Hence we have zero information on what the authors are suggesting is at all correct," cautions Vincent Racaniello, a virologist at Columbia University who was not involved in the work, in an email to *The Scientist*. He also questioned the idea that the cleavage of the SARS-CoV-2 spike protein by human furin could usurp cleavage of the epithelial sodium channel.

It's also not clear that this sodium channel is downregulated during viral infection. But if furin has a higher affinity for the virus and there is a high viral load in the same region where this sodium channel is expressed, "there is potential there that you'd have less processing of that alpha subunit of the sodium channel and this potentially could also [affect] sodium channel function locally," says Perlin. "Is that what's happening? I'm not sure, but it's an interesting hypothesis."

"Most computational analysis requires some experimental validation," says Dario Ghersi, a computational biologist at the University of Nebraska Omaha who did not participate in the study. That this recognition site is present in the majority of SARS-CoV-2 isolates implies that it is important to the virus, meaning the sequence could be of interest for vaccine and therapeutic development. "What they found seems pretty solid to me," he adds.

P. Anand et al., "SARS-CoV-2 strategically mimics proteolytic activation of human ENaC," eLife, doi:10.7554/eLife.58603, 2020.

https://nyti.ms/30doz3q

U.S. and Chinese Scientists Trace Evolution of Coronaviruses in Bats

Researchers whose canceled U.S. grant caused an outcry from other scientists urge preventive monitoring of viruses in southwestern China.

By James Gorman

An international team of scientists, including a prominent researcher at the Wuhan Institute of Virology, has analyzed all known coronaviruses in Chinese bats and used genetic analysis to trace the likely origin of the novel coronavirus to horseshoe bats.

In their report, posted online Sunday, they also point to the great variety of these viruses in southern and southwestern China and urge closer monitoring of bat viruses in the area and greater efforts to change human behavior as ways of decreasing the chances of future pandemics.

The horseshoe bat genus, Rhinolophus, seems to have originated in China tens of millions of years ago and has a long history of co-evolution with coronaviruses. **Credit...DeAgostini/Getty Images**

The research was supported by a U.S. grant to EcoHealth Alliance, a New York-based nonprofit, that was recently canceled by the National Institutes of Health. The grant, for more than $3 million, was well on its way to renewal, and the sudden reversal prompted an outcry in the scientific community.

Thirty-one U.S. scientific societies signed a letter of protest on May 20 to the N.I.H., and 77 Nobel laureates sent another letter to the N.I.H. and the Department of Health and Human Services seeking an investigation of the grant denial. The Nobelists said the cancellation appeared to be based on politics rather than a consideration of scientific merit. The report on the research, which has been accepted by the journal Nature Communications, was posted on the BioRxiv (pronounced bio-archive), where scientific research is often released before publication.

The report gives a glimpse of the work the grant had supported.

The researchers, mostly Chinese and American, conducted an exhaustive search for and analysis of coronaviruses in bats, with an eye to identifying hot spots for potential spillovers of these viruses into humans, and resulting disease outbreaks.

The genetic evidence that the virus originated in bats was already overwhelming. Horseshoe bats, in particular, were considered likely hosts because other spillover diseases, like the SARS outbreak in 2003, came from viruses that originated in these bats, members of the genus Rhinolophus.

None of the bat viruses are close enough to the novel coronavirus to suggest that it jumped from bats to humans. The immediate progenitor of the new virus has not been found, and may have been present in bats or another animal. Pangolins were initially suspected, although more recent analysis of pangolin coronaviruses suggests that although they probably have played a part in the new virus's evolution, there is no evidence that they were the immediate source.

The new research includes an analysis of bat and viral evolution that strongly supports the suspected origin of the virus in horseshoe bats, but isn't definitive, largely because a vast amount about such viruses remains unknown.

The report also adds detail to what scientists know of coronaviruses in bats, how they have evolved and what kind of threat they pose. Renewal of the grant would have supported a continuation of this work.

N.I.H. canceled the grant shortly after President Trump was asked at a news conference about money erroneously described as going to the Wuhan institute. That lab has been the target of conspiracy

theorists who promote the idea that the novel coronavirus was made in a lab. Scientists and U.S. intelligence agencies agree that the overwhelming likelihood is that the virus evolved in nature.

Richard Ebright, a microbiologist and biosafety expert at Rutgers University, has argued that there could have been an accidental leak of a naturally evolved virus that was present in the lab, and that lab safety should be investigated. Many scientists view the leak scenario as unlikely given the many opportunities for infection in the wildlife trade, markets and farming.

There is also no reported evidence that the new virus was ever present at the Wuhan Institute of Virology. It was first discovered after numerous human cases appeared in late December, most in people with connections to a wet market in Wuhan.

Zheng-Li Shi, the director of the Center for Emerging Infectious Diseases at the institute, known for work tracking down the source of the original SARS virus in bats and identifying SARS-CoV-2, as the novel coronavirus is known, is one of the authors of the new paper, along with Peter Daszak, the president of EcoHealth Alliance. The researchers collected oral and rectal swabs, as well as fecal pellets from bats in caves across China from 2010 to 2015, and used genetic sequencing to derive 781 partial sequences of the viruses. They compared these to sequence information already documented in computer databases on bat and pangolin coronaviruses.

They found evidence that the novel coronavirus may have evolved in Yunnan Province, but could not rule out an origin elsewhere in Southeast Asia outside China.

The family of bats that included the horseshoe genus, Rhinolophus, seems to have originated in China tens of millions of years ago. They have a long history of co-evolution with coronaviruses, which the report shows commonly jump from one bat species to another.

Dr. Daszak said that the region where China, Laos, Vietnam and Myanmar converge may be "the real hot spot for these viruses."

He said the region was characterized not only by bat and coronavirus diversity, but by urbanization, population growth and intense poultry and livestock farming, all of which could lead to viruses jumping from one species to another, and to the spread of human disease.

Not only bats should be monitored, Dr. Daszak said, but humans. "People are farming wildlife all across Southern China, tens of thousands of people involved in the industry, they should be getting regular tests, not just for Covid-19, but for what other viruses they are picking up."

He acknowledged that such an effort would be very costly, but said that compared to the cost of a pandemic, "You're definitely getting a good return on investment."

https://bit.ly/3cFDrdo

Urban foxes may be self-domesticating in our midst

It appears UK rural red foxes are turning tame on their own

By Virginia Morell

A fox on the prowl in its Bristol, U.K., home **Sam Hobson/Minden Pictures**

In a famous ongoing experiment started in 1960, scientists turned foxes into tame, doglike canines by breeding only the least aggressive ones generation after generation. The creatures developed stubby snouts, floppy ears, and even began to bark.

Now, it appears that some rural red foxes in the United Kingdom are doing this on their own. When the animals moved from the forest to city habitats, they began to evolve doglike traits, new research reveals, potentially setting themselves on the path to domestication.

"I'm not so much surprised as delighted," by this study, says Lee Dugatkin, an evolutionary biologist at the University of Louisville, who has written about the Russian fox experiment but was not involved with the new work. "This is a 'natural experiment' that is very much in line with what the Russian experiment has found."

The renowned Siberian study immediately came to mind when Kevin Parsons heard about a large collection of red fox skulls at National Museums Scotland. A native Canadian and evolutionary biologist at the University of Glasgow, Parsons had already been struck by the number of foxes he regularly saw on Glasgow's streets, particularly in the early morning. "They'd walk by me and stare, as if asking, 'Why are you looking at me?'" he recalled. "They were fearless."

Curious to see whether the animals had somehow evolved to suit their urban lifestyle, Parsons examined National Museums Scotland's fox skull collection. Some 1500 skulls had been collected from 1971 to 1973 in London and the adjacent countryside, when a fox culling campaign was underway. All were marked with their locations, rural or urban. Urban areas were defined as having buildings, streetlights, and no wooded areas, whereas rural sites were wooded and lacked human development.

Parsons photographed 57 female and 54 male skulls and identified key features. A fox's habitat greatly affected the shape of its skull, he and his colleagues report today in the *Proceedings of the Royal Society B*.

Most significantly, the urban foxes, like those in the Russian experiment, had noticeably shorter and wider muzzles, and smaller brains, than their rural fellows. And males and females had very similar skull shapes. All of these changes are typical of what Charles Darwin labeled domestication syndrome.

Overall, urban foxes' skulls seemed to be designed for a stronger bite than were those of rural foxes, which are shaped for speed. Perhaps that's because in the city, a fox can simply stand at a human trash pile and feed on the food we've tossed out, where they may encounter more bones that can only be crushed with stronger jaws, Parsons speculates.

Still, he emphasizes that the urban red foxes are not domesticated. But the study does show how exposure to human activity can set an animal down this path, says Melinda Zeder, an emeritus archaeologist at the Smithsonian Institution's National Museum of Natural History.

Like early dogs, urban foxes would need to overcome their fear of humans to get close enough to eat our trash. And that may have been the spark that led to a host of other biological changes.

Foxes have started down this domestication path before in many parts of the world, Zeder notes. Their bones show up in early farming communities, for example. But unlike wildcats, who entered these communities and transformed into the furballs we know today, these foxes never become fully domesticated. "They never move any farther down the path to domestication," Zeder says. "We don't know why."

***Correction, 3 June, 1:40 p.m.:** This story has been updated to reflect the fact that the famed Siberian fox experiment is still ongoing.*

https://bit.ly/2UdX3P9

Tulane scientists find a switch to flip and turn off breast cancer growth and metastasis

Team is now working on FDA approval to begin clinical trials

Researchers at Tulane University School of Medicine identified a gene that causes an aggressive form of breast cancer to rapidly grow. More importantly, they have also discovered a way to "turn it off" and inhibit cancer from occurring. The animal study results have been so compelling that the team is now working on FDA approval to begin clinical trials and has published details in the journal *Scientific Reports*.

The team led by Dr. Reza Izadpanah examined the role two genes, including one whose involvement in cancer was discovered by Tulane researchers, play in causing triple negative breast cancer (TNBC). TNBC is considered to be the most aggressive of breast cancers, with a much poorer prognosis for treatment and survival. Izadpanah's team specifically identified an inhibitor of the TRAF3IP2 gene, which was proven to suppress the growth and spread (metastasis) of TNBC in mouse models that closely resemble humans.

In parallel studies looking at a duo of genes - TRAF3IP2 and Rab27a, which play roles in the secretion of substances that can cause tumor formation - the research teams studied what happens when they were stopped from functioning. Suppressing the expression of either gene led to a decline in both tumor growth and the spread of cancer to other organs.

Izadpanah says that when Rab27a was silenced, the tumor did not grow but was still spreading a small number of cancer cells to other parts of the body. However, when the TRAF3IP2 gene was turned off, they found no spread (known as "metastasis" or "micrometastasis") of the original tumor cells for a full year following the treatment. Even more beneficial, inhibiting the TRAF3IP2 gene not only stopped future tumor growth but caused existing tumors to shrink to undetectable levels.

"Our findings show that both genes play a role in breast cancer growth and metastasis," says Izadpanah. "While targeting Rab27a delays progression of tumor growth, it fails to affect the spread of tiny amounts of cancer cells, or micrometastasis. On the contrary, targeting TRAF3IP2 suppresses tumor growth and spread, and interfering with it both shrinks pre-formed tumors and prevents additional spread. This exciting discovery has revealed that TRAF3IP2 can play a role as a novel therapeutic target in breast cancer treatment."

"It is important to note that this discovery is the result of a truly collaborative effort between basic science researchers and clinicians." Izadpanah continued.

Members of the team included Eckhard Alt, David Jansen, Abigail Chaffin, Stephen Braun, Aaron Dumont, Ricardo Mostany and Matthew Burow of Tulane University. Dr. Bysani Chandrasekar of the University of Missouri has joined in the Tulane research efforts and found that targeting TRAF3IP2 can stop the spread of glioblastoma, a deadly brain cancer with limited treatment options. The team is now working on getting FDA approval and hopes to begin clinical trials soon.

https://bit.ly/2Ujeaz8

Paleontologists Find World's Oldest Fossil Bug

425-million-year-old fossil millipede from Scotland is the oldest-known 'bug'

***Kampecaris obanensis*. Image credit: British Geological Survey.**

A 425-million-year-old fossil millipede from Scotland is the oldest-known 'bug' (an insect, arachnid or other related creature), according to new research published in the journal *Historical Biology*.

Named *Kampecaris obanensis*, the prehistoric millipede lived during the Silurian period, about 425 million years ago.

The ancient creature was a small (2-3 cm in length), short-bodied animal with three recognizable sections.

It likely lived near a lake in a semi-arid forested environment and ate decomposing plants.

Its fossilized remains were unearthed on the island of Kerrera in the Scottish Inner Hebrides.

The specimen is about 75 million years younger than the age other paleontologists have estimated the oldest millipede to be using a technique known as molecular clock dating.

The oldest fossil of a land-dwelling, stemmed plant, *Cooksonia*, has the same age as *Kampecaris obanensis* and is also from Scotland.

"Although it's certainly possible there are older fossils of both bugs and plants, the fact they haven't been found — even in deposits known for preserving delicate fossils from this era — could indicate that the ancient millipede and plant fossils that have already been discovered are the oldest specimens," said Dr. Michael Brookfield, a researcher in the Department of Geological Sciences at the Jackson School of Geosciences at the University of Texas at Austin and the University of Massachusetts Boston.

If that's the case, it also means both bugs and plants evolved much more rapidly than the timeline indicated by the molecular clock.

Bountiful bug deposits have been dated to just 20 million years later than the fossils.

And by 40 million years later, there's evidence of thriving forest communities filled with spiders, insects and tall trees.

"Who is right, us or them? We're setting up testable hypotheses — and this is where we are at in the research right now," said Dr. Elizabeth Catlos, also from the Department of Geological Sciences at the Jackson School of Geosciences at the University of Texas at Austin.

"It's a big jump from these tiny guys to very complex forest communities, and in the scheme of things, it didn't take that long," Dr. Brookfield said.

"It seems to be a rapid radiation of evolution from these mountain valleys, down to the lowlands, and then worldwide after that."

M.E. Brookfield et al. Myriapod divergence times differ between molecular clock and fossil evidence: U/Pb zircon ages of the earliest fossil millipede-bearing sediments and their significance. Historical Biology, published online May 13, 2020; doi: 10.1080/08912963.2020.1761351

https://bit.ly/30qAai2

New pill could prevent anaphylaxis in people with food, drug allergies

Drug would be the first known treatment to prevent anaphylaxis

CHICAGO --- For someone with a food or drug allergy, the risk of life-threatening anaphylactic shock lurks around every corner.

A new Northwestern Medicine study shows there might be a pill that can be taken proactively to prevent mild to life-threatening anaphylaxis, no matter the cause.

Anaphylaxis is a severe, potentially life-threatening systemic allergic reaction that can occur within seconds or minutes of exposure to an allergen.

It occurs in about one in 50 Americans, though many believe the rate is higher (closer to one in 20), according to the Asthma and Allergy Foundation of America.

If a person's blood pressure drops so low during anaphylaxis or their airway closes up enough that they can't get enough oxygen to their organs, they enter anaphylactic shock.

How do the drugs stop an allergic reaction before it begins?

The drugs used in the study are known as BTK inhibitors. BTK stands for an enzyme called Bruton's tyrosine kinase, which is found inside cells, including mast cells.

The reason BTK inhibitors work to block allergic reactions is that by inhibiting, or blocking, the BTK enzyme, the mast cells cannot be triggered by allergens and allergic antibody to release histamine and other allergic mediators.

The study used three different BTK inhibitors, which blocked allergic reactions when tested on human mast cells in a test tube. Additionally, the study used one U.S. Food and Drug Administration-approved oral drug, which successfully reduced or prevented allergic reactions, including severe, life-threatening

anaphylactic reactions, in a new "humanized" mouse model of anaphylaxis.

The mouse's organs contained transplanted human cells that, over several months, matured into human mast cells, the primary cells that react during allergic reactions.

This would be the first known treatment to prevent anaphylaxis other than avoiding the allergen.

The findings could pave the way for future human clinical trials of such oral drugs to be used as a preventive treatment to avoid serious allergic reactions, said senior and corresponding author Dr. Bruce Bochner, the Samuel M. Feinberg Professor of Medicine at Northwestern University Feinberg School of Medicine.

"This pill could quite literally be life-changing and life-saving," Bochner said. "Imagine being able to take medication proactively to prevent a serious allergic reaction." The study was published June 2 in the *Journal of Clinical Investigation*.

Many potential uses for the pill

"I've heard parents say, 'It would be nice to have my child take something while we're on vacation in case they accidentally eat the wrong food,' and we think these drugs could one day serve that purpose," Bochner said.

Additionally, Bochner said people who are at high risk of allergic exposures to life-saving antibiotics or people about to undergo oral food desensitization (gradually eating foods to build up a threshold to an allergic reaction) could take the pill as a preventive measure. If such drugs turn out to be safe and cheap enough for daily use, theoretically anyone with a serious allergy, including food allergies, could take it and be able to eat the foods they've been strictly avoiding, Bochner said.

For now, Bochner said the drug would likely be used preventatively, not for emergencies, like an EpiPen, which injects epinephrine into someone experiencing an allergic reaction to reverse the symptoms. But he and his team are considering exploring whether this sort of medication could be reformulated to be added to the EpiPen to be injected along with the epinephrine to see if it would better stop or abort anaphylaxis after it has begun.

Previous allergy research using these cancer drugs

In previous research, Dr. Jennifer Regan and Dr. Melanie Dispenza, both former allergy fellowship trainees working with Bochner, found that cancer patients taking the BTK inhibitor ibrutinib who were allergic to airborne allergens such as cat dander and ragweed pollen saw their allergic skin test reactivity reduced by 80 to 90% in one week.

A subsequent study led by Dispenza showed the same thing happened to food allergy skin test reactions when healthy adults with food allergy took the drug for just a few days. Both pilot studies involved small numbers of subjects, but the findings were consistent.

"Inhibition of skin tests is a kind of a surrogate test for whether the drug is actually working," Bochner said. "So, one future goal is to give this medication to food- or drug-allergic subjects, show by skin testing that their allergic sensitivity has been blocked by the drug's effect and then give them the food or drug, expecting they will have little or no reaction."

BTK inhibitors are currently on the market for approximately $500 per day as a successful and less-toxic alternative to chemotherapy for patients with blood cancers like chronic lymphocytic leukemia and mantle cell lymphoma. They are not yet approved for use in children, who are more likely to have food allergies.

Other Northwestern study authors include Rebecca Krier-Burris, Krishan Chhiba and Piper Robida.

Funding for this study was provided by NIH T32 training grant AI083216, and a grant from Acerta Pharma, LLC, the maker of acalabrutinib, one of the BTK inhibitors studied.

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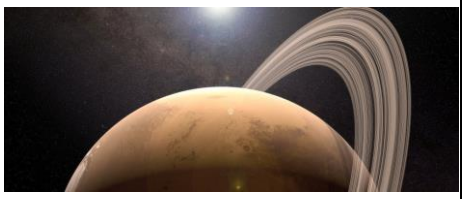
We Just Got Even More Evidence Mars Once Had a Ring

Mars - glorious, dusty, complex Mars - may once have been even more dazzling. New research provides even more evidence that a rubbly ring once circled the Red Planet.

Michelle Starr

The new clue lies in Deimos, the smaller of the two Martian moons. It's orbiting Mars at a slight tilt with respect to the planet's equator - and this could very well be the result of the gravitational shenanigans caused by a planetary ring.



(Kevin Gill/Flickr, CC BY 2.0)

Ring systems aren't actually all that uncommon. When you think about ring systems, your mind immediately leaps to Saturn, no doubt - but half the planets in the Solar System have rings, Saturn, Uranus, Neptune, and Jupiter. Dwarf planet Haumea, and centaurs Chiron and Chariklo also have rings.

In 2017, a pair of researchers theorised that Mars, too, once had a ring. They conducted simulations of the larger of the two Martian moons, Phobos, and found that it could have formed after an asteroid slammed into Mars, sending debris flying into space, forming a ring that then clumped together into an earlier form of Phobos that was much more massive than it is today.

Now this new research has added Deimos into the mix - and the findings are in total agreement with the previous model.

"The fact that Deimos's orbit is not exactly in plane with Mars's equator was considered unimportant, and nobody cared to try to explain it," said astronomer Matija Ćuk of the SETI Institute.

"But once we had a big new idea and we looked at it with new eyes, Deimos's orbital tilt revealed its big secret."

Deimos' orbital tilt isn't huge - just 1.8 degrees off Mars' equator. Aside from that, its orbit is pretty normal - it swings around Mars every 30 hours or so, with extremely low eccentricity - so you can see why no one thought anything screwy was going on.

But there is something screwy going on with Phobos. It's much closer to Mars, on an orbit of 7 hours and 39 minutes, and it's getting closer to Mars by 1.8 centimetres a year.

Within 100 million years, it's expected that Phobos will reach the Roche limit, the distance from Mars at which the planet's tidal forces tear the moon apart.

Much of the debris could form a ring that rains down on Mars; but some of it could re-form into a smaller, newer Phobos that gets pushed outwards as the ring is pulled in.

This, according to the 2017 research, could have happened several times in the past. And this is where Deimos comes in.

Using numerical simulations, Ćuk and his team attempted to model how such an outward-moving proto-Phobos would have affected Deimos' orbital inclination. And they arrived at a proto-Phobos 20 times the moon's current mass, which would have entered a 1:3 orbital resonance with Deimos at a distance of 3.3 Mars radii that pushed the latter's orbit into a slight tilt.

This neatly produced the Deimos orbit we see today, which then remained relatively unchanged for billions of years.

This had to have taken place, Ćuk said, after the Late Heavy Bombardment of asteroids around 3.9 billion years ago, which likely would have destroyed Deimos; afterwards, the moon would have reassembled, but at zero (or close to) inclination. But it also can't have occurred too much after, because the proto-Phobos-Deimos resonance requires low inclination at the start.

"Something like 3.5 billion years ago is our best bet," he told ScienceAlert. "That agrees beautifully with Hesselbrock and

Minton calculation on when Mars had an inner moon with 20 times the mass of Phobos."

That probable destruction of and reformation at low inclination of Deimos also means the asteroid bombardment is unlikely to have caused the disruption to the moon's orbit. And an asteroid that flew by would have disrupted both inclination and eccentricity. Since Deimos' eccentricity is crazy low, that's unlikely too.

As for proto-Phobos, it would have been gravitationally smushed by Mars again.

"Once the ring was gone, the moon also started falling because of Martian tides (just like Phobos)," Ćuk told ScienceAlert.

"Once it was too close to Mars, tidal forces would pull it apart into a new ring, and the cycle would repeat, probably twice, to get to Phobos that we see."

That means current Phobos probably formed around 200 million years ago - and that's something scientists can use to test the theory.

The Japanese space agency, JAXA, is planning to send a probe to Phobos in 2024. This probe will collect surface samples and bring them to Earth.

Those surface samples could then be dated to estimate the age of Phobos' surface. If it's no more than a couple of hundreds of millions of years old, that would validate the team's prediction.

The research has been presented at the 236th Meeting of the American Astronomical Society, and accepted into *The Astrophysical Journal Letters*. It is currently available on arXiv.

https://bit.ly/3eZJsTU

Widely available indigestion drug may curb COVID-19 symptoms in mild to moderate disease

Effects felt within 1-2 days; clinical trial of those who don't require hospital admission warranted

A widely available and inexpensive drug that is used to ease the symptoms of indigestion may prove a worthy contender for treating COVID-19 infection in those whose disease doesn't require admission to hospital, suggest the findings of a small case series, published online in the journal *Gut*.

The effects were felt within 24 to 48 hours of taking famotidine, and a rigorous clinical trial is now warranted to see if the drug could be an effective treatment for COVID-19, say the researchers.

Famotidine (Pepcid AC) belongs to a class of drugs known as histamine-2 receptor antagonists, which reduce the amount of stomach acid produced. Famotidine can be taken in doses of 20-160 mg, up to four times a day, for the treatment of acid reflux and heartburn.

The researchers report on 10 people (6 men; 4 women) who developed COVID-19 infection, all of whom happened to have been taking famotidine during their illness.

The severity of five cardinal symptoms--cough; shortness of breath; fatigue; headache and loss of taste/smell as well as general unwellness--was measured using a version of a 4-point scale normally applied to assess the severity of cancer symptoms (ECOG PS).

Seven of the patients tested positive for COVID-19, using a swab test; two had antibodies to the infection; and one patient wasn't tested but was diagnosed with the infection by a doctor.

Their ages ranged from 23 to 71 and they had a diverse range of ethnic backgrounds and known risk factors for COVID-19 severity, including high blood pressure and obesity.

All started taking famotidine when they were feeling very poorly with COVID-19, the symptoms of which had been going on from 2 up to 26 days at that point.

The most frequently used dose was 80 mg taken three times a day, with the average treatment period lasting 11 days, but ranging from 5 to 21 days. All 10 patients said that symptoms quickly improved

within 24-48 hours of starting famotidine and had mostly cleared up after 14 days.

Improvement was evident across all symptom categories assessed, but respiratory symptoms, such as cough and shortness of breath, improved more rapidly than systemic symptoms, such as fatigue.

Seven of the patients didn't experience any side effects while on famotidine, and in the three who did, these were mild, and all but temporary forgetfulness were known side effects associated with taking the drug.

While promising, the researchers point out that the findings might have been affected by 'the placebo effect,' and/or hazy recall, added to which the number of case study participants was small.

"Our case series suggests, but does not establish, a benefit from famotidine treatment in outpatients with COVID-19," they caution.

And it's not clear how famotidine might work: if it might incapacitate the virus in some way or alter a person's immune response to it.

"Clinically, we unreservedly share the opinion that well designed and informative studies of efficacy are required to evaluate candidate medications for COVID-19 as for other diseases," they emphasise.

Nevertheless, they suggest their findings warrant further more detailed study, adding that a clinical trial, testing the combination of famotidine with the antimalarial drug hydroxychloroquine in patients admitted to hospital with COVID-19, is already under way.

"An outpatient study of oral famotidine that investigates efficacy for symptom control, viral burden and disease outcome and assesses the effects of medication use on long term immunity should be considered to establish if famotidine may be of use in controlling COVID-19 in individual patients while also reducing the risk of SARS-CoV-2 transmission," they conclude.

Peer reviewed? *Yes* ***Evidence type:*** *Case series* ***Subjects:*** *People*

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Scientists discover that nicotine promotes spread of lung cancer to the brain

Why non-small-cell lung cancer so often spreads to the brain has been poorly understood

Winston-Salem, N.C. - Among people who have the most common type of lung cancer, up to 40% develop metastatic brain tumors, with an average survival time of less than six months.

But why non-small-cell lung cancer so often spreads to the brain has been poorly understood.

Now scientists at Wake Forest School of Medicine have found that nicotine, a non-carcinogenic chemical found in tobacco, actually promotes the spread, or metastasis, of lung cancer cells into the brain.

"Based on our findings, we don't think that nicotine replacement products are the safest way for people with lung cancer to stop smoking," said Kounosuke Watabe, Ph.D., professor of cancer biology at Wake Forest School of Medicine and lead author of the study.

In the study, published in the June 4 edition of the *Journal of Experimental Medicine*, Watabe's team first examined 281 lung cancer patients and found that cigarette smokers exhibited a significantly higher incidence of brain cancer.

Then, using a mouse model, the researchers discovered that nicotine enhanced brain metastasis by crossing the blood-brain barrier to change the microglia - a type of immune cell in the brain - from being protective to supporting tumor growth.

Watabe and colleagues then looked for drugs that might reverse the effects of nicotine and identified parthenolide, a naturally occurring substance in the medicinal herb feverfew, which blocked nicotine-induced brain metastasis in the mice.

Because feverfew has been used for years and is considered safe, Watabe believes parthenolide may provide a new approach to fight brain metastasis, particularly for patients who have smoked or still smoke.

"Currently, the only treatment for this devastating illness is radiation therapy," Watabe said. "Traditional chemotherapy drugs can't cross the blood-brain barrier, but parthenolide can, and thus holds promise as a treatment or possibly even a way to prevent brain metastasis."

Watabe said he hopes to work with oncologists at Wake Forest School of Medicine, part of Wake Forest Baptist Health, to develop a clinical trial to test parthenolide in the near future.

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Some types of prostate cancer may not be as aggressive as originally thought

Gleason grade group 5 cancer can actually be subdivided into four subtypes with distinct differences

FINDINGS

Researchers at the UCLA Jonsson Comprehensive Cancer Center analyzed gene-expression patterns in the most aggressive prostate cancer grade group -- known as Gleason grade group 5 -- and found that this grade of cancer can actually be subdivided into four subtypes with distinct differences. The findings may affect how people are treated for the disease.

One subtype, which accounts for about 15% of the grade group 5 cancers, has highly aggressive features and is associated with much worse outcomes than the other subtypes. Another, which makes up about 20% of the tumors, appears to be much less aggressive and may not require intensified and aggressive treatments. Traditionally, all tumors in Gleason grade group 5 have been treated in the same way.

BACKGROUND

Prostate cancer is the leading solid-tumor cancer among men in the United States and a major cause of morbidity globally. While early-stage, localized prostate cancer is curable, current treatments don't always work for everyone. To find out why standard treatment may work for some and not others, the UCLA researchers looked at tumors in the Gleason grade group 5 subset of prostate cancer. These tumors are at the highest risk to fail standard treatment, leading to metastasis and death. The researchers thought that studying the gene expression -- the unique "signature" -- of each cancer cell in these tumors might provide insight into how to make treatments more personalized for each patient.

METHOD

The researchers first analyzed data from more than 2,100 Gleason grade group 5 tumors, looking at how the genetic blueprints differed among the tumors. They identified distinct clusters of subgroups and validated their findings by analyzing an additional cohort of more than 1,900 Gleason grade group 5 prostate cancers.

IMPACT

By using the genetic information from tumors in men with prostate cancer, physicians hope to one day create more personalized treatments based on the actual characteristics of the cancer. This information will help optimize quality of life and avoid overtreating subgroups of men who may not need aggressive treatments.

AUTHORS

The study's lead author is Dr. Amar Kishan, an assistant professor of radiation oncology at the David Geffen School of Medicine at UCLA and a researcher at the UCLA Jonsson Comprehensive Cancer Center. The co-senior authors are Dr. Joanne Weidhaas, a professor of radiation oncology and director of translational research at the Geffen School of Medicine, and Paul Boutros, a professor of urology and human genetics and director of cancer data science for the Jonsson Cancer Center. Boutros is also a member of

the UCLA Institute of Urologic Oncology and the Eli and Edythe Broad Center for Regenerative Medicine and Stem Cell Research at UCLA. Other UCLA authors include David Elashoff, Dr. Rob Reiter and Dr. Matthew Rettig.

JOURNAL

The study was published in the journal *European Urology*.

FUNDING *The research was funded in part by an award from the American Society for Radiation Oncology and the Prostate Cancer Foundation, the Radiological Society of North America, and the National Institutes of Health.*

https://bit.ly/2XHXQdH

How to make plastic bottles from sugarcane and captured CO_2

Running the numbers shows it might even be commercially viable.

Scott K. Johnson

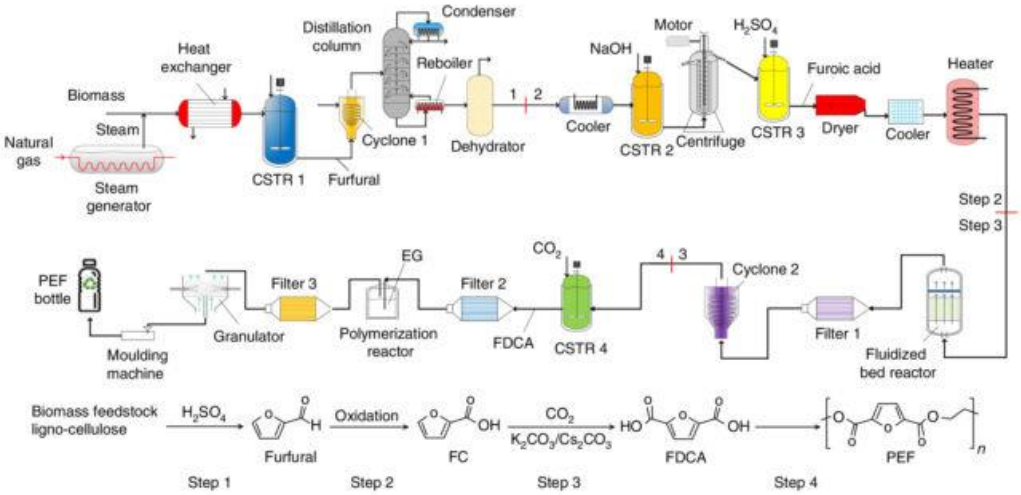
While most plastics have generally been produced from petroleum, that's not an inherent requirement. Chemistry is chemistry, and it's possible to grow many of the hydrocarbons we need. But crops are the things we are best at growing, and plastics made from crops can have problems. They tend to cost more, and unless we're willing to accept impacts on our ability to grow food, pathways to bioplastics have to be pretty clever about their starting materials.

A new study led by Durham University's Long Jiang, Abigail Gonzalez-Diaz, and Janie Ling-Chin lays out a pathway to making plastic bottles from waste organic material and CO_2 captured from power plants. A thorough analysis of the economics shows this process could even be cost competitive for making things like plastic bottles.

The process could start with something like the leftover plant material from sugarcane pressing. After a few reaction steps, which include the addition of some captured CO_2 and some ethylene glycol produced from corn plants, you'd end up with a plastic polymer called polyethylene furandicarboxylate—otherwise known as PEF. Functionally, it's similar to the PET plastic used for water and soda bottles, denoted by the number 1 recycling symbol.

Every step in the process has been at least demonstrated before, and some are quite common, so the paper doesn't spend much space on the chemistry. Instead, the researchers engage in life cycle analysis of the manufacturing process to estimate exactly how this method of making PEF would stack up with the competition.

That includes greenhouse gas emissions. Compared to the manufacturing of PET, their PEF process emits about one-third less greenhouse gas. This assumes that the heat and electricity required for manufacturing is coming from natural gas rather than renewable alternatives. But the process itself includes the consumption of some captured CO_2, offsetting some emissions.



Enlarge */ It's that easy!* **Jiang et al./Nature Sustainability**

Interestingly, other proposed methods for making PEF are actually associated with lower emissions than that. However, those methods rely on using food sugars rather than leftover plant material—something the researchers wanted to avoid.

Sustainability benefits aside, the cost of this process seems to put it at a disadvantage on the surface. The study estimates we could make PEF for about $2,400 per ton, while conventional PET is produced for $1,800 per ton. That would require PEF to fetch a premium on the market to be profitable as a business venture.

But there is one additional thing to consider: it might well be that you could make a PEF bottle with 25-percent less plastic. While PEF and PET have similar enough properties that they fit the same niche, PEF is a little sturdier. "As such, the PEF production cost per bottle could be the same as or lower than that of PET," the researchers write.

So it's at least possible that an approach like this would be commercially viable—especially if some cost savings were found along the way. Then you might see sugarcane-derived bottles holding your fizzy sugar fix.

Nature Sustainability, 2020. DOI: 10.1038/s41893-020-0549-y (About DOIs).

https://bit.ly/3fduKc3

This cow's antibodies could be the newest weapon against COVID-19

Genetically engineered cows are making human antibodies that neutralize SARS-CoV-2.

By Mitch Leslie

The latest recruits in the fight against COVID-19 are munching hay in a South Dakota barn. A biotech company has coaxed genetically modified cows to pump out human antibodies that subdue SARS-CoV-2, the pathogen causing the deadly disease, and it plans to start clinical trials of them this summer.

"This is promising," says Amesh Adalja, an infectious disease physician at the Johns Hopkins University Center for Health Security. "We want to have as many countermeasures as we can."

To manufacture antibodies for treating or preventing diseases, companies typically turn to sources such as cultured cells or tobacco plants. But almost 20 years ago, researchers began to develop the approach now pursued by SAb Biotherapeutics of Sioux Falls, South Dakota, to produce antibodies on the hoof. The company genetically alters dairy cows so that certain immune cells carry the DNA that allows people to make antibodies. That upgrade enables the animals to manufacture large quantities of human antibodies against a pathogen protein injected into them, such as the "spike" surface protein of the new coronavirus.

"Essentially, the cows are used as a giant bioreactor," says viral immunologist William Klimstra of the University of Pittsburgh, who has been analyzing the bovine made antibodies' potency against SARS-CoV-2.

Cows make good antibody factories, and not just because they have more blood than smaller animals engineered to synthesize human versions of the proteins. Their blood can also contain twice as many antibodies per milliliter as human blood, says Eddie Sullivan, SAb Biotherapeutics's president and CEO.

The animals may provide another advantage. Most companies trying to produce antibodies to combat COVID-19 have pinned their hopes on mass-producing identical copies of a single version, a so-called monoclonal antibody that homes in on and attaches tightly to a particular section of a virus. Instead of making just one antibody variety, the cows fashion polyclonal antibodies, a range of the molecules that recognize several parts of the virus. "That's the natural way that our bodies fight disease," Sullivan says. This diversity may make the cow's proteins more powerful than monoclonal antibodies, he says, and they may remain effective even if a virus mutates.

When the COVID-19 pandemic erupted, SAb Biotherapeutics had already completed a clinical trial with cow-generated antibodies against Middle East respiratory syndrome, which is caused by a coronavirus related to SARS-CoV-2. Developing that treatment

"gave us the initial knowledge to focus on the right target," Sullivan says. Within 7 weeks the cows were generating antibodies against SARS-CoV-2's spike.

Before the animals start to release these antibodies into their blood, the cows need a starter immunization—a DNA vaccine based on a portion of the virus' genome that preps their immune system. Then comes the injection that contains a piece of SARS-CoV-2's spike protein, which serves as the virus' passkey to cells. Each month, one cow can yield enough antibodies to treat several hundred patients, Sullivan says.

In test tube studies, Klimstra and colleagues recently pitted the antibodies against so-called convalescent plasma from the blood of COVID-19 survivors. Rich in polyclonal antibodies, the plasma is being tested in clinical trials as a treatment for the virus. The cow antibodies were four times better than convalescent plasma at preventing the virus from entering cells, the company announced last week.

The biotech hopes to begin a clinical trial within the next couple of months, Sullivan says, and wants to test whether infusions of antibodies sifted from the cows' blood prevent healthy people from getting infected by SARS-CoV-2 and prove beneficial for patients who are already sick.

Not everyone thinks the cows are the best choice for making antibodies, however. Infectious disease physician Manish Sagar of Boston University Medical Center says he will remain skeptical "until I see further proof that production of antibodies in cows is a lot more feasible and economically viable" than other methods. So far, no antibodies generated by the animals have been approved for treating any disease.

But infectious disease specialist Jeffrey Henderson of Washington University School of Medicine in St. Louis describes the cow-produced antibodies as "the logical next step" to the convalescent plasma he has been studying. "The whole approach," he says, "is based on sound science and on past experience going back more than a century."

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A newly discovered disease may lead to better treatment of cystic fibrosis

Better understand cystic fibrosis / Study in 'Journal of Medical Genetics'

Cystic fibrosis is the most frequent severe inherited disorder worldwide. Every year, hundreds of families are confronted with this diagnosis - and to date, there is no cure for this disease that mainly affects the respiratory system. Besides supportive treatments, a lung transplant is often the only option to save a patient's live.

Researchers of the Universities of Münster and Regensburg have now discovered a novel disease that might lead to a better understanding of cystic fibrosis and new treatment options in the future. The results have been published in the scientific journal *Journal of Medical Genetics*.

Comparison between the normal TMEM16A protein and the mutated variant showing the truncating effect that leads to the loss of vast portions of the protein. This leads to severe structural alterations. **J. Park et al. 2020/ Journal of Medical Genetics**

The cause of cystic fibrosis are mutations in the cystic fibrosis transmembrane conductor regulator gene (CFTR). This gene contains the blueprint for a chloride channel on the surface of cells in the body. Normally, this channel mediates the accumulation of salt and fluids on the surface of the airways thereby leading to a continuous cleaning of the airways.

Defects in the CFTR channel prevent the transport of chloride ions and thus the humidification of the respiratory tract. As a result, the airways of affected individuals literally get plugged by a thickened,

viscous mucus that leads to airway obstruction - patients are at the risk of suffocating.

At the University of Münster, the lab of Prof. Thorsten Marquardt has now discovered a new disease that is caused by defects in another chloride channel, TMEM16A. This channel is also present on the surface of airway cells. In cooperation with the lab of Prof. Karl Kunzelmann of the University of Regensburg, the researchers evaluated the cellular effects of the disorder that is caused by a total loss of TMEM16A function.

Surprisingly, they discovered that not only TMEM16A but also CFTR is not functional in these patients. Excitingly, this has the potential to improve the treatment of patients suffering from cystic fibrosis.

"We were astonished that children with TMEM16A deficiency don't have any respiratory symptoms at all. A loss of CFTR function due to lack of TMEM16A does not lead to clinincal symptoms of cystic fibrosis in these kids", states Dr. Julien Park, first author and researcher at the Marquardt lab at the Department of General Pediatrics at the University Hospital Münster.

Similarly, the group of Prof. Karl Kunzelmann found in a mouse model that a double knock out of CFTR and TMEM16A does not develop lung disease.

Taken together, these results raise an intriguing question: Could the pharmacological inhibition of TMEM16A improve the respiratory symptoms of patients with cystic fibrosis? A significant reduction of mucus production and secretion as a consequence of TMEM16A inhibition has previously been shown under laboratory conditions. The researchers want to study this approach further in the future: "As a next step, we are planning clinical trials to evaluate a treatment of cystic fibrosis with TMEM16A inhibitors", states Karl Kunzelmann.

https://bit.ly/3eYS258

Approved drug may help calm cytokine storm in COVID-19

Acalabrutinib improved oxygenation levels and decreased molecular markers of inflammation in a majority of 19 patients

The drug acalabrutinib, FDA-approved for the treatment of several types of B cell cancers, improved the oxygenation levels and decreased molecular markers of inflammation in a majority of 19 patients hospitalized for the treatment of severe COVID-19, according to a new study by Mark Roschewski and colleagues.

The drug was administered to 11 patients on supplemental oxygen and 8 patients on mechanical ventilation over a 10-to-14-day course of treatment.

At the end of treatment, 8 of 11 patients on supplemental oxygen were breathing room air, and 4 of 8 patients on ventilation were extubated, with 2 of the 8 breathing room air.

Measurements of two proteins related to inflammation decreased in the majority of patients, with no signs of toxicity from the drug.

The study is not a clinical trial, but rather an off-label observational study to see if acalabrutinib could help dampen the massive immune response - sometimes called a "cytokine storm" - that is associated with the most severe cases of COVID-19.

Acalabrutinib inhibits the Bruton tyrosine kinase (BTK) protein, which aids immune cells called macrophages in activating a variety of other proteins in the body's innate immune response.

Patients with severe COVID-19 have a hyperinflammatory immune response that appears to be driven by macrophage activation, leading to acute respiratory distress syndrome (ARDS) and often death.

Roschewski *et al.* also studied BTK activation and immune markers in whole blood from 4 COVID-19 patients and 5 healthy individuals.

BTK activation levels and the presence of the inflammatory protein IL-6 were higher in the COVID-19 patients, further suggesting that BTK may play a critical role in the disease's progression. An international prospective randomized controlled clinical trial is now underway to confirm the safety and efficacy of this BTK inhibitor as a therapeutic strategy against COVID-19, the authors note.

https://bit.ly/2UnNZHF

Volcanic glass spray shows promise in controlling mosquitoes

Spray made by combining a type of volcanic glass with water showed effective control of mosquitoes that carry malaria

by Mick Kulikowski

An indoor residual spray made by combining a type of volcanic glass with water showed effective control of mosquitoes that carry malaria, according to a new study. The findings could be useful in reducing disease-carrying mosquito populations—and the risk of malaria—in Africa.

Malaria, an infectious disease transmitted by mosquitoes, annually kills some 400,000 people in Africa. The use of insecticide-treated bed nets and indoor residual sprays are the most common and effective methods of reducing mosquito populations in Africa. But mosquitoes are becoming increasingly resistant to the commonly used insecticides such as pyrethroids, so the need for alternative safe chemistry to use in controlling mosquitoes is important.

The volcanic glass material used in this new intervention is perlite, an industrial mineral most frequently used in building materials and in gardens as a soil additive. The tested insecticide created from perlite, called Imergard WP, can be applied to interior walls and ceilings—and perhaps even inside roofs—as an indoor residual spray. The spray contains no additional chemicals, is not toxic to mammals and will be cost effective. Early results show that mosquitoes do not appear to have resistance to the perlite spray.

In the study, North Carolina State University entomologists worked with the Innovative Vector Control Consortium (IVCC) based at the Liverpool School of Tropical Medicine and Imerys Filtration Minerals Inc. to test Imergard WP. Researchers used the spray in experimental huts in the Republic of Benin (West Africa) to test the effects of the spray on both wild and more susceptible strains of Anopheles gambiae mosquitoes, the primary malaria vector in sub-Saharan Africa.

Researchers used four different tests to verify the efficacy of Imergard WP. Control study huts had no mosquito-prevention spray. In the second group hut walls were coated with a common pyrethroid. Hut walls were sprayed with Imergard WP in the third group, while in the fourth group hut walls were sprayed with a mixture of Imergard WP and the common pyrethroid.

The lower portion of a mosquito's leg after contact with a volcanic rock powder. Statically transferred perlite particles dehydrate mosquitoes, killing them. **Credit: Michael Roe, NC State University.**

Huts with walls treated with Imergard WP, with and without the pyrethroid, showed the largest mosquito mortality rates. Results showed mortality rates of mosquitos alighting on Imergard WP-treated walls were greater than 80% up to five months after treatments, and 78% at six months. The treatments were effective against both susceptible and wild-type mosquitoes.

"The statically transferred perlite particles essentially dehydrate the mosquito," said Mike Roe, William Neal Reynolds Distinguished Professor of Entomology at NC State and the corresponding author of the paper. "Many die within a few hours of contact with the treated surface. Mosquitoes are not repelled from a treated surface because there is no olfactory mechanism to smell rock."

Huts sprayed with only the common pesticide had mosquito mortality rates of around 40 to 45% over five months, with those rates dropping to 25% in month six of the study.

"The processing of perlite as an insecticide is novel," said David Stewart, commercial development manager for Imerys, the company that created Imergard WP, and co-author of the paper. "This material is not a silver bullet but a new tool that can be considered as part of an insect vector management program."

More information: *Jean M. Deguenon et al, ImergardTMWP: A Non-Chemical Alternative for an Indoor Residual Spray, Effective against Pyrethroid-Resistant Anopheles gambiae (s.l.) in Africa, Insects (2020).* *DOI: 10.3390/insects11050322*

https://bit.ly/2Ui1KYo

Archaeologists find a way to look for ancient beer

In the process, they discovered the oldest evidence of malted drinks in central Europe.

Kiona N. Smith

Over the last few years, archaeologists have learned a lot from ancient people's dirty dishes. Microscopic residues clinging to the inside of potsherds contain chemical traces of ancient food and drink, which have revealed remarkable details of ancient people's diets.

But as much as we now know about when people started eating certain grains or fermenting milk to make cheese, we're still not sure when people first started brewing beer. It's hard to tell a container used for beer from one that was just storing plain old grain.

But by looking at the remains of ancient grains under a microscope, archaeologists can tell whether the grains had been malted—the first step in the process of brewing beer.

Barley grain used in the production of beer at the Asahi Kanagawa Brewery in Japan. **Tomohiro Ohsumi/Bloomberg/Getty Images**

When grains start to germinate, or sprout, they release an enzyme called diastase, which converts the grain's stockpile of starch into sugar. The whole point of malting is to make the grains release diastase but then stop the process before the starch gets turned into sugar.

Once the brewer adds yeast to the malted grain, then, the diastase can produce more sugar to feed the yeast—and that produces carbon dioxide, alcohol, and a sweet taste. To make this happen, brewers soak grains in water so they start to germinate, then stop the process by air-drying the grains and heating them in an oven.

Austrian Academy of Science bioarchaeologist Andreas Heiss and his colleagues discovered that when barley germinates, the outer layer of the seed's food store gets partially digested. That makes it easy to recognize malted barley under a microscope, because that outer layer looks unusually thin. The same is true of other grains in the grass family, like corn, rye, and wheat.

By looking for that thinned outer wall under a microscope, archaeologists can tell whether ancient grains were malted, "even if the grains concerned are only preserved as pulverized and burnt crusts on pottery," said Heiss.

It's for science—really!

To test the idea, Heiss and his colleagues malted their own barley by charring it then examined the results under a scanning electron microscope. They compared their freshly malted barley with 5,000-year-old ancient samples from Egypt and Central Europe. The results looked very similar.

Both Egyptian sites in the study were known as ancient breweries. Archaeologists sampled charred clumps of wheat from ceramic vats at a predynastic political center called Hierakonpolis in Upper Egypt and at Tell el-Farkha, a sandy island in the eastern Nile Delta. They looked very similar to the charred barley from the archaeologists' lab.

Heiss and his colleagues also studied grain residues left in containers from three lakeshore settlements in Germany and Switzerland, also dating back to around 5,000 years ago.

None of these three sites offered any clear evidence that people brewed beer alongside the lakes, but under Heiss and his colleagues' microscope, the grains had the same thinned outer walls as the barley they'd malted in the lab and the wheat from the ancient Egyptian breweries.

It's the first evidence of malted drinks or food in Neolithic Europe. Heiss called that discovery "a small side effect" of the team's research. "It took us quite a while to realize that, en passant, we had also provided the earliest evidence for malt-based food in central Europe."

Drinking beer by the lake

But it's still not proof of beer. "Malt-based food" can mean a lot of things. Brewing beer is only one reason people might malt grains like barley; throughout history, malted but unfermented grains have also been fed to infants being weaned, taken as tonics, or just eaten as a snack.

In addition, archaeologists don't have a way to recognize the fermentation process itself using ancient grains. Although malting is a very common first step in the brewing process for beer and malted whiskeys, you don't need malted grains in order to make alcohol. That means we may still be missing a lot of ancient booze.

For the Neolithic people who lived on the shores of Lake Constance in Germany and Lake Zurich in Switzerland, however, beer makes sense. The lumps of charred grain recovered from the site came from cooking vessels, which had shapes that don't seem very likely for cooking bread or storing sourdough.

Other studies show that the lake waters around those settlements were teeming with intestinal parasites. "The inhabitants of these settlements definitely had good reason to produce and consume beer," wrote Heiss and his colleagues.

Don't we all.

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https://bbc.in/2MGe0xK

Coronavirus: This is not the last pandemic

Scientists believe another pandemic will happen during our lifetime

By Victoria Gill Science correspondent, BBC News

We have created "a perfect storm" for diseases from wildlife to spill over into humans and spread quickly around the world, scientists warn. Human encroachment on the natural world speeds up that process. This outlook comes from global health experts who study how and where new diseases emerge.

As part of that effort, they have now developed a pattern-recognition system to predict which wildlife diseases pose most risk to humans. This approach is led by scientists at the University of Liverpool, UK, but it is part of a global effort to develop ways to prepare better for future outbreaks.

'We dodged five bullets'

"In the last 20 years, we've had six significant threats - SARS, MERS, Ebola, avian influenza and swine flu," Prof Matthew Baylis from the University of Liverpool told BBC News. "We dodged five bullets but the sixth got us. "And this is not the last pandemic we are going to face, so we need to be looking more closely at wildlife disease."

As part of this close examination, he and his colleagues have designed a predictive pattern-recognition system that can probe a vast database of every known wildlife disease.

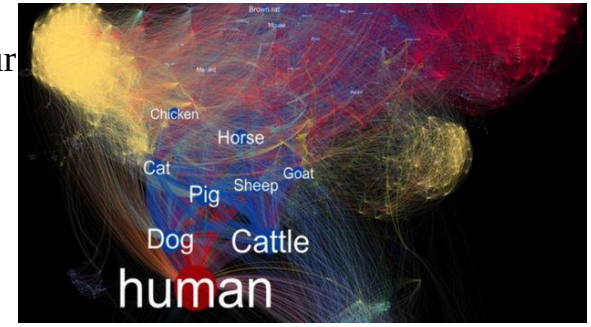
Across the thousands of bacteria, parasites and viruses known to science, this system identifies clues buried in the number and type of species they infect. It uses those clues to highlight which ones

pose most of a threat to humans. If a pathogen is flagged as a priority, scientists say they could direct research efforts into finding preventions or treatments before any outbreak happens.

"It will be another step altogether to find out which diseases could cause a pandemic, but we're making progress with this first step," Prof Baylis said.

Lessons from lockdown

Many scientists agree that our behaviour - particularly deforestation and our encroachment on diverse wildlife habitats - is helping diseases to spread from animals into humans more frequently.



In this data visualisation by Maya Wardeh, each line represents a disease shared between more than one species **Maya Wardeh**

According to Prof Kate Jones from University College London, evidence "broadly suggests that human-transformed ecosystems with lower biodiversity, such as agricultural or plantation landscapes, are often associated with increased human risk of many infections".

"That's not necessarily the case for all diseases," she added. "But the kinds of wildlife species that are most tolerant of human disturbance, such as certain rodent species, often appear to be more effective at hosting and transmitting pathogens. "So biodiversity loss can create landscapes that increase risky human-wildlife contact and increase the chances of certain viruses, bacteria and parasites spilling over into people."

There are certain outbreaks that have demonstrated this risk at the "interfaces" between human activity and wildlife with devastating clarity. In first outbreak of Nipah virus in 1999 in Malaysia, a viral infection - carried by fruit bats - spilled over into a large pig farm built at the edge of a forest. Wild fruit bats fed on the fruit trees and the pigs munched on half-eaten fruit that fell from the trees and was covered in bat saliva.

More than 250 people who worked in close contact with the infected pigs caught the virus. More than 100 of those people died.

The case fatality rate of the coronavirus is still emerging, but current estimates put it at around 1%. Nipah virus kills 40-75% of people it infects.

Prof Eric Fevre from the University of Liverpool and the International Livestock Research Institute in Nairobi, Kenya, says researchers need to be on constant watch in areas where there is a higher risk of disease outbreaks.

Farms on the edge of forests, markets where animals are bought and sold - all are blurred boundaries between humans and wildlife, and places where diseases are more likely to emerge.

"We need to be constantly on the look-out at these interfaces and have systems in place to respond if we see anything unusual", like a sudden disease outbreak in a particular location. "New diseases pop-up in the human population probably three to four times per year," Prof Fevre said. "It's not just in Asia or Africa, but in Europe and the US as well."

Matthew Baylis added that this ongoing surveillance for new disease is increasingly important. "We've created almost a perfect storm here for the emergence of pandemics," he told BBC News.

Prof Fevre agreed. "This kind of event is likely to happen again and again," he said. "It's been happening all throughout our interaction with the natural world. What's important now is how we understand it and respond to it.

The current crisis, Prof Fevre said, provides a lesson for many of us about the consequence of our own impact on the natural world. "All of the things we use and take for granted - the food we eat, the

materials in our smart phones; the more we consume, the more someone will make money by extracting them and moving them around the world. "So it's incumbent on all of us to think about the resources we consume and the impact it has."

https://bit.ly/2Yj23DI

Cluster Headaches Are More Than 'Just a Headache'. But They're Often Misdiagnosed

Cluster headache is more than just a headache. It is a severe neurological condition

Lisa Dikomitis, The Conversation

Cluster headache is more than just a headache. It is a severe neurological condition, sometimes known as a "suicide headache" because many patients have suicidal thoughts during attacks.

The pain experienced during a cluster headache attack is excruciating and is said to be comparable to the pain of childbirth. Such attacks can last from 15 minutes to three hours and can occur several times per day.

The pain is almost always on one side and typical features of an attack may include bloodshot or teary eyes, droopy eyes and a runny nose or blocked nostrils.

Around one in 1,000 people experience cluster headache. It's perceived as a rare disease, but in fact is as common as well-known neurological conditions such as multiple sclerosis or Parkinson's disease. Getting the right treatment for this condition is difficult, as our recent study showed.

We found that many healthcare professionals do not know cluster headache or how to diagnose the condition. This has serious consequences for those suffering. Our research also shows patients regularly face long delays and undergo unnecessary procedures and referrals to specialist care before receiving the correct diagnosis and treatment.

Our team examined the understandings and experiences of cluster headache and the impact of the condition. GPs and neurologists who work in the north of England, were interviewed by a medical sociologist.

We explored their knowledge around the diagnosis and treatment of cluster headache, how they usually refer patients to a specialist, and the ways they communicate with other clinicians.

Our main finding is that cluster headache is neglected among health professionals. Many healthcare professionals do not know what a cluster headache is. This frequently leads to misdiagnosis of the condition and huge delays in receiving the correct diagnosis.

Some clinicians interviewed in the study were not aware of cluster headache, while others thought that cluster headache is the same as "cluster migraine", which can cause nausea and sensitivity to light alongside severe head pain.

Our interviewees gave plenty of examples of the consequences a patient faces when they don't receive a timely and correct diagnosis. Cluster headache is often misdiagnosed as migraine or trigeminal neuralgia (a severe, sudden form of face pain), but also as sinusitis or dental problems.

Patients occasionally undergo unnecessary procedures, such as teeth extraction, sinus washouts and intracranial surgery because they are in despair.

The condition has a huge impact on sufferers' everyday life and they try all kinds of treatments hoping to find some relief from the excruciatingly painful attacks. Indeed, cluster headache can have significant influence on a patient's mental health and on their ability to remain in employment.

People with cluster headache often suffer from severe mental health conditions, such as chronic depression, suicidal thoughts and may self-harm. Family, friends and employers often don't grasp the severity of the condition and the enormous impact it has.

Challenges with treatment

Due to the nature of the attacks, cluster headache is treated differently compared to other headache conditions, like migraine or a tension-type headache. These are normally treated with painkillers – but if these occur frequently they will require regular preventive treatment. Cluster headache attacks are treated with nasal sprays or injectable medication (triptans) and inhalation of oxygen.

Our study also highlights tensions between primary and secondary care around prescribing these treatments because of the cost. Sometimes GPs don't follow the treatment instructions received from neurologists in secondary care. This is especially the case if GPs think the suggested medication is not cost effective.

For example, the injectable triptans were often not prescribed because of their high cost. Some GPs instead prescribed cheaper oral triptans. But these are not effective for cluster headache patients. Many interviewed clinicians were not aware of the prescription policies for oxygen, which is an effect treatment for cluster headache.

GP participants in our study rarely referred patients with cluster headache symptoms to neurologists. When patients get referred, it is more likely to provide the patient with reassurance that their condition is not life-threatening. In some cases, patients with cluster headache get referred to neurologists to begin specialised treatments for cluster headache, such as the drugs verapamil and lithium. Our study shows an urgent need to increase awareness of cluster headache among health professionals and the general public. This will prevent misdiagnosis and delays in diagnosis.

Lisa Dikomitis, Professor in Anthropology and Sociology of Health, Keele University; Alina Buture, PhD researcher, Hull York Medical School, University of Hull, and Fayyaz Ahmed, Professor of Clinical Neurology, University of Hull.