https://go.nature.com/2MRpX7d

Meet the food pioneer whose meat replacements are rocking the gravy boat

Pat Brown explains how he's slicing into the market with plant-based steaks that are eco-friendly and good to eat.

Jack Leeming

The use of animals for mass food production is the most destructive technology on Earth: the number of wild mammals, birds, reptiles, amphibians and fish worldwide is less than one-third of what it was 50 years ago because so much land has been converted to pasture or farmland to feed livestock.

Our only realistic chance of reversing climate change is to replace the animal-farming industry. In 2009, when I was a biochemist at Stanford University in California, I was interested in meat replacements. So I started an 18-month sabbatical to work out how I could make the biggest positive impact on humanity and the planet. In 2011, I founded Impossible Foods, a company based in Redwood City, California, that competes with the meat industry. I am now emeritus at Stanford.

At Impossible, we try to deliver what consumers value in animal products, but in a more sustainable way. Most of that is easy: we can match the nutritional value of any type of meat, for about one-twentieth of the cost, using readily available plant ingredients. The hard part is making our food taste delicious. And that's where haem comes in.

Haem is the part of the haemoglobin molecule that contains iron: it's haem that turns the amino acids, sugars, fats and vitamins in food into an explosion of flavours and aromas.

We make our own haem molecules by using genetically modified yeast to produce soy leghaemoglobin — the form of haemoglobin found in legumes.

In this photo, I'm at our pilot facility in Redwood City, where we optimize the fermentation and purification process for haem. My job is to wander around and talk to the scientists, share ideas and hear what they're doing. I love tasting the prototypes. I've tried plant-based milk, Brie and fish and chips. We have a plant-based steak project.

We're doubling the size of our research and development team this year, and whoever we recruit should feel able to be creative. That requires a fun environment.

Nature ***590****, 176 (2021) doi: https://doi.org/10.1038/d41586-021-00264-z*

http://bit.ly/3oRLycF

NIH study shows hyaluronan is effective in treating chronic lung disease

Naturally produced by the body, hyaluronan represents a new class of biologic that significantly improves lung health in patients with severe COPD.

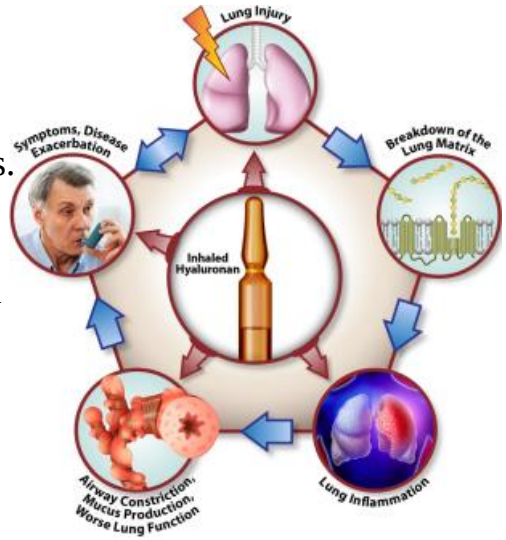
Researchers at the National Institutes of Health and their collaborators found that inhaling unfragmented hyaluronan improves lung function in patients suffering from severe exacerbation of chronic obstructive pulmonary disease (COPD). Hyaluronan, a sugar secreted by living tissue that acts as a scaffold for cells, is also used in cosmetics as a skin moisturizer and as a nasal spray to moisturize lung airways.

Utilized as a treatment, hyaluronan shortened the amount of time COPD patients in intensive care needed breathing support, decreased their number of days in the hospital, and saved money by reducing their hospital stay.

The study, published online in *Respiratory Research*, is a good example of how examining the impacts of environmental pollution on the lungs can lead to viable treatments.

Several years ago, co-senior author Stavros Garantziotis, M.D.,

medical director of the Clinical Research Unit at the National Institute of Environmental Health Sciences (NIEHS), part of NIH, showed that exposure to pollution causes hyaluronan in the lungs to break down into smaller fragments. These fragments irritate lung tissue and activate the immune system, leading to constriction and inflammation of the airways. He determined that inhalation of healthy, unfragmented hyaluronan reduces inflammation by outcompeting the smaller hyaluronan fragments.



The research shows that inhaling hyaluronan interferes at almost every step of the COPD cycle, making it a potent treatment for chronic lung disease.
Credit: Stavros Garantziotis, M.D.

Garantziotis offered an analogy for how the inflammation occurs. He said hyaluronan surrounds cells like mortar surrounds bricks. Introducing pollution causes cracks in the mortar, breaking it into smaller chunks.

"These smaller chunks irritate the body and activate the immune system, leading to inflammation," Garantziotis said. "Reintroducing the full-length hyaluronan, like a fresh coat of mortar, means it is less irritating and reduces the amount of inflammation."

Since hyaluronan was approved in Italy for airway moisturization, Garantziotis worked with colleagues in Rome to see if inhalation of full-size hyaluronan could improve lung function in critically ill COPD patients.

He explained that the patients were using a breathing apparatus similar to a continuous positive airway pressure (CPAP) machine to treat their acute exacerbation of COPD. This apparatus provided breathing support by blowing air into the airways through a mask.

"Inhaled hyaluronan qualifies as a stimulating aid for patients with exacerbated COPD, as it is safe and easy to administer," said co-senior author Raffaele Incalzi, M.D., Department of Medicine, Campus Bio-Medico University and Teaching Hospital, Rome. "Furthermore, it acts locally, only in the bronchial tree, and, thus, cannot interfere with any systemic drug."

Garantziotis also wanted to know what was producing airway constriction in the lungs of COPD patients. He theorized that thick mucus may be involved.

Collaborating with scientists at the University of Alabama at Birmingham (UAB), they grew airway cells from emphysema patients in culture and looked at how mucus moved in the cells. They saw that mucus flowed more easily after administering hyaluronan.

Co-author Steven Rowe, M.D., director of the Gregory Fleming James Cystic Fibrosis Research Center at UAB, said if patients with severe COPD took hyaluronan, the treatment would improve mucus transport and aid their recovery.

Current treatments for lung disease include inhaled steroids, antibiotics, and bronchodilators, so using a molecule that is already found in the body is a new concept.

The goal now for Garantziotis is to study this treatment in more patients in the U.S., so he can understand the optimal conditions and dosing that will produce the most benefit.

Grant Numbers: Z01ES102605 Z01ES102465 R35HL135816 P30DK072482
Reference: Galdi F, Pedone C, McGee CA, George M, Rice AB, Hussain SS, Vijaykumar K, Boitet ER, Tearney GJ, McGrath JA, Brown AR, Rowe SM, Incalzi RA, Garantziotis S. 2021. Inhaled high molecular weight hyaluronan ameliorates respiratory failure in acute COPD exacerbation: a pilot study. Respir Res: doi: 10.1186/s12931-020-01610-x [Online 1 February 2021].

http://bit.ly/39O7nWq

Closer look shows Neanderthals on La Cotte de St Brelade interbred with modern humans

Evidence of interbreeding between Neanderthals and modern humans on Jersey island

by Bob Yirka , Phys.org

A team of researchers affiliated with multiple institutions in the U.K. and one in Germany has found evidence of interbreeding between Neanderthals and modern humans on Jersey island. In their paper published in *Journal of Human Evolution*, the group describes their study of teeth found at La Cotte de St Brelade, a cave on the southwest side of the island, back in 1911.

Jersey island is located off the northwest coast of France—prior research has shown that Neanderthals had been living in the cave as far back as 250,000 years ago. Prior research has also shown Neanderthals first came to exist in parts of Europe and Siberia approximately 400,000 years ago. Modern humans are thought to have traveled to Europe approximately 40,000 years ago—5,000 years later, the Neanderthals were gone.

In this new effort, the researchers focused their effort on two teeth found on a small granite ledge in the cave in 1910 or 1911. At the time of their discovery, it was assumed the teeth, like so many others in the cave, were Neanderthal.

In taking a new look at the teeth using computed tomography, the researchers found evidence of human-like differences from Neanderthals. The neck of the teeth were shaped like those of modern humans, but they also lacked the transverse crest of Neanderthal teeth. This suggested that the teeth came from the offspring of both a Neanderthal and a modern human. It also suggests that the teeth may represent some of the most recent remains ever found of a Neanderthal.

The researchers also found that the two teeth belonged to two individuals—prior researchers had assumed they came from the same individual. The teeth were also dated to 48,000 years ago.

The researchers suggest that interbreeding between modern humans and Neanderthals was more common than thought. The study also hints at the possibility that Neanderthals never went extinct at all, but were instead subsumed into the human genome.

Prior research has suggested that the genome of modern non-African people is approximately 2% to 3% Neanderthal. The study is also the first to show interbreeding between modern humans and Neanderthals in such a western part of Europe.

More information: *Tim Compton et al. The morphology of the Late Pleistocene hominin remains from the site of La Cotte de St Brelade, Jersey (Channel Islands), Journal of Human Evolution (2021). DOI: 10.1016/j.jhevol.2020.102939*

http://bit.ly/3ayNxxx

Mummy with a gold tongue found in Egypt

Could they speak to the gods?

By Owen Jarus - Live Science Contributor

This 2,000-year-old mummy was buried with a golden tongue, likely to help the deceased speak in the afterlife. **© Egyptian antiquities ministry**

Archaeologists have found a 2,000-year-old mummy with a gold tongue at an ancient Egyptian site called Taposiris Magna. Embalmers perhaps placed the golden tongue on the mummy to ensure that the deceased would be able to speak in the afterlife, the Egyptian antiquities ministry said in a statement released Jan 29.

For instance, if the golden-tongued mummy encountered Osiris, the god of the underworld, in the afterlife, they would have needed to be able to speak to the god, the statement said. It isn't clear if the mummy had a speech impediment when they were alive. It's also not clear why the tongue was made out of gold specifically.

The archaeologists, led by Kathleen Martinez, from the Dominican

Republic, discovered the mummy in one of 16 burials at Taposiris Magna, which has temples dedicated to Osiris and Isis, a goddess who was both the wife and sister of Osiris. Previously, archaeologists found a hoard of coins decorated with the face of Cleopatra VII, suggesting the temples were in use during the queen's reign.

More mummies

The other 15 burials also date back around 2,000 years and contain remarkable treasure. In one, a female mummy is wearing a death mask that covers much of her body and depicts her with a headdress while smiling.

Two of the mummies were found with the remains of scrolls, which scholars are currently analyzing and deciphering. The plastered layers, or cartonnage, encasing one of these mummies has golden decorations of Osiris, the statement said.

The researchers also found several statues that depict the people who were buried at the site; the statues are so well preserved, you can still make out the individual's hairstyles and headdresses, the statement said. The statues give the people a formal look, with no smiles on their faces.

Though the archaeologists aren't sure exactly when the individuals died, they can tell that the people lived at a time when Egypt was ruled either by the Ptolemies (304 B.C. to 30 B.C.), who were the descendants of one of Alexander the Great's generals, or by the Roman Empire, which took over the country after the death of Cleopatra VII in 30 B.C.

A team made of archaeologists from Egypt and the University of Santo Domingo in the Dominican Republic are conducting these excavations at Taposiris Magna. It is led by Kathleen Martinez, an archaeologist from the Dominican Republic. Excavation of the site and analysis of the remains is ongoing.

http://bit.ly/3rkjBMh

Nasal spray that protects against COVID-19 is also effective against the common cold

Researchers were able to use cells from human donors and re-grow the structure of the airway surface, the epithelium, to recreate the first line of defense against respiratory viruses.

Research into a new drug which primes the immune system in the respiratory tract and is in development for COVID-19 shows it is also effective against rhinovirus. Rhinovirus is the most common respiratory virus, the main cause of the common cold and is responsible for exacerbations of chronic respiratory diseases such as asthma and chronic obstructive pulmonary disease. In a study recently published in the *European Respiratory Journal* (LINK), the drug, known as INNA-X, is shown to be effective in a pre-clinical infection model and in human airway cells.

Treatment with INNA-X prior to infection with rhinovirus significantly reduced viral load and inhibited harmful inflammation. University of Newcastle and Hunter Medical Research Institute (HMRI) researcher Associate Professor Nathan Bartlett, who led the study, said INNA-X showed great promise as a new way to protect people from diseases caused by common respiratory viruses such as rhinovirus. These diseases range from the common cold to potentially life-threatening exacerbations of chronic respiratory diseases, which cost the global economy billions of dollars each year.

"Consistent with what we have reported for other respiratory viruses including SARS-CoV-2 (the virus that causes COVID-19), INNA-X treatment prior to infection reduced the level of virus in the respiratory tract," Associate Professor Bartlett said.

"We have also examined the effect of INNA-X in airway cells from patients with asthma which we know have a less effective anti-viral immune response and found that INNA-X treatment was effective

providing a rationale for the use of INNA-X in at risk populations."

INNA-X is developed by the Australian biotech company Ena Respiratory and works by stimulating the innate immune system in the airways, the first line of defense against the invasion of respiratory viruses into the body. This immune priming makes it much more difficult for viruses such as rhinoviruses to take hold, cause serious symptoms and spread.

INNA-X has been also shown to be highly effective at reducing virus shedding of SARS-CoV-2 and human trials of Ena Respiratory's clinical candidate INNA-051 will begin in Australia in the coming weeks.

"If found protective, this could be used by at risk populations including elderly or asthma patients, to reduce the severity of rhinovirus, COVID-19 and other respiratory viruses' infections in conjunction with vaccine approaches," Associate Professor Bartlett said.

** HMRI is a partnership between the University of Newcastle, Hunter New England Health, and the community.*

http://wb.md/3cKf1mw

Newer iPhones Disable Implanted Defibrillators

Newer models of smartphones equipped with magnets, such as the iPhone 12, can disable their device, inhibiting its lifesaving functions

Ted Bosworth

Patients with an implantable cardioverter defibrillator (ICD) should be warned that some newer models of smartphones equipped with magnets, such as the iPhone 12, can disable their device, inhibiting its lifesaving functions, according to investigators who tested and confirmed this effect.

"Once the iPhone was brought close to the ICD over the left chest area, immediate suspension of ICD therapies was noted which persisted for the duration of the test," reported the investigating team led by Joshua C. Greenberg, MD, who is an electrophysiology fellow at Henry Ford Hospital, Detroit. The results were published in Heart Rhythm.

The American Heart Association has already cautioned that magnetic fields can inhibit the pulse generators for ICDs and pacemakers. On the AHA website, there is a list of devices and their potential for functional interference, but cell phones and other common devices are identified as posing a low risk.

The most recent iPhone and perhaps other advanced smartphones appear to be different. According to the authors of a study that tested the iPhone 12, this model has a circular array of magnets around a central charging coil. This array interacts with Apple's proprietary MagSafe technology, which accelerates charging. The magnets also serve to orient the phone on the charger and enable other MagSafe accessories.

The authors of the new study were concerned that this array of magnets might be sufficiently strong to interfere with ICDs or other devices at risk. In a previously published study, the strength of a magnetic field sufficient to interfere with implantable cardiac devices was estimated to be at least 10 gauss.

Tests were performed on a patient wearing a Medtronic ICD.

"Once the iPhone was brought close to the ICD over the left chest area, immediate suspension of ICD therapies was noted," according to the authors of the study. The functional loss of the ICS persisted for the duration of proximity. It was reproduced multiple times and with multiple phone positions.

Previous studies have provided evidence that earlier models do not share this risk. In a study testing the iPhone 6 and an Apple Watch in 148 patients with various types of implantable electronic devices, including pacemakers, cardioverter defibrillators, resynchronization defibrillators, and resynchronization pacemakers, only one instance of interference was observed in 1,352 tests.

With wand telemetry, iPhone-induced interferences could be detected with the iPhone 6 in 14% of the patients, but these did not appear to be clinically meaningful, and this type of interference could not be detected with the Apple Watch, according to the report. The single observed interaction, which was between an iPhone 6 and a dual-chamber pacemaker, suggested device–device interactions are uncommon.

More recently, a woman with a single-chamber Medtronic ICD who went to sleep wearing an Apple Watch was awoken by warning beeps from her cardiac device, according to a case report published online. The Apple watch became the prime suspect in causing the ICD warning when proximity of the watch reproduced the warning during clinical examination. However, the magnetic interference was ultimately found to be emanating from the wristband, not the watch.

This case prompted additional studies with Fitbit and other Apple Watch wristbands. Both wristbands contain magnets used to track heart rate. Both were found capable of deactivating ICDs at distances of approximately 2 cm.

On the basis of these results, the authors concluded that patients should be counseled about the risk posed by wristbands used in fitness tracking, concluding that they should be kept at least 6 inches away from ICDs and not worn while sleeping.

On their website, Apple maintains a page that specifically warns about the potential for interactions between iPhone 12s and medical devices.

Although there is an acknowledgment that the iPhone 12 contains more magnets than prior iPhone models, it is stated that iPhone 12 models are "not expected to pose a greater risk of magnetic interference to medical devices than prior iPhone models." Nevertheless, the Apple instructions advise keeping the iPhone and MagSafe accessories more than 6 inches away from medical devices.

Greenberg and coinvestigators concluded that the iPhone 12 does pose a greater risk to the dysfunction of ICDs and other medical devices because of the more powerful magnets. As a result, the study brings forward "an important public health issue concerning the newer generation iPhone 12."

Well aware of this issue and this study, Bruce L. Wilkoff, MD, director of cardiac pacing and tachyarrhythmia devices, Cleveland Clinic, agreed. He said the focus should not be restricted to the iPhone 12 series but other wearable devices as alluded to in the study.

"Pacemakers and implantable defibrillators are designed to respond to magnets for important reasons, but magnets have many common uses," he said. These can change the function of the implantable cardiac devise, but "it is temporary and only when placed in close proximity."

The solution is simple. "Patients should be careful to avoid locating these objects near these devices," Wilkoff said.

However, the first step is awareness. According to the study authors, devices with magnets powerful enough to impair function of implantable devices, such as the iPhone 12 "can potentially inhibit lifesaving therapy."

Patients should be counseled and provided with practical steps, according to the authors. This includes keeping these devices out of pockets near implantable devices.

They called for more noise from makers of smartphones and other devices with strong enough magnets to alter pacemaker and ICD function, and they advised physicians to draw awareness to this issue.

Greenberg reported no potential conflicts of interest.

This article originally appeared on MDEdge.com.

http://bit.ly/36Nf79n

This Flower Is Really a Fungus in Disguise

In Guyanese savannas, a fungus infects grasslike plants, sterilizes them and produces bizarre all-fungal "flower" doppelgängers

By Priyanka Runwal

On a collection trip to Guyana in 2006, botanist Kenneth Wurdack was strolling along an airstrip at Kaieteur National Park when he noticed something unusual about the flowers on two species of yellow-eyed grasses.

Unlike the species' typical blooms, they were a more orange shade of yellow, tightly clustered and spongy in texture. "I just sort of filed it away as an incidental thing," Wurdack says.

Two orange-yellow "blooms" at right are fungal mimics of flowers produced by yellow-eyed grasses, such as the one at left. **Credit: K. Wurdack Smithsonian Institution**

On subsequent trips, he observed more examples of the strange phenomenon. Digging through relevant botanical literature, Wurdack learned what was actually going on: The orange oddities were not really flowers at all. And the yellow-eyed grasses—which belong to a genus called *Xyris*—had not made them.

Instead they were mimics—the product of a fungus that Wurdack, who works at the Smithsonian National Museum of Natural History, and his colleagues recently described. The fungus, *Fusarium xyrophilum*, infects an *Xyris* plant and sterilizes it to block the plant's own blooms. Then *F. xyrophilum* hijacks an as yet unknown aspect of the plant's operations to host pseudoflowers made entirely of fungal tissue—potentially tricking pollinators to disperse its spores rather than pollen from the plant's flowers. The finding is thought to be a first of its kind on record.

Fascinated by this likely case of floral mimicry, scientists are now left wondering how this fungus evolved to deceive—and to do it so well. "This is the only example that we know of, anywhere on planet Earth, where the false flower is all fungal," says Kerry O'Donnell, a microbiologist at the U.S. Department of Agriculture's Agricultural Research Service and a co-author of the recent study about the pseudoflowers, which was published in *Fungal Genetics and Biology*.

A handful of other fungal imposters only go partway, typically modifying a host's leaves rather than building their own mock flower. For instance, some rust fungi belonging to the order Pucciniales induce hosts to produce rosettes of leaves (in place of their own flowers) on which the fungus erupts, resembling nearby yellow-colored flowers.

Another fungal species called *Monilinia vaccinii-corymbosi*, which infects the leaves of blueberry bushes, does not form flowerlike structures. But the blighted leaves reflect UV light, emit a fermented tea odor similar to that of blueberry flowers and provide nectar, all of which could attract insects.

So the authors of the new paper wondered if there were more to *F. xyrophilum*'s elaborate mimicry in yellow-eyed grasses, given that many insects navigate by smell and are able to perceive ultraviolet light.

The study's lead author Imane Laraba, also a microbiologist at the Agricultural Research Service, used an ultraviolet filter to photograph F. xyrophilum pseudoflowers that Wurdack collected in 2010 and 2012. As speculated, the fungus's tissues reflected UV light, a property of many yellow-hued flowers that could help pollinators locate them. In the wild, Laraba says, *Xyris* flowers likely also reflect UV light.

Two pigments isolated from the pseudoflowers—and also confirmed in lab-grown *F. xyrophilum*—could be responsible for this UV reflectivity and fluoresce at ranges especially visible to

bees, the researchers say. In the lab, they also documented the species emitting up to 10 chemical compounds, many of them known to attract insect visitors.

Did this fragrant chemical cocktail recorded in the lab match the scents of the wild *Xyris* flowers that *F. xyrophilum* mimics? Because of the COVID-19 pandemic, Laraba's team could not travel to South America to study live Guyanese *Xyris* flowers and *F. xyrophilum* pseudoflowers. So they looked at a proxy species that grows in the southern U.S.'s savanna habitats: *Xyris laxifolia* var. *iridifolia*, a perennial that looks similar to the Guyanese plants. Comparisons of the chemical cocktails produced by the uninfected *X. laxifolia* flowers and *F. xyrophilum* cultures revealed that both emit 2-ethylhexanol, a compound that attracts pollinators and others insects, such as honeybees, bumblebees, whiteflies and cowpea weevils.

Still, floral scents can vary between species of the same genus. And aromas are better understood as a blended profile than individual compounds. "I think it's a case of mimicry that still needs more documentation," says Jonathan Gershenzon, a biochemist at the Max Planck Institute for Chemical Ecology in Jena, Germany, who was not involved in the new study. "But when you look at the shape, the color [of the pseudoflowers], it's hard not to be incredibly impressed with what nature has done."

Terry Torres-Cruz, a plant pathology graduate student at Pennsylvania State University, who was also not involved in the recent work, plans to separately explore the *Fusarium* fraud. Once the pandemic wanes, she intends to travel to Guyana's tropical savannas to trap the fragrances produced by both *Xyris* and *F. xyrophilum* flowers and to track their insect guests.

By studying how the whole system functions in the field, her work could solve the mystery of these fungal doppelgängers.

http://bit.ly/39NoI1M

White dwarf atmospheres might contain the pulverized crusts of their dead planets

Astronomers have developed a new technique to search for exoplanets—by looking for their crushed up bones in the atmospheres of white dwarfs. And it's working.

by Paul M. Sutter, Universe Today

The search for planets outside the solar system, known as exoplanets, has one significant limitation: We can only find exoplanets that exist right now. But our universe has been hanging around for over 13 billion years, and many generations of planetary systems have come and gone in that vast expanse of cosmic time.

Unfortunately, when stars die, they usually take their planets with them. Especially the most massive stars, which die as supernovae—those deaths usually obliterate any orbiting planet completely. But even when less massive stars like the sun die, it's generally bad news for their planets.

But as a new research paper has pointed out, that doesn't remove all evidence of the planetary system off the galactic map. If any planets (or remnant cores of planets) survive, they can occasionally gravitationally scatter off of each other. This doesn't usually happen in stable systems, but in the death throes of a star anything is possible (gravitationally speaking).

Some of those scattered objects can head inward to the white dwarf, the leftover core of the parent star. That white dwarf is made of almost completely pure carbon and oxygen, surrounded by a dense but thin shell of hydrogen and helium. Naturally, any object passing too close will get torn to shreds by the extreme gravity of the white dwarf, with the debris making its way to the surface to mix and mingle with the hydrogen and helium.

Once there, any elements in the destroyed object, like lithium and calcium, can release their own light, giving a spectral fingerprint

that astronomers can potentially spot. Most white dwarfs are too hot, though, and that light outshines any contamination. But the recent Gaia mission was able to map dozens of old, cool white dwarfs, and astronomers have detected the distinct signature of crushed up planets in their atmospheres.

The astronomers found that the abundance of enriched elements matches what we know from our own solar system, indicating that planetary systems like ours have been in the universe for a very, very long time.

More information: *Mark A. Hollands, et al. Alkali metals in white dwarf atmospheres as tracers of ancient planetary crusts. arXiv:2101.01225v1 [astro-ph.EP]*
arxiv.org/abs/2101.01225

http://bit.ly/2YNChrI

A new way to make wood transparent, stronger and lighter than glass

An idea that scientists have been working on for some time

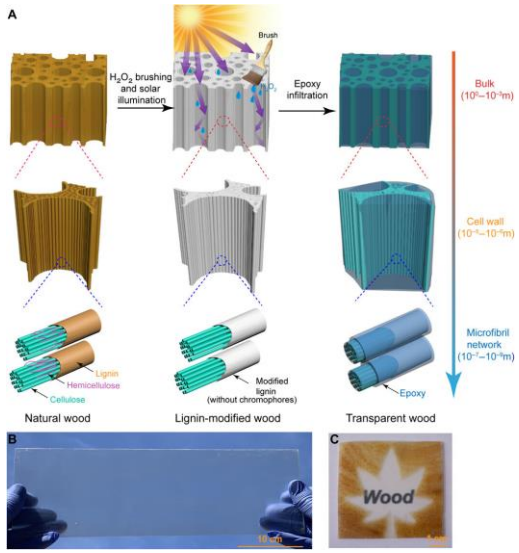
by Bob Yirka , Phys.org

A team of researchers at the University of Maryland, has found a new way to make wood transparent. In their paper published in the journal *Science Advances*, the group describes their process and why they believe it is better than the old process.

Transparent wood is an idea that scientists have been working on for some time. Home builders see it as a new option for houses because wood is stronger than glass—it would not shatter if struck by an errant baseball, for example. But despite much effort, transparent wood has not made it into commercial use—mostly because of the way it is made.

The conventional method for making wood transparent involves using chemicals to remove the lignin—a process that takes a long time, produces a lot of liquid waste and results in weaker wood. In this new effort, the researchers have found a way to make wood transparent without having to remove the lignin.

The process involved changing the lignin rather than removing it. The researchers removed lignin molecules that are involved in producing wood color. First, they applied hydrogen peroxide to the wood surface and then exposed the treated wood to UV light (or natural sunlight). The wood was then soaked in ethanol to further clean it. Next, they filled in the pores with clear epoxy to make the wood smooth.



Schematic illustration of fabricating transparent wood and demonstration of its patterning. (A) Schematic illustration of this simple yet effective, eco-friendly, scalable, and low-cost method of fabricating transparent wood. Lignin not only endows natural wood with a brownish color but also serves as a binder for cellulose and hemicellulose. After chemical brushing and solar illumination, the lignin chromophore and hemicellulose are removed and the natural wood becomes colorless, but the modified lignin remains and can still effectively bind and wrap around the cellulose microfibrils to maintain the material's mechanical properties. Then, epoxy can be easily infiltrated into the loosely packed lignin-modified wood microchannels to prepare the final transparent wood. (B) A digital image of a large-scale sheet of transparent wood (400 mm by 110 mm by 1 mm) along the longitudinal direction (i.e., the fiber direction). (C) A digital image of the transparent wood along the transverse direction (i.e., perpendicular to the fiber direction) patterned with a "tree leaf" shape. **Photo credit: Qinqin Xia, University of Maryland, College Park. Credit: Science Advances (2021). DOI: 10.1126/sciadv.abd7342**

The wood that resulted was found to be 50 times stronger than transparent wood made the conventional way—it also allowed 90% of light to pass through. The researchers also found it to be both stronger and lighter than glass—and it provided better insulation.

The researchers suggest that it could be used for both windows and roofs. They note that the wood could in theory be used to create an entirely see-through house because it can also be used as a load-bearing material.

The researchers claim wood made using their process is clean and could be easily scaled for use in large buildings. They suggest also that it could be used in other applications, such as touch-sensitive displays for use in harsh environments or inside of cars.

More information: *Qinqin Xia et al. Solar-assisted fabrication of large-scale, patternable transparent wood, Science Advances (2021). DOI: 10.1126/sciadv.abd7342*

http://wb.md/3cG63Xz

COVID-19 Virus May Prompt Body to Attack Itself

An international team of researchers studying COVID-19 has made a startling and pivotal discovery: The virus appears to cause the body to make weapons to attack its own tissues.

Brenda Goodman

The finding could unlock a number of COVID's clinical mysteries. They include the puzzling collection of symptoms that can come with the infection; the persistence of symptoms in some people for months after they clear the virus, a phenomenon dubbed long COVID; and why some children and adults have a serious inflammatory syndrome, called MIS-C or MIS-A, after their infections.

"It suggests that the virus might be directly causing autoimmunity, which would be fascinating," says lead study author Paul Utz, MD, who studies immunology and autoimmunity at Stanford University in Stanford, CA.

The study also opens the question of whether other viruses might also break the body's tolerance to itself, setting people up for autoimmune diseases like multiple sclerosis, rheumatoid arthritis, and lupus later in life.

Utz says he and his team are next going to study flu patients to see if that virus might also cause this phenomenon. "My prediction is that it isn't going to be specific just to SARS-CoV-2. I'm willing to bet that we will find this with other respiratory viruses," he says.

The study comes on the heels of a handful of smaller, detailed investigations that have come to similar conclusions. The study included data from more than 300 patients from four hospitals: two in California, one in Pennsylvania, and another in Germany.

Researchers used blood tests to study their immune responses as their infections progressed. Researchers looked for autoantibodies -- weapons of the immune system that go rogue and launch an attack against the body's own tissues. They compared these autoantibodies to those found in people who were not infected with the virus that causes COVID.

As previous studies have found, autoantibodies were more common after COVID -- 50% of people hospitalized for their infections had autoantibodies, compared to less than 15% of those who were healthy and uninfected.

Some people with autoantibodies had little change in them as their infections progressed. That suggests the autoantibodies were there to begin with, allowing the infection to burn out of control in the body. "Their body is set up to get bad COVID, and it's probably caused by the autoantibodies," Utz says.

But in others, about 20% of people who had them, the autoantibodies became more common as the infection progressed, suggesting they were directly related to the viral infection, instead of being a preexisting condition.

Some of these were antibodies that attack key components of the immune system's weapons against the virus, like interferon. Interferons are proteins that interfere with a virus's ability to copy itself. Taking them out is a powerful evasive tactic, and previous studies have shown that people who are born with genes that cause them to have lower interferon function, or who make autoantibodies

against these proteins, appear to be at higher risk for life-threatening COVID infections. "It seems to give the virus a powerful advantage," says study author, John Wherry, PhD, who directs the Institute for Immunology at the University of Pennsylvania.

"Now your immune system, instead of having a tiny little hill to climb, is staring at Mount Everest. That really is devious." "I'm not aware of another viral infection where that happens," he says.

In addition to those that counterpunch the immune system, some people in the study had autoantibodies against muscles and connective tissues that are seen in some rare disorders

Utz says they started the study after seeing COVID patients with strange collections of symptoms that looked more like autoimmune diseases than viral infections -- skin rashes, joint pain, fatigue, aching muscles, brain swelling, dry eyes, blood that clots easily, and inflamed blood vessels.

"One thing that's very important to note is that we don't know if these patients are going to go on to develop autoimmune disease," Utz says. "I think we'll be able to answer that question in the next 6 to 12 months as we follow the long haulers and study their samples."

Utz says it will be important to study autoantibodies in long haulers to see if they can identify exactly which ones seem to be at work in the condition. If you can catch them early, it might be possible to treat those at risk for enduring symptoms with drugs that suppress the immune system.

What this means, he says, is that COVID will be with us for a long, long time. "We have to realize that there's going to be long-term damage from this virus for the survivors. Not just the long haulers, but all the people who have lung damage and heart damage and everything else. We're going to be studying this virus and it's badness for decades," Utz says.

Sources *BioRxiv, Jan. 29, 2021.*

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https://go.nature.com/3jjnz5j

The Arctic Ocean might have been filled with freshwater during ice ages

A geochemical study of sediments suggests that, during recent glacial periods, the Arctic Ocean was completely isolated from the world ocean, with fresh water filling the basin for thousands of years.

Sharon Hoffmann

The Arctic region is undergoing rapid climatic and environmental change[1], so knowledge of its past variability is crucial for understanding modern trends and predicting future ones. Ancient climate conditions and ocean behaviour are often reconstructed by analysing marine sediments. But Arctic sediments can be difficult to interpret, and much is still unknown about how the Arctic Ocean changed during specific glacial and interglacial periods over the past few million years[2,3]. Writing in *Nature*, Geibert *et al.*[4] report analyses of an isotope of the element thorium in sea-floor sediments, which suggest that the Arctic Ocean swung between being filled with salt water and fresh water during periods of the two most recent glacials.

The authors base their argument on records of thorium-230, produced from the decay of dissolved uranium that is naturally present in seawater. Thorium is highly insoluble and sticks to solid particles such as dust grains or biological material, which sink to the sea floor and become buried in sediments[5]. Thorium that derives from the water column in this way is known as excess thorium-230 ($^{230}Th_{ex}$). It is typically present in sediments deposited during the past 450,000 years and is often measured to determine sediment-

deposition rates[5,6]. Geibert and colleagues' innovation is instead to use these measurements to reconstruct how much $^{230}Th_{ex}$ was produced in the Arctic Ocean over time, and thereby to determine how the salinity has changed.

The authors examined sediment cores from across the Arctic and Nordic seas, and found that $^{230}Th_{ex}$ is absent in several layers of sediment deposited during the past 200,000 years. The cores suggest that no ^{230}Th was produced in the water above the study sites between about 150,000 and 131,000 years ago (during the next-to-last glacial), 70,000 and 62,000 years ago (during early parts of the last glacial) and perhaps even as recently as about 15,000 years ago (at the end of the last glacial).

Thorium-230 produced in seawater is removed so rapidly by sinking particles that its net horizontal transport across the ocean is typically low[5], even in the particle-poor Arctic. The intervals of absent $^{230}Th_{ex}$ in the sediment cores therefore imply that the uranium concentration was low to non-existent in the water above the study sites when those sediments were deposited. This, in turn, implies that the entire water column was essentially fresh down to the sea floor — there were no dissolved salts of any type.

Thick ice shelves covered regions of the Arctic during previous glacials[7]. Geibert *et al.* posit that such ice shelves could have extended into the Nordic seas, possibly grounding on the Greenland–Scotland Ridge — the tall underwater feature that separates the Nordic seas from the rest of the Atlantic basin (Fig. 1). The ice shelves might, in effect, have dammed the Arctic and Nordic seas, isolating them from salty inflows from the Atlantic. The low sea levels at that time blocked the exchange of water with the Pacific Ocean through the Bering Strait. Fresh water from melting land ice and precipitation could therefore have entered and eventually filled the isolated northern basins.

An advantage of Geibert and co-workers' $^{230}Th_{ex}$ method is that, unlike many other techniques used in palaeoceanography, no biologically produced material is needed for the analysis. It can therefore be used to probe environments that would have had low to no biological productivity, such as a freshwater Arctic Ocean beneath ice shelves. Indeed, microfossils in the $^{230}Th_{ex}$-free sediment layers are absent or extremely rare, or are derived from older deposits rather than being contemporaneous with the $^{230}Th_{ex}$ minima.

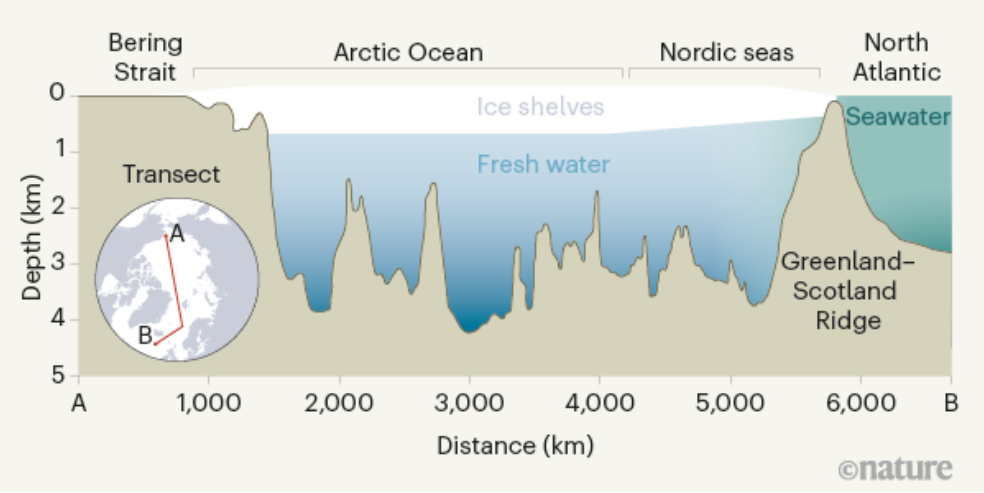

Figure 1 | Isolation of a freshwater Arctic Ocean during glacial periods. ***By analysing marine sediments, Geibert et al.[4] infer that the Arctic Ocean was filled with fresh water during periods of the two most recent glacials. They propose that thick ice shelves covering the region extended into the Nordic seas, and grounded on the undersea Greenland–Scotland Ridge, as shown in this transect. This would effectively have dammed the Arctic Ocean and Nordic seas, isolating them from salty inflows from the Atlantic Ocean. The low sea levels at that time would also have blocked exchange of water with the Pacific Ocean through the Bering Strait. Fresh water from melting land ice and precipitation could therefore have entered and eventually filled the isolated basins beneath the ice shelves.*** **(Adapted from Extended Data Fig. 5 of ref. 4.)**

This new interpretation of $^{230}Th_{ex}$ might also provide an intriguing means of reconciling contrasting results previously obtained from

different methods of estimating past sea levels. The relative abundances of oxygen isotopes in global seawater are recorded in microfossils, and, in part, reflect the sequestration of evaporated ocean water into ice sheets or other freshwater reservoirs, which can affect sea level. For certain times during recent ice ages, sea-level records obtained from isotopic analyses of microfossils are inconsistent with records derived from corals[8]. Geibert *et al.* suggest that these inconsistencies could be explained by the proposed storage of large volumes of fresh water in the Arctic Ocean.

Various complications in the analysis will no doubt raise questions. Arctic sediments are notoriously hard to date owing to the lack of microfossils, and because sedimentation rates varied[2,3]. It is therefore uncertain whether the $^{230}Th_{ex}$-deficient intervals in the cores were produced at exactly the same times at all sites across the ocean basins. Moreover, the authors had to correct their data to account for ^{230}Th that was produced from uranium decay in sediment grains, rather than in the water column[5], and this contributed to the uncertainty in measured $^{230}Th_{ex}$. These corrections become proportionally more important for older sediments because $^{230}Th_{ex}$ itself decays away; thorium decay also limits the time span over which the method can be used to investigate Arctic salinity. Finally, no freshwater fauna have been identified in the sediments concerned, so direct evidence of freshwater intrusion into deep Arctic basins remains to be found.

However, the various absences — of $^{230}Th_{ex}$, of microfossils and biological productivity, and of elements such as sulfur, which partly derive from salinity in marine sediments[9] — suggest exciting avenues for future research. Computational modelling of Arctic Ocean circulation and ice-sheet behaviour will be needed to determine realistic estimates of the circulation and freshwater run-off from land that could produce a basin filled with fresh water. Further geochemical and fossil analyses might help to support or challenge the assertion that the Arctic Ocean could have been fresh. Geibert and colleagues' innovative use of ^{230}Th might spur a re-evaluation of what is possible in the Arctic Ocean, and of how dramatically this region can change.

Nature ***590***, *37-38 (2021) doi: https://doi.org/10.1038/d41586-021-00208-7* ***References***

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https://bit.ly/2YM50No

How enlisting dentists can speed up Covid-19 vaccinations

OPINION: Dental care providers have the skills, the facilities and the trust of patients who might otherwise miss out

By Mary E. Northridge

Even as the Biden administration has upped its Covid-19 vaccine goal to 1.5 million per day, early reports say vaccination rates are lagging in hard-hit Black and Latino communities. On both fronts, America's dentists can help.

Dental professionals — dentists, dental hygienists and dental assistants — have been responding to the pandemic from the outset, even as many practices were shut down by the emergency. At the health center where I work in Brooklyn, dental providers first donated their personal protective equipment (PPE) to the affiliated

hospital. Then many of them were redeployed to perform arterial blood gas measurements and even transport deceased patients to makeshift morgues.

Today, the urgent need is to get millions of shots in arms. States should immediately authorize dental providers to administer Covid-19 vaccines. That would not only expand the trained immunization workforce, it would open up additional sites to dispense the vaccine and bolster vaccine acceptance among patients who do not routinely go to the doctor.

This is not without precedent. In 2019, Oregon became the first state to allow dentists to offer any vaccine to patients. Other states, including Illinois and Minnesota, allow dentists to administer influenza vaccines. Since late 2020, Arkansas, Massachusetts and California have permitted dentists to administer Covid-19 vaccines.

During this devastating public health emergency, this idea needs to be extended to all states.

There are more than 110,000 dentists – excluding specialists — and over 200,000 hygienists in the United States, and they already have the skills needed. Dentists routinely administer intra- and extra-oral injections to provide anesthesia, so any additional training would be minimal. In California, for instance, dentists will do four hours of online training before joining the vaccination effort.

California currently plans to utilize dentists just as extra manpower at vaccine clinics. But dental offices, too, will be valuable in vaccinating hard-to-reach populations.

Dental offices and clinics are a safe location. Despite early concerns that they might be particularly vulnerable to aerosol-borne transmission of the novel coronavirus, evidence is mounting that transmission at dental sites is rare. As in medical settings, precautions such as using PPE and increasing ventilation are effective. Nearly all dental practices and clinics have reopened to provide care. And that has been essential during the pandemic: Treating damaged teeth, tooth decay, gum disease and oral sores before they become acute prevents patients from going to emergency departments because of dental pain.

Interrupting community spread, however, is the chief imperative to prevent Covid-19 cases from overwhelming hospitals today. And that means adding vaccines to dental services.

Inoculating patients who are already in chairs for dental visits could improve vaccine acceptance. At the health center where I work, a simple workflow change for preventive tooth sealant placement nearly doubled the number of eligible children treated, from 37 percent to nearly 78 percent. Rather than schedule a separate appointment, sealants were applied during the kids' initial or recall visits. Fewer visits meant greater acceptance of the treatment and higher rates of completion. The same could be true for vaccines.

Community dental clinics also serve hard-to-reach patients — minorities, immigrants, impoverished people — those who may be hesitant to seek out the vaccine because of historical injustices, fear of deportation or lack of health insurance. But dental providers have often earned trust through longstanding service in these communities. Ongoing quality improvement studies at our health center, for instance, document no racial/ethnic bias in treatment by dental providers. When patients are treated with respect regardless of their ability to pay for services, they may be more willing to accept a vaccine that will protect them, their families and their communities.

Many states have suspended regulations and expanded the scope of dental practices to combat the pandemic. To help ensure health equity and successfully immunize the whole US population, all states ought to enlist dental providers to administer Covid-19 vaccines as well.

This article is part of "Reset: The Science of Crisis & Recovery," an ongoing Knowable Magazine *series exploring how the world is navigating the coronavirus pandemic, its consequences and the way forward. "Reset" is supported by a grant from the Alfred P.*

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http://bit.ly/3aCsD0F

MESSENGER saw a meteoroid strike Mercury

MESSENGER may have seen an impact take place back in 2013

by Nancy Atkinson, Universe Today

Telescopes have captured meteoroids hitting the Moon and several spacecraft imaged Comet Shoemaker–Levy 9 smacking into Jupiter in 1994. But impacts as they happen on another rocky world have never been observed.

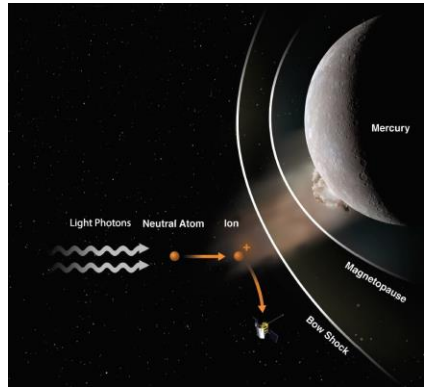
However, the MESSENGER (MErcury Surface, Space ENvironment, GEochemistry and Ranging) mission may have seen an impact take place back in 2013. In looking at archival data from the mission, scientists found evidence of a meteoroid impact on Mercury. While this data isn't a 'no-doubt' photo of the event, it does tell scientists more about impacts and how they affect Mercury's wispy-thin atmosphere.

"It's just incredible that MESSENGER could watch this happen," said Jamie Jasinski, a space physicist at the Jet Propulsion Laboratory, and the lead author on the study, published in *Nature Commmunications*. "This data plays a really important role in helping us understand how meteoroid impacts contribute material to Mercury's exosphere."

Mercury's tiny atmosphere, called an exosphere, has a pressure that's one-quadrillionth of that felt at sea level on Earth. The exosphere forms on Mercury's Sun-facing side from material originally on the planet's surface. Scientists think meteoroid impacts, in part, are responsible for putting such material into the exosphere.

The archival data revealed a strange anomaly: on December 21, 2013, MESSENGER's Fast Imaging Plasma Spectrometer (FIPS) saw an unusually large number of sodium and silicon ions blowing in the Sun's solar wind, the powerful charged gases that spew from the Sun. Oddly, these particles were traveling in a tight beam, nearly all in the same direction, and at the same speed.

Using the particles' speed and direction, the researchers "rewound the clock, tracking the particles' motion back to their source." They found the particles clustered in a dense plume, one that had erupted from Mercury's surface and extended nearly 3,300 miles into space.



Artist's illustration depicting how MESSENGER observed the first meteoroid impact on another planet's surface. Particles (neutral atoms) ejected by the meteoroid skyrocketed over 3,000 miles above Mercury's surface, outside the bow shock of Mercury's magnetosphere. There, photons of light turned the neutral particles into charged particles (ions), which one of MESSENGER's instruments could detect. **Credit: Jacek Zmarz**

They estimate the meteoroid was likely just a little over three feet long, which is relatively small. But computer models suggest something that size would create a plume with a height and density closely matching what FIPS detected.

Interestingly enough, before the MESSENGER mission, scientists expected the spacecraft would capture some impacts on Mercury—perhaps up to two impacts per year during its four years in orbit. But none were seen in images during the mission, which lasted from 2011 to 2015. But in sifting through the old spectrometer data, the anomaly stood out.

"It just shows how rare it is to have the spacecraft at the right place and time to be able to measure something like this," said study co-author Leonardo Regoli, from Johns Hopkins Applied Physics Laboratory in Maryland—where MESSENGER was built and operated. "This was a special observation, and really cool to see the story come together."

Perhaps the European Space Agency's BepiColombo mission, which launched for Mercury in 2018 and will approach the planet in late 2025, will be able to capture more meteoroid impacts during its mission. Regoli noted that researchers will need to hone their models before using BepiColombo to make new observations, but the opportunity to see another Mercurian impact would be invaluable, he said.

More information: *Jamie M. Jasinski et al. A transient enhancement of Mercury's exosphere at extremely high altitudes inferred from pickup ions, Nature Communications (2020).* *DOI: 10.1038/s41467-020-18220-2*

http://bit.ly/3cM6yPL

A mysterious disease is killing chimps in West Africa. Scientists may now know the culprit

"Sometimes they'd go to bed healthy and be dead in the morning."

By Ann Gibbons

Disease ecologist Tony Goldberg was stunned in 2016 when he learned that a mysterious infection was swiftly killing chimpanzees at a lush sanctuary in Sierra Leone's rainforest. "It was not subtle—the chimpanzees would stagger and stumble, vomit, and have diarrhea," recalls Goldberg of the University of Wisconsin, Madison. "Sometimes they'd go to bed healthy and be dead in the morning."

Even when veterinarians gave ill chimps antibiotics and fluids, wrapped them in warm blankets, and isolated them in smaller enclosures to try to prevent the spread of infection, they died. At least 53 perished at the Tacugama Chimpanzee Sanctuary between 2005 and 2018.

The refuge is home to nearly 100 chimps rescued from illegal trade, hunting, or abandonment as pets. "It was really upsetting for the staff because there was no end in sight," says biologist Gregg Tully, executive director of the Pan African Sanctuary Alliance.

He sought Goldberg's help to identify the disease, which is 100% fatal.

Now, after studying tissue samples and DNA from chimpanzees at the sanctuary, Goldberg and his colleagues have identified the likely culprit.

In *Nature Communications* today, they report that a new species of clover-shaped bacterium infected tissue samples from 13 chimps that died, but not samples from 14 healthy chimps.

The mysterious gastrointestinal and neurological disease has not infected veterinarians or other humans. Its closest relative is *Sarcina ventriculi*, however, a rare cause of gastrointestinal disease that does infect people, as well as cattle, cats, and horses. Although researchers worry about any new disease that might jump between apes and humans, their biggest concern is that it will spread to chimpanzees in other sanctuaries and the wild.

"Wildlife in sanctuaries are always the most vulnerable to pathogens that are transmissible by air," says veterinary epidemiologist Sharon Deem of the St. Louis Zoo, not part of the team.

The big break came in 2018, when Goldberg's graduate student Leah Owens spotted a strange-looking bacterium in the brain tissue of one of the deceased chimpanzees.

"Late at night, I was looking through the microscope and I saw this really weird-looking cubic structure," she recalls. The team had spent several years screening tissues, feces, and blood samples from the sanctuary chimps for pathogens, finding no smoking gun. Owens realized the bacteria on her slide looked like the clover-shaped *Sarcina*—a finding confirmed by pathologists.

The researchers then sequenced the genome from the bacteria in the sample, finding it most closely matched that of *S. ventriculi*. Yet it was distinct enough to classify it as a new species, which they propose to call *Sarcina troglodytae*, after the species of chimpanzee

it infects—*Pan troglodytes*.

Further studies of the DNA from the new species of bacterium show it has genes that make it more virulent than *S. ventriculi*. The team also wonders whether cases in other animal species that were classified as *S. ventriculi* might belong to this new species—or other unidentified types of *Sarcina*.

Owens is applying for grants to try to identify the source of the bacterium by testing samples of water, air, food, and vegetation she and Goldberg gathered at the sanctuary in 2019.

One possibility is that the bacterium is ubiquitous, but something in the environment at the sanctuary or in the apes' physiology is triggering disease. Most cases occur every March during the hot, dry season, when the animals are provisioned with more food.

Veterinarians at the Tacugama sanctuary are already using the new findings: They're treating a sick chimp with antacids, anticonvulsive, and antibiotics—similar to the treatment in humans—in hopes of saving its life. In the meantime, other researchers hope to test chimpanzees in other sanctuaries for the infection, as well.

http://bit.ly/2MX5UnM

Fecal transplant turns cancer immunotherapy non-responders into responders

Changing gut microbiome can transform patients with advanced melanoma who never responded to immunotherapy into patients who do

Pittsburgh - Researchers at UPMC Hillman Cancer Center and the National Cancer Institute (NCI) demonstrate that changing the gut microbiome can transform patients with advanced melanoma who never responded to immunotherapy--which has a failure rate of 40% for this type of cancer--into patients who do.

The results of this proof-of-principle phase II clinical trial were published online today in Science. In this study, a team of researchers from UPMC Hillman administered fecal microbiota transplants (FMT) and anti-PD-1 immunotherapy to melanoma patients who had failed all available therapies, including anti-PD-1, and then tracked clinical and immunological outcomes. Collaborators at NCI analyzed microbiome samples from these patients to understand why FMT seems to boost their response to immunotherapy.

"FMT is just a means to an end," said study co-lead author Diwakar Davar, M.D., a medical oncologist and member of the Cancer Immunology and Immunotherapy Program (CIIP) at UPMC Hillman and assistant professor of medicine at the University of Pittsburgh School of Medicine.

"We know the composition of the intestinal microbiome--gut bacteria--can change the likelihood of responding to immunotherapy. But what are 'good' bacteria? There are about 100 trillion gut bacteria, and 200 times more bacterial genes in an individual's microbiome than in all of their cells put together."

Fecal transplant offers a way to capture a wide array of candidate microbes, testing trillions at once, to see whether having the "good" bacteria on board could make more people sensitive to PD-1 inhibitors.

This study is among the first to test that idea in humans.

Davar and colleagues collected fecal samples from patients who responded extraordinarily well to anti-PD-1 immunotherapy and tested for infectious pathogens before giving the samples, through colonoscopy, to advanced melanoma patients who had never previously responded to immunotherapy. The patients were then given the anti-PD-1 drug pembrolizumab. And it worked.

Out of 15 advanced melanoma patients who received the combined FMT and anti-PD-1 treatment, six showed either tumor reduction or disease stabilization lasting more than a year.

"The likelihood that the patients treated in this trial would

spontaneously respond to a second administration of anti-PD-1 immunotherapy is very low," said study co-senior author Hassane Zarour, M.D., a cancer immunologist and co-leader of the CIIP at UPMC Hillman as well as a professor of medicine at Pitt. "So, any positive response should be attributable to the administration of fecal transplant."

Analysis of samples taken from FMT recipients in this study revealed immunologic changes in the blood and at tumor sites suggesting increased immune cell activation in responders as well as increased immunosuppression in non-responders. Artificial intelligence linked these changes to the gut microbiome, likely caused by FMT.

Davar and Zarour hope to run a larger trial with melanoma patients, as well as evaluating whether FMT may be effective in treating other cancers. Ultimately, their goal is to replace FMT with pills containing a cocktail of the most beneficial microbes for boosting immunotherapy--but that's still several years away.

"Even if much work remains to be done, our study raises hope for microbiome-based therapies of cancers," said Zarour, who holds the James W. and Frances G. McGlothlin Chair in Melanoma Immunotherapy Research at UPMC Hillman.

Additional authors on the study include Amiran Dzutsev, M.D., John McCulloch, Ph.D., Richard Rodriguez, M.B.A., Jonathan Badger, Ph.D., Marie Vetizou, Ph.D., Alicia Cole, Miriam Fernandes, Ph.D., Stephanie Prescott, M.S.N., C.R.N.P., Rachel Costa, M.S., Ascharya Balaji and Giorgio Trinchieri, M.D., of the National Cancer Institute; Joe-Marc Chauvin, Ph.D., Robert Morrison, M.D., Richelle Deblasio, Carmine Menna, Quanquan Ding, Ph.D., Ornella Pagliano, Bochra Zidi, Ph.D., Shuowen Zhang, Hong Wang, Ph.D., Scarlett Ernst, Amy Rose, Yana Najjar, M.D., and John Kirkwood, M.D., of UPMC Hillman Cancer Center; Andrey Morgun, M.D., Ph.D., of Oregon State University; Ivan Vujkovic-Cvijin, Ph.D., and Yasmine Belkaid, Ph.D., of the National Institute of Allergy and Infectious Diseases; and Amir Borhani, M.D., Marc Schwartz, M.D., and Howard Dubner, M.D., of Pitt.

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Open Insulin Can Actually Be Stored at Warm Temperatures For Weeks, Scientists Find

Opened insulin can be stored for four weeks in warm conditions without losing efficacy, a study showed Wednesday, giving hope to diabetics in hot countries without access to refrigerators.

The research by the medical charity Doctors Without Borders (MSF) and the University of Geneva showed that a vial of insulin could be stored for four weeks after opening at temperatures fluctuating between 25 and 37 degrees Celsius (77 and 98.6 degrees Fahrenheit).

The study was published in the *PLOS One* medical journal.

"The current pharmaceutical protocol requires insulin vials to be stored between 2 Celsius and 8 Celsius until opened, after which most human insulin can be stored at 25 C for four weeks," said Philippa Boulle, a non-communicable diseases advisor at MSF.

"This is obviously an issue in refugee camps in temperatures hotter than this, where families don't have refrigerators."

In some poorer regions of the world with temperatures well above 25 Celsius, diabetics without home refrigerators have to go to hospital for their injections, sometimes several times a day.

For people living with diabetes, access to treatment, including insulin, is critical to their survival.

Diabetes is a chronic, metabolic disease characterised by elevated blood sugar levels, which leads over time to serious damage to the heart, blood vessels, eyes, kidneys, and nerves. The most common is type-2 diabetes, usually in adults, which occurs when the body becomes resistant to insulin or doesn't make enough insulin.

Type-1 diabetes is a chronic condition in which the pancreas produces little or no insulin by itself.

Potency matches cold storage

MSF recorded temperatures in the Dagahaley refugee camp in

northern Kenya fluctuating between 25 Celsius at night and 37 Celsius during the day.

Those changes were reproduced in a laboratory over four weeks – the time it usually takes a diabetic to finish one vial of insulin.

The findings showed that "the stability of insulin stored under these conditions is the same as that of cold-stored insulin, with no impact on efficacy", they said in a joint news release.

"This allows people with diabetes to manage their illness without having to visit a hospital multiple times daily." The research found that the insulin preparations recorded a potency loss of no more than 1 percent – the same as in a control batch kept in cold storage.

"These results can serve as a basis for changing diabetes management practices in low-resource settings, since patients won't have to go to hospital every day for their insulin injections," said Boulle. She said she hoped the findings would be endorsed by the World Health Organization.

The WHO says that about 422 million people worldwide have diabetes, the majority living in low-and middle-income countries, and 1.6 million deaths are directly attributed to diabetes each year.

The prevalence of diabetes has been steadily increasing in recent decades.

http://bit.ly/3ayabGc

How elephants evolved to become big and cancer-resistant

A study shows that elephants possess a large toolbox of genes for evading cancer, and suggests that evolution of tumor suppression capabilities contributed to the development of big bodies

BUFFALO, N.Y. -- All things being equal, large, long-lived animals should have the highest risk of cancer.

The calculation is simple: Tumors grow when genetic mutations cause individual cells to reproduce too quickly. A long life creates more opportunities for those cancerous mutations to arise. So, too, does a massive body: Big creatures -- which have many more cells -- should develop tumors more frequently.

Why, then, does cancer rarely afflict elephants, with their long lifespans and gargantuan bodies? They are some of the world's largest land animals.

A new study delves into this sizeable mystery, showing that elephants possess extra copies of a wide variety of genes associated with tumor suppression.

But this phenomenon is not unique to elephants, scientists say: The research concluded that duplication of tumor suppressor genes is quite common among elephants' living and extinct relatives, including in small ones like Cape golden moles (a burrowing animal) and elephant shrews (a long-nosed insectivore). The data suggest that tumor suppression capabilities preceded or coincided with the evolution of exceptionally big bodies, facilitating this development.

The study was published on Jan. 29 in the journal *eLife* by biologists Vincent Lynch at the University at Buffalo and Juan Manuel Vazquez at the University of California, Berkeley.

"One of the expectations is that as you get a really big body, your burden of cancer should increase because things with big bodies have more cells," says Lynch, PhD, assistant professor in the Department of Biological Sciences in the UB College of Arts and Sciences. "The fact that this isn't true across species -- a long-standing paradox in evolutionary medicine and cancer biology -- indicates that evolution found a way to reduce cancer risk."

In the new study, "We explored how elephants and their living and extinct relatives evolved to be cancer-resistant," Lynch says. "We have past research looking at TP53, a well-known tumor suppressor. This time, we said, 'Let's just look at whether the entire elephant genome includes more copies of tumor suppressors than what you'd expect.' Is the trend general? Or is the trend specific to one gene?

We found that it was general: Elephants have lots and lots and lots of extra copies of tumor suppressor genes, and they all contribute probably a little bit to cancer resistance." Elephants do have enhanced cancer protections, compared with relatives

Though many elephant relatives harbor extra copies of tumor suppressor genes, the scientists found that elephant genomes possess some unique duplications that may contribute to tumor suppression through genes involved in DNA repair; resistance to oxidative stress; and cellular growth, aging and death.

"By determining how big, long-lived species evolved better ways to suppress cancer, we can learn something new about how evolution works and hopefully find ways to use that knowledge to inspire new cancer treatments," says Vazquez, PhD, a postdoctoral researcher at UC Berkeley who completed much of the project while earning his PhD at the University of Chicago.

A related mystery: How did giant sloths and ancient mega-armadillos get so big?

Elephants are a great case study for understanding the evolution of cancer protection because they belong to a group of mammals -- the Afrotherians -- that are mostly small-bodied.

The study searched for extra copies of tumor suppressor genes in the DNA of Asian, African savanna and African forest elephants, as well as in the genomes of a number of fellow Afrotherians, such as Cape golden moles, elephant shrews, rock hyraxes, manatees, extinct woolly mammoths, extinct mastodons and more. The team also studied certain species belonging to a group of mammals called Xenarthra that is closely related to Afrotherians, and found some extra copies of tumor suppressors in those animals' genomes as well.

Given the findings, Lynch wonders whether the duplication of tumor suppressors may have aided the evolution of other ancient large bodies within these groups.

"If you pick a weird mammal, there's a good chance that it will be in these groups, the Afrotherians and Xenarthrans: armadillos, aardvarks, sloths, anteaters, all of these weird mammals," Lynch says. "We found that within these groups of organisms, the ones we studied all seem to have extra copies of tumor suppressor genes. That may be why in the last Ice Age, there were giant sloths and ancient mega-armadillos. There's even an extinct species of manatee relative called the Steller's sea cow that was elephant-big. Extra copies of tumor suppressors may have helped all of these animals get really, really big."

http://bit.ly/39WyVc4

Spicy perfection isn't to prevent infection

This is the chef's kiss of scientific discovery

The next time you tuck in to a tikka masala you might find yourself asking a burning question: are spices used in dishes to help stop infection?

It's a question many have chewed the fat over. And now thanks to new research from The Australian National University (ANU) we have an answer. The quick takeaway is: probably not.

Professor Lindell Bromham and her colleagues asked why hot countries across the world tend to have spicy food? This pattern has led to what some have termed "Darwinian gastronomy" - a tummy-led cultural evolutionary process in countries with hotter climates.

To find out the answer to their question, the researchers feasted on a true smorgasbord of data, examining more the 33,000 recipes from 70 cuisines containing 93 different spices.

"The theory is that spicy foods helped people survive in hot climates where the risk of infection from food can have a big cost in terms of health and survival," Professor Bromham said.

"But we found that this theory doesn't hold up.

"Spicier food is found in hotter countries, but our analysis provides no clear reason to believe that this is primarily a cultural adaptation to reducing infection risk from food."

The study instead shows that while use of spice is related to the risk of foodborne illness, it's also associated with a wide range of health outcomes. In fact, spice use is even related to causes of death that have nothing to do with infection risk, such as fatal car accidents.

"So there is a significant relationship between life expectancy and spicy food," Professor Bromham said.

"But this doesn't mean that spicy food shortens your life span or makes you crash your car. Instead, there are many socioeconomic indicators that all scale together, and many of them also scale with spice use."

Professor Bromham said that because the spiciness of cuisines scales with many socio-economic factors, like gross domestic product per capita and life expectancy, it is difficult to tease apart the key causes. However, the researchers could rule out some possible explanations of why some areas use more spices in their cooking. "Spicier foods are not explained by variation in climate, human population density or cultural diversity," she said.

"And patterns of spice use don't seem to be driven by biodiversity, nor by the number of different crops grown, nor even by the number of spices growing naturally in the area."

Whatever the key drivers for the use of spice, one thing is certain - our palettes and plates are a lot better for it!

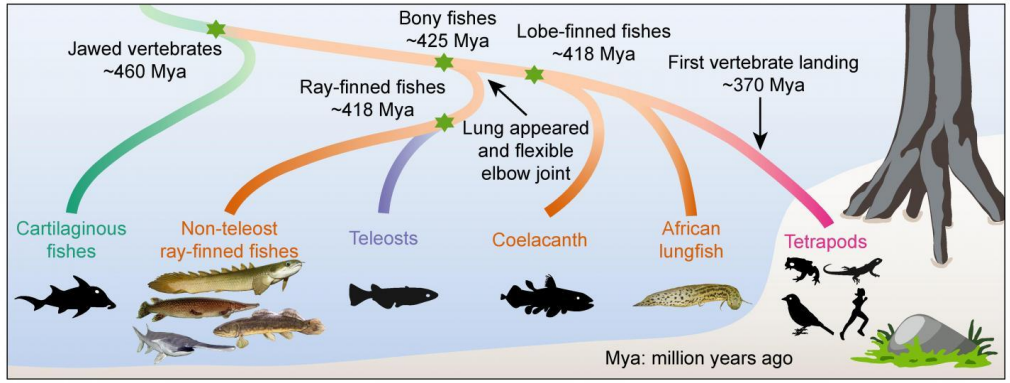
The study's findings are published in *Nature Human Behaviour*.

http://bit.ly/3aJyYY0

Surprising new research: We're more like primitive fishes than once believed

People traditionally think that lungs and limbs are key innovations that came with the vertebrate transition from water to land.

But in fact, the genetic basis of air-breathing and limb movement was already established in our fish ancestor 50 million years earlier. This, according to a recent genome mapping of primitive fish conducted by the University of Copenhagen, among others. The new study changes our understanding of a key milestone in our own evolutionary history.



Vertebrate evolution timeline **Credit: Dr. Guojie Zhang**

There is nothing new about humans and all other vertebrates having evolved from fish. The conventional understanding has been that certain fish shimmied landwards roughly 370 million years ago as primitive, lizard-like animals known as tetrapods. According to this understanding, our fish ancestors came out from water to land by converting their fins to limbs and breathing under water to air-breathing.

However, limbs and lungs are not innovations that appeared as recent as once believed. Our common fish ancestor that lived 50 million years before the tetrapod first came ashore already carried the genetic codes for limb-like forms and air breathing needed for landing. These genetic codes are still present in humans and a group of primitive fishes.

This has been demonstrated by recent genomic research conducted by University of Copenhagen and their partners. The new research reports that the evolution of these ancestral genetic codes might have contributed to the vertebrate water-to-land transition, which changes the traditional view of the sequence and timeline of this big evolutionary jump. The study has been published in the scientific

journal *Cell*.

"The water-to-land transition is a major milestone in our evolutionary history. The key to understanding how this transition happened is to reveal when and how the lungs and limbs evolved. We are now able to demonstrate that the genetic basis underlying these biological functions occurred much earlier before the first animals came ashore," stated by professor and lead author Guojie Zhang, from Villum Centre for Biodiversity Genomics, at the University of Copenhagen's Department of Biology.

A group of ancient living fishes might hold the key to explain how the tetrapod ultimately could grow limbs and breathe on air. The group of fishes includes the bichir that lives in shallow freshwater habitats in Africa. These fishes differ from most other extant bony fishes by carrying traits that our early fish ancestors might have had over 420 million years ago. And the same traits are also present in for example humans.

Through a genomic sequencing the researchers found that the genes needed for the development of lungs and limbs have already appeared in these primitive species.

Our synovial joint evolved from fish ancestor

Using pectoral fins with a locomotor function like limbs, the bichir can move about on land in a similar way to the tetrapod. Researchers have for some years believed that pectoral fins in bichir represent the fins that our early fish ancestors had.

The new genome mapping shows that the joint which connects the socalled metapterygium bone with the radial bones in the pectoral fin in the bichir is homologous to synovial joints in humans - the joints that connect upper arm and forearm bones. The DNA sequence that controls the formation of our synovial joints already existed in the common ancestors of bonefish and is still present in these primitive fishes and in terrestrial vertebrates. At some point, this DNA sequence and the synovial joint was lost in all of the common bony fishes - the socalled teleosts.

"This genetic code and the joint allows our bones move freely, which explains why the bichir can move around on land," says Guojie Zhang.

First lungs, then swim bladder

Moreover, the bichir and a few other primitive fishes have a pair of lungs that anatomically resembles ours. The new study reveals that the lungs in both bichir and alligator gar also function in a similar manner and express same set of genes as human lungs.

At the same time, the study demonstrates that the tissue of the lung and swim bladder of most extant fishes are very similar in gene expression, confirming they are homologous organs as predicted by Darwin. But while Darwin suggested that swim bladders converted to lungs, the study suggests it is more likely that swim bladders evolved from lungs.

The research suggests that our early bony fish ancestors had primitive functional lungs. Through evolution, one branch of fish preserved the lung functions that are more adapted to air breathing and ultimately led to the evolution of tetrapods. The other branch of fishes modified the lung structure and evolved with swim bladders, leading the evolution of teleosts. The swim bladders allow these fishes to maintain buoyancy and perceive pressure, thus better survive under water.

"The study enlightens us with regards to where our body organs came from and how their functions are decoded in the genome. Thus, some of the functions related to lung and limbs did not evolve at the time when the water-to-land transition occurred, but are encoded by some ancient gene regulatory mechanisms that were already present in our fish ancestor far before landing. It is interesting that these genetic codes are still present in these 'living-fossil" fishes, which offer us the opportunity to trace back the root of these genes," concludes Guojie Zhang.

FACT BOX 1: Not just limbs and lungs, but also the heart

Primitive fish and humans also share a common and critical function in the cardio-respiratory system: The conus arteriosus, a structure in the right ventricle of our heart which might allow the heart to efficiently deliver the oxygen to the whole body, and which is also found in the bichir. However, the vast majority of bony fish have lost this structure. The researchers discovered a genetic element that appears to control the development of the conus arteriosus. Transgenic experiments with mice showed that when researchers removed this genetic element, the mutated mice died due to thinner, smaller right ventricles, which lead to congenital heart defects and compromised heart function.

FACT BOX 2:

The vast majority of extant fish species belong to the ray-finned fishes, a subclass of bony fish. These are typically fish with gills, fins and a swim bladder.

The terrestrial group of vertebrates are known as tetrapod. The tetrapod includes all vertebrates that descended from the first animals adapted to a life on land by developing four limbs and lungs, i.e., all mammals, birds, reptiles and amphibians.

The researchers' theory is that the air-breathing ability in these primitive fishes allowed them to survive the second mass extinction roughly 375-360 million years ago. At that time, oxygen depletion in Earth's oceans caused a majority of species to be wiped out. Lungs allowed some fish to survive on land.

The study has been published in the scientific journal Cell. Access the research article here. The research team also contributed to another paper which reported the genome for another primitive fish, the lungfish. The genome is the biggest vertebrate genome decoded so far. This paper was published in Cell at the same time.

The research is supported by the Villum Foundation, among others.

http://bit.ly/3oRRvqc

Neanderthals' gut microbiota and the bacteria helping our health

Neanderthals' gut microbiota already included some beneficial micro-organisms that are also found in our own intestine.

An international research group led by the University of Bologna achieved this result by extracting and analysing ancient DNA from 50,000-year-old faecal sediments sampled at the archaeological site of El Salt, near Alicante (Spain).

Published in *Communication Biology*, their paper puts forward the hypothesis of the existence of ancestral components of human microbiota that have been living in the human gastrointestinal tract since before the separation between the Homo Sapiens and Neanderthals that occurred more than 700,000 years ago.

"These results allow us to understand which components of the human gut microbiota are essential for our health, as they are integral elements of our biology also from an evolutionary point of view" explains Marco Candela, the professor of the Department of Pharmacy and Biotechnology of the University of Bologna, who coordinated the study. "Nowadays there is a progressive reduction of our microbiota diversity due to the context of our modern life: this research group's findings could guide us in devising diet- and lifestyle-tailored solutions to counteract this phenomenon".

The Issues Of The "Modern" Microbiota

The gut microbiota is the collection of trillions of symbiont micro-organisms that populate our gastrointestinal tract. It represents an essential component of our biology and carries out important functions in our bodies, such as regulating our metabolism and immune system and protecting us from pathogenic micro-organisms.

Recent studies have shown how some features of modernity - such as the consumption of processed food, drug use, life in hyper-

sanitized environments - lead to a critical reduction of biodiversity in the gut microbiota. This depletion is mainly due to the loss of a set of microorganisms referred to as "old friends".

"The process of depletion of the gut microbiota in modern western urban populations could represent a significant wake-up call," says Simone Rampelli, who is a researcher at the University of Bologna and first author of the study. "This depletion process would become particularly alarming if it involved the loss of those microbiota components that are crucial to our physiology".

Indeed, there are some alarming signs. For example, in the West, we are witnessing a dramatic increase in cases of chronic inflammatory diseases, such as inflammatory bowel disease, metabolic syndrome, type 2 diabetes and colorectal cancer.

How The "Ancient" Microbiota Can Help

How can we identify the components of the gut microbiota that are more important for our health? And how can we protect them with targeted solutions? This was the starting point behind the idea of identifying the ancestral traits of our microbiota - i.e. the core of the human gut microbiota, which has remained consistent throughout our evolutionary history. Technology nowadays allows to successfully rise to this challenge thanks to a new scientific field, paleomicrobiology, which studies ancient microorganisms from archaeological remains through DNA sequencing.

The research group analysed ancient DNA samples collected in El Salt (Spain), a site where many Neanderthals lived. To be more precise, they analysed the ancient DNA extracted from 50,000 years old sedimentary faeces (the oldest sample of faecal material available to date). In this way, they managed to piece together the composition of the micro-organisms populating the intestine of Neanderthals. By comparing the composition of the Neanderthals' microbiota to ours, many similarities aroused.

"Through the analysis of ancient DNA, we were able to isolate a core of microorganisms shared with modern Homo sapiens", explains Silvia Turroni, researcher at the University of Bologna and first author of the study. "This finding allows us to state that these ancient micro-organisms populated the intestine of our species before the separation between Sapiens and Neanderthals, which occurred about 700,000 years ago".

Safeguarding The Microbiota

These ancestral components of the human gut microbiota include many well-known bacteria (among which Blautia, Dorea, Roseburia, Ruminococcus and Faecalibacterium) that are fundamental to our health. Indeed, by producing short-chain fatty acids from dietary fibre, these bacteria regulate our metabolic and immune balance. There is also the Bifidobacterium: a microorganism playing a key role in regulating our immune defences, especially in early childhood. Finally, in the Neanderthal gut microbiota, researchers identified some of those "old friends". This confirms the researchers' hypotheses about the ancestral nature of these components and their recent depletion in the human gut microbiota due to our modern life context.

"In the current modernization scenario, in which there is a progressive reduction of microbiota diversity, this information could guide integrated diet- and lifestyle-tailored strategies to safeguard the micro-organisms that are fundamental to our health", concludes Candela. "To this end, promoting lifestyles that are sustainable for our gut microbiota is of the utmost importance, as it will help maintain the configurations that are compatible with our biology".

THE AUTHORS OF THE STUDY

The study titled "Components of a Neanderthal gut microbiome recovered from fecal sediments from El Salt" was published in Communication Biology. The University of Bologna participated in this study thanks to Marco Candela, Simone Rampelli, Silvia Turroni and Elena Biagi from the Department of Pharmacy and Biotechnology; Annalisa Astolfi from the Interdepartmental Center for Cancer Research "Giorgio Prodi"; Patrizia Brigidi from the Department of Medical and Surgical Sciences; and Stefano Benazzi from

the Department of Cultural Heritage.
Moreover, this study saw the participation of researchers from the Universidad de La Laguna (Spain), from the Massachusetts Institute of Technology (USA) as well as the University of Oklahoma (USA) and Konrad Lorenz Institute for Evolution and Cognition Research (Austria).

http://bit.ly/39Z9Kps

Signs that SARS-CoV-2 is evolving to avoid immune responses

Mutations are changing, but not eliminating, the antibody response to the virus.

John Timmer

Over the summer, you could almost hear a sigh of relief rising from the portion of the research community that was tracking the evolution of the SARS-CoV-2 virus. Viruses, especially those new to their hosts, often pick up mutations that help them adapt to their new habitat, or they evade drugs or immune attacks. But SARS-CoV-2 seemed to be picking up mutations at a relatively sedate pace, in part because its virus-copying enzymes had a feature that lets them correct some errors.

But suddenly, new variants appear to be everywhere, and a number of them appear to increase the threat posed by the virus. A new study helps explain the apparent difference: while new base changes in the virus's genetic material remain rare, some deletions of several bases appear to have evolved multiple times, indicating that evolution was selecting for them. The research team behind this new work found evidence that these changes alter how the immune system can respond to the virus.

This looks familiar

The researchers' interest in deletions started with their involvement with an immunocompromised cancer patient, who held off the infection for over two months without being able to clear the virus. Samples obtained from late in the infection revealed two different virus strains that each had a deletion in the gene encoding the spike protein that SARS-CoV-2 uses to attach to and enter cells.

When the researchers searched a database of other viral genomes, they found six other cases where the same or similar deletions seem to have evolved in other patients. This caused them to go back and look at a collection of nearly 150,000 viral genomes. They found that over 1,100 of them carried deletions in the spike protein. But critically, they found that these weren't distributed randomly. Ninety percent of the deletions clustered into four distinct areas of the spike gene.

That could be for one of two reasons. It's possible that these viruses are related by common descent and all inherited the same ancestral deletion. Or these deletions could be useful from an evolution perspective, and so whenever they happen to occur, they end up being kept around.

To figure out what's going on, the researchers built an evolutionary tree of the viruses using mutations that occurred outside the spike protein. This showed that, outside of the deletions, the viruses were often distantly related. This indicates the latter option is likely to be true: the deletions often occurred independently and were just kept around at an unusually high rate. One specific deletion seems to have occurred at least 13 different times, and some of the deletions have been around since early in the pandemic.

Selected

If these deletions are being kept around, then the obvious question is "Why?" To find out, the researchers figured out how each of the deletions would alter the spike protein produced by the mutant form of the gene. They then compared this information to what we know about the structure and function of the spike protein. None of the regions turned out to be essential for the spike protein to do its job (which you'd expect, given that deleting those would probably inactivate it). Instead, some of the sites had already been identified as locations where antibodies to the spike protein would stick to it.

So, the researchers produced these deletion versions of the spike protein and tested whether an antibody that can neutralize the virus can stick to them. For one antibody, the answer was "yes": two of the deletions completely blocked its ability to stick to spike, while the other two had no effect.

That's bad news. But the immune response typically involves a collection of different antibodies that can stick to a virus. And, when the researchers tested patients' plasma (which should have a mix of antibodies) against the mutant forms, some of the antibodies present were still able to stick to it. So, while any of these deletions seems to be capable of limiting the immune system's ability to neutralize the virus, the deletions don't eliminate that ability entirely. And, while these mutations are worrying, they're not yet a clear threat.

Some of these deletions have already been seen in strains that seem to have increased spread in recent months. And, while the research team was doing all these experiments, reports came out of four additional strains that were spreading quickly and carried deletions in spike.

Again, so far, there's no indication that any of these strains can evade the immunity built up by earlier infection or one of the vaccines currently in use. But the results make clear that the virus is evolving in response to the immune system's reaction to it, and we can't guarantee that further changes won't make COVID-19 harder for our immune systems to keep at bay.

Science, 2021. DOI: 10.1126/science.abf6950 (About DOIs).

http://bit.ly/3cWAOaZ

Critical flaw found in lab models of the human blood-brain barrier

Throws nearly a decade's worth of research into question

NEW YORK, NY - Cells used to study the human blood brain barrier in the lab aren't what they seem, throwing nearly a decade's worth of research into question, a new study from scientists at Columbia University Vagelos College of Physicians and Surgeons and Weill Cornell Medicine suggests.

The team also discovered a possible way to correct the error, raising hopes of creating a more accurate model of the human blood-brain barrier for studying certain neurological diseases and developing drugs that can cross it.

The study was published online Feb. 4 in the *Proceedings of the National Academy of Sciences* (PNAS).

"The blood-brain barrier is difficult to study in humans and there are many differences between the human and animal blood-brain barrier. So it's very helpful to have a model of the human blood-brain barrier in a dish," says co-study leader Dritan Agalliu, PhD, associate professor of pathology and cell biology (in neurology) at Columbia University Vagelos College of Physicians and Surgeons.

The in vitro human blood-brain barrier model, developed in 2012, is made by coaxing differentiated adult cells, such as skin cells, into stem cells that behave like embryonic stem cells. These induced pluripotent stem cells can then be transformed into mature cells of almost any type--including a type of endothelial cell that lines the blood vessels of the brain and spinal cord and forms a unique barrier that normally restricts the entry of potentially dangerous substances, antibodies, and immune cells from the bloodstream into the brain.

Agalliu previously noticed that these induced human "brain microvascular endothelial cells," produced using the published approach in 2012, did not behave like normal endothelial cells in the human brain. "This raised my suspicion that the protocol for making the barrier's endothelial cells may have generated cells of the wrong identity," says Agalliu.

"At the same time the Weill Cornell Medicine team had similar suspicions, so we teamed up to reproduce the protocol and perform

bulk and single-cell RNA sequencing of these cells."

Their analysis revealed that the supposed human brain endothelial cells were missing several key proteins found in natural endothelial cells and had more in common with a completely different type of cell (epithelial) that is normally not found in the brain.

The team also identified three genes that, when activated within induced pluripotent cells, lead to the creation of cells that behave more like bona fide endothelial cells. More work is still needed, Agalliu says, to create endothelial cells that produce a reliable model of the human blood-brain barrier. His team is working to address this problem.

"The misidentification of human brain endothelial cells may be an issue for other types of cells made from induced pluripotent cells such as astrocytes or pericytes that form the neurovascular unit," Agalliu says. The protocols to generate these cells were created before the advent of single-cell technologies that are better at uncovering a cell's identity. "Cell misidentification remains a major problem that needs to be addressed in the scientific community in order to develop cells that mirror those found in the human brain. This will allow us to use these cells to study the role of genetic risk factors for neurological disorders and develop drug therapies that target the correct cells that contribute to the blood-brain barrier."

More Information

The study is titled, "Pluripotent stem cell-derived epithelium misidentified as brain microvascular endothelium requires ETS factors to acquire vascular fate."

The other contributors are: Tyler M. Lu (Weill Cornell Medicine), Sean Houghton (Weill Cornell Medicine), Tarig Magdeldin (Weill Cornell Medicine), José Gabriel Barcia Durán (Weill Cornell Medicine), Andrew P. Minotti (Weill Cornell Medicine), Amanda Snead (Columbia), Andrew Sproul (Columbia), Duc-Huy T. Nguyen (Weill Cornell Medicine), Jenny Xiangh (Weill Cornell Medicine), Howard A. Fine (Weill Cornell Medicine), Zev Rosenwaks (Weill Cornell Medicine), Lorenz Studer (Memorial Sloan-Kettering Cancer Center and Weill Cornell), Shahin Rafii (Weill Cornell Medicine), David Redmond (Weill Cornell Medicine), and Raphaël Lis (Weill Cornell Medicine).

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The authors report no financial or other conflicts of interest.

http://wb.md/3pTHXfH

Some COVID Vaccine Reactions Could Be Pseudoallergy, Experts Say

Cases of complement-activation-related pseudoallergy resemble a severe allergic reaction

Michele Cohen Marill

On January 13, two days after a drive-through vaccination "superstation" opened in San Diego, a cluster of six people were treated for anaphylaxis after they received the Moderna vaccine, leading the California state epidemiologist to recommend pausing the administration of that particular lot.

A group of allergy and immunology experts and public health officials reviewed the cases, as well as an incident that occurred the day before, and concluded that at least some of the responses were angioedema, or swelling — a serious allergic reaction — but none were actually anaphylaxis. No similar clusters had occurred with the same vaccine lot in other states, and California resumed using the doses.

Yet questions remain about the reactions and the mechanisms for them. Some might have been triggered by an allergy to a vaccine component, most likely the polyethylene glycol (PEG) that stabilizes the lipid surrounding the mRNA, the key vaccine component in both the Moderna and Pfizer vaccines. Another possible explanation is that some could be pseudoallergic reactions to a blood protein known as complement, a little-understood process that resembles an antigen-based reaction but doesn't leave an immune memory and might not recur.

Cases of complement-activation-related pseudoallergy look like a severe allergic reaction but occur through a different mechanism

and don't require previous exposure to an allergen.

"It has the same signs and symptoms and is treated the same way, but it occurs through a different pathway," explained Neal Halsey, MD, director emeritus of the Institute for Vaccine Safety and emeritus professor at the Johns Hopkins Bloomberg School of Public Health in Baltimore.

Pseudoallergies are not well understood, but they have been associated with reactions to the contrast media used in imaging, such as with MRI. "If people have had an anaphylaxis-type reaction following the injection of contrast-dye material, that is a strong signal that it might be a complement-activation-related pseudoallergy," said Halsey, who is a member of the Clinical Immunization Safety Assessment Network. "Those are the people who definitely need to consider seeing an allergist before getting the COVID vaccines."

When Aleena Banerji, MD, clinical director of the allergy and clinical immunology unit at Massachusetts General Hospital in Boston, talks to patients about vaccine reactions, she addresses the risk for COVID-19 infection. All of the people who developed allergies after the Pfizer and Moderna vaccines recovered, but more than 445,000 Americans have died from COVID.

Most people with common allergies, such as to food or oral medications, don't need to worry about reactions, said Banerji, who is lead author of a review that assessed the risk for allergic reactions to the Pfizer and Moderna vaccines.

Investigating Reactions

As investigators search for the answers to what causes reactions, transparency is crucial to trust, said Kathryn Edwards, MD, principal investigator of the Clinical Immunization Safety Assessment (CISA) Project, a vaccine safety network funded by the Centers for Disease Control and Prevention (CDC).

"Unless the public knows that we're really investigating and we're taking this seriously, then I think the vaccine hesitancy is going to increase," said Edwards, who is professor of pediatrics at Vanderbilt University Medical Center and scientific director of the Vanderbilt Vaccine Research Program in Nashville, Tennessee.

First reports of anaphylaxis came quickly after COVID-19 vaccinations began. In the 2 weeks before the holidays, almost 2 million healthcare workers received the Pfizer vaccine, and 21 of them developed anaphylaxis, according to CDC researchers who reviewed case reports from the Vaccine Adverse Event Reporting System (VAERS). That rate of about one in 100,000 is 10 times higher than the occurrence with other vaccines. No deaths from anaphylaxis were reported.

As the vaccinations ramped up, the rate declined. As of January 18, 50 cases of anaphylaxis were reported to VAERS after the administration of 9,943,247 Pfizer doses, for a rate of 5.0 per million, according to data presented at the January 27 meeting of the CDC Advisory Committee on Immunization Practices. And 21 cases of anaphylaxis were reported to VAERS after the administration of 7,581,429 Moderna doses, for a rate of 2.8 per million.

The anaphylaxis occurred almost exclusively in women; only three of the VAERS anaphylaxis reports were from men. Only 24% had a history of anaphylaxis.

The earlier CDC report explored the potential link to allergies. One person with anaphylaxis had a history of allergy to iodinated contrast media, and others had allergies to various medications, vaccines, foods, and animals. The researchers reported 86 nonanaphylaxis allergic reactions and 61 nonallergic adverse events among the 175 case reports they reviewed as possible cases of severe allergic reaction.

Of 1266 reports that VAERS received from December 21 to January 10, the CDC identified 108 possible cases of severe allergic

reaction after the Moderna vaccine. Only 10 met the case definition of anaphylaxis put forward by the Brighton Collaboration, a vaccine safety organization. All but one case involved a history of allergies or allergic reactions; only five had a previously experienced anaphylaxis.

There were 47 nonanaphylaxis allergic reactions.

The San Diego cluster also met the Brighton case definition for anaphylaxis, Edwards reported. This discrepancy highlights the difficulties in characterizing vaccine reactions.

Measuring a pseudoallergic reaction is a challenge. It requires that a blood sample be drawn soon after the incident and then frozen to protect heat-sensitive blood markers, Edwards explained.

And as vaccinations rise, so do adverse-event reports. But unlike in clinical trials, there is no control group for comparison. That is why vaccine safety experts urge caution when evaluating events and, where possible, advise looking at background rates.

"A major way to determine whether the adverse event is causally related is to assess the incidence of the adverse event in vaccines versus nonvaccines," said Walter Orenstein, MD, who directed the US Immunization Program from 1988 to 2004 and is now associate director of the Emory Vaccine Center and professor of infectious diseases at Emory University School of Medicine in Atlanta. Public health officials could then identify vaccine risk factors, he said.

When a reaction occurs almost immediately after vaccination, vaccine safety investigators look for probable triggers. If allergy to PEG is the culprit in anaphylactic reactions, then the individuals would have had a previous exposure, perhaps from injectable medications, Edwards said.

It might be feasible to perform a skin test for allergy to PEG. "If the skin testing is negative, that doesn't completely rule out allergy, but it can be used in the decision-making about giving the first or second vaccine dose," Banerji said.

Other vaccines, such as childhood vaccines, contain polysorbate as a stabilizer, which has a similar chemical structure, and it's not clear why someone would react to PEG but not to polysorbate, Edwards said.

Meanwhile, other illnesses and even deaths sometimes occur in the days after vaccination, but that doesn't mean the vaccine caused them, cautioned Steve Black, MD, emeritus professor of pediatrics at Cincinnati Children's Hospital and cofounder of the Global Vaccine Data Network, an international vaccine safety collaboration.

"Different events and clusters of events will occur by chance alone, as these events can occur without vaccines. We need to not immediately assume that they're due to the vaccine," he said. "You don't want to undermine the whole vaccine program every time something comes up and assume that it's associated with the vaccine."

The CDC only has three contraindications for the vaccines:

- ***Severe allergic reaction (such as anaphylaxis) after a previous dose of an mRNA COVID-19 vaccine or any of its components***
- ***Immediate allergic reaction of any severity to a previous dose of an mRNA COVID-19 vaccine or any of its components (including PEG)***
- ***Immediate allergic reaction of any severity to polysorbate (due to potential cross-reactive hypersensitivity with PEG).***

People who have had an immediate allergic reaction to other vaccines or injectable therapies should consider consulting with an allergist or immunologist before getting the Pfizer or Moderna vaccines, the CDC advises.

The CDC also says that people with a history of anaphylaxis from any cause should be observed for 30 minutes after vaccination. Vaccination protocol calls for everyone else to wait on site for 15 minutes after vaccination.

http://nyti.ms/3oZsTMm

How Scientists Shot Down Cancer's 'Death Star'

No drug could touch a quivering protein implicated in a variety of tumors. Then one chemist saw an opening.

By Gina Kolata

After 40 years of effort, researchers have finally succeeded in switching off one of the most common cancer-causing genetic mutations in the human body. The finding promises to improve treatment for thousands of patients with lung and colorectal cancer, and may point the way to a new generation of drugs for cancers that resist treatment.

The finding has already led to a new medication, sotorasib, by the drugmaker Amgen. Other companies are close behind with their own versions.

Amgen tested its drug in patients with the most common type of lung cancer, called non-small cell cancer. The disease is diagnosed in 228,000 Americans a year, and for most patients in the advanced stages, there is no cure.

The new drug attacks a cancer-causing mutation, known as KRAS G12C, that occurs in 13 percent of these patients, almost all of whom are current or former smokers. Sotorasib made the cancers shrink significantly in patients with the mutation, Amgen reported last week at the World Conference on Lung Cancer.

On average, tumors in the patients stopped growing for seven months. In three out of 126 patients, the drug seems to have made the cancer disappear entirely, at least so far, although side effects included diarrhea, nausea and fatigue.

It already is routine to test lung cancer patients for the mutation, because they are often resistant to other drugs, said Dr. John Minna, a lung cancer specialist at the University of Texas Southwestern Medical Center in Dallas.

Amgen's drug is not as drastically effective as some new cancer medicines, said Dr. Bruce Johnson, the chief clinical research officer at the Dana-Farber Cancer Institute in Boston. But in combination with other drugs, those targeting specific mutations can change the course of the disease in many patients, he added.

For example, drugs targeting specific mutations in melanoma patients at first seemed unimpressive, but when combined with other medicines, they eventually changed prospects for patients with this deadly disease.

"The more I looked at it, the more optimistic I became," Dr. Johnson said of Amgen's new data.

While the KRAS G12C mutation is most common in lung cancer, it also occurs in other cancers, especially in colorectal cancer, where it is found in up to 3 percent of tumors, and particularly in pancreatic cancer. KRAS mutations of some type are present in 90 percent of pancreatic tumors.

How the off-switch was discovered is a story of serendipity and persistence by an academic chemist who managed the seemingly impossible.

In 2008, that chemist, Kevan Shokat, a professor at the University of California, San Francisco, decided to focus on the mutated gene. It had been discovered 30 years earlier in rats with sarcomas, a type of cancer that begins in bones and soft tissues.

Researchers found the mutation in human tumor cells, and then discovered that it was one of the most frequently mutated genes in cancers of many types. Different cancers tend to spring from different mutations in the KRAS gene and the protein it encodes. The G12C mutation occurs mostly in lung cancers.

The search for drugs to block previously discovered cancer-causing mutations was always straightforward: Researchers had to find a molecule that attached to the mutated protein and could stop it from functioning. That strategy worked for so-called kinase inhibitors, which also block a protein created by gene mutations. There are 50

approved kinase inhibitors on the market now.

KRAS was different. The gene directs production of a protein that normally flexes and relaxes thousands of times a second, as if it is panting. In one position, the protein signals cells to grow; in the other, it stops the growth. With the KRAS mutation, the protein remains mostly in an "on" position, and cells are constantly forced to grow.

The standard solution would be a drug that would hold the mutated protein in the "off" position. But that seemed impossible. The protein is large and globular, and it doesn't have deep pockets or clefts on its surface where a drug could slip in. It was like trying to drive a wedge into a ball of solid ice.

"Our medicinal chemists referred to it as the Death Star," said Dr. David Reese, executive vice president for research and development at Amgen. "It was so smooth."

So Dr. Shokat and his colleagues began looking for a molecule that could do the trick. Five years later, after screening 500 molecules, they found one and discovered why it worked.

Their drug held the protein steady, making a crevice visible on its surface. "We never saw that pocket before," Dr. Shokat said. The protein normally flexes and relaxes so quickly that the narrow groove had almost been impossible to see.

There was more good news. The drug attached itself to cysteine, an amino acid that occurs in the groove only because of the KRAS mutation. The drug worked only against the mutated protein, and therefore only against cancer cells.

"It is really specific," Dr. Shokat said. "That's what's amazing." He published his findings in 2013, causing a sensation in the field.

Dr. Reese, of Amgen, said that the data "gave us the proof that we could actually do this," and that "it silenced many of the doubters."

Dr. Shokat, too, began working on a drug, which is now being developed by Johnson and Johnson. At least eight companies have their own KRAS inhibitors in clinical trials.

Lung cancer is only the beginning, Dr. Shokat said. The next challenge is pancreatic cancer, one of the most lethal types: "KRAS is the signature mutation for pancreatic cancer," he added.

Most patients have such a mutation, and while it makes the disease very difficult to treat, now it may also make the cancer particularly vulnerable. Researchers have already found drugs that seem promising.

http://bit.ly/2N5QE8q

Scientists switch on tissue repair in inflammatory bowel disease

Method instructs immune system cells to help repair damaged tissues in the intestine, opening the way for more effective treatment of IBD

A method that instructs immune system cells to help repair damaged tissues in the intestine has been developed by researchers at KU Leuven and Seoul National University. This opens the way for more effective treatment of inflammatory bowel disease, including ulcerative colitis and Crohn's disease. The study was carried out on humans and mice.

When functioning correctly, the immune system protects against harmful agents such as bacteria that get into the body. But in conditions such as inflammatory bowel disease (IBD), the immune system attacks the tissues that line the gut, forming ulcers and causing pain and discomfort. Nearly 3.9 million women and 3.0 million men are living with IBD worldwide, and the number of cases is rising.

Since the origin of IBD is unknown, treatments often focus on reducing the immune response in order to limit inflammation and the resulting symptoms. But this also hinders those parts of the immune system involved in repairing the damaged intestine. For example, the white blood cells known as macrophages (literally 'big

eaters' in Greek) play a variety of roles in both inflammation and tissue repair. They consume foreign bodies, clear up debris from damaged cells, and release substances that direct other steps in the inflammatory or repair processes.

"Our idea is that the migration of macrophages to the damaged tissue in IBD is essential to stimulate its recovery," explains Professor Gianluca Matteoli, an immunologist at the Translational Research Center for Gastrointestinal Disorders (TARGID) KU Leuven and lead author of the research, published this week in the journal Gut. His team, and that of Professor Seung Hyeok Seok from Seoul National University, set out to test this theory.

When the researchers looked at macrophages in the intestines of a handful of people with IBD, a sub-group of cells able to respond to prostaglandin E2 (PGE2) stood out. Prostaglandins are messenger molecules in the immune system, associated with tissue regeneration.

"If the patients had acute disease, they had a lower amount of these beneficial cells, and if they went into remission, then amounts of macrophages went up. This suggests that they are part of the reparative process," Professor Matteoli says.

To investigate further, the researchers turned to a mouse model for ulcerative colitis, one of the main forms of IBD. The number of macrophages sensitive to the prostaglandin was lower in the model than in healthy mice, but if PGE2 levels were increased, the few sensitive macrophages present responded, releasing a substance that in turn stimulated tissue regeneration.

If the PGE2 receptors on the macrophages were knocked out, making them unable to respond to the prostaglandin, the level of tissue regeneration dropped. But it could be restored by getting the macrophages to swallow a liposome (a bubble of material similar to a fragment of cell wall) containing a substance able to trigger the release of the repair stimulating agent.

"We already knew that prostaglandins were important for inducing proliferation of tissue cells, but this study shows that they are also important for controlling the inflammatory effect, so moving the body from the acute stage where inflammation dominates to the reparative stage," Professor Matteoli says.

The prospects for new treatments lie in liposomes used to jump-start the macrophages into stimulating tissue repair. The technique is well-established as an experimental tool, but applications like this are rare. "This is one of the first times it has been used to produce a beneficial, therapeutic effect," says Professor Seok. However, a lot of work will be needed before it can be used in patients.

The next step is to look in detail at human macrophages at different stages of IBD. "We want to identify other factors that trip the switch that turns macrophages from inflammatory cells to non-inflammatory cells," says Professor Matteoli. "Then, using the liposome technology that Professor Seok has developed, these could be used to target the macrophages and so produce very precise drugs.

The project was funded through a scientific cooperation agreement between the governments of Flanders via the Research Foundation - Flanders (FWO) and National Research Foundation of Korea (NRF), and supported by the two universities.

http://bit.ly/3rxngXn

Fossil may be of one of oldest mammals in Japan

Japanese researchers believe that a jawbone fossil discovered in Fukui Prefecture in 2019 might be from the earliest mammal to ever live within its shores.

Researchers at Fukui Prefectural Dinosaur Museum have analyzed a lower jaw fossil that was unearthed in June, 2019. It was found in the early Cretaceous stratum, which dates back about

127 million years.
The jaw has three teeth, each measuring 13.1 millimeters long and 5.8 millimeters high.
Researchers suspect that the jawbone belonged to a primitive mammal that was about 16 to 17 centimeters long.
Researchers say Japan's earliest currently known mammal fossil was found in the stratum dating back about 130 to 121 million years.
The latest discovery was excavated from the stratum of almost the same age. They say that suggests this mammal lived in the same age, or even earlier.
Chief researcher Miyata Kazunori says the specimen is valuable as it suggests a diversity of mammals in the time of dinosaurs.

http://bit.ly/39WU85H

AstraZeneca vaccine: delaying the second dose increases protection, according to new data

Delaying the second dose to 12 weeks after the first works especially well

Paul Hunter*

The Oxford/AstraZeneca vaccine is effective at preventing people from developing COVID-19 and could reduce viral transmission, according to a new scientific paper from the team behind the vaccine.
The paper also suggests that delaying the second dose to 12 weeks after the first works especially well. The protective effect of the first dose doesn't appear to wane during these 12 weeks, and leaving a longer gap between doses ultimately seems to make the second more protective.
These promising new findings come from an analysis of clinical trial data, updating a previous paper on the vaccine's trial results published in early December. However, it's important to keep in mind that the paper is a preprint – meaning its results haven't yet been scrutinised formally by other scientists.
The main difference between this paper and the last is that more cases of COVID-19 have been included. In the December paper, 192 cases of illness were included in the analysis, enough to give a general estimate of the amount by which the vaccine reduces the risk of developing symptomatic COVID-19 – otherwise known its efficacy. This new paper analyses 332 cases.
Join 130,000 people who subscribe to free evidence-based news.
More cases appearing among trial participants doesn't mean the vaccine isn't working as well. As before, the majority occurred in those who didn't get the vaccine, meaning its overall efficacy is broadly the same: 67% (still lower than other authorised COVID-19 vaccines, but nevertheless offering important protection).
Rather, having more cases to look at means the authors can now make more robust estimates of the vaccine's efficacy. It's also allowed them to address the dosing regimen, whether the vaccine prevents asymptomatic infection and how protective a single dose actually is.

The half-dose debate

One surprising trial outcome reported in the earlier paper was that efficacy seemed to be much higher in volunteers given only half a dose in their first injection. The half-dosing was apparently an error and so was considered to be a serendipitous mistake. In the UK part of the trial, giving two standard doses resulted in 59% efficacy, whereas the efficacy of a half dose followed by a standard dose was 90%.
In an earlier Conversation article, I raised concerns about the reliability of any conclusions drawn on starting with a half-dose. The UK Medicines and Health Products Regulatory Agency licensed the standard-dosing schedule, saying that when assessing the data, the benefits of the initial half-dose "were not borne out by the full analysis".
It's very clear in this second paper that the dosing error was not

serendipitous at all. Rather, the greater efficacy for those receiving an initial half-dose appears to be down to many of them receiving their second injection much later.

This new analysis shows that vaccine efficacy after the second dose was only 55% if the gap between doses was less than six weeks, but was 81% if the gap was 12 weeks or more. Although not directly presented in the paper, it appears that with a 12-week gap between doses there was very little difference in efficacy for those receiving an initial half or full dose.

Mind the gap

One of the more intense debates around the UK vaccine rollout has concerned increasing the gap between doses to 12 weeks. The thinking was that although a single injection may not be as protective as two, delaying the second dose would allow more people to be given some protection with the first, leading to fewer deaths.

In light of this, this paper also looks at the efficacy of a single injection of the Oxford/AstraZeneca vaccine. Of course, this is only relevant to people receiving this vaccine. Anyone receiving the Pfizer/BioNTech or Moderna vaccines in the UK will also have their doses spaced out by 12 weeks, but we don't have a clear view yet of what effect – if any – this has on these vaccines' efficacy.

From 22 days after being given, the paper states that the efficacy of the first dose of the Oxford/AstraZeneca vaccine is 76%. The paper also finds no evidence of efficacy declining during the 90 days following the first injection – meaning a first dose should remain protective until the second is given 12 weeks later.

At first sight, it appears that a single-dose regimen may even provide better protection than two doses (76% vs 63%). However, the confidence intervals for these figures overlap, meaning that in reality these results may not be that different.

Indeed, overall we need to be a little cautious here. Testing the vaccine's efficacy after delaying the second dose for different amounts of time wasn't an original aim of the trial. This means that people weren't randomly assigned how long they would have to wait for their second dose to eliminate potential bias. Because of this, it could be that these findings have been influenced by other factors.

Preventing transmission?

One aspect of this paper picked up by the media is the suggestion that the vaccine could substantially cut the spread of the virus. However, we also have to be somewhat cautious with accepting this conclusion.

As well as recording symptomatic infections, the authors also took regular throat swabs for PCR testing to see what effect the vaccine had on asymptomatic infections. The overall efficacy at preventing symptomatic infections after two standard doses was 67%, but for preventing any infection (as measured by a positive PCR test) it was 50% – a worthwhile reduction, but not enough to prevent all transmission.

Any vaccine that reduces the incidence of symptomatic infections will also reduce the transmission of the virus somewhat. But people with asymptomatic infections can still spread the virus, albeit rather less effectively. So unless a vaccine is highly effective at preventing these, it won't be able to fully prevent the disease spreading.

And, as others have noted, seeing a reduction in the number of people carrying the virus as a result of being vaccinated doesn't definitively prove that it will reduce transmission – this is still quite a big inference to make.

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