https://bit.ly/3eXBQDc

Why do wisdom teeth come in so late?

Were these late-blooming teeth ever useful to humans?

By Tara Santora

Wisdom-teeth removal is a rite of passage for many people in their late teens and early 20s. But why don't they come in during childhood with the rest of our permanent teeth?

The answer comes down to child development. There's not enough room in a child's jaw for wisdom teeth to come in. But as a kid grows, their jaw grows too, and there's more room for wisdom teeth to emerge, according to an October 2021 study in the journal Science Advances.

However, many modern human jaws don't grow long enough for wisdom teeth to come in without issue, which is why wisdom teeth removal is so common. Again, this is because of child development. Ancient humans ate diets full of hard nuts, uncooked vegetables, gamey meats and other tough foods. Following this diet as a youngster actually makes the jaw grow longer, Julia Boughner, anthropologist at the University of Saskatchewan College of Medicine in Canada, wrote in The Conversation. But as people in industrialized nations have shifted to eating softer foods, we've stopped maxing out our potential of jaw growth.

Another reason wisdom teeth come in during young adulthood is that they're not needed until then. When ancient people would grind down or lose their molars to tough food, wisdom teeth — the third set of molars — would take their place. "They're meant as kind of a backup for somebody who may have lost another molar tooth," said Steven Kupferman, an oral surgeon at Cedars Sinai in Los Angeles. But because most people don't lose their molars as young children, wisdom teeth wait until adulthood to arrive. In other words, if you lost your molars or ground them down as a child or teenager, your wisdom teeth are programmed to erupt to fill the gap.

The first set of permanent molars, or teeth in the back of the mouth that are designed to grind food, first come in around 6 years of age, when a child starts losing their baby teeth. Around age 12, the second molars emerge, serving as a backup to the 6-year molars in case they develop cavities, Kupferman told Live Science. Third molars, or wisdom teeth, come in around the ages of 17 to 21.

Nowadays, dentists often remove wisdom teeth because their emergence can cause pain in crowded mouths. Even if a person doesn't have pain, removing wisdom teeth in young adulthood can prevent health issues later in life, such as gum infections. Dentists and oral surgeons generally don't remove wisdom teeth as a preventive measure past age 27, because the risks of complications, such as damage to nearby nerves, increase. However, people may get their wisdom teeth removed past this age, usually due to issues such as pain.

Most people have 32 teeth, including four wisdom teeth. But some have more or less, and some people may be missing their wisdom teeth altogether, Kupferman said. Others may have a fourth molar, called a paramolar, behind each wisdom tooth. There is almost never enough space for paramolars in the modern human mouth, so they are always removed at the same time as the wisdom teeth.

Not everyone gets their wisdom teeth removed, though. "Even today, when people have teeth pulled for braces purposes, they often will keep their wisdom teeth because there's enough room for them," Kupferman said.

However, keeping your wisdom teeth can lead to issues down the line. Not all wisdom teeth pop through the gums during the late teens and early 20s. But as a person gets older and their gums recede, their wisdom teeth may peek through. In this case, the wisdom teeth come through the gums only partway, so they are prone to cavities and thus must be removed, Kupferman said.

"There are naysayers that [claim] all surgeons are just trying to

make money by taking out wisdom teeth, but I think if you know any teenagers and you've seen just a few X-rays, you know that there's good reason to take out third molars," Kupferman said.

https://bit.ly/3zyIaL1

What Antarctica's 'Doomsday' Glacier Could Mean For The World

The massive Thwaites glacier in West Antarctica contains enough ice to raise global sea levels by 65cm if it were to completely collapse.

Ella Gilbert, The Conversation

And, worryingly, recent research suggests that its long-term stability is doubtful as the glacier hemorrhages more and more ice.

Adding 65cm to global sea levels would be coastline-changing amounts. For context, there's been around 20cm of sea-level rise since 1900, an amount that is already forcing coastal communities out of their homes and exacerbating environmental problems such as flooding, saltwater contamination, and habitat loss.

But the worry is that Thwaites, sometimes called the "doomsday glacier" because of its keystone role in the region, might not be the only glacier to go. Were it to empty into the ocean, it could trigger a regional chain reaction and drag other nearby glaciers in with it, which would mean several meters of sea-level rise.

That's because the glaciers in West Antarctica are thought to be vulnerable to a mechanism called Marine Ice Cliff Instability or MICI, where retreating ice exposes increasingly tall, unstable ice cliffs that collapse into the ocean.

A sea level rise of several meters would inundate many of the world's major cities – including Shanghai, New York, Miami, Tokyo, and Mumbai.

It would also cover huge swathes of land in coastal regions and largely swallow up low-lying island nations like Kiribati, Tuvalu, and the Maldives.

As big as Britain

Thwaites is a frozen river of ice approximately the size of Great Britain. It already contributes around 4 percent of the global sea-level rise.

Since 2000, the glacier has had a net loss of more than 1000 billion tons of ice and this has increased steadily over the last three decades. The speed of its flow has doubled in 30 years, meaning twice as much ice is being spewed into the ocean as in the 1990s.

Thwaites glacier, the widest in the world at 80 miles wide, is held back by a floating platform of ice called an ice shelf, which restrains the glacier and makes it flow less quickly.

But scientists have just confirmed that this ice shelf is becoming rapidly destabilized. The eastern ice shelf now has cracks crisscrossing its surface and could collapse within ten years, according to Erin Pettit, a glaciologist at Oregon State University.

This work supports research published in 2020 which also noted the development of cracks and crevasses on the Thwaites ice shelf. These indicate that it is being structurally weakened.

This damage can have a reinforcing feedback effect because cracking and fracturing can promote further weakening, priming the ice shelf for disintegration.

If Thwaites' ice shelf did collapse, it would spell the beginning of the end for the glacier. Without its ice shelf, Thwaites glacier would discharge all its ice into the ocean over the following decades to centuries.

Other unstable glaciers

The ice shelf – which can be thought of as the floating extension of Thwaites glacier – is one of several that scientists are watching closely in the Amundsen Sea Basin, West Antarctica. Several ice shelves that hold back glaciers there, including Thwaites and its next-door neighbor, the Pine Island glacier, are being eroded by rising ocean temperatures.

Warmer ocean water is able to undercut these floating ice shelves, driving melting from below that can thin the ice and weaken it, allowing the cracks and fractures that have been observed at the surface to develop.

This ocean-driven melting at the bottom of the ice shelf also pushes the anchoring point where the ice meets the seabed backwards. Because the seabed slopes downwards in the Amundsen Sea, that could eventually trigger a shift as the glaciers lose their footing and retreat rapidly. Ultimately, if the ice shelves retreat, it means there is less holding the West Antarctic glaciers back – allowing them to accelerate and add more to global sea levels.

However, scientists are still getting to grips with MICI and questions remain about the future of West Antarctic glaciers. While the collapse of Thwaites certainly could trigger a wholesale collapse event, not everyone believes this will happen.

Other work suggests that the destabilization of the Thwaites ice shelf and glacier may not lead to the kind of catastrophic outcomes that some fear. Sea ice and chunks of ice that break away from the collapsing ice shelf and glacier might have a similar restraining effect to the intact ice shelf, nipping the chain reaction in the bud and preventing the sustained collapse of the entire West Antarctic ice sheet.

But while uncertainty remains about exactly what will happen in West Antarctica, one thing is for sure – the retreating Thwaites glacier will continue to add to global sea levels for many years to come.

https://bit.ly/3q2Jxyj

Newly-discovered protein in the rod cells of the retina helps us see in dim light

Responsible for relaying optical signals from the eye to the brain

PSI scientists have shed light on an important component of the eye: a protein in the rod cells of the retina which helps us see in dim light. Acting as an ion channel in the cell membrane, the protein is responsible for relaying the optical signal from the eye to the brain. If a genetic disorder disrupts the molecular function in a person, they will go blind. Scientists have deciphered the protein's three-dimensional structure, preparing the way for innovative medical treatments. The study is published in the scientific journal *Nature Structural & Molecular Biology*.

"It's thanks to the rod cells in our eye that we can observe the stars in the night sky," explains Jacopo Marino, a biologist with PSI's Laboratory of Biomolecular Research.

"These photo cells are so sensitive to light that they can detect even a single photon reaching us from a very remote part of the universe—a truly incredible feat." The ability of our brain to eventually translate these light beams into a visual impression is partly down to the cyclic nucleotide-gated (CNG) ion channels whose three-dimensional structure has now been illuminated by a PSI research group led by Jacopo Marino.

The ion channel acts as a gatekeeper controlling whether specific particles are allowed through to the interior of the receptor cell. It is embedded in the protein-rich shell—the cell membrane—of the rod cells. In darkness, the ion channel, and thus the gate to the cell, is completely open.

But when light hits the eye, it triggers a cascade of processes in the rod cells. This ultimately causes the gate to close, with the result that positively charged particles, such as calcium ions, can no longer enter into the cell.

This electrochemical signal continues via the nerve cells into the brain's visual cortex, where a visual impression—such as a flash of light—is created. "The idea of solving the structure of this channel dates back to nearly 20 years ago, when Gebhard Schertler and Benjamin Kaupp already collaborated on this topic," says Jacopo Marino. Both are co-authors of the new study.

Endurance paid off

Ph.D. student Diane Barret first had to extract the channel protein from cows' eyes supplied by an abattoir—a complicated and arduous process. "This was a very challenging task, as the protein is extremely sensitive and decomposes very quickly. In addition, it is only available in tiny quantities in the source material," Barret explains. It took a whole two years to obtain enough protein to work with. "We were both too stubborn to simply give up," says Jacopo Marino, laughing. "But in the end that stubbornness paid off."

The scientists then used cryo-electron microscopy to reveal the three-dimensional structure of the ion channel. "In contrast to previous studies on the structure of the ion channel, we investigated the native protein as it exists in the eye. We are therefore much closer to the real conditions that exist in living creatures," Diane Barret says.

One of the reasons why a clearer understanding of the channel protein's natural structure is important is to advance the development of treatments for genetic disorders for which there is no known cure, such as retinitis pigmentosa. With this disease, photoreceptors gradually die off, leaving people blind. One possible cause is that the body is unable to correctly produce the CNG channel protein due to a genetic defect. As a result, the ion channel does not close completely when light hits the eye, disrupting the cell's electrochemical balance and causing the cells to die.

"If we could find molecules that affect the protein in such a way that the channel would completely close, we could prevent the cells from dying—and thus stop people going blind," explains Jacopo Marino. Now that researchers have identified the precise structure of the protein they are able to search specifically for such molecules.

Additional barrier

The protein comprises four parts: three lots of subunit A, and one lot of subunit B. A correctly functioning ion channel is only possible in this combination. In their study, PSI scientists show why the B subunit seems to play such an important role: a side arm of the protein—a single amino acid—protrudes from the rest of the protein, like a barrier across a gateway. This narrows the passage in the channel to the point where no ions can pass through.

"No one expected that—it came as a total surprise," says Diane Barret. Other narrow places already exist in the A subunit—like main gateways—which were previously thought to be the only ones. It is interesting to note that the additional barrier is found not only in the protein from the cow's eye, but seems to apply to all types of animal, as the scientists showed. Whether crocodiles, eagles or humans—all living creatures with an ion channel in their eye have the same protruding amino acid at this position in the protein. As it has been preserved so consistently during evolution, it must be essential for the functioning of the channel.

More information: *Diane C. A. Barret et al, The structure of the native CNGA1/CNGB1 CNG channel from bovine retinal rods, Nature Structural & Molecular Biology (2021). DOI: 10.1038/s41594-021-00700-8*

Journal information: *Nature Structural & Molecular Biology*

https://bit.ly/33ayURd

Mysterious Footprints Suggest Neanderthals Climbed a Volcano Right After It Erupted

According to legend, the devil once took a walk down the side of a volcano in southern Italy, each step preserved forever in solid rock.

Mike Mcrae

The tracks are known as the "Ciampate del Diavolo"' or "Devil's Trail" – but details published in 2020 reveal a less diabolical yet far more interesting story on how they came to be.

The mysterious footprints are well known to those living near Roccamonfina, an extinct volcano in southern Italy that hasn't erupted in tens of thousands of years.

Since 2001, researchers have sought to explain the dozens of impressions left by a small group of human ancestors and even a few animals snaking their way down the mountainside.

***Footprints on the Ciampate del Diavolo.* (edmondo gnerre/Wikimedia Commons/CC BY 2.0)**

But a paper published in January 2020 suggested some individuals were actually heading back up.

Over recent years numerous expeditions have provided detailed measurements on a total of 67 indentations left by the scuffle of feet, hands, and legs, all divided across three distinct tracks headed away from the mountain's summit.

Thanks to the contributions by a team of scientists from institutes across Italy, we obtained details on a further 14 prints – these even larger than the others – some of which head up the mountain rather than down.

Radiometric and geological dating of the various rock strata have already established that the imprints were cast in the soft blanket of ash left in the wake of an eruption around 350,000 years ago, making them some of the oldest preserved human footprints on record.

But just who left these tracks? It's impossible to say for certain based on an assortment of dull shapes pressed awkwardly in time-worn volcanic sediment.

There seemed to be at least five different bodies behind the marks. Further investigations could help whittle down ideas on the sex, body mass, and perhaps even heights of the trekkers.

Given our own *Homo sapiens* ancestors developed their characteristic traits only 315,000 years ago, we can be pretty confident they weren't members of our own species.

But the researchers have some clues.

One of the clearer imprints provides clear evidence of a grown human male.

And the shapes of many of the footprints point to an interesting possibility. The broad nature of the hindfoot area, with the low rise of the arch, looks suspiciously like the feet of individuals buried in the Sima de los Huesos "Pit of Bones".

The owners of those 430,000-year-old remains have been a topic of debate of the years, progressing from *Homo heidelbergensis* to Neanderthal, to Denisovan, back to Neanderthal.

Assuming they truly are Neanderthals, it's a reasonable – even if not solid – bet that the footprints were left by a gang of young Neanderthal adults.

Still, the researchers were careful about jumping to conclusions.

"We have decided to keep the attribution to a specific species still pending," lead researcher Adolfo Panarello told *New Scientist*'s Michael Marshall back in January 2020.

Just what inspired an ancient group of hominids to go trouncing through the cooling soot and debris after the mountain violently blew its lid is anybody's guess, though it's clear from the impressions that nobody was in a hurry.

Based on the leisurely pace of around 1 meter per second (3.2 feet per second), the handful of footsteps heading uphill, and a scattering of basalt artifacts found in the vicinity, we might imagine this was just another day in the life by an active volcano.

Slowly treading barefoot through material freshly deposited by a 300 degree Celsius (572 Fahrenheit) flow of billowing pyroclastic insanity isn't exactly for the faint-hearted either, no matter how tough your soles might be.

Going on a back-of-the-envelope calculation, the researchers estimated the blanket would need to have cooled to at least 50 degrees Celsius (122 Fahrenheit), meaning at least several hours needed to have passed between an eruption and the trek.

We might well imagine members of a community living in the shadow of a mountain known to occasionally spew out hot clouds of poisonous gas and muddy ash, with a small band setting across a familiar path to check out the carnage.

Perhaps disaster tourism isn't a recent thing, after all.

This research was published in the *Journal of Quaternary Science*.

https://bit.ly/3zyRcYr

Researchers Discover Respiratory Tract Bacterial Extracts Could Prevent COVID-19

Bacterial lysate blocked SARS-CoV-2 infection by decreasing the ability of the coronavirus to bind to ACE2

Researchers from the UArizona College of Medicine – Tucson found that the bacterial lysate OM-85 blocked SARS-CoV-2 infection by decreasing the ability of the coronavirus to bind to the lung cell surface receptor ACE2.

A team of University of Arizona Health Sciences researchers at the UArizona College of Medicine – Tucson found that a combination of bacterial extracts used in Europe to treat respiratory infections may offer a new way to prevent or reduce infection by SARS-CoV-2, the virus that causes COVID-19.

The study, published in the *Journal of Allergy and Clinical Immunology*, showed that a specific combination of bacterial extracts known as OM-85 inhibited SARS-CoV-2 infection by reducing the virus's ability to attach to lung cells. OM-85 is a bacterial lysate, a combination of molecules extracted from the cell walls of bacteria, marketed outside the U.S. under the brand name Broncho-Vaxom as a preventive treatment for upper respiratory infections in children and adults.

"Current infection prevention strategies rely on vaccines that trigger our immune system to respond primarily by producing antibodies. The antibodies attach to a specific part of the virus that acts like the key and prevent it from being able to attach to the lung cell receptor, which is like a lock on the outside of the lung cell. This study is unique because it is the first time researchers have targeted the receptor – the lock – with a bacterial extract and shown it protects against infection with live virus. We're essentially removing the lock from the cell wall so there's nothing for the virus' key to attach to," said senior author Dr. Donata Vercelli, professor of cellular and molecular medicine at the UArizona College of Medicine – Tucson and professor of genetics at the BIO5 Institute.

When SARS-CoV-2 enters the lungs, it binds to receptors including the angiotensin converting enzyme 2 receptor, known as ACE2, on the outer membranes of lung cells. A cellular enzyme changes the shape of a protein on the virus to enable SARS-CoV-2 to breach the membrane and infect the cell.

When the pandemic began, Vercelli and Vadim Pivniouk, associate professor in the Department of Cellular and Molecular Medicine, along with other members of the research team, turned to data they collected in an asthma prevention study to determine whether OM-85 treatment affected the ACE2 receptor and enzyme involved in COVID-19.

Vercelli collaborated with Dr. Janko Nikolich-Žugich, professor and chair of the Department of Immunobiology and BIO5 member, and Jennifer Uhrlaub, associate research scientist, and found that pretreatment of cells with OM-85 prevented infection by SARS-CoV-2. The ability of OM-85 to prevent viral infection was found to be dependent on its ability to decrease the expression of the ACE2 receptor.

"ACE2 is the critical piece that tips the scale," said Vercelli, who also serves as director for molecular genomics at the Asthma and Airway Disease Research Center. "Without that initial attachment – the key fitting into a lock – the entire infectious process is derailed and blocked."

The mechanism by which OM-85 prevents viral infection is unlike

that of vaccines or antibody treatments, which focus on a viral protein. By targeting the receptor, OM-85 may shut the very door that allows the coronavirus to infect cells, which could make it effective against any variants that infect cells through the ACE2 receptor.

"Original studies of this type require us to test whether infection by the live virus can be blocked by the potential preventive treatment in question," Nikolich-Žugich said. "This must be done in specialized biosafety containment facilities, so our long-time experience with this type of work and our biosafety facility at BIO5 enabled us to help Dr. Vercelli and her team with this study."

Vercelli and Pivniouk also enlisted the help of Dr. Monica Kraft, the Robert and Irene Flinn Endowed Chair in the College of Medicine – Tucson, who collected primary lung cells from healthy patients.

The rationale for using bacterial extracts to prevent viral infection relates to a previous study led by Vercelli, who also is the director of the Arizona Center for the Biology of Complex Diseases. In 2016, her team found that exposure to environmental microbial products protected Amish farm children from asthma and allergies.

"Our innate immune system has evolved under environmental pressures like bacteria, but our current lifestyles often don't give us the chance to develop this protective immunity," Vercelli said."Our idea is to use bacterial lysate to train our immune system to protect us from viruses, in the same way those who are regularly exposed to farm animals are protected against a multitude of bacteria and other microbes."

According to Vercelli, treatment with bacterial lysates such as OM-85 could promote a more interactive exchange between the immune system and microbes.

Reference: "The OM-85 bacterial lysate inhibits SARS-CoV-2 infection of epithelial cells by downregulating SARS-CoV-2 receptor expression" by Vadim Pivniouk, PhD; Oksana Pivniouk, MA; Avery DeVries, PhD; Jennifer L. Uhrlaub, MS; Ashley Michael, BS; Denis Pivniouk, BS; Sydney R. VanLinden, BS; Michelle Y. Conway, BS; Seongmin Hahn, MS; Sean P. Malone; Peace Ezeh, PhD; Jared M. Churko, PhD; Dayna Anderson, BS; Monica Kraft, MD; Janko Nikolich-Zugich, MD, PhD and Donata Vercelli, MD, 9 December 2021, Journal of Allergy and Clinical Immunology.
DOI: 10.1016/j.jaci.2021.11.019
This research was supported in part by OM Pharma SA, and by the National Institutes of Health's National Institute of Environmental Health Sciences (T32ES007091), National Heart, Lung and Blood Institute (T32 HL007249, R25HL126140), and National Institute of Allergy and Infectious Diseases (P01AI148104, R21AI144722).

https://bit.ly/3GkKYhv

Study reveals more hostile conditions on Earth as life evolved

During long portions of the past 2.4 billion years, the Earth may have been more inhospitable to life than scientists previously thought, according to new computer simulations.

Using a state-of-the-art climate model, researchers now believe the level of ultraviolet (UV) radiation reaching the Earth's surface could have been underestimated, with UV levels being up to ten times higher.

UV radiation is emitted by the sun and can damage and destroy biologically important molecules such as proteins.

The last 2.4 billion years represents an important chapter in the development of the biosphere. Oxygen levels rose from almost zero to significant amounts in the atmosphere, with concentrations fluctuating but eventually reaching modern day concentrations approximately 400 million years ago.

During this time, more complex multicellular organisms and animals began to colonize land.

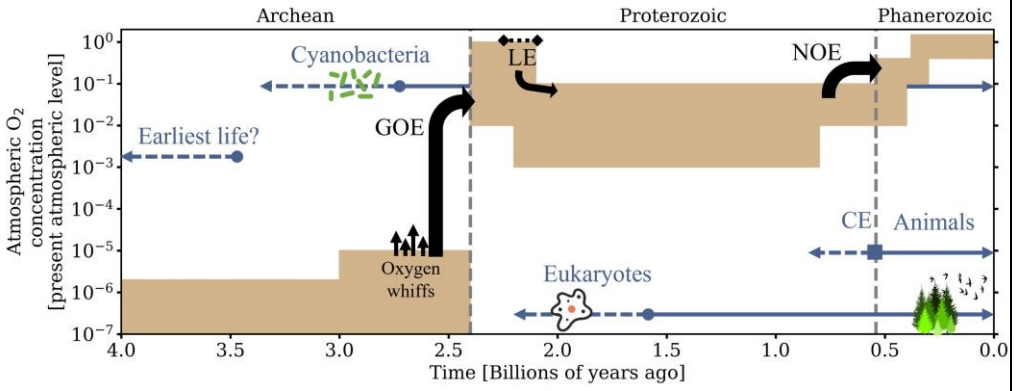
Gregory Cooke, a Ph.D. researcher at the University of Leeds who led the study, said the findings raise new questions about the evolutionary impact of UV radiation as many forms of life are known to be negatively affected by intense doses of UV radiation.

He said: "We know that UV radiation can have disastrous effects if life is exposed to too much. For example, it can cause skin cancer

in humans. Some organisms have effective defense mechanisms, and many can repair some of the damage UV radiation causes.

"Whilst elevated amounts of UV radiation would not prevent life's emergence or evolution, it could have acted as a selection pressure, with organisms better able to cope with greater amounts of UV radiation receiving an advantage."

The research "A revised lower estimate of ozone columns during Earth's oxygenated history" is published today in the scientific journal *Royal Society Open Science*.



A rough outline of oxygen (O_2) concentrations in Earth's atmosphere through time are illustrated in this figure. Brown blocks show the estimated range for O_2 in terms of its present atmospheric level (which is 21% by volume). Grey-blue lines indicated various important events for the evolution of life, including the emergence of eukaryotes and animals. Black arrows refer to important events where atmospheric oxygen concentration changed. The Archean, Proterozoic, and Phanerozoic are geological eons. GOE = Great Oxidation Event; NOE = Neoproterozoic Oxidation Event; CE = Cambrian Explosion; LE = Lomagundi Excursion. **Credit: Please credit: Gregory Cooke/ Royal Society Open Science**

The amount of UV radiation reaching the Earth is limited by the ozone in the atmosphere, described by the researchers as "...one of the most important molecules for life" because of its role in absorbing UV radiation as it passes into the Earth's atmosphere.

Ozone forms as a result of sunlight and chemical reactions—and its concentration is dependent on the level of oxygen in the atmosphere.

For the last 40 years, scientists have believed that the ozone layer was able to shield life from harmful UV radiation when the level of oxygen in the atmosphere reached about one percent relative to the present atmospheric level.

The new modeling challenges that assumption. It suggests the level of oxygen needed may have been much higher, perhaps 5% to 10% of present atmospheric levels.

As a result, there were periods when UV radiation levels at the Earth's surface were much greater, and this could have been the case for most of the Earth's history.

Mr Cooke said: "If our modeling is indicative of atmospheric scenarios during Earth's oxygenated history, then for over a billion years the Earth could have been bathed in UV radiation that was much more intense than previously believed.

"This may have had fascinating consequences for life's evolution. It is not precisely known when animals emerged, or what conditions they encountered in the oceans or on land. However, depending on oxygen concentrations, animals and plants could have faced much harsher conditions than today's world. We hope that the full evolutionary impact of our results can be explored in the future."

The results will also lead to new predictions for exoplanet atmospheres. Exoplanets are planets that orbit other stars. The presence of certain gases, including oxygen and ozone, may indicate the possibility of extra-terrestrial life, and the results of this study will aid in the scientific understanding of surface conditions on other worlds.

More information: *A revised lower estimate of ozone columns during Earth's oxygenated history, Royal Society Open Science (2022). DOI: 10.1098/rsos.211165.*
royalsocietypublishing.org/doi/10.1098/rsos.211165

https://bit.ly/3fiKj4h

Herd the moos? Latvia's symbolic blue cow back from the brink

Once a rarity, cows with light blue or dark ultramarine hides may again be glimpsed grazing on the Latvian countryside among the regular brown, black or white spotted cattle.

by Imants Liepinsh

The unique and hardy breed, driven to near extinction during the Soviet era, has made a comeback over the last few decades as an unlikely symbol of Latvian national identity.

"Their worst days are over," said Arnis Bergmanis, head of the Ciruli animal park in the village of Kalvene, which serves as a breeding facility for the cattle. "Blue cows are unique and wonderful. I'm glad we can help them thrive," he told AFP while examining a baby calf.

Driven to near extinction during the Soviet era, the Latvian blue cow has made a comeback over the last few decades.

In 2000 there were only 18 blue cows in Latvia, but today they number around 1,500—thoroughbreds as well as hybrids.

Originally found only on the Baltic coast in the Kurzeme region, they are increasingly popular in central areas too.

"We are happy to help every new farmer or guesthouse owner get their own special blue cow," Bergmanis said.

Rural innkeepers acquire the cattle as a tourist attraction, while farmers include a token blue cow in their herd for its strong maternal instinct.

"If a calf of any colour loses its mother or gets separated, the blue cow will take the calf and raise it as its own," Bergmanis said.

Cultural symbol

Blue cows evolved on the coast, where they led a spartan lifestyle, able to subsist on bush branches and dune grass—fodder considered inedible by other cattle. Legend has it that they get their colour from the sea, though in fact they are born almost beige. Their coat soon turns blue however and gets darker with the years.

The pigment also influences the muscular tissue, producing beef that is exceptionally dark, though their numbers have always been too low for meat sales on a mass scale.

When the communists came to power under the Soviet occupation, they put an emphasis on mass production of beef and dairy. They favoured more generic cattle, causing the blue cow to almost go extinct.

But theatre, of all things, saved the day. Following the highly popular 1970s play "The Blue One" by Latvian playwright Gunars Priede, the special cattle returned to public consciousness, becoming a symbol of vanishing national identity.

In 2006, farmers, scientists and enthusiasts founded the Blue Cow Association to safeguard the breed. The government meanwhile offers special subsidies for owners of blue cows.

'Strong, independent'

Blue cows provide less milk than your average cattle—around 5,000 litres (1,300 gallons) per cow per year compared to 8,000 for the Holstein breed—but the milk is healthier and more nutritious.

They also stand out for their ability to thrive in harsh conditions, according to Daiga Simkevica, head of the Blue Cow Association.

"The strong, independent and robust blue cow can live all year round outdoors, even during the winter frosts, which many other cattle breeds can't endure," she told AFP.

The Blue Cow Association organises seminars for farmers, keeps meticulous records to avoid inbreeding, works to keep the population growing and also does research on the cattle.

"In the future we hope to carry out full DNA analysis to identify those genes that are unique to the blue cow," Simkevica said.

"We've never had a blue cow catch the bovine leukosis virus, therefore we hope to identify genes that might benefit all other cows too."

https://bit.ly/3FdcsUU

How changing parental beliefs can build stronger vocabulary and math skills for young children

Parents were more likely to believe that parental investments affect child development

by Julie Pernaudet, Dana Suskind, John List, The Conversation

The key to improving young children's vocabulary and math skills may lie in changing their parents' beliefs. We describe these findings in an article published in October 2021 in the peer-reviewed scientific journal *Nature Communications*.

When we measured parental beliefs about child development among 479 parents of newborns living in the Chicago area, a striking pattern emerged: Better educated parents were significantly more likely than parents with lower levels of education to believe that activities such as telling stories to their children, playing with them and spending time having conversations with them affect child development. We call such activities "parental investments."

To understand how socioeconomic differences in these beliefs may drive inequality in children's skills, we designed two interventions among low-income families in the Chicago area. Both intervention programs promote language-rich interactions between caregivers and children.

Our first intervention consisted of a series of short educational videos that provided tips and information about babies' capabilities. Parents watched the videos when they visited their pediatrician for their child's immunizations in the first six months after birth.

The second intervention was more intensive. Families with a child 24 to 30 months old received home visits by specifically trained members of our research team every other week for six months. During the 12 visits, the home visitors showed an educational video to the parents and then did an activity that demonstrated how to put the concepts covered in the video into practice. These demonstrations included, for example, how to use descriptive language with their child or incorporate math into everyday routines. Finally, the home visitors gave feedback and set goals for the next visit.

At the end of both experiments, parents were more likely to believe that parental investments affect child development than parents that did not get the interventions.

But we also found that parents in the more intensive program had significantly more interactions with their children than parents that did not get the intervention. The less intensive program had a similar but smaller effect on parent-child interactions.

Importantly, our results also indicate that the children whose parents received the home visits developed higher vocabulary and math skills—as well as improved socio-emotional health—immediately after the intervention and six months later, compared to those that did not get the interventions. As these are indicators of school readiness, it means that kids who got the treatment were better prepared for school. The first intervention, on the other hand, did not improve children's vocabulary, which was the main outcome of interest for that program.

Why it matters

Research shows that socioeconomic inequalities in child development begin well before school starts. Investing in the early years of a child's development can improve a variety of outcomes later in life, such as employment, earnings and physical health.

During the first years of life, parental investments are critical for the healthy development of children. Yet socioeconomic

differences in parental investments, which have been consistently observed over time and across countries, exacerbate the educational and income inequalities that are often seen in modern economies.

What's next

The fact that only our more intensive intervention succeeded in making kids better prepared for school suggests that simply providing families with more information on child development and parenting is insufficient.

Our future work will address how to personalize support for families. We are developing a computer-adaptive version of the survey we used to elicit parental beliefs. This will tailor to each parent's specific knowledge and needs and help us identify the most appropriate programs for each family.

More information: *John A. List et al, Shifting parental beliefs about child development to foster parental investments and improve school readiness outcomes, Nature Communications (2021). DOI: 10.1038/s41467-021-25964-y*

https://bit.ly/3JQlhXY

Superbug MRSA arose in hedgehogs long before clinical use of antibiotics

Staphylococcus aureus first developed resistance to the antibiotic methicillin around 200 years ago

Staphylococcus aureus first developed resistance to the antibiotic methicillin around 200 years ago, according to a large international collaboration including the University of Cambridge, the Wellcome Sanger Institute, Denmark's Serum Statens Institut and the Royal Botanic Gardens, Kew, which has traced the genetic history of the bacteria.

They were investigating the surprising discovery—from hedgehog surveys from Denmark and Sweden—that up to 60% of hedgehogs carry a type of MRSA called mecC-MRSA. The new study also found high levels of MRSA in swabs taken from hedgehogs across their range in Europe and New Zealand.

The study is published today in the journal *Nature*.

The researchers believe that antibiotic resistance evolved in Staphylococcus aureus as an adaptation to having to exist side-by-side on the skin of hedgehogs with the fungus Trichophyton erinacei, which produces its own antibiotics.

The resulting methicillin-resistant Staphylococcus aureus is better known as the superbug MRSA. The discovery of this centuries-old antibiotic resistance predates antibiotic use in medical and agricultural settings.

Photo shows fungus Trichophyton erinacei growing in the centre of an agar plate streaked with MRSA on the left half and methicillin-susceptible Staphylococcus aureus bacteria on the right. The fungus produces antibiotics, which kill methicillin-susceptible Staphylococcus aureus bacteria but not MRSA, resulting in a clear zone on the right with no bacterial growth. Credit: Claire L. Raisen

"Using sequencing technology we have traced the genes that give mecC-MRSA its antibiotic resistance all the way back to their first appearance, and found they were around in the nineteenth century," said Dr. Ewan Harrison, a researcher at the Wellcome Sanger Institute and University of Cambridge and a senior author of the study.

He added: "Our study suggests that it wasn't the use of penicillin that drove the initial emergence of MRSA, it was a natural biological process. We think MRSA evolved in a battle for survival on the skin of hedgehogs, and subsequently spread to livestock and humans through direct contact."

Antibiotic resistance in bugs causing human infections was previously thought to be a modern phenomenon, driven by the clinical use of antibiotics. Misuse of antibiotics is now accelerating the process, and antibiotic resistance is rising to dangerously high levels in all parts of the world.

Since almost all the antibiotics we use today arose in nature, the

researchers say it is likely that resistance to them already exists in nature too. Overuse of any antibiotic in humans or livestock will favor resistant strains of the bug, so it is only a matter of time before the antibiotic starts to lose its effectiveness.

"This study is a stark warning that when we use antibiotics, we have to use them with care. There's a very big wildlife 'reservoir' where antibiotic-resistant bacteria can survive—and from there it's a short step for them to be picked up by livestock, and then to infect humans," said Professor Mark Holmes, a researcher in the University of Cambridge's Department of Veterinary Medicine and a senior author of the report.

In 2011, previous work led by Professor Holmes first identified mecC -MRSA in human and dairy cow populations. At the time it was assumed the strain had arisen in the cows because of the large amount of antibiotics they are routinely given.

MRSA was first identified in patients in 1960, and around 1 in 200 of all MRSA infections are caused by mecC-MRSA. Due to its resistance to antibiotics, MRSA is much harder to treat than other bacterial infections. The World Health Organization now considers MRSA one of the world's greatest threats to human health. It is also a major challenge in livestock farming.

The findings are not a reason to fear hedgehogs, say the researchers: humans rarely get infections with mecC-MRSA, even though it has been present in hedgehogs for more than 200 years.

"It isn't just hedgehogs that harbor antibiotic-resistant bacteria—all wildlife carries many different types of bacteria, as well as parasites, fungi and viruses," said Holmes.

He added: "Wild animals, livestock and humans are all interconnected: we all share one ecosystem. It isn't possible to understand the evolution of antibiotic resistance unless you look at the whole system."

More information: *Jesper Larsen, Emergence of methicillin resistance predates the clinical use of antibiotics, Nature (2022). DOI: 10.1038/s41586-021-04265-w. www.nature.com/articles/s41586-021-04265-w*

https://bit.ly/3tiq3aO

Researchers pioneer new method to edit genes in human cells

Researchers have fine-tuned a system for more efficient gene editing, using molecules called retrons

by Sarah C.p. Williams, Gladstone Institutes

Over the past decade, the CRISPR genome-editing system has revolutionized molecular biology, giving scientists the ability to alter genes inside living cells for research or medical applications.

Now, researchers at Gladstone Institutes have fine-tuned an additional system for more efficient gene editing, using molecules called retrons.

Retrons, the group reported in the journal *Nature Chemical Biology*, can be optimized for efficiency and used to edit genes in a variety of cell types, from fungi to human cells.

"This work really solidifies retrons as a platform that can be used across organisms," says Gladstone Assistant Investigator Seth Shipman, Ph.D., senior author of the new study.

"We can make precise modifications to genes more easily, quickly, and efficiently than with current approaches."

A one-stop shop for gene editing

Most current gene-editing technologies based on the CRISPR system involve cutting a section of DNA out of a cell's genome, and then introducing new genetic material called "template DNA" to replace it. As the cell repairs the places where an existing gene was cut, the template DNA is integrated.

That template DNA is normally produced in the lab and then introduced to cells from the outside. The protein that cuts the cell's genome—called Cas9—is delivered separately.

Neither Cas9 nor the template DNA penetrate every cell, limiting

the efficiency of CRISPR gene editing.

Retrons, however, act like DNA factories, producing abundant copies of template DNA from inside cells.

Moreover, retrons can be delivered along with the rest of the CRISPR components so that cells get all the material needed for gene editing simultaneously—the genetic codes for template DNA, Cas9, and molecules that help researchers track the edits that have been made.

"This means we only have to introduce one element to each cell," says Santiago Lopez, a graduate student in the Shipman Lab and first author of the new paper. "That significantly simplifies the process and opens the door for new types of experiments."

Re-engineering retrons

Both retrons and CRISPR originate from bacteria; both are defense mechanisms that bacteria use to alter DNA in response to infections.

After the advent of CRISPR genome editing, in which the CRISPR system was co-opted to selectively target genes in other cell types, some researchers began probing whether retrons could be used to supply the templates for precise gene editing.

However, the roles of different sections of the retron's structure in its function—and how to tweak those sections to improve retrons—has been unknown.

"The retron system evolved to help defend bacteria," says Shipman, who is also an assistant professor of bioengineering and therapeutic sciences at UC San Francisco (UCSF). "But we wanted to change it from what it does normally to what we want it to do—produce templates for gene editing."

In the new study, Shipman's group engineered E. coli retrons to create hundreds of new variants.

They tested each new variant and discovered a series of changes, that together, led to an 8-to-10-fold increase in how much template DNA was eventually produced by the retron in E. coli cells.

Next, the researchers tested the new re-engineered retron system in the fungus Saccharomyces cerevisiae (baker's yeast) and in cultured human cells, and they found that this optimized system worked in all cases.

This was the first demonstration of retrons' use in human cells and their portability across cell types.

Since the team could now fine-tune exactly how much template DNA the retrons produced, they were also able to show that when the retrons produce high levels of template DNA, this boosts gene editing efficiency.

"Our study demonstrates for the first time that the more template DNA we can produce, the better the genome editing," says Shipman. "Better and more precise editing ultimately means more effective and safer genomic medicines and more advanced fundamental research."

Taking tools from bacteria

Retrons, Shipman says, are immediately useful as a research tool for editing genes in different cell types in the lab.

While the platform isn't yet ready for use in humans, it also holds the potential to help edit genes for therapeutic purposes—for example by repairing gene mutations that cause disease.

Since different bacteria contain different retrons, his group also plans to explore whether other retron variations have benefits over the E. coli retron they optimized in this study.

"We're taking a general approach in which we're mining parts that we find in bacteria and domesticating them for our own use," says Shipman.

"This has already been incredibly fruitful for developing new tools, but I think we're only just beginning to reap the benefits of applying these tools in biotechnology."

More information: *Santiago C. Lopez et al, Precise genome editing across kingdoms of life using retron-derived DNA, Nature Chemical Biology (2021). DOI: 10.1038/s41589-021-00927-y*

https://bit.ly/3n5OVyD

Horned 'Viking' helmets were actually from a different civilization, archaeologists say

Spectacular helmets worn by Bronze Age leaders as power symbols.

By Tom Metcalfe

Two spectacular bronze helmets decorated with bull-like, curved horns may have inspired the idea that more than 1,500 years later, Vikings wore bulls' horns on their helmets, although there is no evidence they ever did. Rather, the two helmets were likely emblems of the growing power of leaders in Bronze Age Scandinavia.

The two Viksø helmets were found in pieces a bog in eastern Denmark in 1942. Archaeologists think they were deliberately deposited there as religious offerings. **(Image credit: National Museum of Denmark)**

In 1942, a worker cutting peat for fuel discovered the helmets — which sport "eyes" and "beaks" — in a bog near the town of Viksø (also spelled Veksø) in eastern Denmark, a few miles northwest of Copenhagen. The helmets' design suggested to some archaeologists that the artifacts originated in the Nordic Bronze Age (roughly from 1750 B.C. to 500 B.C.), but until now no firm date had been determined. The researchers of the new study used radiocarbon methods to date a plug of birch tar on one of the horns.

"For many years in popular culture, people associated the Viksø helmets with the Vikings," said Helle Vandkilde, an archaeologist at Aarhus University in Denmark. "But actually, it's nonsense. The horned theme is from the Bronze Age and is traceable back to the ancient Near East."

The new research by Vandkilde and her colleagues confirms that the helmets were deposited in the bog in about 900 B.C. — almost 3,000 years ago and many centuries before the Vikings or Norse dominated the region.

That dates the helmets to the late Nordic Bronze Age, a time when archaeologists think the regular trade of metals and other items had become common throughout Europe and foreign ideas were influencing Indigenous cultures, the researchers wrote in the journal Praehistorische Zeitschrift.

Horned helmets

In 1942, a man cutting peat for fuel found broken pieces of the helmets, according to the Danish Ministry of Culture.

When the muddy helmet fragments were first discovered, the man who found them thought they were bits of buried waste, so he set them aside. Later, a foreman noticed the fragments and stored them in a shed for later examination. Later examinations by archaeologists from the National Museum of Denmark showed that the "buried waste" fragments were actually parts of two bronze helmets decorated with curved horns. When excavating the peat pit, researchers also found the remains of a wooden slab that one of the helmets seemed to have stood on, which suggested they had been deliberately deposited in the bog.

But metal can't be reliably dated, and further research suggested the wooden slab might have been placed in the bog earlier than the helmets. It wasn't until 2019 that one of Vandkilde's colleagues spotted the birch tar on one of the horns when she was preparing to take new photographs of the helmets at the National Museum of Denmark.

"She noticed that there was primary organic material in the horns and spoke to a colleague at the National Museum responsible for the collection, and they agreed to send a sample for absolute dating," Vandkilde said.

Previously, any information about the helmets was based on their typology — the style they were made in and any symbols they were

decorated with. But the new date is based on the radioactive decay of the isotope carbon 14, which can determine when the organic matter originated. This method let archaeologists pinpoint when the helmets were created and theorize their purpose, she said.

"Typology is quite often a good first step, chronologically speaking, but it is very important when we can have absolute dates, as we can with carbon 14," Vandkilde said. "We now know with this new date that the helmets were deposited in the bog, perhaps by someone standing on a wooden platform, around 900 B.C."

Sun symbolism

As well as the having eyes and beak of a bird of prey and curving bull's horns, archaeologists think the helmets were decorated with plumes of feathers and manes of horsehair. **(Image credit: Thomas Bredsdorff/National Museum of Denmark)**

As well as their prominent horns, the Viksø helmets are adorned with symbols meant to look like the eyes and beak of a bird of prey; plumage that has since eroded was likely stuck into the ends of the horns with birch tar, and each helmet also may have had a mane of horsehair.

Both the bulls' horns and the bird of prey were probably symbols of the sun, as similar iconography from the time has been found in other parts of Europe, such as on the Mediterranean island of Sardinia and in southwest Iberia. "It's certainly not coincidental — there must have been some sort of connection there," Vandkilde said.

It's possible that the symbology of sun worship may have reached Scandinavia along a sea route, from the Mediterranean and along the Atlantic coast, that was used by the seafaring Phoenicians for trade after about 1000 B.C., "independent of the otherwise flourishing transalpine trading route," the researchers wrote.

There is no sign that the Viksø helmets were ever used for war, which was usually carried out in Bronze Age Scandinavia with only rudimentary helmets or no helmets at all. "They were never used for battle," Vandkilde said.

Instead, leaders probably wore the helmets as symbols of authority at a time when the region was becoming more politicized and centralized, she said.

"There are many signs of this, and our new dating of the Viksø helmets actually suits this very well — this picture of centralization and the importance of political leadership," she said. "And those leaders must have used religious beliefs and innovative traits, like the horns, to further their power."

https://bit.ly/3HP3dvw

Vaccines for animals, based on viruses that spread on their own, are being developed in Europe and the U.S.

Any mammal species that lives in groups could theoretically be targeted to rapidly vaccinate whole populations

Since the first lab-modified virus capable of replication was generated in 1974, an evidence-based consensus has emerged that many changes introduced into viral genomes are likely to prove unstable if released into the environment. On this basis, many virologists would question the release of genetically modified viruses that retain the capacity to spread between individual vertebrate hosts. Researchers from Germany, South Africa, the United Kingdom and the United States now point out in a policy piece that despite these concerns, self-spreading vaccines for animals are being researched in Europe and the US. They are intended to limit the spread of animal diseases or disease spillover to humans.

Non-spreading lab-modified viral vaccines are already in use today, for example as vaccines for wild animals against rabies or for

humans against polio. However, in all modified virus applications to date, rigorous efforts have been made to eliminate (or if this is not possible, minimize) the capacity of viruses to spread in the environment between host individuals.

The molecular tools necessary to generate viral vaccines that retain their capacity to be self-spreading have existed for some time. In 2000, researchers demonstrated the transmission of a self-spreading rabbit vaccine in a field trial on a Spanish island. However, the European Medicines Agency declined to grant marketing approval for the vaccine. "No new technologies are needed to produce self-spreading vaccines; they can be developed using methods that already exist today," says Filippa Lentzos of King's College London.

Viral vaccine against swine fever

In Spain, scientists are currently vaccinating pigs with self-spreading viruses (that have not been modified in a laboratory) against African swine fever as part of contained experiments. In the U.S., a four-year research project that sought to mathematically identify strategies for deploying self-spreading vaccines has just ended. The U.S. Department of Defense's research agency, DARPA, is also funding experimentation to determine if lab-modified self-spreading animal vaccines can prevent the spillover of pathogens to U.S. military personnel in areas where they operate.

"If, as is argued, self-spreading vaccines are potentially transformational in a wide array of agricultural, medical and conservation uses, then developers and funders should commit to address needs within their own borders, rather than continue to propose equatorial nations for field testing," says Guy Reeves of the Max Planck Institute for Evolutionary Biology in Plön, Germany. "This will maximize the chances of a robust debate among fellow citizens and nations about the wisdom of self-spreading viral approaches in the environment. In this respect the EU funded project to address a serious pig disease within its own territories could be viewed as a step in this direction."

More information: *Filippa Lentzos et al, Eroding norms over release of self-spreading viruses, Science (2022). DOI: 10.1126/science.abj5593*

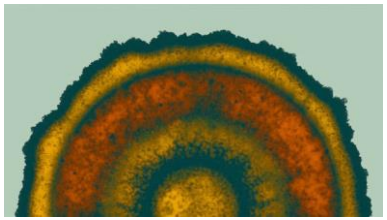
https://bit.ly/330yM6Y

Bacterial Communities are More Advanced than Previously Thought

Biologists from the University of California San Diego and elsewhere have found that biofilm cells are organized in elaborate patterns, a feature previously only associated with higher-level organisms such as plants and animals.

“We are seeing that biofilms are much more sophisticated than we thought,” said Professor Gürol Süel, a researcher in the Division of Biological Sciences at the University of California San Diego, the San Diego Center for Systems Biology, the BioCircuits Institute, and Center for Microbiome Innovation.

“From a biological perspective our results suggest that the concept of cell patterning during development is far more ancient than previously thought. Apparently, the ability of cells to segment themselves in space and time did not just emerge with plants and vertebrates, but may go back over a billion years.”



Chou et al. found that Bacillus subtilis, a bacterium found in soil, creates concentric rings reminiscent of developmental stripes created by a segmentation clock; they discovered that bacterial biofilms use a clock-and-wavefront process for cell patterning similar to plants and animals. **Image credit: Kwang-Tao Chou.**

Biofilms, which are prevalent in the living world, inhabiting sewer pipes, kitchen counters and even the surface of our teeth, are made up of cells of different types.

Biologists previously had not thought that these disparate cells could be organized into regulated complex patterns.

For the new study, Professor Süel and colleagues developed experiments and a mathematical model that revealed the genetic basis for a 'clock and wavefront' mechanism, previously only seen in highly evolved organisms ranging from plants to fruit flies to humans.

As the biofilm expands and consumes nutrients, a 'wave' of nutrient depletion moves across cells within the bacterial community and freezes a molecular clock inside each cell at a specific time and position, creating an intricate composite pattern of repeating segments of distinct cell types.

The breakthrough for the authors was the ability to identify the genetic circuit underlying the biofilm's ability to generate the biofilm community-wide concentric rings of gene expression patterns. They were then able to model predictions showing that biofilms could inherently generate many segments.

"Our discovery demonstrates that bacterial biofilms employ a developmental patterning mechanism hitherto believed to be exclusive to vertebrates and plant systems," they said.

The results appear in the journal *Cell*.

Kwang-Tao Chou et al. 2022. A segmentation clock patterns cellular differentiation in a bacterial biofilm. Cell 185 (1): 145-157.e13; doi: 10.1016/j.cell.2021.12.001

https://bit.ly/3GagOqx

COVID-19 Can Trigger Self-Attacking Antibodies – Even in People That Had No Symptoms of Infection

Cedars-Sinai Investigators Found Evidence of an Overactive Immune Response.

Infection with the virus that causes COVID-19 can trigger an immune response that lasts well beyond the initial infection and recovery—even among people who had mild symptoms or no symptoms at all, according to Cedars-Sinai investigators. The findings are published in the *Journal of Translational Medicine*.

When people are infected with a virus or other pathogen, their bodies unleash proteins called antibodies that detect foreign substances and keep them from invading cells. In some cases, however, people produce autoantibodies that can attack the body's own organs and tissues over time.

The Cedars-Sinai investigators found that people with prior infection with SARS-CoV-2, the virus that causes COVID-19, have a wide variety of autoantibodies up to six months after they have fully recovered. Prior to this study, researchers knew that severe cases of COVID-19 can stress the immune system so much that autoantibodies are produced. This study is the first to report not only the presence of elevated autoantibodies after mild or asymptomatic infection, but their persistence over time.

"These findings help to explain what makes COVID-19 an especially unique disease," said Justyna Fert-Bober, PhD, research scientist in the Department of Cardiology at the Smidt Heart Institute and co-senior author of the study. "These patterns of immune dysregulation could be underlying the different types of persistent symptoms we see in people who go on to develop the condition now referred to as long COVID-19."

To conduct their study, the Cedars-Sinai research team recruited 177 people with confirmed evidence of a previous infection with SARS-CoV-2. They compared blood samples from these individuals with samples taken from healthy people prior to the pandemic. All those with confirmed SARS-CoV-2 infection had elevated levels of autoantibodies. Some of the autoantibodies also have been found in people with diseases in which the immune system attacks its own healthy cells, such as lupus and rheumatoid arthritis.

"We found signals of autoantibody activity that are usually linked to chronic inflammation and injury involving specific organ systems and tissues such as the joints, skin and nervous system," said Susan Cheng, MD, MPH, MMSc, director of the Institute for

Research on Healthy Aging in the Department of Cardiology at the Smidt Heart Institute and co-senior author of the study.

Some of the autoantibodies have been linked to autoimmune diseases that typically affect women more often than men. In this study, however, men had a higher number of elevated autoantibodies than women.

“On the one hand, this finding is paradoxical given that autoimmune conditions are usually more common in females,” Fert-Bober said. “On the other hand, it is also somewhat expected given all that we know about males being more vulnerable to the most severe forms of COVID-19.”

The research team is interested in expanding the study to look for the types of autoantibodies that may be present and persist in people with long-haul COVID-19 symptoms. Because this study was in people infected before the advent of vaccines, the researchers will also examine whether autoantibodies are similarly generated in people with breakthrough infections.

“If we can better understand these autoantibody responses, and how it is that SARS-CoV-2 infection triggers and drives these variable responses, then we can get one step closer to identifying ways to treat and even prevent these effects from developing in people at risk,” Cheng said.

Reference: “Paradoxical sex-specific patterns of autoantibody response to SARS-CoV-2 infection” by Yunxian Liu, Joseph E. Ebinger, Rowann Mostafa, Petra Budde, Jana Gajewski, Brian Walker, Sandy Joung, Min Wu, Manuel Bräutigam, Franziska Hesping, Elena Rupieper, Ann-Sophie Schubert, Hans-Dieter Zucht, Jonathan Braun, Gil Y. Melmed, Kimia Sobhani, Moshe Arditi, Jennifer E. Van Eyk, Susan Cheng and Justyna Fert-Bober, 30 December 2021, Journal of Translational Medicine.
DOI: 10.1186/s12967-021-03184-8

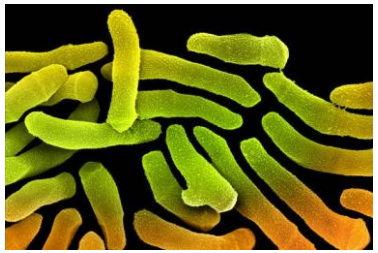
https://nyti.ms/3qZKvuC

Every Pore on Your Face Is a Walled Garden -

A close examination of human skin found that each pore had a single variety of bacteria living inside

By Veronique Greenwood

Your skin is home to a thousand kinds of bacteria, and the ways they contribute to healthy skin are still largely mysterious. This mystery may be getting even more complex: In a paper published Thursday in the journal Cell Host & Microbe, researchers studying the many varieties of Cutibacterium acnes bacteria on 16 human volunteers found that each pore was a world unto itself. Every pore contained just a single type of C. acnes.



A colored scanning electron micrograph of Cutibacterium acnes, the most abundant bacteria on skin. **Credit...Science Photo Library/Science Source**

C. acnes is naturally occurring, and the most abundant bacteria on skin. Its link to acne, the skin disease, is not clear, said Tami Lieberman, a professor at M.I.T. and an author of the new paper. If biologists want to unpack the relationship between your face’s inhabitants and its health, it will be an important step to understand whether varying strains of C. acnes have their own talents or niches, and how the strains are distributed across your skin.

To collect their samples, Dr. Lieberman and her colleagues used commercially available nose strips and old-fashioned squeezing with a tool called a comedone extractor. They then smeared samples, each a bit like a microscopic glacial core, from within pores on Petri dishes. They did the same with samples from toothpicks rubbed across the surface of participants’ foreheads, cheeks and backs, which picked up bacteria living on the skin’s surface rather than in the pores. They allowed the bacteria to grow, then sequenced their DNA to identify them.

Each person’s skin had a unique combination of strains, but what surprised the researchers most was that each pore housed a single variety of C. acnes. The pores were different from their neighbors, too — there was no clear pattern uniting the pores of the left cheek or forehead across the volunteers, for instance.

What's more, judging from the sequencing data, the bacteria within each pore were essentially identical.

"There's a huge amount of diversity over one square centimeter of your face," said Arolyn Conwill, a postdoctoral researcher who is the study's lead author. "But within a single one of your pores, there's a total lack of diversity."

What the scientists think is happening is that each pore contains descendants of a single individual. Pores are deep, narrow crannies with oil-secreting glands at the bottom, Dr. Lieberman said. If a C. acnes cell manages to get down there, it may proliferate until it fills the pore with copies of itself.

This would also explain why strains that don't grow very quickly manage to avoid being outcompeted by speedier strains on the same person. They're not competing with each other; they're living side by side in their own walled gardens.

Intriguingly, these gardens are not very old, the scientists think. They estimate that the founding cells in the pores they studied took up residence only about one year before.

What happened to the bacteria that previously lived there? The researchers don't know — perhaps they were destroyed by the immune system, fell prey to viruses or were unceremoniously yanked out by a nose strip, clearing the way for new founders.

Dr. Lieberman said the finding has implications for microbiome research more broadly. Taking a simple swab of someone's skin would never hint at the complexity uncovered in this study, for instance. And as scientists consider the possibility of manipulating our microbiomes to help treat disease, the patterns uncovered in this study imply the need for information about the location and arrangement of microbes, not just their identities. In the future, should doctors hope to replace someone's current skin inhabitants with others, they may need to clean out their pores first.

And could it be that another inhabitant on our faces plays a role in how each pore's bacteria comes and goes?

"We have mites on our faces that live in pores and eat bacteria," Dr. Lieberman said. What role they play in this ecosystem, as far as the maintenance of gardens of C. acnes, has yet to be determined.

https://bit.ly/33iVbfG

Endometriosis Drug Shows Promise in Preliminary Phase 3 Trial Results

A new drug with the potential to treat endometriosis-associated pain with very few side effects is getting closer to official approval.

Carly Cassella

Endometriosis is a chronic inflammatory condition and the leading cause of pelvic pain worldwide. With no known cause or cure, many patients have run out of options and are living with chronic and unrelenting symptoms.

Safe and effective long-term treatments that can help patients live pain-free lives are desperately needed, and yet to date, very few drugs have been approved for clinical use.

Those that have, like elagolix and leuprorelin (aka Orilissa and Lupron), don't work for everyone and cannot be taken for more than two years because of adverse effects.

These drugs can not only lead to significant and potentially irreversible loss of bone density, they can also induce menopausal-like symptoms, such as hot flushes, insomnia, and mood changes.

An experimental drug in the same class, called linzagolix, could one day prove a much better alternative. It is currently being tested by the biopharmaceutical company ObsEva as a potential way to treat endometriosis-associated pain, as well as heavy menstrual bleeding from uterine fibroids.

At the end of 2021, in fact, the results of two, phase-3 clinical trials were enough to convince the United States Federal Drug Advisory (FDA) to review linzagolix as a treatment for uterine fibroids.

It might not be long until officials also consider the drug as a

treatment for people with endometriosis.

ObsEva has recently announced "topline" results when using linzagolix to treat women with moderate-to-severe endometriosis-associated pain. The findings from their phase-3 clinical trial have not yet been peer-reviewed, so they need to be taken with a grain of salt. But preliminary results are encouraging – hopefully we'll have more details soon.

Two different daily doses of linzagolix were tested in the trial, including a 200 mg dose and a 75 mg dose.

With the higher dose, patients were also given an "add-back" hormonal therapy, as linzagolix works on the brain to reduce estrogen production in the ovaries.

Endometriosis occurs when tissue similar to the uterus grows elsewhere in the body, where it then responds to hormones, including estrogen, as it would on the inside of the uterus, thickening and bleeding with the menstrual cycle.

This can be associated with a significant amount of pain and not only during menstruation.

Compared to a placebo, both doses of linzagolix resulted in a significant reduction in severe and frequent menstrual cramps, menstrual-related constipation (known as dyschezia), and overall pelvic pain after three months. At six months, improvements continued. Even better, side effects were limited.

In 2019, during phase 2b clinical trials, hot flushes were the most common adverse outcome of taking linzagolix, impacting about 20 percent of people on the low dose and nearly half of those on the high dose. Even better, during these trials, low-dose linzagolix showed "no clinically significant impact on bone mineral density", while the high-dose only showed minimal loss.

"While there have been recent advances in non-surgical endometriosis treatment, there is still a critical need for therapeutic options for women who suffer from this chronic condition," says Hugh Taylor, an endometriosis researcher at Yale University who is leading the clinical trials.

"Once daily linzagolix 200 mg with add-back therapy demonstrated excellent efficacy along with minimal changes in bone mineral density, suggesting this dose may be used for long-term treatment."

While both doses of the drug are reported as being significantly and clinically effective, researchers at ObsEva say the low dose is being tested as an option for patients who cannot or do not wish to take hormones with add-back therapy.

The company also intends to explore a higher dose option of linzagolix that does not include add-back hormonal therapy for the same reasons.

The drug may not appeal to everyone with endometriosis, but it is promising that drug researchers and pharmaceutical companies have finally begun to take gynecological pain seriously. The more treatment choices we can give people with incurable conditions, the better chance they have of finding what works for them.

https://go.nature.com/32UgJiZ

Immunity against Omicron from breakthrough infection could be a matter of timing

Laboratory studies hint that a longer interval between vaccination and infection is better than a shorter one.

Saima May Sidik

Good timing is a key to success — even for riding out the Omicron wave. Research from Japan suggests that COVID-19 vaccination followed months later by a breakthrough SARS-CoV-2 infection offers greater protection against the Omicron variant than do closely spaced vaccination and infection[1].

A medical worker administers a COVID-19 vaccine in a gaming arcade in Osaka, Japan. **Credit: Jiji Press/AFP/Getty**

The finding implies that countries that saw large numbers of non-Omicron infections in late 2021 have an advantage as 2022 rolls in with the new variant. The study has not yet been peer reviewed.

Many countries' populations have gained immunity through a combination of vaccination and infection with an array of variants. But Japan's population is protected mainly by vaccination with mRNA vaccines. Study co-author Takeshi Arashiro, an infectious disease researcher at Japan's National Institute of Infectious Diseases in Tokyo, and his colleagues wanted to understand whether the country's mostly single-source immunity would leave the population especially susceptible to Omicron. So far, the country has had few breakthrough cases, but "we are afraid that once the Omicron variant is in high transmission in Japan, we might see a whole different picture", Arashiro says.

The team collected antibodies from people in Japan who had received two doses of the Pfizer–BioNTech COVID-19 vaccine and later been infected with either the Alpha or Delta variant. The researchers tested these antibodies' ability to protect cultured cells from SARS-CoV-2 infection, and found that the length of time between a person's vaccination and the breakthrough infection was strongly correlated with how well the individual's antibodies protected cells against infection — particularly with Omicron.

"It's an interesting study," says immunologist Jenna Guthmiller at the University of Chicago in Illinois. She cautions that the results are solely correlative, but adds that they are in line with immunologists' general understanding of how antibody responses mature over time.

Guthmiller explains that vaccination leads to an emergency blast of antibody production, as a natural infection would. If a person gets infected soon after vaccination, these antibodies are probably still circulating in the blood, where they'll bind to the virus and quickly eliminate it.

But when a person becomes infected months after vaccination, the antibodies that respond come from a new and improved batch made by long-lived cells that carry a memory of the pathogen. When the body encounters the pathogen again, these memory cells are called back to duty and have a chance to refine the antibodies, providing better protection against subsequent infections.

Boosters versus breakthroughs

Guthmiller says she would like to see similar data focused on vaccine boosters instead of breakthrough infections. "Does the amount of time between your first two doses, and then your booster, impact how many cross-reactive antibodies you have?" she asks.

Arashiro and his colleagues have not investigated that, but he thinks boosters are still Japan's best bet for combating the Omicron wave. "We're trying to push for booster doses as soon as possible — especially among vulnerable populations — because we are only protected by vaccines, not by natural infections," he says.

doi: https://doi.org/10.1038/d41586-022-00004-x

References

1. Miyamoto, S. et al. Preprint at medRxiv https://doi.org/10.1101/2021.12.28.21268481 (2022).

https://wb.md/3zKcnXE

A High-Risk Medical Device Didn't Meet Federal Standards. The Government Paid Millions for More.

FDA threatened to notify other federal health agencies about the inspection's findings, but never sent out the letter

Neil Bedi

In 2014, when the Food and Drug Administration found serious problems with a life-sustaining heart pump, its warning letter to the manufacturer threatened to notify other federal health agencies about the inspection's findings.

But for years, no such alert ever went out. Instead, the agency added the warning letter to an online database alongside thousands of others, following its typical procedures, an FDA spokesperson

said.

Agencies such as the Centers for Medicare & Medicaid Services and the U.S. Department of Veterans Affairs went on paying to implant the HeartWare Ventricular Assist Device, or HVAD, in new patients even though federal inspectors had found problems with the device linked to patient deaths and injuries.

Taxpayer dollars continued to flow to the original device maker, HeartWare, and then to the company that acquired it in 2016, Medtronic, for seven years while the issues raised in the warning letter remained unresolved.

If crucial safety information in FDA warning letters doesn't make it to other arms of the government responsible for deciding which medical devices to pay for, experts said patients are the ones put at risk.

"It's clearly a breakdown of communication," said Dr. Rita Redberg, a cardiologist at the University of California San Francisco who researches medical device safety and regulation. "It's not just the money, obviously. It's people's lives."

The FDA acknowledged that it doesn't directly notify other agencies when it issues warning letters, pointing instead to its online database, which is accessible to both government officials and the public. "The FDA's decisions are intended to be patient-centric with the health and safety of device users as our highest priority," the agency spokesperson said in an email.

The HeartWare letter was removed from the public database about two years ago, even though the problems remained unresolved and patients were still receiving implants. The database clears out letters that are more than five years old.

CMS, which oversees the Medicare and Medicaid programs, would not say why it continued paying for a device that didn't meet government standards. It directed questions about the HeartWare warning letter to the FDA. "CMS does not have oversight of the manufacturing and related safety assessments of a medical device manufacturer," a spokesperson said in an email.

The spokesperson noted that CMS requires heart pump patients to have specialized medical teams managing their care, which should monitor FDA communications regarding safety of devices.

CMS doesn't track data on devices by manufacturer, so it's essentially impossible to calculate its total spending on HVADs. One 2018 medical journal study found that Medicare and Medicaid paid for more than half the cost of all heart pump implants from 2009 to 2014. If that rate of spending continued, CMS may have spent more than $400 million on implanting HVADs since 2014.

A spokesperson for the VA said his agency was never notified about the HeartWare warning letter. The VA paid HeartWare and Medtronic more than $3 million after the FDA issued the letter in 2014. It offered this explanation for why: "It's important to note that FDA Warning Letters are notifications issued to manufacturers found to be in significant violation of federal regulations. They are not product recalls."

In the case of the HVAD, the FDA's failure to make sure its warning reached beyond the manufacturer may have had life-and-death consequences.

In August, ProPublica reported that federal inspectors continued finding problems at the HVAD's manufacturing plant for years. Meanwhile, the FDA received thousands of reports of suspicious deaths and injuries and more than a dozen high-risk safety alerts from the manufacturer.

The documents detailed one horrifying device failure after another. A father of four died after his device suddenly failed and his teenage daughter couldn't resuscitate him. Another patient's heart tissue was charred after a pump short-circuited and overheated. A teenager died after vomiting blood as his mother struggled to restart a defective pump.

In June, Medtronic ended sales and implants of the device, citing new data that showed patients with HVADs had a higher rate of deaths and strokes than those with a competing heart pump.

Medtronic declined to comment for this story. It has previously said it believed that after the 2014 warning letter the benefits of the HVAD still outweighed the risks for patients with severe heart failure.

Experts said the lack of communication between federal agencies when serious device problems are found is baffling but not surprising. It fits a broader trend of device regulators focusing more on evaluating new products than monitoring the ones already on the market.

"The priority is to get more medical devices out there, paid for and getting used," said Dr. Joseph Ross, a professor of medicine and public health at Yale University who studies medical device regulation.

Other U.S. health care regulators move more forcefully when providers and suppliers don't meet the government's minimum safety requirements for an extended period, putting patients at risk.

Take hospitals. When inspectors find a facility is not meeting safety standards, CMS can issue an immediate jeopardy citation and, if problems aren't fixed, move to withhold federal payments, which make up substantial portions of most hospitals' revenues. In the rare cases when hospitals don't take sufficient action, CMS follows through and revokes funding.

Redberg, the UCSF cardiologist, said the lack of similar action for medical devices offers a clear "opportunity for improvement." At minimum, the FDA could establish processes to directly inform other agencies when it issues warning letters and finds serious problems with devices being sold in the United States.

"If the agency's mission is to protect public health, they would want to do these things and move quickly," she said.

https://bit.ly/3n9ewqs

How 'Flower Power' Quite Literally Transformed Earth Millions of Years Ago

Following the time of the dinosaurs, it might well be that the evolution of flowering plants drove the explosion in the diversity of life on Earth, according to a 2021 paper.

Tessa Koumoundouros

Most of the plants we now eat, drink, wear, and build with are of the flowering variety. They're called angiosperms, which roughly translates from Greek as 'seed vessels'.

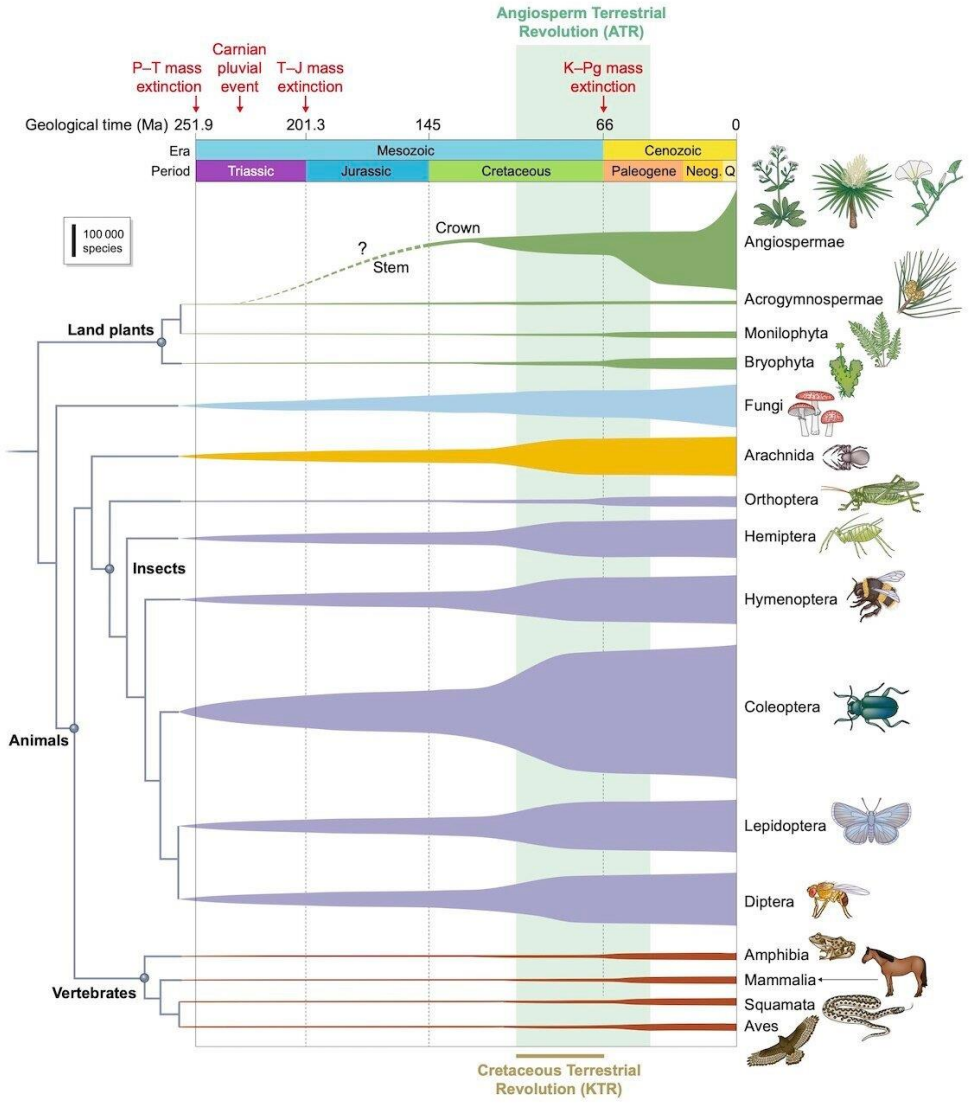
"More than a million species of modern insects owe their livelihoods to angiosperms, as pollinators such as bees and wasps, as leaf-eaters such as beetles, locusts, and bugs, or feeding on nectar such as butterflies," says Pennsylvania State University paleobotanist Peter Wilf. "And these insects are eaten by spiders, lizards, birds, and mammals."

Hundreds of millions of years ago, it's been suggested that most species on Earth lived in the oceans – which makes sense given these watery places cover over 70 percent of our planet's surface. But today, most of life's diversity is found on land.

In a recently published literature review, University of Bristol paleobiologist Michael Benton and colleagues argue this changeover, which is thought to have occurred around 100 million years ago, was driven by flowering plants. It coincided with several innovations in angiosperm biology.

This was around the time when many of the plant families we know today arose according to molecular timelines, which included a massive increase in fruit and seed size – a driver for the evolution of more fruit-eating animals.

"Flowering plants might have been around for some time, but they began to appear more commonly in the Cretaceous, in the last 70 million years of the age of dinosaurs," says Benton.



Above: The rise of angiosperms coincided with massive expansions in the biodiversity of modern plants, fungi, and animals. **(Mike Benton/New Phytologist Trust)**

"But it seems that dinosaurs didn't choose to eat them, and continued chomping ferns and conifers such as pines. However, it was only after the dinosaurs had gone that angiosperms really took off on evolutionary terms."

The team has called this event the Angiosperm Terrestrial Revolution, and suspects we've overlooked it previously because it was punctured by the dramatic extinction event that knocked non-avian dinosaurs out of the picture.

That asteroid impact destroyed many types of creatures, including 70 percent of marine species; but when life rebounded, it was the insects, birds, mammals, and reptiles on land who won out.

"It is even possible that the removal of the dinosaurs and their constant trampling and disturbance was the trigger for these events," says paleobotanist Peter Wilf from Pennsylvania State University.

These floral evolutionary experiments seem to have driven life on land to diversify in four main ways, the team suggests.

Firstly, as flowering plants spread into different habitats, evolution twisted them into a dazzling array of new forms.

These new varieties of structures, chemicals, and reproductive strategies created new opportunities for the other life evolving around them.

"The angiosperms became hugely diverse themselves, but they also created enormous numbers of niches for other plants and animals, so you get tens more species on each hectare of Earth's surface than you would if angiosperms had not become established when they did," says Benton.

In turn, the increase in productivity means these plants were producing and trading more energy.

"They can also capture much more of the Sun's energy than conifers and their relatives, and this extra energy passes through the whole ecosystem," says evolutionary biologist Hervé Sauquet from Sydney's Royal Botanic Gardens.

The resulting new food sources, from luscious vegetation to

enticing high-energy treats for pollinators, created many mutualistic relationships between these plants and animals, triggering a cascade of other new opportunities for biodiversity through to the very top predators.

"Angiosperms also drive the evolution of the animals that pollinate them, mainly insects, and they can build complex forest structures which are homes to thousands of species," explains Sauquet.

Finally, as the flowering invaders increased in abundance, they also started influencing their local climate. Higher rates of transpiration mean the plants draw more water from the soil and pass it into the atmosphere, altering the climate and water cycles.

This allowed angiosperms to increase the extent of wet tropic environments and therefore expand the suitable habitats of many other species, from frogs to fungi and even for the other plants that preceded them like ferns. It was a win-win situation.

"On the other hand, conifer forests, based around the pine family, for example, contain fewer species of other plants or animals, and they probably were never as species-rich," notes Sauquet.

Benton and colleagues suggest differences in genetics enabled angiosperms to diversify so much more than other plants. Despite past genome duplications (a trait common in all plants that can result in more chromosomes), they have relatively small genomes with fewer chromosomes. The mechanisms that reduce their genomes may be what lets flowering plants create new genotypes so easily.

Angiosperms show considerably higher reinvention and trait flexibility – the ability to rapidly evolve physiologically – than gymnosperms like conifers, the researchers explain.

This may have allowed flowering plants to usher in a whole new regime of life on Earth. Ultimately, it became our regime.

The review was published in *New Phytologist*.

https://bit.ly/3HJwMyw

Risk of Death For Female Patients Is Much Higher if Surgeon Is a Man, Study Reveals

For female patients, operation outcomes tend to be significantly better when their surgeon is also female, recent research out of Canada has found.

Carly Cassella

No one really knows why that is just yet, but a new model comparing the sex of the surgeon, the sex of the patient, and the outcomes of the surgery have now revealed an implicit bias that could be costing patients their health and even their lives.The data is based on more than 1.3 million patients who underwent one of 21 common elective surgeries in Ontario, Canada between 2007 and 2019.

Overall, the analysis suggests that when a male surgeon treats a female patient, that patient is 16 percent more likely to experience complications, 20 percent more likely to remain in the hospital for longer, and 32 percent more likely to die than if they were treated by a female surgeon.

On the other hand, male patients treated by a female surgeon were only 2 percent more likely to experience complications, and 13 percent less likely to die than if they had seen a male surgeon.

The underlying reason or reasons for this discrepancy in care remains unclear, but this isn't the first time a study has found a patient's sex might impact how their doctor treats them.

In 2018, female patients in Florida hospitals who were seeking care for heart attacks were found to have higher mortality when treated by male physicians. In comparison, female physicians had more consistent outcomes no matter whether their patient was male or female. Interestingly, male surgeons who had more exposure to female physicians and female patients had better outcomes for women.

While some past studies suggest female physicians prescribe different follow-up tests and medications compared to male doctors, or that they listen more to their patients, further research is needed to determine which factors are influencing these outcomes the most. Once we can figure that out, we can start to mend the bias.

"Surgeons likely believe they provide the same quality of care to patients irrespective of identity," reads an invited commentary to the current paper, written by surgeons Amalia Cochran and Andrea Riner at the University of Florida College of Medicine.

"However, these data underscore an under-appreciated phenomenon and highlight a measurable repercussion of implicit bias. Metrics of surgeon outcomes with regard to patient identity should be developed and incorporated into performance reviews."

Medical experts could also be better trained to improve their care and communication with patients, especially those with identities different from their own, Cochran and Riner suggest.

While most findings to date suggest patients are generally better off in the hands of female surgeons and physicians, the significant gender disparity in these professions means many patients don't ever get to make that choice.

In 2020, slightly more than 27 percent of general surgeons in Canada were female. In the United States, the percentage is slightly lower. In both nations, female surgeons are paid significantly less than their male counterparts. "Female patients with surgical disease should not be disadvantaged because there simply are not enough female surgeons or surgeons who are competent in the care of female patients," the commentary concludes.

"While data are lacking, the concerns faced by female patients undergoing surgery may be even greater for gender-nonconforming and transgender patients. We owe it to patients to provide them with the best outcomes, regardless of how their identities may align with ours." The study was published in *JAMA Surgery*.

https://bit.ly/3f5rn8G

'Deltacron' Covid Variant That Combines Delta and Omicron Reportedly Discovered in Cyprus

Strain of Covid-19 combining Delta and Omicron variants dubbed "Deltacron"

By Katherine Huggins

A researcher in Cyprus has reportedly discovered a strain of Covid-19 that combines the Delta and Omicron variants. According to *Bloomberg News*, the discovery was dubbed "Deltacron."

Leondios Kostrikis, a biological sciences professor at the University of Cyprus and head of the Laboratory of Biotechnology and Molecular Virology, told Sigma TV on Friday that "there are currently omicron and delta co-infections and we found this strain that is a combination of these two." Kostrikis' team have identified 25 cases of "Deltacron," 11 of which came from people hospitalized for Covid and 14 from the general population. "The frequency of the mutations was higher among those in hospital which could mean there is a correlation between Deltacron and hospitalizations," Kostrikis said.

Kostrikis said it was too early to tell whether Deltacron could became the dominant strain, but "his personal view is that this strain will also be displaced by the highly contagious omicron variant," *Bloomberg* reported.

The health minister of Cyprus will hold a press conference in the coming week to address the Deltacron variant, according to the news organization *Greek Reporter*.

https://bit.ly/3zF9KpQ

Gene Involved in Sense of Smell Could Play Role in Spread of Breast Cancer to the Brain

A huge unmet need exists for therapeutic targets to prevent or delay metastasis of breast cancer to the brain, the leading cause of

***death from the malignancy*.**

An olfactory receptor gene that aids in the sense of smell may also play a role in the metastasis of breast cancer to the brain, bones, and lung, researchers from Massachusetts General Hospital (MGH) have found. The team further discovered that inhibiting the gene, OR5B21, significantly decreased the metastasis of breast cancer cells to these organs and could thus be an important target for future therapy to prevent its spread, according to a paper published in *iScience*.

"The common perception is that the only role of olfactory receptors, which line the nasal cavity and relay sensory data to the brain, is to recognize odor and smell," says Bakhos Tannous, PhD, director of the Experimental Therapeutics Unit in the Department of Neurology at MGH and senior author of the study. "Our work suggests that the olfactory receptor 5B21 is also a novel oncogene that may figure prominently in cancer progression by driving breast cancer cells to the brain and other sites in the body."

Breast cancer is the second most frequently diagnosed malignancy behind lung cancer, and the leading cause of cancer in women, with more than two million new cases reported each year. Moreover, migration of breast cancer to the brain is the leading cause of mortality from the disease, underscoring the urgent need for new therapeutic targets to delay or halt its metastasis.

"The olfactory receptor family of genes is known to be overexpressed in a variety of cancers, including prostate, melanoma, lung and liver, though its role in breast cancer has been understudied in the past," says Litia Carvalho, PhD, co-corresponding author of the study and an instructor in Neurology at MGH. The team learned through its research with animal models that OR5B21 enhances or primes breast cancer cells to metastasize through a signaling pathway that activates a process known as the epithelial to mesenchymal transition (EMT). EMT prompts multiple biochemical or phenotypical changes in the olfactory cells which include enhanced migratory capacity to distant organs, especially the brain.

"This activation converts a wide range of extracellular signals into intracellular messages through the signaling pathway NF-κB/STAT, resulting in cell proliferation, invasion and metastasis," explains lead author Mao Li, a graduate student researcher in the Experimental Therapeutics Unit. "Our findings are novel for the field, though further research is needed to determine exactly *how* OR5B21 induces metastasis."

Future research might also lead to a molecular inhibitor of OR5B21 in response to the team's discovery that downregulating the olfactory receptor resulted in a significant decrease in cancer cell metastasis. "Our hope," says Tannous, "is that using OR5B21 as a target for adjuvant therapy could help fill a huge unmet medical need by preventing breast cancer metastasis to the brain and other organs, and thus prolong survival of patients."

Reference: "Olfactory receptor 5B21 drives breast cancer metastasis" by Mao Li, Markus W. Schweiger, Daniel J. Ryan and Ichir, 26 November 2021, iScience.
DOI: 10.1016/j.isci.2021.103519

Tannous is an associate professor of Neurology at Harvard Medical School and an associate neuroscientist at MGH.