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French pharma firm found guilty over medical scandal in which up to 2,000 died

Servier accused of covering up potentially fatal side-effects of the Mediator diabetes drug

Kim Willsher in Paris

A French court has fined one of the country's biggest pharmaceutical firms €2.7m (£2.3m) after finding it guilty of deception and manslaughter over a pill linked to the deaths of up to 2,000 people.

In one of the biggest medical scandals in France, the privately owned laboratory Servier was accused of covering up the potentially fatal side-effects of the widely prescribed drug Mediator. The former executive Jean-Philippe Seta was sentenced to a suspended jail sentence of four years. The French medicines agency, accused of failing to act quickly enough on warnings about the drug, was fined €303,000.

The amphetamine derivative was licensed as a diabetes treatment, but was widely prescribed as an appetite suppressant to help people lose weight. Its active chemical substance is known as Benfluorex.

As many as 5 million people took the drug between 1976 and November 2009 when it was withdrawn in France, long after it was banned in Spain and Italy. It was never authorised in the UK or US.

The French health minister estimated it had caused heart-valve damage killing at least 500 people, but other studies suggest the death toll may be nearer to 2,000. Thousands more have been left with debilitating cardiovascular problems. Servier has paid out millions in compensation.

"Despite knowing of the risks incurred for many years, … they [Servier] never took the necessary measures and thus were guilty of deceit," said the president of the criminal court, Sylvie Daunis.

The pharmaceutical group was acquitted of charges of fraud.

The scandal, which forced the resignation of the head of France's public health agency, sparked a furore about drugs regulation and the lobbying power of French pharmaceutical companies.

The trial, which opened in 2019, aimed to establish how the medication was allowed to remain on the market for so long in France. The alarm was raised in 2007 by Irène Frachon, a lung specialist from a Brittany hospital, two years before Mediator was withdrawn. Frachon assessed patients' records and warned of a link between the drug and serious heart and pulmonary damage.

In the 677-page French indictment, magistrates accused Servier of having "knowingly concealed the medication's true characteristics" from the 1970s and hidden medical studies unfavourable to the product, perpetrating a long-term fraud. The court case involved 21 defendants and more than 6,500 plaintiffs.

Lawyers for Servier argued that the company was unaware of the risks associated with Mediator before 2009, and said it had never pretended it was a diet pill.

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Apes constantly reinvent the wheel

Great apes do not pass on their behavior to the next generation.

Unlike humans, they do not copy the specific knowledge of those around them, instead learning it anew in each generation. This is shown in a study by Dr. Alba Motes-Rodrigo and Dr. Claudio Tennie of the "Tools and Culture in Early Hominins" research group at the University of Tübingen. "Metaphorically speaking, apes constantly have to reinvent the wheel. But the shape of the wheel does not change in the process," Tennie explains.

The Early Prehistory and Quaternary Ecology team searched all published reports on great apes for statements about locally unique behavioral patterns present in a single great ape population, such as the use of leaves as spoons to drink water by chimpanzees. These were then systematically examined for accuracy. By searching for

locally unique behaviors, the researchers indirectly tested whether great ape cultures are built on the same transmission mechanisms as human cultures. The resulting study has been published in the journal *Biological Reviews*.

In human culture, behaviors are learned by people observing and copying each other's behavior. In this way, valuable know-how is passed on to the next generation. In the process, behaviors are often slightly modified, because people make mistakes when copying or add their own alterations. As a result, human culture changes from generation to generation. Alba Motes-Rodrigo compares this to the telephone game, in which each player whispers a term into the next player's ear. The term passes among players and, due to errors in hearing, is likewise frequently changed from the original word.

Exactly when humans began copying each other in this way is hotly debated. According to one theory, the ability to copy behavior goes back millions of years and is also present in modern apes. Another theory proposes that modern apes are incapable of copying each other's behavior, as were many human ancestors.

Alba Motes-Rodrigo and Claudio Tennie used a new approach to look for evidence of the process of know-how copying in great apes. They sought to identify behaviors in ape populations that have undergone changes from generation to generation. "If ape behavior is really based on copying, as it is in humans, we would expect behavioral details to have changed culturally, and therefore there should by now be individual behaviors that are restricted to only one population in one place," Motes-Rodrigo explains.

The team therefore searched for locally unique behavioral patterns in great apes, both in all published reports on the animals and in interviews with experts. They found that the overwhelming majority of great ape behaviors are not locally unique. Out of hundreds of ape behavior patterns, only three could not be found elsewhere.

According to the research team, these results show that ape culture is maintained by different learning mechanisms than those of human culture. Unlike humans, apes do not copy each other's know-how, but reinvent each of their behaviors over and over again in each population and in each generation. "In the process, they are merely stimulated to these reinventions by others, but without copying the particular form of behavior. This finding seems surprising, but it is supported by recent experimental studies in comparative cognitive science," Tennie says. In these studies, great apes copied new behaviors only if they had previously been trained by humans to do so. Therefore, more and more evidence suggest that modern humans and great apes acquire their behavior in different ways.

More information: *Alba Motes-Rodrigo et al. The Method of Local Restriction: in search of potential great ape culture-dependent forms, Biological Reviews (2021).* *DOI: 10.1111/brv.12710*

https://bit.ly/3mbVzlx

A visit to 'Dr. Google' makes patients better at diagnosis

Study finds patients made modest improvements in diagnostic accuracy and experienced no change in anxiety after conducting an internet search for symptoms

BOSTON - Medical professionals often advise patients not to search the Internet for their symptoms before coming into the clinic, yet many people turn to "Dr. Google" when feeling sick. Concerns about "cyberchondria" -- or increased anxiety induced by the Internet -- have made the value of using Internet searches controversial. In a new study that used case vignettes, researchers from Brigham and Women's Hospital and Harvard Medical School Department of Health Care Policy explored the impact Internet searches have on patients' abilities to reach a correct diagnosis. They found that study outcomes suggest the Internet may not be so

harmful after all. Participants across the board demonstrated modest improvements in reaching an accurate diagnosis after looking up symptoms on the Internet. Participants additionally showed no difference in reported anxiety nor in triage abilities. Results are published in *JAMA Network Open*.

"I have patients all the time, where the only reason they come into my office is because they Googled something and the Internet said they have cancer. I wondered, 'Is this all patients? How much cyberchondria is the Internet creating?'" said corresponding author David Levine, MD, MPH, of the Division of General Internal Medicine & Primary Care at the Brigham.

In a study of 5,000 participants, each person was asked to read a short case vignette describing a series of symptoms and imagine someone close to them was experiencing the described symptoms. Participants were asked to provide a diagnosis based on the given information then look up their case symptoms on the Internet and again offer a diagnosis. Cases ranged from mild to severe, but described illnesses that commonly affect everyday people, such as viruses, heart attacks and strokes. In addition to diagnosing a given condition, participants each selected a triage level, ranging from "let the health issue get better on its own" to "call 911." Study members then recorded their individual anxiety levels.

Notably, Levine and co-author Ateev Mehrota, MD, MPH, a hospitalist at Harvard Medical School, found that people were slightly better at diagnosing their cases correctly after performing an Internet search. Participants demonstrated no difference in their abilities to triage nor did they report a change in anxiety after using the Internet.

"Our work suggests that it is likely OK to tell our patients to 'Google it,'" said Levine. "This starts to form the evidence base that there's not a lot of harm in that, and, in fact, there may be some good."

Authors note that a limitation to this study is that participants were asked to pretend as if a loved one was having the symptoms described by the case vignette. It isn't completely clear that people would behave the same way upon experiencing symptoms themselves. Additionally, the authors note that this study is not representative of all people that use the Internet for health-related searches.

Levine also plans to expand the scope of this study by investigating the ability of artificial intelligence (AI) to use the Internet to correctly diagnose patients.

"This next study takes a generalized AI algorithm, trained on all of the open-source text of the Internet such as Reddit and Twitter, and then uses that to respond when prompted," said Levine. "Can AI supplement how people use the Internet? Can it supplement how doctors use the Internet? That's what we're interested in investigating."

Funding for this work was provided by a gift to Harvard Medical School from Mell Hall.
Levine reports receiving funds from Biofourmis for a PI-initiated study regarding home hospital patients, separate from the present work.
Paper cited: Levine et al. "Assessment of Diagnosis and Triage in Validated Case Vignettes Among Nonphysicians Before and After Internet Search." JAMA Network Open DOI:10.1001/jamanetworkopen.2021.3287

https://bit.ly/3cK0WFf

Uprooting cancer: Hydrogel rapidly reverts cancer cells back to cancer stem cells

Hydrogel successfully reverted six types of cancer cells back to cancer stem cells within 24 hours

A hydrogel, a type of soft matter, developed at Hokkaido University successfully reverted cancer cells back to cancer stem cells within 24 hours, in six different human cancer types. This could lead to the development of anti-cancer stem cell drugs and personalized medicines.

An innovative hydrogel - called a double network (DN) gel - can

rapidly reprogram differentiated cancer cells into cancer stem cells, researchers at Hokkaido University and the National Cancer Center Research Institute have reported in the journal *Nature Biomedical Engineering*. The hydrogel can be used to help develop new cancer therapies and personalized medicines targeting cancer stem cells.

Cancer is the leading cause of death in developed countries, and more than 8.6 million people die from cancer annually worldwide. Despite the advancement of treatments, the 5-year survival rate of patients with advanced-stage cancer remains low. One reason is that cancer tissues contain cancer stem cells, which are resistant to chemotherapies and radiotherapies. These cells can hide as 'roots' or circulate in the body, causing cancer recurrence.

"Cancer stem cells are a major target for anti-cancer drugs, but they are difficult to identify because they are present in very small numbers in cancer tissues," explained Professor Shinya Tanaka of Hokkaido University's Faculty of Medicine. "Understanding the molecular mechanisms of cancer stem cells is crucial for developing better cancer treatments."

Cancer stem cells require a very specific microenvironment. In this study, the research team investigated whether their DN gel could recreate the right conditions to induce cancer stem cells. The DN gel consists of a network of two chemicals and incorporates a high volume of water, giving it soft and wet characteristics resembling biological tissues.

In the study, the DN gel rapidly reprogrammed differentiated cancer cells into cancer stem cells in just 24 hours in six different human cancer cell lines -- brain cancer, uterine cancer, lung cancer, colon cancer, bladder cancer, and sarcoma. After cancer cells were placed on the DN gel, they started to form spherical structures and produce specific molecules known to be markers of cancer stem cells such as SOX2 and Oct3/4, aka Yamanaka factors, named after the Nobel Prize laureate, suggesting they had been reprogrammed.

The researchers also uncovered some of the molecular mechanisms involved in cancer cell reprogramming. They found that calcium channel receptors and the protein osteopontin were essential for the induction of cancer stem cells. They also found that brain cancer cells from a patient that had been cultured on the DN gel produced receptors called platelet-derived growth factor receptors. By adding a molecular inhibitor of these receptors, they were able to target and eradicate the cancer stem cells, suggesting that the DN gel could be used to select therapeutic drugs. In addition, they showed that the brain cancer cells that had been cultured on DN gel formed tumors efficiently when transplanted into mice brain, suggesting the stemness of the cancer cells.

This study paves the way for research into drugs that can target cancer stem cells. "In the future, the DN gel could be used to enhance cancer cell type diagnosis and to produce personalized medicines, which could improve the prognosis of cancer patients," said Shinya Tanaka.

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The Genetic Signal of Ancient Australians in South America Goes Deeper Than We Knew

The extent of Australasian influence into the ancient bloodlines of early South American cultures looks to be even greater than scientists thought, according to new research.

Peter Dockrill

In 2015, a pair of scientific studies identified an intriguing link: evidence of Indigenous Australian, Melanesian, and South Asian genetics embedded in modern Native American populations living in the Amazon.

How this mysterious connection was forged between peoples living a globe apart has never been fully understood or agreed upon, although it's thought Australasian genes flowed into the Americas via an epic, land-based migration through Eurasia roughly 20,000

years ago, back when the ancient, now submerged landmass of Beringia still served as a convenient bridge to Alaska.

By about 15,000 years ago, some of the trekkers had made it as far as South America, where the Australasian genes can still be found in the blood of Indigenous Amazonian groups today.

But not all those on the journey necessarily settled in the rainforest. A new study suggests the Australasian contribution to the Native American gene pool of South America was broader in scope than we realized.

One of the previously identified hallmarks of the Australasian influence in South America is what's known as the 'Ypikuéra population' signal (Y signal) – a genetic variant so far only seen in present-day Amazonian populations.

Now, however, this signal has been seen outside the Amazon for the first time, with a genomic analysis comprising 383 individuals from a number of indigenous groups in South America revealing that the Y signal not only exists in Amazonian groups – but also in the indigenous peoples of Chotuna (living near the Pacific coast of Peru), Guaraní Kaiowá (central west Brazil), and Xavánte (close to the center of Brazil).

"Our results showed that the Australasian genetic signal, previously described as exclusive to Amazonian groups, was also identified in the Pacific coastal population, pointing to a more widespread signal distribution within South America, and possibly implicating an ancient contact between Pacific and Amazonian dwellers," the researchers, led by first author and evolutionary biologist Marcos Araújo Castro e Silva from the University of São Paulo (USP) in Brazil, explain in their study.

In addition to suggesting that the Australasian genetic signature spread within Native American populations from the coast to the center of South America, the new findings indicate that at least two migratory waves likely occurred, with one branch of people with the Y variation settling in the Pacific coastal regions, before another group with the same Australasian ancestry later migrated eastwards, inhabiting the Amazon and central Brazil.

As for how the Y signal hasn't been picked up northwards of South America – even though these ancient migrants must once have passed through that territory – it's possible that by sticking to the Pacific coastal route, the migrants' bloodlines, and the Australasian genetic component it carried, may not have thoroughly mixed in with the contemporaneous populations of North and Central America.

Another possibility, as senior author and USP evolutionary geneticist Tábita Hünemeier told *Science*, is that those carrying the Y variant in North and Central America may simply not have survived the violent transitions of European colonization.

It may also be that the Y signal just hasn't been searched for widely enough in more northerly located populations. As these ongoing discoveries show, it may be just a matter of time and further testing before more of these ancient, surprising connections become known.

The findings are reported in *PNAS*.

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New drug to regenerate lost teeth

Antibody for USAG-1 shown to stimulate tooth growth

Japan -- The tooth fairy is a welcome guest for any child who has lost a tooth. Not only will the fairy leave a small gift under the pillow, but the child can be assured of a new tooth in a few months. The same cannot be said of adults who have lost their teeth.

A new study by scientists at Kyoto University and the University of Fukui, however, may offer some hope. The team reports that an antibody for one gene -- uterine sensitization associated gene-1 or USAG-1 -- can stimulate tooth growth in mice suffering from *tooth agenesis*, a congenital condition. The paper was published in *Science Advances*.

Although the normal adult mouth has 32 teeth, about 1% of the population has more or fewer due to congenital conditions. Scientists have explored the genetic causes for cases having too many teeth as clues for regenerating teeth in adults.

According to Katsu Takahashi, one of the lead authors of the study and a senior lecturer at the Kyoto University Graduate School of Medicine, the fundamental molecules responsible for tooth development have already been identified.

"The morphogenesis of individual teeth depends on the interactions of several molecules including BMP, or bone morphogenetic protein, and Wnt signaling," says Takahashi.

BMP and Wnt are involved in much more than tooth development. They modulate the growth of multiple organs and tissues well before the human body is even the size of a raisin. Consequently, drugs that directly affect their activity are commonly avoided, since side effects could affect the entire body.

Guessing that targeting the factors that antagonize BMP and Wnt specifically in tooth development could be safer, the team considered the gene USAG-1.

"We knew that suppressing USAG-1 benefits tooth growth. What we did not know was whether it would be enough," adds Takahashi.

The scientists therefore investigated the effects of several monoclonal antibodies for USAG-1. Monoclonal antibodies are commonly used to treat cancers, arthritis, and vaccine development.

USAG-1 interacts with both BMP and Wnt. As a result, several of the antibodies led to poor birth and survival rates of the mice, affirming the importance of both BMP and Wnt on whole body growth. One promising antibody, however, disrupted the interaction of USAG-1 with BMP only.

Experiments with this antibody revealed that BMP signaling is essential for determining the number of teeth in mice. Moreover, a single administration was enough to generate a whole tooth. Subsequent experiments showed the same benefits in ferrets.

"Ferrets are diphyodont animals with similar dental patterns to humans. Our next plan is to test the antibodies on other animals such as pigs and dogs," explains Takahashi.

The study is the first to show the benefits of monoclonal antibodies on tooth regeneration and provides a new therapeutic framework for a clinical problem that can currently only be resolved with implants and other artificial measures.

"Conventional tissue engineering is not suitable for tooth regeneration. Our study shows that cell-free molecular therapy is effective for a wide range of congenital tooth agenesis," concludes Manabu Sugai of the University of Fukui, another author of the study.

The paper "Anti-USAG-1 therapy for tooth regeneration through enhanced BMP signaling" appeared 12 February 2021 in the journal Science Advances, with doi: 10.1126/sciadv.abf1798

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Researchers discover how animals grow their pointy body parts

Universal rule of biological growth explains surprising similarities in shapes of sharp structures across the tree of life

An interdisciplinary team at Monash University discovered a new universal rule of biological growth that explains surprising similarities in the shapes of sharp structures across the tree of life, including teeth, horns, claws, beaks, animal shells, and even the thorns and prickles of plants.

Animals and plants often grow in specific patterns, like logarithmic spirals following the golden ratio. There are very simple processes that generate these patterns—a logarithmic spiral is produced when one side of a structure grows faster than another at a constant ratio. We can call these 'rules of growth', and they help us understand why organisms are certain shapes.

In the new study published today in *BMC Biology*, the research team demonstrates a new rule called the 'power cascade' based on how the shape 'cascades' down a tooth following a power law.

When an elephant tusk grows longer, it grows wider at a very specific rate following a 'power law'—a mathematical pattern where there is a straight-line relationship between the logarithm of the tooth's width and length. Power laws are found throughout nature, such as in the magnitudes of earthquakes, the sizes of cities, and the movement of the stock market.

This pattern applies across many animals, in the teeth of giant sharks, Tyrannosaurus rex, mammoths, and even humans. Remarkably, this power law works for claws, hooves, horns, spider fangs, snail shells, antlers, and the beaks of mammals, birds, and dinosaurs. Beyond animals, the team also observed it in the thorns of the rose bush and lemon tree.

Associate Professor Alistair Evans in the School of Biological Sciences at Monash University led the research team.

"The diversity of animals, and even plants, that follow this rule is staggering," Associate Professor Evans said.

"We were quite shocked that we found it almost everywhere we looked across the kingdoms of life—in living animals and those extinct for millions of years."

The new pattern expands on the ideas of the polymath anatomist, physicist and mathematician Sir Christopher Wren, the designer of London's St Paul's Cathedral. In 1659, Wren suggested that a snail shell could be a cone twisted to be a logarithmic spiral. The new study shows that shells and other shapes such as teeth and horns are in fact the power cascade shape (called a 'power cone').

"This new rule is the missing piece of a 350-year-old puzzle of how animals and their parts grow," Associate Professor Evans said.

"Because so many structures follow this growth pattern, we can use it to predict the likely pattern of evolution. Whenever animals evolve teeth, horns, or claws, it seems most likely that they will be this shape. It even allows us to predict what mythical animals would look like if they follow the same patterns of nature."

"Now we can know what the dragons from Game of Thrones and fantastic beasts of Harry Potter would look like," Associate Professor Evans said.

More information: *BMC Biology (2021).* *DOI: 10.1186/s12915-021-00990-w*

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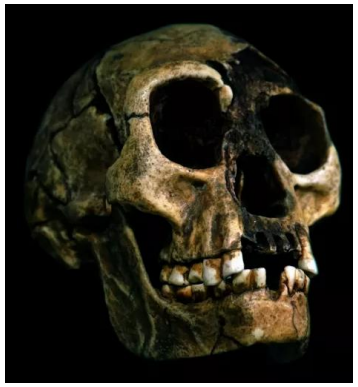
Identity of mysterious 'Hobbits' possibly found

Hobbits may be members of the mysterious close relatives of modern humans known as Denisovans

By Charles Q. Choi - Live Science Contributor



The remains of an individual Homo floresiensis were discovered in 2003 in the Liang Bua cave on the island of Flores. **(Image credit: Universal History Archive/Universal Images Group via Getty Images)**

The extinct human lineage nicknamed "the hobbit" may not be a distant relative of modern humans as previously thought. Instead, hobbits may be members of the mysterious close relatives of modern humans known as Denisovans, and may have interbred with ancestors of modern humans on the islands of Southeast Asia, researchers say.

Although modern humans, *Homo sapiens*, are now the only surviving human lineage, other human species once roamed across Earth.

For instance, previous research suggested *Homo erectus*, the most likely ancestor of modern humans, made its way out of Africa by at least 1.8 million years ago. In contrast, modern humans may have only begun migrating out of Africa about 200,000 years ago.

In the past 20 years, researchers have discovered many new branches of the human family tree on the islands of maritime

Southeast Asia, which includes Brunei, Indonesia, Malaysia, the Philippines, Singapore and East Timor. These human ancestors include the extinct species *Homo floresiensis*, often known as "the hobbit" for its miniature body, as well as the even smaller *Homo luzonensis*. Both species survived until about 50,000 to 60,000 years ago, meaning they may have lived in the region at the same time as modern humans.

Recently, scientists have detected signs that extinct groups of humans not only overlapped timewise but also had sex with the modern humans of maritime Southeast Asia. For example, fossil DNA suggests the ancestors of modern Papuans and South Asians interbred with a southern branch of the mysterious Denisovans, who were close relatives of Neanderthals.

But even though modern people in these regions have relatively high levels of Denisovan DNA, suggesting significant interbreeding, no Denisovan fossils have been found in the region — the only traces of this enigmatic group found so far were a finger bone and jawbone unearthed in Siberia and Tibet.

Now, researchers suggest that either the hobbit *H. floresiensis* or its smaller cousin *H. luzonensis* or both may actually be southern Denisovans. They detailed their findings online March 22 in the journal Nature Ecology and Evolution.

To shed light on the prehistory of maritime Southeast Asia, the study researchers analyzed more than 400 modern human genomes from across the world, including more than 200 from the islands of Southeast Asia and New Guinea.

Scientists hunted specifically for genetic sequences that were significantly different from those usually detected in modern humans, because such DNA may have come from extinct human lineages such as *H. floresiensis* or *H. luzonensis*.

The new study confirmed prior work that found relatively high levels of Denisovan ancestry in people of maritime Southeast Asia, New Guinea and Australia — up to 3% to 6% of their DNA comes from Denisovans.

It did not show evidence of interbreeding between modern humans and older lineages, such as *Homo erectus*.

The researchers also found traces of highly divergent genetic sequences in Denisovan DNA — extracted from specimens found in Siberia — that may have come from very distant relations of modern humans, which might suggest Denisovans could have interbred with an archaic human lineage such as *H. erectus* about 1 million years ago, before Denisovans split into southern and East Asian branches.

So what might these new findings suggest? One possibility is that *H. floresiensis* and *H. luzonensis* are very distant relatives of modern humans as currently thought, evolving from *H. erectus* or a similarly ancient lineage, and that Denisovans are a completely separate lineage. In this scenario, neither of these smaller-sized *Homo* species would have interbred with either Denisovans or modern humans.

Another more extraordinary possibility is that *H. floresiensis* and *H. luzonensis* may differ significantly from modern humans in terms of anatomy, but either or both might be closer relatives of modern humans than often suggested.

In this scenario, these human species might not have differed from modern humans as much genetically as previously thought, explained study author João Teixeira, a population geneticist at the University of Adelaide in Australia.

If so, either or both of these lineages might be examples of southern Denisovans, in which case, they would have interbred with the ancestors of the modern humans of maritime Southeast Asia, potentially explaining the high levels of Denisovan ancestry found in modern people there, he noted.

"Maybe *H. floresiensis* and *H. luzonensis* are not very divergent

super-archaic groups as we currently assume," Teixeira told Live Science.

However, not everyone who was part of the study agreed with that conclusion. Study co-author Chris Stringer, a paleoanthropologist at the Natural History Museum in London, noted archaeological evidence suggested *H. floresiensis* and *H. luzonensis* were living in maritime Southeast Asia since at least 700,000 to 1 million years ago, long before the Denisovan lineage first evolved. Given that, he argued the hobbit and its cousin may be too ancient to be the southern Denisovans.

However, the oldest supposed fossils associated with *H. floresiensis* and *H. luzonensis* in the region may not actually have belonged to these species, Texeira noted.

Instead, those fossils may be traces of an earlier group. So it might still be possible that either *H. floresiensis* or *H. luzonensis* — or both — arrived later to their respective isles and could still potentially be Denisovans.

This suggested connection between hobbits and Denisovans remains uncertain because scientists have yet to successfully analyze DNA from any fossils of *H. floresiensis* or *H. luzonensis*, Teixeira cautioned.

"It's hard for DNA to preserve in the tropics," he said. "At the moment, this idea is only speculation. But *H. floresiensis* and *H. luzonensis* are definitely at the right place at the right time to be southern Denisovans."

To help fill in the missing branches of the human family tree in the islands of Southeast Asia, researchers should not only continue searching for DNA in human fossils from this region, but also look for fossils in other areas such as Australia, Teixeira said.

All in all, Teixeira predicted, "the next big find in human evolution is due to occur in island Southeast Asia."

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Infants' language skills more advanced than first words suggest

Babies can recognize combinations of words even before they have uttered their first word, a study suggests, challenging ideas of how children learn language

Babies can recognise combinations of words even before they have uttered their first word, a study suggests, challenging ideas of how children learn language. Assessments in 11-12 month-olds show that infants at the cusp of talking are already processing multiword phrases such as 'clap your hands'.

Researchers say the study is the first to provide evidence that young children can pick up and understand multiword sequences before they can talk or begin producing such combinations themselves.

The findings suggest that babies learn individual words and more complex phrases at the same time, which challenges the perspective that they progress from single words to phrases and sentences, experts say. It may also explain why adults who learn a new language in later life by focusing on individual words often do not achieve native-like proficiency.

Linguists at the University of Edinburgh assessed 36 infants' language learning behaviour in a series of attention tests using recorded adult speech. They looked at how the babies responded to multiword combinations of three-word sequences used in parent-child conversations. The researchers compared the infants' responses using a testing method called central fixation, which measures infants' looking behaviour in response to sounds.

They assessed if the babies could distinguish more frequently used three-word sequences such as 'clap your hands' from similar but less common phrases such as 'take your hands'.

On average, fixation times were longer for the frequently used phrases. This pattern was found in 23 of the 36 infants.

Researchers say this suggests babies who are still learning their first words are simultaneously learning word combinations.

This development happens months before parents hear their children's first attempts at sequences of words, experts say.

Dr Barbora Skarabela, of the School of Philosophy, Psychology and Languages Sciences, said: "Previous research has shown that young infants recognise many common words. But this is the first study that shows that infants extract and store more than just single words from everyday speech. This suggests that when children learn language, they build on linguistic units of varying sizes, including multiword sequences, and not just single words as we often assume. This may explain why adults learning a second language, who tend to rely on individual words, often fall short of reaching native-like proficiency in the way they string words together into phrases and sentences."

The study is published in Cognition - https://authors.elsevier.com/a/1cYnj2Hx2luLz (doi.org/10.1016/j.cognition.2021.104612).

Researchers at the Hebrew University of Jerusalem contributed to the study.

https://bit.ly/3ulN2zj

People living 100,000 years ago spent time collecting crystals

A cache of beautiful crystals collected 105,000 years ago in South Africa is shedding new light on the emergence of complex behaviours in our species.

By Alison George

A team led by Jayne Wilkins at Griffith University, Australia, discovered 22 distinctively shaped white calcite crystals at a site in the Kalahari desert called Ga-Mohana Hill North Rockshelter. “They are little rhomboids, really visually striking,” says Wilkins.

These geometric crystals didn’t originate at the site and haven’t been modified, so seem to have been deliberately collected and brought to the rock shelter for ornamental purposes. “They don’t seem to have been used for everyday tasks,” she says.

The collection of beautiful items seems like a normal thing for humans to do today, but this so-called symbolic behaviour only emerged around 100,000 years ago. “Collecting these kinds of pretty objects for non-utilitarian reasons could have its roots in symbolism and arts and culture,” says Wilkins.

Calcite crystals collected by humans more than 100,000 years ago **Jayne Wilkins**

Also found at the site were 42 fragments of burnt ostrich egg shell. The large egg shells may have been used by humans to store and transport water – offering more evidence of human innovation.

These discoveries in the Kalahari, 600 kilometres from the sea, are challenging the prevailing assumption that the emergence of complex behaviours like symbolism and technological innovation emerged at the coast, where humans had access to seafood containing nutrients thought to support brain growth.

Until now, the earliest evidence of symbolic behaviour was found at sites close to the sea, such as 100,000-year-old engraved ochre from Blombos cave and 60,000-year-old decorated ostrich egg shells from the Diepkloof rock shelter, both on the South African coast.

“In the Kalahari, which is really far from the coast, we are seeing the same kinds of behaviours, at the same time,” says Wilkins.

Journal reference: Nature, DOI: 10.1038/s41586-021-03419-0

https://bit.ly/3wk7lPk

Study provides first evidence of DNA collection from air

Researchers from Queen Mary University of London have shown for the first time that animal DNA shed within the environment can be collected from the air.

The proof-of-concept study, published in the journal *PeerJ*, opens up potential for new ecological, health and forensic applications of environmental DNA (eDNA), which to-date has mainly been used to survey aquatic environments.

Living organisms such as plants and animals shed DNA into their surrounding environments as they interact with them. In recent years, eDNA has become an important tool to help scientists identify species found within different environments. However, whilst a range of environmental samples, including soil and air, have been proposed as sources of eDNA until now most studies have focused on the collection of eDNA from water.

In this study, the researchers explored whether eDNA could be collected from air samples and used to identify animal species. They first took air samples from a room which had housed naked mole-rats, a social rodent species that live in underground colonies, and then used existing techniques to check for DNA sequences within the sampled air.

Using this approach, the research team showed that airDNA sampling could successfully detect mole-rat DNA within the animal's housing and from the room itself. The scientists also found human DNA in the air samples suggesting a potential use of this sampling technique for forensic applications.

Dr Elizabeth Clare, Senior Lecturer at Queen Mary University of London and first author of the study, said: "The use of eDNA has become a topic of increasing interest within the scientific community particularly for ecologists or conservationists looking for efficient and non-invasive ways to monitor biological environments. Here we provide the first published evidence to show that animal eDNA can be collected from air, opening up further opportunities for investigating animal communities in hard to reach environments such as caves and burrows."

The research team are now working with partners in industry and the third sector, including the company NatureMetrics, to bring some of the potential applications of this technology to life. Dr Clare added: "What started off as an attempt to see if this approach could be used for ecological assessments has now become much more, with potential applications in forensics, anthropology and even medicine."

"For example, this technique could help us to better understand the transmission of airborne diseases such as Covid-19. At the moment social distancing guidelines are based on physics and estimates of how far away virus particles can move, but with this technique we could actually sample the air and collect real-world evidence to support such guidelines."

The project was supported by Queen Mary's Impact Acceleration Accounts (IAAs), strategic awards provided to institutions by UK Research and Innovation (UKRI) that support knowledge exchange (KE) and help researchers generate impact from their research.

** Research publication: 'eDNAir: proof of concept that animal DNA can be collected from air sampling' Elizabeth L Clare, Chloe Economou, Chris G Faulkes, James D Gilbert, Frances Bennett, Rosie Drinkwater, Joanne E Littlefair, PeerJ.*

** A supporting video is available here: https://www.youtube.com/watch?v=YhUPIx4fiGc*

https://bit.ly/3umKXTN

Teens fully protected by Pfizer's COVID-19 vaccine, company says

Vaccinated adolescents had higher levels of neutralizing antibodies than older groups.

Beth Mole

Adolescents ages 12 to 15 were completely protected from symptomatic COVID-19 after being vaccinated with the Pfizer/BioNTech mRNA vaccine in a small Phase III clinical trial, Pfizer reported in a press release Wednesday.

The company also said that the vaccine was well-tolerated in the age group, spurring only the standard side effects seen in people ages 16 to 25. The vaccine is already authorized for use in people

age 16 and over.

The vaccine appeared more effective at spurring defensive immune responses in adolescents ages 12 to 15 than in the 16- to 25-year-old group, producing even higher levels of antibodies that were able to neutralize SARS-CoV-2. In a measure of neutralizing antibodies, vaccinated youths in the new trial had geometric mean titers (GMTs) of 1,239.5, compared with the GMTs of 705.1 previously seen in those ages 16 to 25, Pfizer noted.

The trial involved 2,260 adolescents ages 12 to 15, of which 1,131 were vaccinated and 1,129 received a placebo. There were 18 cases of symptomatic COVID-19 in the trial, all of which were in the placebo group. In today's press release, the company trumpeted that the vaccine demonstrated "100 percent efficacy." The trial was not primarily designed to assess efficacy, however. It was primarily assessing relative immune responses, so it will require more data to fully evaluate efficacy. Additionally, Pfizer and BioNTech have only released top-line trial results, not the full data from the trial, which has not been peer-reviewed.

Last year, a Phase III trial involving more than 46,000 people found the vaccine to be 95 percent effective at preventing symptomatic COVID-19 in adults.

The hardy immune responses and demonstrated protection in the new adolescent trial are positive signs. Pfizer and BioNTech are now planning to submit the data to the US Food and Drug Administration, as well as regulators in the European Union, to expand use of the vaccine to adolescents.

"We share the urgency to expand the authorization of our vaccine to use in younger populations and are encouraged by the clinical trial data from adolescents between the ages of 12 and 15," Albert Bourla, Pfizer's CEO, said in the press release. "We plan to submit these data to FDA as a proposed amendment to our Emergency Use Authorization in the coming weeks and to other regulators around the world, with the hope of starting to vaccinate this age group before the start of the next school year."

Last week, the companies announced the start of trials looking at safety and immune responses in infants and children ages 6 months to 11 years. The trial splits the children into three groups: ages 6 months to 2 years, 2 to 5 years, and 5 to 11 years. First doses went to children in the 5- to 11-year-old group last week, and the companies plan to start the 2- to 5-year group next week.

https://bit.ly/3uouP4d

In search of the first bacterium

Introducing the ancient cell named 'LBCA'

by Arne Claussen, Heinrich-Heine University Duesseldorf

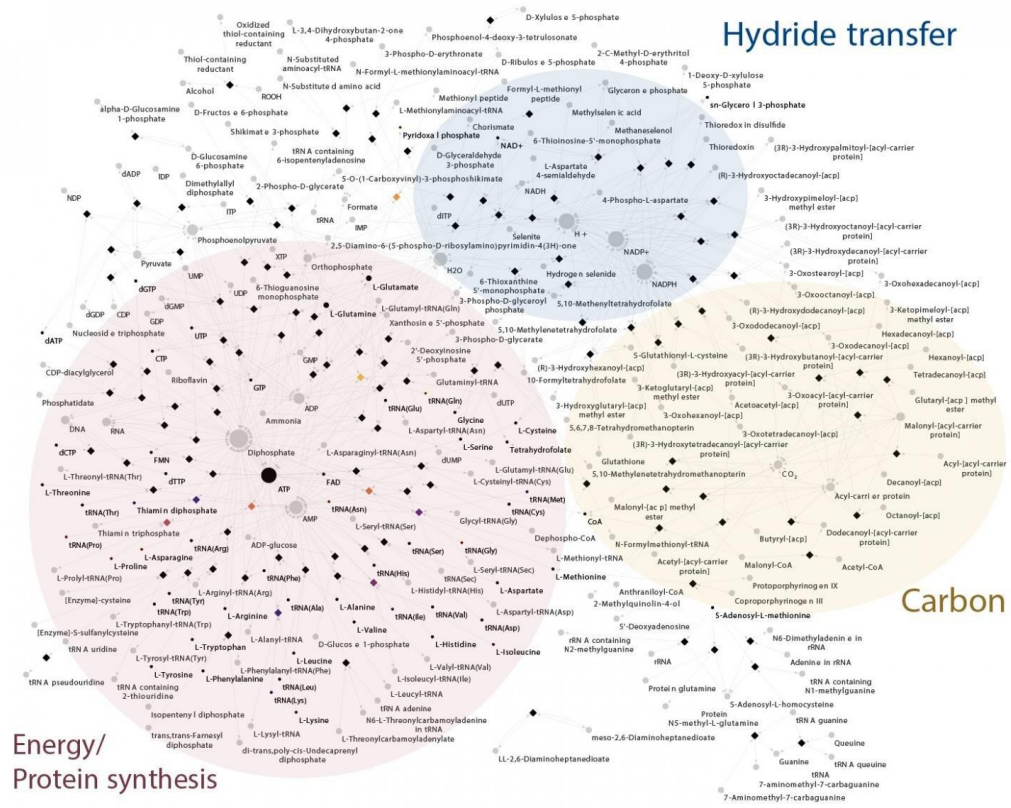
Roughly five years ago, Institute Head Prof. Dr. William (Bill) Martin and his team introduced the last universal common ancestor of all living organisms and named it 'LUCA.' It lived approximately 3.8 billion years ago in hot deep sea hydrothermal vents.

Now the evolutionary biologists in Duesseldorf have described a further ancient cell named 'LBCA' (last bacterial common ancestor). It is the ancestor of today's largest domain of all living organisms: Bacteria. In *Communications Biology*, they report on their new research approaches which led to the successful prediction of the biochemistry of LBCA and its phylogenetic links.

Bacteria are almost as old as life itself. LBCA lived around 3.5 billion years ago in a similar environment to LUCA. In order to unlock LBCA's genetic code, its properties and its story, the research team examined the genomes of 1,089 bacterial anaerobes or bacteria that survive without oxygen. "Abandoning aerobes made sense for our work", explains first author Dr. Joana C. Xavier. "If bacteria originated at a time when the Earth was anoxic, it does not make sense to investigate their origin considering species full of adaptations caused by oxygen."

Higher life forms pass on their genetic code from parent to

offspring via vertical gene transfer. As a result, the genome provides information on phylogenetic history. But bacteria are masters in another form of gene transfer, namely lateral gene transfer (LGT). This allows bacteria to exchange genetic information across different strains. This posed a major challenge in reconstructing the LBCA genome, as it renders the traditional phylogenetic methods incapable of inferring the root in the bacterial evolutionary tree.



The metabolic network of the last bacterial common ancestor, LBCA. The small circles are metabolites or compounds; the diamonds are reactions. Arrows indicate the flow of compounds to and from reactions. Three large functional modules of the network are highlighted as large regions. Credit: HHU / Joana Xavier

For this reason, the researchers in Duesseldorf used biochemical networks together with thousands of individual trees. They investigated 1,089 anaerobic genomes and identified 146 protein families conserved in all bacteria. These proteins make up a nearly complete core metabolic network.

To complete LBCA's biochemistry, just nine further genes had to be added for the reconstructed metabolic network to include all essential and universal metabolites. To be fully independent and self-generated, LBCA's network would still require further genes inherited from the last universal common ancestor, LUCA, and nutrients from the environment.

With LBCA's metabolic network in hand, the authors then used statistical methods to determine which of the modern bacterial groups are most similar to LBCA. They did this using a method called Minimal Ancestor Deviation, MAD, previously developed by one of the co-authors, Fernando D. K. Tria: "The analyses revealed that the earliest branch of Bacteria to diverge was most similar to modern Clostridia, followed closely by Deltaproteobacteria, Actinobacteria and some members of Aquifex. In common, these groups have the acetyl-CoA pathway for carbon fixation and/or energy metabolism."

Prof. William Martin, senior author of the study, explains: "This is the only carbon fixation pathway present in both archaea and bacteria and that traces to LUCA. This result, obtained independently, is also in line with our most recent findings on the origin and early evolution of life in hydrothermal vents."

"We can infer with confidence that LBCA was most likely rod-shaped", says Xavier. "If it was similar to Clostridia, it is possible that LBCA was able to sporulate." This hypothesis was recently laid out by other researchers "and is highly compatible with our results", says Xavier. Forming spores would allow early cells to survive the inhospitable environment of the early Earth.

More information: *Joana C. Xavier et al, The metabolic network of the last bacterial common ancestor, Communications Biology (2021).* [DOI: 10.1038/s42003-021-01918-4](https://doi.org/10.1038/s42003-021-01918-4)
Journal information: [Communications Biology](https://www.nature.com/commsbio/)

https://bit.ly/2PnEN77

Flowers!

How the Chicxulub impactor gave rise to modern rainforests

Tropical rainforests today are biodiversity hotspots and play an important role in the world's climate systems. A new study published today in *Science* sheds light on the origins of modern rainforests and may help scientists understand how rainforests will respond to a rapidly changing climate in the future.

The study led by researchers at the Smithsonian Tropical Research Institute (STRI) shows that the asteroid impact that ended the reign of dinosaurs 66 million years ago also caused 45% of plants in what is now Colombia to go extinct, and it made way for the reign of flowering plants in modern tropical rainforests.

"We wondered how tropical rainforests changed after a drastic ecological perturbation such as the Chicxulub impact, so we looked for tropical plant fossils," said Mónica Carvalho, first author and joint postdoctoral fellow at STRI and at the Universidad del Rosario in Colombia. "Our team examined over 50,000 fossil pollen records and more than 6,000 leaf fossils from before and after the impact."

In Central and South America, geologists hustle to find fossils exposed by road cuts and mines before heavy rains wash them away and the jungle hides them again. Before this study, little was known about the effect of this extinction on the evolution of flowering plants that now dominate the American tropics.

Carlos Jaramillo, staff paleontologist at STRI and his team, mostly STRI fellows--many of them from Colombia--studied pollen grains from 39 sites that include rock outcrops and cores drilled for oil exploration in Colombia, to paint a big, regional picture of forests before and after the impact. Pollen and spores obtained from rocks older than the impact show that rainforests were equally dominated by ferns and flowering plants. Conifers, such as relatives of the of the Kauri pine and Norfolk Island pine, sold in supermarkets at Christmas time (Araucariaceae), were common and cast their shadows over dinosaur trails. After the impact, conifers disappeared almost completely from the New World tropics, and flowering plants took over. Plant diversity did not recover for around 10 million years after the impact.

Leaf fossils told the team much about the past climate and local environment. Carvalho and Fabiany Herrera, postdoctoral research associate at the Negaunee Institute for Conservation Science and Action at the Chicago Botanic Garden, led the study of over 6,000 specimens. Working with Scott Wing at the Smithsonian's National Museum of Natural History and others, the team found evidence that pre-impact tropical forest trees were spaced far apart, allowing light to reach the forest floor. Within 10 million years post-impact, some tropical forests were dense, like those of today, where leaves of trees and vines cast deep shade on the smaller trees, bushes and herbaceous plants below. The sparser canopies of the pre-impact forests, with fewer flowering plants, would have moved less soil water into the atmosphere than did those that grew up in the millions of years afterward.

"It was just as rainy back in the Cretaceous, but the forests worked differently." Carvalho said.

The team found no evidence of legume trees before the extinction event, but afterward there was a great diversity and abundance of legume leaves and pods. Today, legumes are a dominant family in tropical rainforests, and through associations with bacteria, take nitrogen from the air and turn it into fertilizer for the soil. The rise of legumes would have dramatically affected the nitrogen cycle.

Carvalho also worked with Conrad Labandeira at the Smithsonian's

National Museum of Natural History to study insect damage on the leaf fossils.

"Insect damage on plants can reveal in the microcosm of a single leaf or the expanse of a plant community, the base of the trophic structure in a tropical forest," Labandeira said. "The energy residing in the mass of plant tissues that is transmitted up the food chain--ultimately to the boas, eagles and jaguars--starts with the insects that skeletonize, chew, pierce and suck, mine, gall and bore through plant tissues. The evidence for this consumer food chain begins with all the diverse, intensive and fascinating ways that insects consume plants."

"Before the impact, we see that different types of plants have different damage: feeding was host-specific," Carvalho said. "After the impact, we find the same kinds of damage on almost every plant, meaning that feeding was much more generalistic."

How did the after effects of the impact transform sparse, conifer-rich tropical forests of the dinosaur age into the rainforests of today--towering trees dotted with yellow, purple and pink blossoms, dripping with orchids? Based on evidence from both pollen and leaves, the team proposes three explanations for the change, all of which may be correct. One idea is that dinosaurs kept pre-impact forests open by feeding and moving through the landscape. A second explanation is that falling ash from the impact enriched soils throughout the tropics, giving an advantage to the faster-growing flowering plants. The third explanation is that preferential extinction of conifer species created an opportunity for flowering plants to take over the tropics.

"Our study follows a simple question: How do tropical rainforests evolve?" Carvalho said. "The lesson learned here is that under rapid disturbances--geologically speaking--tropical ecosystems do not just bounce back; they are replaced, and the process takes a really long time."

The Smithsonian Tropical Research Institute, headquartered in Panama City, Panama, is a unit of the Smithsonian Institution. The institute furthers the understanding of tropical biodiversity and its importance to human welfare, trains students to conduct research in the tropics and promotes conservation by increasing public awareness of the beauty and importance of tropical ecosystems. Promo video.

Reference: Carvalho, M.R., Jaramillo, C., de la Parra, F., et al. 2021. Extinction at the end-Cretaceous and the origin of modern neotropical rainforests. Science.

The authors of this paper are affiliated with STRI in Panama, the Universidad del Rosario Bogota, Colombia; The Université de Montpellier, CNRS, EPHE, IRD, France; Universidad de Salamanca, Spain; the Instituto Colombiano del Petróleo, Bucaramanga, Colombia; the Chicago Botanic Garden; National Museum of Natural History, Washington, D.C.,; University of Florida, U.S.; Universidade Federal de Mato Grosso, Cuiabá, Brazil; ExxonMobil Corporation, Spring, Texas, U.S.; Centro Científico Tecnológico-CONICET, Mendoza, Argentina; Universidad de Chile, Santiago; University of Maryland, College Park, U.S.; Capital Normal University, Beijing, China; Corporación Geológica Ares, Bogota, Colombia; Paleoflora Ltda., Zapatoca, Colombia; University of Houston, Texas, U.S.; Instituto Amazónico de Investigaciones Científicas SINCHI, Leticia, Colombia; Universidad Nacional de Colombia, Medellín, Colombia; Boise State University, Boise, Idaho, U.S.; BP Exploration Co. Ltd., UK; and University of Fribourg, Switzerland.

https://bit.ly/3cLkpWc

Factory mix-up spoils 15 million doses of J&J COVID vaccine

The error at a manufacturing facility will delay future shipments of the vaccine.

Beth Mole

About 15 million doses of Johnson & Johnson's one-shot COVID-19 vaccine were ruined, and future vaccine shipments will be delayed. This all follows a mix-up at a manufacturing facility in Baltimore, according to multiple media reports.

Johnson & Johnson had partnered with Emergent BioSolutions to manufacture the active ingredient of its vaccine. But according to two US officials who spoke with Politico, workers at the West Baltimore facility mixed up the ingredients in Johnson &Johnson's vaccine with those for a different coronavirus vaccine. Emergent BioSolutions is also a manufacturing partner of AstraZeneca, according to The New York Times, which first reported the

problem.

The mishap with Johnson & Johnson's vaccine began before the Food and Drug Administration had authorized the facility to produce the vaccine. Now, that authorization has been delayed, and shipments are stalled.

In a statement Wednesday, Johnson & Johnson acknowledged the problem but noted that none of the vaccines in use are affected. The company explained that a "quality control process identified one batch of drug substance that did not meet quality standards at Emergent Biosolutions... This batch was never advanced to the filling and finishing stages of our manufacturing process." The vaccines currently in use in the US were manufactured in the Netherlands, according to the Times.

In light of the error, the Biden administration has asked Johnson & Johnson to step up oversight of manufacturing at the Emergent BioSolutions facility. But getting the facility up to regulatory standards could take days or weeks, a senior administration official told Politico.

The delay is significant for Johnson & Johnson, which has struggled to ramp up production of its vaccine. The company barely met its pledge to provide 20 million doses by the end of March, Politico notes. Yet, accelerated production by Johnson & Johnson is critical to the Biden administration's plans to have enough vaccine available by the end of May to immunize every adult in the country. For now, Johnson & Johnson is planning to have 100 million doses delivered by that time.

White House officials are now hedging their projections for vaccine deliveries to states. In a call to governors Tuesday, White House coronavirus coordinator Jeff Zients forecasted shipments of Pfizer and Moderna vaccines but cautioned that deliveries from Johnson & Johnson could fluctuate.

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COVID-19 survivors might need just one dose of two-part vaccine

Cedars-Sinai research involving more than 260 individuals supports earlier findings from small studies about efficacy of single vaccine dose for those with prior coronavirus infections; further study needed

LOS ANGELES - A single dose of the Pfizer-BioNTech vaccine for individuals who previously had COVID-19 generates an immunologic response similar to that of individuals receiving the two-dose recommended sequence, according to a Cedars-Sinai study published today by the journal *Nature Medicine*.

"Our findings extend those from smaller studies reported elsewhere and support a potential strategy of providing a single dose of vaccine to persons with a confirmed prior history of coronavirus infection, along with two doses for people not previously infected," said Susan Cheng, MD, MPH, MMSc, associate professor of Cardiology and director of Public Health Research at the Smidt Heart Institute at Cedars-Sinai. "This approach could maximize the reach of a limited vaccine supply, allowing potentially millions more people to be vaccinated in the U.S. alone."

The vaccine that was studied, produced by Pfizer Inc. and BioNTech SE, normally is administered in two doses, 21 days apart, to provide nearly full protection against the novel coronavirus, known as SARS-CoV-2.

The Cedars-Sinai research strongly suggests the second dose may not be needed for individuals who have successfully recovered from a prior coronavirus infection.

"Overall, individuals who had recovered from COVID-19 developed an antibody response after a single vaccine dose that was comparable to that seen after a two-dose vaccination course administered to individuals without prior infections," said Kimia

Sobhani, PhD, medical director of the clinical core laboratories and associate professor of Pathology and Laboratory Medicine at Cedars-Sinai. "It appears that a single booster dose given to previously infected individuals offers the same benefit as two doses given to people without prior infection." Sobhani and Cheng, along with Jonathan Braun, MD, PhD, professor of Medicine at the F. Widjaja Foundation Inflammatory Bowel and Immunobiology Research Institute at Cedars-Sinai, co-senior-authored this study.

For their research, the investigators administered surveys to 1,090 healthcare workers in the Cedars-Sinai Health System who had received the Pfizer-BioNTech vaccine. The surveys asked the workers about prior coronavirus infections and any symptoms they might have experienced after being vaccinated.

The healthcare workers also took antibody tests to gauge the response of their immune systems to the vaccinations. Antibody levels were measured at three points in time: before or up to three days after the first dose, within seven to 21 days after the first dose, and within seven to 21 days after the second dose.

Based on the surveys, the research team identified 35 individuals with prior coronavirus infections who had received a single vaccine dose and 228 individuals without prior infection who had received both vaccine doses. Based on the antibody tests, the team found that levels and responses of coronavirus-specific antibodies were similar in both of these groups.

Post-vaccine symptoms were more prominent for those with prior infection after the first dose, but symptomatology was similar between the two groups after the second dose.

The investigators said their study had limitations and that more research will be needed to confidently guide vaccine policy.

They noted that they measured antibody levels only up to 21 days following each vaccine dose and that longer-term follow-up likely would provide additionally informative data, especially regarding the duration of the immunity acquired from receiving a single versus double dose of the vaccine.

They also noted that even larger cohort samples will be needed to examine differences across demographic and clinical subgroups that are known to exhibit variation in antibody response following vaccination. More studies also are needed to determine if the results seen after a single dose of the Pfizer-BioNTech vaccine might also apply to other SARS-CoV-2 vaccines, they added.

The vaccine study and related research are part of the Coronavirus Risk Associations and Longitudinal Evaluation (CORALE) study conducted by a network of clinicians and scientists from multiple institutions, primarily in Southern California. The network receives support from the National Cancer Institute of the National Institutes of Health as part of the National Serological Sciences Network, an initiative to advance knowledge of immunology and COVID-19 in the U.S. Cedars-Sinai is one of eight institutions that have been awarded NCI grants to conduct multiple research projects for the initiative.

Funding: *Research reported in this publication was supported in part by Cedars-Sinai, the Erika J. Glazer Family Foundation, the F. Widjaja Family Foundation, the Helmsley Charitable Trust, the National Institutes of Health under grant number K23-HL1538 and the National Cancer Institute of the National Institutes of Health under grant number U54-CA260591-01.*

Competing interests: *John C. Prosko, Edwin C. Frias and James L. Stewart work for Abbott Diagnostics, a company that performed the serological assays on the biospecimens that were collected for this study. The remaining authors have no competing financial interests.*

https://wb.md/3miCxK1

Six Pregnancy Complications Flag Later Heart Disease Risk

Six pregnancy-related complications increase a woman's risk of developing risk factors for cardiovascular disease (CVD) and subsequently developing CVD, the American Heart Association (AHA) says in a new scientific statement.

Megan Brooks

They are hypertensive disorders of pregnancy, preterm delivery, gestational diabetes, small-for-gestational-age (SGA) delivery, placental abruption (abruptio placentae), and pregnancy loss.

A history of any of these adverse pregnancy outcomes should

prompt "more vigorous primordial prevention of CVD risk factors and primary prevention of CVD," the writing group says.

"Adverse pregnancy outcomes are linked to women having hypertension, diabetes, abnormal cholesterol, and cardiovascular disease events, including heart attack and stroke, long after their pregnancies," Nisha I. Parikh, MD, MPH, chair of the writing group, said in a news release.

Adverse pregnancy outcomes can be a "powerful window" into CVD prevention "if women and their healthcare professionals harness the knowledge and use it for health improvement," said Parikh, associate professor of medicine in the Cardiovascular Division at the University of California San Francisco.

The statement was published online March 29 in the journal *Circulation*.

For the scientific statement, the writing group reviewed the latest scientific literature on adverse pregnancy outcomes and CVD risk.

The evidence in the literature linking adverse pregnancy outcomes to later CVD is "consistent over many years and confirmed in nearly every study we examined," Parikh said. Among their key findings:

- Gestational hypertension is associated with an increased risk ***of CVD later in life by 67% and the odds of stroke by 83%. Moderate and severe preeclampsia is associated with a more than twofold increase in the risk for CVD.***
- ***Gestational diabetes is associated with an increase in the risk for CVD by 68% and the risk of developing type 2 diabetes after pregnancy by 10-fold.***
- ***Preterm delivery (before 37 weeks) is associated with double the risk of developing CVD and is strongly associated with later heart disease, stroke and CVD.***
- ***Placental abruption is associated with an 82% increased risk for CVD.***
- ***Stillbirth is associated with about double the risk for CVD.***

"This statement should inform future prevention guidelines in terms of the important factors to consider for determining women's risk for heart diseases and stroke," Parikh added.

The statement emphasizes the importance of recognizing these adverse pregnancy outcomes when evaluating CVD risk in women but notes that their value in reclassifying CVD risk may not be established.

It highlights the importance of adopting a heart-healthy diet and increasing physical activity among women with any of these pregnancy-related complications starting right after childbirth and continuing across the life span to decrease CVD risk.

Lactation and breastfeeding may lower a woman's later cardiometabolic risk, the writing group notes.

"Golden Year of Opportunity"

The statement highlights several opportunities to improve transition of care for women with adverse pregnancy outcomes and to implement strategies to reduce their long-term CVD risk.

One strategy is longer postpartum follow-up care, sometimes referred to as the "fourth trimester," to screen for CVD risk factors and provide CVD prevention counseling.

Another strategy involves improving the transfer of health information between ob/gyns and primary care physicians to eliminate inconsistencies in electronic health record documentation, which should improve patient care.

A third strategy is obtaining a short and targeted health history for each woman to confirm if she has any of the six pregnancy-related complications.

"If a woman has had any of these adverse pregnancy outcomes, consider close blood pressure monitoring, type 2 diabetes and lipid screening, and more aggressive risk factor modification and CVD prevention recommendations," Parikh advised.

"Our data lends support to the prior AHA recommendation that

these important adverse pregnancy outcomes should be 'risk enhancers' to guide consideration for statin therapy aimed at CVD prevention in women," Parikh added.

In a commentary in the journal *Circulation*, Eliza C. Miller, MD, assistant professor of neurology at Columbia University, notes that pregnancy and the postpartum period are a critical time window in a woman's life to identify CVD risk and improve a woman's health trajectory.

"The so-called 'Golden Hour' for conditions such as sepsis and acute stroke refers to a critical time window for early recognition and treatment, when we can change a patient's clinical trajectory and prevent severe morbidity and mortality," writes Miller.

"Pregnancy and the postpartum period can be considered a 'Golden Year' in a woman's life, offering a rare opportunity for clinicians to identify young women at risk and work with them to improve their cardiovascular health trajectories," she notes.

This scientific statement was prepared by the volunteer writing group on behalf of the AHA Council on Epidemiology and Prevention; the Council on Arteriosclerosis, Thrombosis and Vascular Biology; the Council on Cardiovascular and Stroke Nursing; and the Stroke Council.

The authors of the scientific statement have disclosed no relevant financial relationships. Miller received personal compensation from Finch McCranie, LLP and Argionis & Associates, LLC for expert testimony regarding maternal stroke; and personal compensation from Elsevier, Inc for editorial work on Handbook of Clinical Neurology, Vols 171 and 172 (Neurology of Pregnancy).

Circulation. Published online March 29, 2021. Full text, Editorial

https://bit.ly/3wnsc4j

Think twice before you ice after an injury

Applying ice to a sprained ankle or wrist decreases blood flow to the area for longer than previously thought

Margaux Lopez

It is common practice to apply an ice pack to a sprained ankle or a sore muscle, and many professional athletes have been reported to use cryotherapy to aid with recovery. However, the benefits of the well-known RICE protocol (rest, ice, compression, and elevation) for injuries and sore muscles have been thoroughly debunked, including by the doctor that originally coined the term four decades ago. While icing an injury does effectively relieve pain, it also constricts blood vessels and reduces blood flow to the cold area. Even though the injury feels better, this impairs the body's ability to heal, extending the recovery process.

But what happens after the ice is removed? In a recent study, scientists hypothesized that once the area warmed up, there would be a large temporary increase in blood flow, aiding in the healing process. This "rebound" phenomenon has been observed after things like removing a tourniquet or unclamping an artery during surgery, but hadn't been studied for restrictions due to cold temperatures.

The researchers found that using ice, compression, and elevation therapy on a muscle immediately after exercise led to significantly reduced blood flow as expected, but instead of bouncing back immediately after treatment, the blood flow remained low for an extended period of time. While we already knew that ice impairs muscle recovery even though it's great for reducing pain, now we can add that the negative effects last longer than previously hypothesized, suggesting that injured athletes should think twice before using ice as pain relief.

https://bit.ly/3fINhA7

Woman gives birth to twins conceived three weeks apart

A woman in England became pregnant while already pregnant.

By Yasemin Saplakoglu - Staff Writer

A woman in England became pregnant while already pregnant, ultimately giving birth to rare twins conceived three weeks apart, according to recent news reports.

Typically, when a woman becomes pregnant, her body kick-starts

several biological processes aimed at preventing a concurrent pregnancy, including releasing hormones to stop ovulation. But in rare instances, a pregnant woman could continue to ovulate, or release an egg, and that egg could then be fertilized by sperm and implanted in the uterus, Live Science previously reported. This rare phenomenon, in which two fertilized eggs are implanted in the uterus at different times, is known as "superfetation."

In this new case, the twins were conceived three weeks apart, according to Good Morning America. The mother, Rebecca Roberts, was 39 years old and became pregnant for the first time last year after trying to conceive for several years and taking fertility medication.

At 12 weeks gestation, doctors discovered a second baby in an ultrasound that had a three-week size difference from the first baby. Because superfetation is so rare, at first Roberts' doctors could not explain the size difference between the two babies.

"My initial reaction was how had I missed the second twin," Dr. David Walker, an OB-GYN at Royal United Hospital in Bath, told Good Morning America. "And following this [I] was slightly relieved that it was not my mistake but a quite extraordinary pregnancy."

The doctors diagnosed Roberts with superfetation and told her that the younger baby might not survive. When Roberts was 33 weeks pregnant, last September, the doctors induced labor because the younger twin, Rosalie, stopped growing properly due to a problem with the umbilical cord.

The older twin, Noah, stayed in a neonatal intensive care unit (NICU) for three weeks, and Rosalie stayed for 95 days. Both infants are now home and healthy.

"When we lay them down next to each other, it's like they instantly know — and they reach out and touch each other's faces, and it's just the most beautiful thing," Roberts told Good Morning America. "Twins have an amazing bond anyways, but the story between these two, when they're old enough to find out, they'll feel even more special."

It's not clear how many cases of superfetation occur; many cases may go undetected because the fetuses are so close in age, and thus size, that they're thought to be ordinary twins, according to the Live Science report. Most known cases of superfetation involve patients who used assisted reproductive techniques such as in vitro fertilization, according to Healthline.

Still, the phenomenon is thought to be extremely rare, because three separate, improbable events must take place for it to occur: ovulation (which is usually stopped by pregnancy hormones), fertilization (which is usually stopped early in pregnancy when a "mucus plug" forms to stop the sperm from passing through the cervix) and implantation (which requires enough space for another embryo in the uterus, as well as hormones that normally wouldn't be released once someone is already pregnant), according to Healthline. But in other animals — such as fish, hares and badgers — superfetation is actually common.

https://bit.ly/31Jtnqt

Sunlight Inactivates Coronavirus 8 Times Faster Than Predicted. We Need to Know Why

A team of scientists is calling for greater research into how sunlight inactivates SARS-CoV-2 after realizing there's a glaring discrepancy between the most recent theory and experimental results.

Tessa Koumoundouros

UC Santa Barbara mechanical engineer Paolo Luzzatto-Fegiz and colleagues noticed the virus was inactivated as much as eight times faster in experiments than the most recent theoretical model predicted. "The theory assumes that inactivation works by having UVB hit the RNA of the virus, damaging it," explained Luzzatto-

Fegiz.

But the discrepancy suggests there's something more going on than that, and figuring out what this is may be helpful for managing the virus.

UV light, or the ultraviolet part of the spectrum, is easily absorbed by certain nucleic acid bases in DNA and RNA, which can cause them to bond in ways that are hard to fix.

But not all UV light is the same. Longer UV waves, called UVA, don't have quite enough energy to cause problems. It's the mid-range UVB waves in sunlight that are primarily responsible for killing microbes and putting our own cells at risk of Sun damage.

Short-wave UVC radiation has been shown to be effective against viruses such as SARS-CoV-2, even while it's still safely enveloped in human fluids. But this type of UV doesn't usually come into contact with Earth's surface, thanks to the ozone layer.

"UVC is great for hospitals," said co-author and Oregon State University toxicologist Julie McMurry. "But in other environments – for instance, kitchens or subways – UVC would interact with the particulates to produce harmful ozone."

In July 2020, an experimental study tested the effects of UV light on SARS-CoV-2 in simulated saliva. They recorded the virus was inactivated when exposed to simulated sunlight for between 10-20 minutes. "Natural sunlight may be effective as a disinfectant for contaminated nonporous materials," Wood and colleagues concluded in the paper.

Luzzatto-Feigiz and team compared those results with a theory about how sunlight achieved this, which was published just a month later, and saw the math didn't add up.

This study found the SARS-CoV-2 virus was three times more sensitive to the UV in sunlight than influenza A, with 90 percent of the coronavirus's particles being inactivated after just half an hour of exposure to midday sunlight in summer.

By comparison, in winter light infectious particles could remain intact for days.

Environmental calculations made by a separate team of researchers concluded the virus's RNA molecules are being photochemically damaged directly by light rays.

This is more powerfully achieved by shorter wavelengths of light, like UVC and UVB. As UVC doesn't reach Earth's surface, they based their environmental light exposure calculations on the medium-wave UVB part of the UV spectrum.

"The experimentally observed inactivation in simulated saliva is over eight times faster than would have been expected from the theory," wrote Luzzatto-Feigiz and colleagues. "So, scientists don't yet know what's going on," Luzzatto-Fegiz said.

The researchers suspect it's possible that instead of affecting the RNA directly, long-wave UVA may be interacting with molecules in the testing medium (simulated saliva) in a way that hastens the inactivation of the virus.

Something similar is seen in wastewater treatment – where UVA reacts with other substances to create molecules that damage viruses.

If UVA can be harnessed to combat SARS-CoV-2, cheap and energy-efficient wavelength-specific light sources might be useful in augmenting air filtration systems at relatively low risk for human health. "Our analysis points to the need for additional experiments to separately test the effects of specific light wavelengths and medium composition," Luzzatto-Fegiz concludes.

With the ability of this virus to remain suspended in the air for extended periods of time, the safest means to avoid it in countries where it's running rampant is still social distancing and wearing masks where distancing isn't possible. But it's nice to know that sunlight may be helping us out during the warmer months.

Their analysis was published in *The Journal of Infectious Diseases*.

https://bit.ly/2OjUCeq

Study identifies possible COVID-19 drugs -- including several that are FDA-approved

Promising candidates include widely used transplant-rejection drug cyclosporine

Philadelphia - A team led by scientists in the Perelman School of Medicine at the University of Pennsylvania has identified nine potential new COVID-19 treatments, including three that are already approved by the Food and Drug Administration (FDA) for treating other diseases.

The team, whose findings were published in *Cell Reports*, screened thousands of existing drugs and drug-like molecules for their ability to inhibit the replication of the COVID-19-causing coronavirus, SARS-CoV-2. In contrast to many prior studies, the screens tested the molecules for anti-coronaviral activity in a variety of cell types, including human airway-lining cells that are similar to the ones principally affected in COVID-19.

Of the nine drugs found to reduce SARS-CoV-2 replication in respiratory cells, three already have FDA approval: the transplant-rejection drug cyclosporine, the cancer drug dacomitinib, and the antibiotic salinomycin. These could be rapidly tested in human volunteers and COVID-19 patients.

The experiments also shed light on key processes the coronavirus uses to infect different cells and found that the antiviral drug remdesivir, which has an FDA Emergency Use Authorization for treating COVID-19, does appear to work against the virus in cell-culture tests on respiratory cells, whereas hydroxychloroquine does not.

"Our discoveries here suggest new avenues for therapeutic interventions against COVID-19, and also underscore the importance of testing candidate drugs in respiratory cells," said co-senior author Sara Cherry, PhD, a professor of Pathology and Laboratory Medicine and scientific director of the High-Throughput Screening (HTS) Core at Penn Medicine. Study collaborators included co-senior authors David Schultz, PhD, technical director of the HTS Core, and Holly Ramage, PhD, assistant professor of microbiology & immunology at Thomas Jefferson University.

Although great progress has been made in the development of vaccines and treatments for the SARS-CoV-2 coronavirus, there is still much room for improvement. In the United States, the only antiviral COVID-19 treatments that have received FDA Emergency Use Authorization -- remdesivir and several anti-SARS-CoV-2 antibody preparations -- are expensive and far from 100 percent effective.

For their screening project, Cherry and colleagues assembled a library of 3,059 compounds, including about 1,000 FDA-approved drugs and more than 2,000 drug-like molecules that have shown activity against defined biological targets. They then tested all of these for their ability to significantly inhibit SARS-CoV-2 replication in infected cells, without causing much toxicity.

Initially, they performed antiviral screens using cell types they could grow easily in the lab and infect with SARS-CoV-2, namely African Green Monkey kidney cells, and a cell line derived from human liver cells. With these screens, they identified and validated several compounds that worked in the monkey kidney cells, and 23 that worked in the human liver cells. Hydroxychloroquine, which is used as a malaria drug, and remdesivir, were effective in both cell types.

Since SARS-CoV-2 is mainly a respiratory virus and is thought to initiate infections via airway-lining cells, the researchers sought a respiratory cell type that they could infect experimentally with the virus. They eventually identified a suitable cell line, Calu-3, that is derived from human airway-lining cells. They used these respiratory-derived cells to test the antiviral compounds identified

through the human liver cell screen, and found that only nine had activity in the new cells. The nine did not include hydroxychloroquine. (Remdesivir worked in the Calu-3 cells but was not included in the list because it is already in use against COVID-19.)

By identifying different sets of drugs that work in different cell types, the researchers also shed light on the mechanisms SARS-CoV-2 uses to gain entry to cells. The findings suggest that in kidney and liver cells, the virus uses a mechanism that can be disrupted, for example, by hydroxychloroquine; yet the virus appears to use a different mechanism in respiratory cells, thus explaining hydroxychloroquine's lack of success in those cells -- and in COVID-19 clinical trials.

The nine antivirals active in respiratory cells did include ***salinomycin***, a veterinary antibiotic that is also being investigated as an anticancer drug; the kinase enzyme inhibitor ***dacomitinib***, an anticancer drug; ***bemcentinib***, another kinase inhibitor now being tested against cancers; the antihistamine drug ***ebastine***; and ***cyclosporine***, an immune suppressing drug commonly used to prevent the immune rejection of transplanted organs.

The study highlights cyclosporine as particularly promising, as it appears to works against SARS-CoV-2 in respiratory and non-respiratory cells, and via two distinct mechanisms: inhibiting cell enzymes called cyclophilins, which the coronavirus hijacks to support itself, and suppressing the potentially lethal inflammation of severe COVID-19.

"There may be important benefits to the use of cyclosporine in hospitalized COVID-19 patients, and ongoing clinical trials at Penn and elsewhere are testing that hypothesis," Cherry said.

The research was supported by funding from the National Institutes of Health (5R01AI140539, 1R01AI1502461, R01AI152362), the Mark Foundation, the Dean's Innovation Fund, the Laddie and Linda Montague Foundation, the Burroughs Wellcome Fund, Mercatus, and the Bill and Melinda Gates Foundation.

https://bit.ly/31JcJNQ

Detecting This Specific Gas in an Alien World's Atmosphere May Be a Good Sign of Life

Another potential biosignature we should be on the lookout for is isoprene

by Matt Williams

It is no exaggeration to say that the study of extrasolar planets has exploded in recent decades. To date, 4,375 exoplanets have been confirmed in 3,247 systems, with another 5,856 candidates awaiting confirmation. In recent years, exoplanet studies have started to transition from the process of discovery to one of characterization. This process is expected to accelerate once next-generation telescopes become operational.

As a result, astrobiologists are working to create comprehensive lists of potential "biosignatures," which refers to chemical compounds and processes that are associated with life (oxygen, carbon dioxide, water, etc.) But according to new research by a team from the Massachusetts Institute of Technology (MIT), another potential biosignature we should be on the lookout for is a hydrocarbon called isoprene (C_5H_8).

The study that describes their findings, "Assessment of Isoprene as a Possible Biosignature Gas in Exoplanets with Anoxic Atmospheres," recently appeared online and has been accepted for publication by the journal *Astrobiology*. For the sake of their study, the MIT team looked at the growing list of possible biosignatures that astronomers will be on the lookout for in the coming years.

To date, the vast majority of exoplanets have been detected and confirmed using indirect methods. For the most part, astronomers have relied on the Transit Method (Transit Photometry) and the Radial Velocity Method (Doppler Spectroscopy), alone or in combination. Only a few have been detectable using Direct Imaging, which makes it very difficult to characterize exoplanet atmospheres

and surfaces.

Only on rare occasions have astronomers been able to obtain spectra that allowed them to determine the chemical composition of that planet's atmosphere. This was either the result of light passing through an exoplanet's atmosphere as it transitted in front of its star or in the few cases where Direct Imaging occurred and light reflected from the exoplanet's atmosphere could be studied.

Much of this has had to do with the limits of our current telescopes, which do not have the necessary resolution to observe smaller, rocky planets that orbit closer to their star. Astronomers and astrobiologists believe that it is these planets that are most likely to be potentially habitable, but any light reflected from their surfaces and atmospheres is overpowered by the light coming from their stars.

However, that will change soon as next-generation instruments like the *James Webb Space Telescope* (JWST) takes to space. Sara Seager, the Class of 1941 Professor of Physics and Planetary Sciences at MIT, leads the research group responsible (aka. the Seager Group) and was a co-author on the paper. As she told Universe Today via email: "With the upcoming October 2021 launch of the James Webb Space Telescope we will have our first capability of searching for biosignature gases—but it will be tough because the atmospheric signals of small rocky planet are so weak to begin with. With the JWST on the horizon the number of people working in the field has grown tremendously. Studies such as this one coming up with new potential biosignature gases, and other work showing potential false positives even for gases such as oxygen."

Once it is deployed and operational, the JWST will be able to observe our Universe at longer wavelengths (in the near- and mid-infrared range) and with greatly improved sensitivity. The telescope will also rely on a series of spectrographs to obtain composition data, as well as coronagraphs to block out the obscuring light of parent stars. This technology will enable astronomers to characterize the atmospheres of smaller rocky planets.

In turn, this data will allow scientists to place much tighter constraints on an exoplanet's habitability and could even lead to the detection of known (and/or potential) biosignatures. As noted, these "biosignatures" include the chemical indications associated with life and biological process, not to mention the types of conditions that are favorable to it.

These include oxygen gas (O_2), which is essential to most forms of life on Earth and is produced by photosynthetic organisms (plants, trees, cyanobacteria, etc.). These same organisms metabolize carbon dioxide (CO_2), which oxygen-metabolizing life emits as a waste product. There's also water (H_2O), which is essential to all life as we know it, and methane (CH_4), which is emitted by decaying organic matter.

Since volcanic activity is believed to play an important role in planetary habitability, the chemical byproducts associated with volcanism – hydrogen sulfide (H_2S), sulfur dioxide (SO_2), carbon monoxide (CO), hydrogen gas (H_2), etc. – are also considered biosignatures. To this list, Zhan, Seager, and their colleagues wished to add another possible biosignature – isoprene. As Zhan explained to Universe Today via email: "Our research group at MIT focuses on using a holistic approach to explore all possible gases as potential biosignature gas. Our prior work led to the creation of the all small molecules database. We proceed to filter the ASM database to identify the most plausible biosignature gas candidates, one of which is isoprene, using machine learning and data-driven approaches – Dr. Zhuchang Zhan."

Like its cousin methane, isoprene is an organic hydrocarbon molecule that is produced as a secondary metabolite by various species here on Earth. In addition to deciduous trees, isoprene is

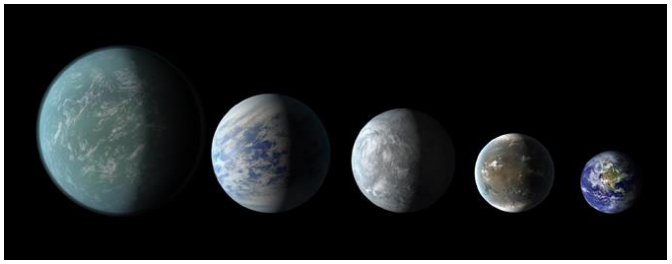
also produced by a diverse array of evolutionary-distant organisms – such as bacteria, plants, and animals. As Seager explained, this makes it promising as a potential biosignature: "Isoprene is promising because it is produced in vast qualities by life on Earth—as much as methane production! Furthermore, a huge variety of life forms (from bacteria to plants and animals), those that are evolutionary distant from each other, produce isoprene, suggesting it might be some kind of key building block that life elsewhere might also make."

While isoprene is about as abundant as methane here on Earth, isoprene is destroyed by interaction with oxygen and oxygen-containing radicals. For this reason, Zhang, Seager, and their team chose to focus on anoxic atmospheres. These are environments that are predominantly composed of H_2, CO_2, and nitrogen gas (N_2), which is similar to what Earth's primordial atmosphere was composed of.

According to their findings, a primordial planet (where life is beginning to emerge) would have abundant isoprene in its atmosphere. This would have been the case on Earth between 4 and 2.5 billion years ago when single-celled organisms were the only life and photosynthetic cyanobacteria were slowly converting Earth's atmosphere into one that was oxygen-rich.

By 2.5 billion years ago, this culminated in the "Great Oxygenation Event" (GOE), which proved toxic to many organisms (and metabolites like isoprene). It was also during this time that complex lifeforms (eukaryotes and multi-celled organisms) began to emerge. In this respect, isoprene could be used to characterize planets that are in the midst of a major evolutionary shift and laying the groundwork for future animal phyla.

But as Zhang noted, teasing out this potential biosignature will be a challenge, even for the JWST: "The caveats with isoprene as a biomarker are that: 1. 10x-100x the Earth's Isoprene production rate is needed for detection; 2. Detecting Near-Infrared isoprene spectral feature can be hindered by the presence of methane or other hydrocarbons. Unique detection of isoprene will be challenging with JWST, as many hydrocarbon molecules share similar spectra features in Near-Infrared wavelengths. But future telescopes that focus on the mid-IR wavelength will be able to detect isoprene spectral features uniquely."



Relative sizes of Kepler habitable zone planets discovered as of 2013 April 18. Left to right: Kepler-22b, Kepler-69c, Kepler-62e, Kepler-62f, and Earth (except for Earth, these are artists' renditions). **Credit: NASA/Ames/JPL-Caltech.**

Beyond the JWST, the *Nancy Grace Roman Space Telescope* (successor to the Hubble mission) will also be taking to space by 2025. This observatory will have the power of "One-Hundred Hubbles" and its recently-upgraded infrared filters will allow it to characterize exoplanets on its own and through collaborations with the JWST and other "great observatories."

There are also several ground-based telescopes currently being built here on Earth that will rely on sophisticated spectrometers, coronographs, and adaptive optics (AOs). These include the Extremely Large Telescope (ELT), the Giant Magellan Telescope (GMT), the Thirty Meter Telescope (TMT) These telescopes will also be able to conduct Direct Imaging studies of exoplanets, and the results are expected to be ground-breaking.

Between improved instruments, rapidly improving data analysis and techniques, and improvements in our methodology, the study of exoplanets is only expected to accelerate further. In addition to

having tens of thousands of more available for study (many of which will be rocky and "Earth-like"), the unprecedented views we will have of them will let us see just how many habitable worlds are out there.

Whether or not this will result in the discovery of extraterrestrial life within our lifetimes remains to be seen. But one thing is clear. In the coming years, when astronomers start combing through all the new data they will have on exoplanet atmospheres, they will have a comprehensive list of biosignatures to guide them.

Seager and Zhan's previous work include a concept for a Martian greenhouse that could provide all the necessary food for a crew of four astronauts for up to two years. This greenhouse, known as the Biosphere Engineered Architecture for Viable Extraterrestrial Residence (BEAVER), took second place in the 2019 NASA BIG Idea Challenge. You can read more about it here.

Further Reading: arXiv

https://bit.ly/3fEMpwr

Cosmic rays causing 30,000 network malfunctions in Japan each year

Most "soft errors" automatically corrected via safety devices, but experts said in some cases they may have led to disruptions.

Cosmic rays are causing an estimated 30,000 to 40,000 malfunctions in domestic network communication devices in Japan every year, a Japanese telecom giant found recently.

Most so-called "soft errors," or temporary malfunctions, in the network hardware of Nippon Telegraph and Telephone Corp. are automatically corrected via safety devices, but experts said in some cases they may have led to disruptions.

It is the first time the actual scale of soft errors in domestic information infrastructures has become evident.

Soft errors occur when the data in an electronic device is corrupted after neutrons, produced when cosmic rays hit oxygen and nitrogen in the earth's atmosphere, collide with the semiconductors within the equipment.

Cases of soft errors have increased as electronic devices with small and high-performance semiconductors have become more common. Temporary malfunctions have sometimes led to computers and phones freezing, and have been regarded as the cause of some plane accidents abroad.

Masanori Hashimoto, professor at Osaka University's Graduate School of Information Science and Technology and an expert in soft errors, said the malfunctions have actually affected other network communication devices and electrical machineries at factories in and outside Japan.

There is a chance that "greater issues" will arise as society's infrastructure becomes "more reliant on electronic devices" that use such technologies as artificial intelligence and automated driving, Hashimoto said.

He emphasized the need for the government and businesses to further research and implement countermeasures.

However, identifying the cause of soft errors and implementing measures against them can be difficult due to them not being reproducible in trials, unlike mechanical failures.

NTT therefore measured the frequency of soft errors through an experiment whereby semiconductors are exposed to neutrons, and concluded there are about 100 errors per day in its domestic servers.

Although NTT did not reveal if network communication disruptions have actually occurred, the company said it was "implementing measures against major issues" and "confirming the quality of the safety devices and equipment design through experiments and presumptions."

https://bit.ly/31OdrJU

When Did Life First Emerge in the Universe?

We don't know, but we could try to find out by searching for it on

planets orbiting the very oldest stars

By Avi Loeb

About 15 million years after the big bang, the entire universe had cooled to the point where the electromagnetic radiation left over from its hot beginning was at about room temperature. In a 2013 paper, I labeled this phase as the "habitable epoch of the early universe." If we had lived at that time, we wouldn't have needed the sun to keep us warm; that cosmic radiation background would have sufficed.

Did life start that early? Probably not. The hot, dense conditions in the first 20 minutes after the big bang produced only hydrogen and helium along with a tiny trace of lithium (one in 10 billion atoms) and a negligible abundance of heavier elements. But life as we know it requires water and organic compounds, whose existence had to wait until the first stars fused hydrogen and helium into oxygen and carbon in their interiors about 50 million years later. The initial bottleneck for life was not a suitable temperature, as it is today, but rather the production of the essential elements.

Given the limited initial supply of heavy elements, how early did life actually start? Most stars in the universe formed billions of years before the sun. Based on the cosmic star formation history, I showed in collaboration with Rafael Batista and David Sloan that life near sunlike stars most likely began over the most recent few billion years in cosmic history. In the future, however, it might continue to emerge on planets orbiting dwarf stars, like our nearest neighbor, Proxima Centauri, which will endure hundreds of times longer than the sun's. Ultimately, it would be desirable for humanity to relocate to a habitable planet around a dwarf star like Proxima Centauri b, where it could keep itself warm near a natural nuclear furnace for up to 10 trillion years into the future (stars are merely fusion reactors confined by gravity, with the benefit of being more stable and durable than the magnetically confined versions that we produce in our laboratories).

As far as we know, water is the only liquid that can support the chemistry of life—but there is much we don't know. Could alternative liquids have existed in the early universe as a result of warming by the cosmic radiation background alone? In a new paper with Manasvi Lingam we show that ammonia, methanol and hydrogen sulfide could exist as liquids just after the first stars formed and that ethane and propane might be liquids somewhat later. The relevance of these substances to life is unknown, but they can be studied experimentally. If we ever succeed in creating synthetic life, as is being attempted in Jack Szostak's laboratory at Harvard University, we could check whether life can emerge in liquids other than water.

One way to determine how early life started in the cosmos is to examine whether it formed on planets around the oldest stars. Such stars are expected to be deficient in elements heavier than helium, which astrophysicists call "metals." (in our language, unlike that of most people, oxygen, for example, is considered a metal). Indeed, metal-poor stars have been discovered in the periphery of the Milky Way, and have been recognized as potential members of the earliest generation of stars in the universe. These stars often exhibit an enhanced abundance of carbon, making them "carbon enhanced metal poor" (CEMP) stars. My former student Natalie Mashian and I suggested that planets around CEMP stars might be made mostly of carbon, so their surfaces could provide a rich foundation for nourishing early life.

We could therefore search for planets that transit, or pass in front of, CEMP stars and show biosignatures in their atmospheric composition. This would allow us to determine observationally how far back in time life may have started in the cosmos, based on the ages of these stars. Similarly, we could estimate the age of interstellar technological equipment that we might discover floating

near Earth (or which might have crashed on the moon), based on long-lived radioactive elements or the extent of scars from impacts of dust particles on its surface.

A complementary strategy is to search for technological signals from early distant civilizations that harnessed enough energy to make them detectable across the vast cosmic scale. One possible signal would be a flash of light from a collimated light beam generated to propel light sails. Others could be associated with cosmic engineering projects, such as moving stars around. Communication signals are not expected to be detectable across the universe, because the signal travel time would require billions of years in each direction and no participant would be patient enough to engage in such a slow exchange of information.

But life's signatures will not last forever. The prospects for life in the distant future are gloomy. The dark and frigid conditions that will result from the accelerated expansion of the universe by dark energy will likely extinguish all forms of life 10 trillion years from now. Until then, we could cherish the temporary gifts that nature had blessed us with. Our actions will be a source of pride for our descendants if they sustain a civilization intelligent enough to endure for trillions of years. Here's hoping that we will act wisely enough to be remembered favorably in their "big history" books.