https://bit.ly/3P6ki8m

Japan Proposes a Wild Concept for Making Artificial Gravity on the Moon

A towering sci-fi space cone, that would stand 400 meters tall and 200 meters across spinning on its axis every 20 seconds

By Jason Dorrier

The list of challenges space explorers will face is formidable. They'll have to produce breathable air, clean water, and food in extremely hostile environments lacking all of the above. They'll also have to peacefully coexist with small groups of fellow explorers in tight quarters for long periods of time, all while minimizing exposure to the searing radiation that's ubiquitous virtually anywhere they go.

Assuming explorers overcome these challenges, there's another that doesn't get the love it deserves, according to researchers at Japan's Kyoto University.

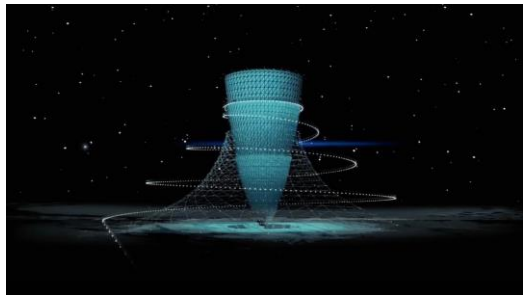


Image Credit: Takuya Ono and Kajima Co. Ltd.

Long-term settlement of Earth orbit, the moon, Mars, and beyond requires explorers forsake Earth's gravity—the steady downward force every Earthly animal has evolved to navigate over billions of years. Studies of astronauts spending weeks or months in microgravity have shown atrophied muscles, bone loss, vision loss, and changes to immune systems. There have, of course, been no studies of humans living on planetary bodies with low-gravity, but it's likely adult explorers would contend with health issues—and how all this might affect childbirth and normal development in kids is unknown.

Assuming some kind of artificial gravity would lessen these risks considerably, Kyoto University partnered with construction company, Kajima Corp, to explore futuristic concepts that might one day offer tourists and settlers a healthy dose of good ol' Earth gravity.

Their far-future vision? A towering sci-fi space cone, called the Glass, that would stand 1,312 feet (400 meters) tall and 656 feet (200 meters) across. This habitat would spin around its axis once every 20 seconds so that people living on its inner walls would enjoy Earth gravity—alongside trees, grass, and a lake that would do MC Escher proud. The plans call for spinning habitats on the moon and Mars, where gravity is notably less than on Earth.

In addition to the habitat itself, the three-part proposal, outlined in a press release and video last week, also sketched out a system for transportation between Earth, Mars, and the moon called Hexatrack, which would include standardized vehicles for travel between habitats on the surface of the planet or moon and base stations in orbit.

Obviously, all this is more of a beautiful concept to solve a real problem than anything remotely practical today.

The sheer size of the endeavor—akin to building the Empire State Building upside-down on the moon or Mars, spinning it like a top, and then layering water, soil, and other internal structures through its interior—would demand huge amounts of resources and technical know-how. And without exceptional design, living in such an environment, where the ground visibly curves at your feet and the the tug of local gravity is at odds with the structure's artificial gravity, could be pretty disorienting. The team envisions our migration to the moon and Mars won't hit its stride until the latter half of this century, but even that timeframe for work on this scale seems optimistic.

For now, the idea is more at home among other futuristic space concepts. Though focused on off-planet living, for example, the vision for O'Neill cylinders, proposed in the mid-70s, came

complete with spin-based gravity, lakes, farmland, and even artificial sunshine. At the moment, though, we're much closer to realizing small, private space bubbles in orbit, like those designed by Axiom Space, than we are to off-Earth megastructures such as these.

Still, as going to space on reusable rockets gets cheaper, and alternative methods of shooting stuff into orbit—like this space catapult—emerge, we may hone our abilities to both build structures and also find, mine, and exploit resources out there. There's an abundance of raw materials for sustaining our presence in space. Eventually, we may begin engineering ever bigger structures in orbit and elsewhere, and wild concepts mooted today, could look a *bit* more realistic.

Regardless, there's little question that bringing some extra gravity with us would help the cause. Maybe someone will build spinning conical towers on the moon—or maybe there'll be a better, more practical alternative by then.

In either case, it's fun to dream.

https://bit.ly/3uSkfoB

Precession Helped Drive Glacial Cycles in the Pleistocene

By studying bits of rock scooped up by ancient glaciers, researchers have pinned down that recent glacial variability was driven, in part, by changes in the direction of Earth's axis of rotation.

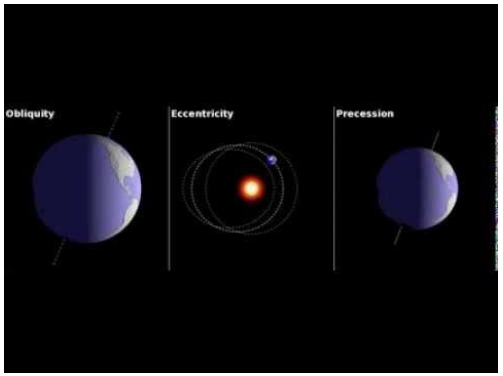
by Katherine Kornei

Ice sheets have ebbed and flowed over Earth's surface for eons. Now scientists have analyzed tiny bits of rock transported by glaciers and gained a better understanding of recent glacial cycles. The team found that precession—gradual changes in the direction of Earth's axis of rotation—has played an important role in the breakup of Northern Hemisphere ice sheets over the past 1.7 million years. And during the late Pleistocene, that precession-driven collapse coincided with deglaciation, the researchers reported in May in *Science*.

Here and Gone, Again and Again

"Over the last million years, there have been seven or eight glacial cycles."

Just 30,000 years ago—a blink in geologic time—significant swaths of Earth's landmasses were covered in glacial ice. That time period was the so-called Last Glacial Maximum, and large ice sheets reigned supreme, said Stephen Barker, a paleoclimatologist at Cardiff University in the United Kingdom. "Where I am here in South Wales, there'd be an ice sheet right next door to me."



But the majority of those ice sheets have since retreated, and the planet is now in an interglacial period. That shift, from a largely ice covered world to one in which ice is sparser, represents a cycle that has repeated many times, said Barker. "Over the last million years, there have been seven or eight glacial cycles."

Eyes on the Sun

The question of what has driven the planet's glacial cycles over the past few million years has long preoccupied scientists. Solar radiation is critically important, researchers have agreed. But the energy received from the Sun at any one point on Earth varies according to two long-term cycles: precession and obliquity. Precession refers to changes in the direction of Earth's axis of rotation, and obliquity is the tilt of Earth's rotational axis as the planet orbits the Sun.

These two so-called Milankovitch cycles modulate the amount of solar energy received by Earth's surface over periods of roughly 23,000 and 41,000 years, respectively. But it's challenging to determine which of those rhythms correlates most strongly with the planet's glacial cycles, said Barker. "People have been trying to pick one or the other."

To help answer that question, Barker and his colleagues analyzed more than 9,000 bits of rock larger than 0.15 millimeter in diameter. The researchers painstakingly picked that material out of a sediment core drilled several hundred kilometers off the southwestern coast of Iceland. These grains of rock reveal the timing of when ancient ice sheets in the Northern Hemisphere grew and ultimately broke up, Barker and his colleagues suggested. That's because ice moving over Earth's surface entrains debris, and such material sinks to the seafloor after it's carried offshore by icebergs.

Barker and his collaborators calculated the rate at which this so-called ice-rafted debris was deposited on the seafloor. "We literally count it," he said. "We work out how much has been delivered per unit time." Spikes in the concentration of ice-rafted debris correspond to the breakup of Northern Hemisphere ice sheets, the researchers concluded.

A Hidden Role

The ice-rafted debris the team studied was deposited over the past roughly 1.7 million years. That time span encompasses two important periods, said Barker. There's the period prior to the Mid-Pleistocene Transition, when glacial cycles were roughly 41,000 years long. And there's the more recent period, during which glacial cycles have consistently lasted about 100,000 years.

Barker and his colleagues found that glacial cycles before and after the Mid-Pleistocene Transition were correlated with both precession and changes in obliquity. The team showed that minima in precession—meaning that summer in the Northern Hemisphere occurs when the planet is closest to the Sun—were tied to ice sheet breakup. And times of decreasing obliquity were associated with ice sheet growth.

It was particularly surprising to uncover the role of precession prior to the Mid-Pleistocene Transition, said Barker. That's because the shorter glacial cycles long have been assumed to have been driven solely by changes in obliquity occurring at the same cadence, without any influence from precession, he said. "I nearly fell off my chair when I saw that."

"Earth's climate system dances to the beat of these Milankovitch cycles."

Furthermore, before the Mid-Pleistocene Transition, ice sheet breakup didn't always spell the end of an ice age, Barker and his colleagues found. That's perhaps because ice sheets at that time were limited to higher latitudes, exactly where the effects of obliquity are felt more acutely than those of precession, the researchers suggested. Conversely, after the Mid-Pleistocene Transition, such breakup was often linked to the end of an ice age. One explanation for that difference is that Northern Hemisphere ice sheets might have been larger after the Mid-Pleistocene Transition, and therefore the effects of both obliquity and precession would have been necessary to catapult the planet into a new state. "We need both to help get rid of these larger ice sheets when their time is up," said Barker.

These results shed light on long-term cycles that affect our planet's climate, said Tim Naish, a paleoclimatologist at Victoria University of Wellington in New Zealand who was not involved in the research. "Earth's climate system dances to the beat of these Milankovitch cycles."

Citation: Kornei, K. (2022), Precession helped drive glacial cycles in the Pleistocene, Eos, 103, https://doi.org/10.1029/2022EO220310. Published on 11 July 2022.

https://bbc.in/3z7Cf0C

World Population Day: India will overtake China in 2023, says the UN

India is set to become the world's most populous country next year, overtaking China with its 1.4bn people, according to UN figures.

By Stephanie Hegarty Population correspondent

By this November, the planet will be home to 8bn.

But population growth is not as rapid as it used to be.

It is now at its slowest rate since 1950 and is set to peak, says the UN, around the 2080s at about 10.4bn though some demographers believe that could happen even sooner.

But the population of the world is expanding unevenly. More than half the growth we will see in the next 30 years will happen in just eight countries - the Democratic Republic of the Congo, Egypt, Ethiopia, India, Nigeria, Pakistan, the Philippines and Tanzania.

At the same time, some of the world's most developed economies are already seeing population decline as fertility rates fall below 2.1 children per woman, which is known as the "replacement rate". In 61 countries, the report says, populations will decline by at least 1% by 2050.

With one of the lowest fertility rates in the world (at 1.15 children per woman), China has announced that its population is due to start declining next year - much earlier than previously thought. That is despite the country abandoning its one child policy in 2016 and introducing incentives for couples to have two or more children.

As India's population continues to grow it will almost certainly overtake China as the country with the biggest population in the world.

Fertility rates are falling globally - even in many of the countries where the population is expanding. That is because, as previous generations expand, there are more people having children, even if individually those people are having fewer children than their parents did.

Growth is also largely thanks to developments in medicine and science which mean that more children are surviving into adulthood and more adults into old age. That pattern is likely to continue, which means that by 2050 the global average life expectancy will be around 77.2 years.

But this pattern means that the share of the global population aged 65 years or above is projected to rise from 10% this year to 16% in 2050. Again the distribution will be unequal with some countries, in East Asia and Western Europe, already seeing more extremes in ageing.

https://bit.ly/3O8l3q0

Challenges Conventional Theory: Research Sheds New Light on the Origin of Civilization

Research challenges the conventional theory that the transition from foraging to farming drove the development of complex, hierarchical societies by creating agricultural surplus, finds the adoption of cereal crops is the key factor.

New research challenges the conventional theory that the transition from foraging to farming drove the development of complex, hierarchical societies by creating agricultural surplus in areas of fertile land. The work was conducted by the University of Warwick, the Hebrew University of Jerusalem, Reichman University, Universitat Pompeu Fabra, and the Barcelona School of Economics.

Professors Joram Mayshar, Omer Moav, and Luigi Pascali show that high land productivity on its own does not lead to the development of tax-levying states in their paper, “In The Origin of the State: Land Productivity or Appropriability?” published in the April issue of the *Journal of Political Economy* – one of the oldest and most prestigious journals in economics.

The key factor for the emergence of hierarchy is the adoption of

cereal crops. In ***this short video***, Professor Moav explains.

The researchers theorize that this is because the nature of cereals requires that they be harvested and stored in accessible locations, making them easier to appropriate as tax than root crops which remain in the ground, and are less storable.

The researchers demonstrate a causal effect of cereal cultivation on the emergence of hierarchy using empirical evidence drawn from multiple data sets spanning several millennia, and find no similar effect for land productivity.

Professor Mayshar said: "A theory linking land productivity and surplus to the emergence of hierarchy has developed over a few centuries and became conventional in thousands of books and articles. We show, both theoretically and empirically, that this theory is flawed."

Underpinning the study, Mayshar, Moav, and Pascali developed and examined a large number of data sets including the level of hierarchical complexity in society; the geographic distribution of wild relatives of domesticated plants; and land suitability for various crops to explore why in some regions, despite thousands of years of successful farming, well-functioning states did not emerge, while states that could tax and provide protection to lives and property emerged elsewhere.

Professor Pascali said: "Using these novel data, we were able to show that complex hierarchies, like complex chiefdoms and states, arose in areas in which cereal crops, which are easy to tax and to expropriate, were de-facto the only available crops. Paradoxically, the most productive lands, those in which not only cereals but also roots and tubers were available and productive, did not experience the same political developments."

They also employed the natural experiment of the Columbian Exchange, the interchange of crops between the New World and the Old World in the late 15th century which radically changed land productivity and the productivity advantage of cereals over roots and tubers in most countries in the world.

Professor Pascali said "Constructing these new data sets, investigating case studies, and developing the theory and empirical strategy took us nearly a decade of hard work. We are very pleased to see that the paper is finally printed in a journal with the standing of the JPE"

Professor Moav said: "Following the transition from foraging to farming, hierarchical societies and, eventually, tax-levying states have emerged. These states played a crucial role in economic development by providing protection, law and order, which eventually enabled industrialization and the unprecedented welfare enjoyed today in many countries."

"The conventional theory is that this disparity is due to differences in land productivity. The conventional argument is that food surplus must be produced before a state can tax farmers' crops, and therefore that high land productivity plays the key role.

Professor Mayshar added: "We challenge the conventional productivity theory, contending that it was not an increase in food production that led to complex hierarchies and states, but rather the transition to reliance on appropriable cereal grains that facilitate taxation by the emerging elite. When it became possible to appropriate crops, a taxing elite emerged, and this led to the state.

"Only where the climate and geography favored cereals, was hierarchy likely to develop. Our data shows that the greater the productivity advantage of cereals over tubers, the greater the likelihood of hierarchy emerging.

"Suitability of highly productive roots and tubers is in fact a curse of plenty, which prevented the emergence of states and impeded economic development."

Reference: "The Origin of the State: Land Productivity or Appropriability?" by Joram Mayshar, Omer Moav and Luigi Pascali, 8 March 2022, Journal of Political Economy.
DOI: 10.1086/718372

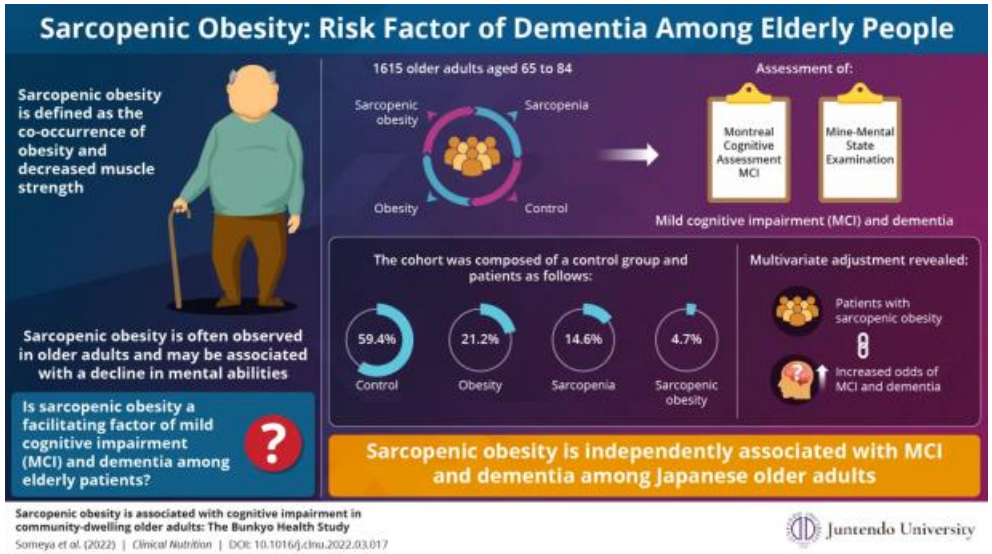
https://bit.ly/3yK3z3D

A Surprisingly Common Condition Has Been Linked to Dementia

Scientists have linked dementia in the elderly to an unexpected candidate: sarcopenic obesity

Over 15% of Japanese adults over 65 suffer from dementia, a severe medical condition. It's well known that dementia drastically reduces the quality of life for older adults, as the condition causes deteriorates their memory, thinking, and social abilities.

Obesity, on the other hand, has become an increasingly prevalent lifestyle disease. It often occurs with poor muscle mass, a condition called sarcopenic obesity which is assessed based on body mass index (BMI) and handgrip strength. Surprisingly, this condition is known to increase the risk of cognitive impairments. This caused scientists to wonder, does this relationship apply to dementia as well?

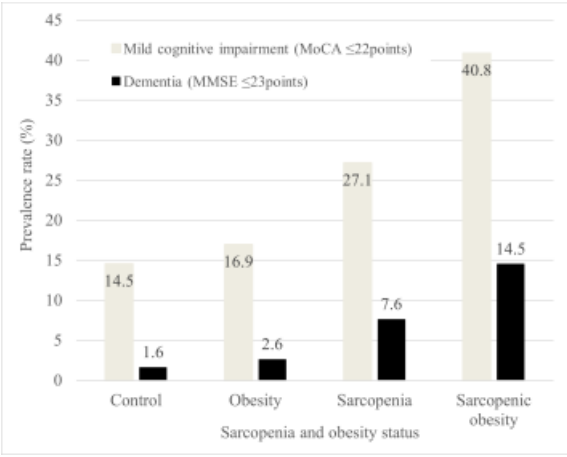


Sarcopenic obesity is independently associated with MCI and dementia among Japanese older adults. **Credit: Juntendo University**

Researchers from Juntendo University in Japan, under the direction of Dr. Yoshifumi Tamura, answered this question in a recent study that was published in *Clinical Nutrition.* Dr. Tamura emphasizes the significance of their work by saying "If the association between sarcopenic obesity and dementia is established, appropriate preventive measures can be taken to reduce the occurrence of this condition and the risk of dementia in elderly patients."

The study involved 1615 older Japanese people who were 65 to 84 years old and taking part in the Bunkyo Health Study. According to the individuals' sarcopenia and obesity status, the researchers separated the participants into four groups: those with obesity, those with sarcopenia, those with sarcopenic obesity, and those without obesity or sarcopenia (control). They then examined the relationship between sarcopenia, obesity, and several mental functions. Handgrip strength of less than 28 kg for males and 18 kg for women indicated sarcopenia or poor muscular strength, whereas individuals with a BMI of more than 25 kg/m2 were classified as obese.

To determine if dementia and moderate cognitive impairment (MCI) existed, two evaluation techniques were used. MCI and dementia were determined by a score of less than 22 on the Montreal Cognitive Assessment and less than 23 on the Mine-Mental State Examination, respectively.



In a brand-new study, researchers from Japan have shown how co-morbidity with sarcopenia and obesity is linked with cognitive impairment in elderly Japanese people. **Credit: Juntendo University**

They found that 59.4% of the population had neither obesity nor sarcopenia, 21.2% had obesity, 14.6% had sarcopenia, and 4.7% of the population had sarcopenic obesity. The participants with sarcopenic obesity had the greatest rate of MCI and dementia, followed by those with sarcopenia, obesity, and finally the control group.

When the team ran multivariate analyses to check for statistically relevant associations, they found that sarcopenic obesity was independently associated with an increased prevalence of MCI and dementia compared with the absence of sarcopenia and obesity. The study also showed that sarcopenia is significantly associated with dementia in women, but not in men. "This study clearly demonstrates that sarcopenic obesity, defined by the combination of BMI and hand grip strength is associated with MCI and dementia among Japan's elderly people," says Dr. Tamura.

But what are the long-term implications of this study?

Dr. Tamura's answer to this question is encouraging. "Since we now know that there is a strong correlation between sarcopenic obesity and dementia, we may develop new treatment methods to manage the condition, thereby even reducing the prevalence of dementia."

Credit: "Sarcopenic obesity is associated with cognitive impairment in community-dwelling older adults: The Bunkyo Health Study" by Yuki Someya, Yoshifumi Tamura, Hideyoshi Kaga, Daisuke Sugimoto, Satoshi Kadowaki, Ruriko Suzuki, Shigeki Aoki, Nobutaka Hattori, Yumiko Motoi, Kazunori Shimada, Hiroyuki Daida, Muneaki Ishijima, Kazuo Kaneko, Shuko Nojiri, Ryuzo Kawamori and Hirotaka Watada, 16 March 2022, Clinical Nutrition. DOI: 10.1016/j.clnu.2022.03.017

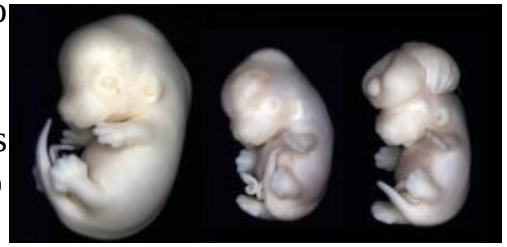
https://bit.ly/3PsMn9z

Why a Widely Used Drug Causes Birth Defects and Autism

Researchers determined that valproic acid prevents nervous system cells from properly developing and dividing

When used during pregnancy, the drug valproic acid, which is used to treat bipolar disorder, migraines, and epilepsy, can lead to birth defects. Now, research recently published in the journal *PLoS Biology* by Bill Keyes of the Institute of Genetics and Molecular and Cellular Biology, France, and associates gives one explanation for why: Valproic acid (VPA) causes certain nervous system development cells to enter a condition known as senescence, which prevents them from properly growing and dividing.

VPA is frequently used to treat a variety of diseases. However, since its first use, there have been many instances of pregnant women using VPA giving birth to kids who had birth abnormalities such as spina bifida, facial changes, and heart malformations A third of exposed newborns also develop cognitive decline and Autism Spectrum Disorder.



Three mouse embryos, representative of the study that describes how the teratogenic drug Valproic acid can cause neurodevelopmental birth defects in mice, including microcephaly and exencephaly. The embryo on the left is a normal embryo, with no exposure to Valproic acid. The embryo in the middle is smaller and has microcephaly, while the embryo on the right exhibits exencephaly. The middle embryo and the one on the right were both exposed to Valproic acid. **Credit: Muriel Rhinn (CC-BY 4.0)**

Keyes and colleagues examined embryonic exposure to VPA in the new study by using both human organoids—three-dimensional collections of human cells generated in the lab—and mice. They found that neuroepithelial cells, which are the stem cells that give rise to the central nervous system, undergo cellular senescence as a result of VPA. The researchers also identified $p19^{Arf}$ as the specific molecule that caused this VPA-induced senescence. Although VPA exposure during pregnancy still resulted in other abnormalities, the scientists found that it no longer produced microcephaly (a small head size) or alterations to gene expression patterns linked to

autism spectrum disorder in mice missing the $p19^{Arf}$ gene.

Valproic acid is used to treat the manic phase of bipolar disorder, seizures, and migraine headaches. This prescription medication goes by various brand names including Depakene, Depakote, Depakote DR, Depakote ER, Depakote Sprinkles, Stavzor, and Alti-Valproic.

The work is one of the first to associate cellular senescence with developmental defects, the authors say. “Overall, the discovery that atypical activation of senescence in the embryo can perturb development raises the intriguing possibility that it may also contribute to defects in developmental contexts beyond those we studied here.”

Muriel Rhinn, the first author of the study, adds, “While cellular senescence has long been associated with aging and age-related disease, we now show that aberrant induction of senescence can also contribute to developmental defects. As valproic acid is strongly linked to cognitive defects and Autism Spectrum Disorder, this study now introduces an exciting link with senescence, supporting how additional studies are needed.”

This study was funded by grants from La Fondation pour la Recherche Medicale (FRM) (AJE20160635985), Fondation ARC pour la Recherche sur le Cancer (PJA20181208104), IDEX Attractivité – University of Strasbourg (IDEX2017), La Fondation Schlumberger pour l’Education et la Recherche FSER 19 (Year 2018)/FRM, Agence Nationale de la Recherche (ANR) (ANR-19-CE13-0023-03) and Ligue Contre le Cancer (all to W.M.K.). I.Z.B. was supported by a 4th-year fellowship from the Fondation ARC pour la Recherche sur le Cancer and a Ph.D. fellowship from INSERM and Conseil Regional Grand-Est. A.K. was supported by a fellowship from Eur IMCBiO. The work was also supported by an institutional grant to the IGBMC, ANR-10-LABX-0030-INRT, a French State fund managed by the Agence Nationale de la Recherche under the frame program Investissements d’Avenir ANR-10-IDEX-0002-02. Sequencing was performed by the GenomEast platform, a member of the “France Génomique” consortium (ANR-10-INBS-0009). The funders had no role in the study’s design, data collection, and analysis, decision to publish, or preparation of the manuscript.

Reference: “Aberrant induction of $p19^{Arf}$-mediated cellular senescence contributes to neurodevelopmental defects” by Muriel Rhinn, Irene Zapata-Bodalo, Annabelle Klein, Jean-Luc Plassat, Tania Knauer-Meyer and William M. Keyes, 14 June 2022, PLoS Biology. DOI: 10.1371/journal.pbio.3001664

https://bit.ly/3aGczz3

We've Finally Pinpointed The Precise Spot on Mars This Famous Meteorite Came From

Millions of years ago, an epic journey began from Mars. A giant asteroid slammed into the surface, gouging out chunks of the Martian crust and hurling them into space.

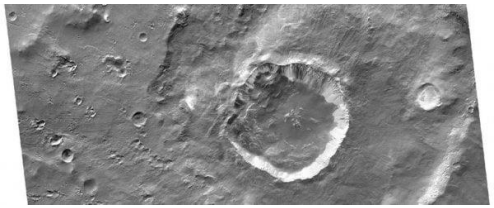
Michelle Starr

In 2011, one of those chunks of rock was fished out of the Sahara Desert. Its trajectory had carried it, by chance, all the way to Earth (that, or Mars deliberately started throwing rocks at us).

Nicknamed Black Beauty for its glorious dark glossy hue, the meteorite catalogued NWA 7034 is thought to be the oldest chunk of Mars we have. And now it has been traced to the precise location where the asteroid that launched it struck.

The team has named that impact crater Karratha, after a region in Australia where some of Earth's oldest rocks can be found. This new geological context for the rock – a volcanic mineral, composed of different kinds of rock (a bit like a fruit cake) in what's known as a breccia – will aid comparisons of the formation history of Earth and Mars.

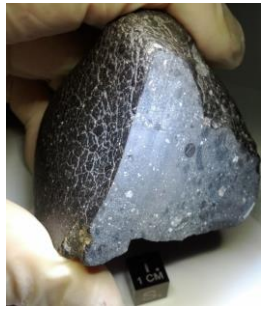
"For the first time, we know the geological context of the only brecciated Martian sample available on Earth," explained planetary scientist Anthony Lagain of Curtin University in Australia, who led the international team of researchers.



Karratha Crater, inside the larger Dampier Crater. **(NASA MRO)**

"Finding the region where the 'Black Beauty' meteorite originates is critical because it contains the oldest Martian fragments ever found, aged at 4.48 billion years old, and it shows similarities between Mars' very old crust, aged about 4.53 billion years old, and today's

Earth continents. The region we identify as being the source of this unique Martian meteorite sample constitutes a true window into the earliest environment of the planets, including the Earth, which our planet lost because of plate tectonics and erosion."



Black Beauty. **(NASA)**

To date, around 300 meteorites from Mars have ended up here on Earth (maybe Mars has a grudge). Black Beauty, consisting of a 320-gram (11-ounce) chunk of rock and a pair of stones, is absolutely one of a kind: In addition to being the oldest piece of Mars we have, it's the only piece of volcanic breccia among all of them.

It's thought to be a record of early conditions on Mars – but where on Mars had remained a mystery. The red planet is positively riddled with impact craters, making tracing a meteorite to any one of them extremely challenging.

To do so, Lagain and his colleagues used the powerful Pawsey Supercomputing Research Centre in Western Australia, and an algorithm developed at Curtin University for the express purpose of detecting impact craters. An analysis of the size and spatial distribution of 90 million craters detected by this algorithm allowed scientists to narrow down the origin of Black Beauty.

Their results revealed multiple impacts went into forming Black Beauty. The oldest fragments of the rock were blasted from the Martian crust around 1.5 billion years ago from a spot marked by the 40-kilometer-across (25 miles) Khujirt crater in the southern hemisphere of Mars. This material fell back to Mars, where it remained until around 5 to 10 million years ago, when the impact that created the Karratha crater threw it up again, sending it flying into space on its journey to Earth.

Previous research at Curtin found shocks in the meteorite's zircon crystals dating back to 4.45 billion years ago, indicative of a massive impact then, too. Although the site of that putative impact remains unknown, it seems that some of the material in Black Beauty may have been involved in at least three impacts on Mars.

The findings suggest that the region from which the rock was initially ejected may be a relic of the primordial Martian crust, and therefore of intense interest for future Mars exploration.

The work, in addition, could be used to trace the origins of some of the other meteorites that Mars has chucked at Earth. This could help reconstruct in greater detail a timeline of Mars' geological history. And there are implications for other heavily cratered bodies in the Solar System too, such as Mercury and the Moon.

"We are … adapting the algorithm that was used to pinpoint Black Beauty's point of ejection from Mars to unlock other secrets from the Moon and Mercury," said astro-geologist Gretchen Benedix of Curtin University.

"This will help to unravel their geological history and answer burning questions that will help future investigations of the Solar System such as the Artemis program to send humans on the Moon by the end of the decade or the BepiColombo mission, in orbit around Mercury in 2025."

The research has been published in *Nature Communications*.

https://bit.ly/3clEAMI

MIT Engineers Work To Harness the Liver's Regenerative Abilities To Treat Chronic Disease

By tracing the steps of liver regrowth, MIT engineers hope to harness the liver's regenerative abilities to help treat chronic disease.

By Anne Trafton, Massachusetts Institute of Technology

The human liver has incredible regeneration capabilities: Even if up to 70% of it is removed, the remaining tissue can regrow a full-sized liver in just months. Being able to take advantage of this regenerative capability could provide doctors with a plethora of

options for treating chronic liver disease. MIT engineers have now taken a step toward that goal, by creating a novel liver tissue model that allows them to more precisely trace the steps involved in liver regeneration than has been possible before.

Using the new model can yield information that couldn't be gleaned from studies of mice or other animals, whose biology is not identical to that of humans, says Sangeeta Bhatia, the leader of the research team.

"For years, people have been identifying different genes that seem to be involved in mouse liver regeneration, and some of them seem to be important in humans, but they have never managed to figure out all of the cues to make human liver cells proliferate," says Bhatia, the John and Dorothy Wilson Professor of Health Sciences and Technology and of Electrical Engineering and Computer Science at MIT and a member of MIT's Koch Institute for Integrative Cancer Research and Institute for Medical Engineering and Science.

The new study, which appears this week in the *Proceedings of the National Academy of Sciences*, has identified one molecule that appears to play a key role, and also yielded several other candidates that the researchers plan to explore further.

The lead author of the paper is Arnav Chhabra, a former MIT graduate student and postdoctoral researcher.

Regeneration on a chip

Most of the patients who need liver transplants suffer from chronic illnesses such as viral hepatitis, fatty liver disease, or cancer. However, if researchers had a reliable way to stimulate the liver to regenerate on its own, some transplants could be avoided, Bhatia says. Or, such stimulation might be used to help a donated liver grow after being transplanted.

From studies in mice, researchers have learned a great deal about some of the regeneration pathways that are activated after liver injury or illness. One key factor is the reciprocal relationship between hepatocytes (the main type of cell found in the liver) and endothelial cells, which line the blood vessels. Hepatocytes produce factors that help blood vessels develop, and endothelial cells generate growth factors that help hepatocytes proliferate.

Another contributor that researchers have identified is fluid flow in the blood vessels. In mice, an increase in blood flow can stimulate the endothelial cells to produce signals that promote regeneration.

"Right now when patients come in with liver failure, you have to transplant them because you don't know if they're going to recover on their own. But if we knew who had a robust regenerative response, and if we just needed to stabilize them for a little while, we could spare those patients from transplant." — *Sangeeta Bhatia*

To model all of these interactions, Bhatia's lab teamed up with Christopher Chen, the William F. Warren Distinguished Professor of Biomedical Engineering at Boston University, who designs microfluidic devices with channels that mimic blood vessels. To create these models of "regeneration on a chip," the researchers grew blood vessels along one of these microfluidic channels and then added multicellular spheroid aggregates derived from liver cells from human organ donors.

The chip is designed so that molecules such as growth factors can flow between the blood vessels and the liver spheroids. This setup also allows the researchers to easily knock out genes of interest in a specific cell type and then see how it affects the overall system.

Using this system, the researchers showed that increased fluid flow on its own did not stimulate hepatocytes to enter the cell division cycle. However, if they also delivered an inflammatory signal (the cytokine IL-1-beta), hepatocytes did enter the cell cycle.

When that happened, the researchers were able to measure what other factors were being produced. Some were expected based on earlier mouse studies, but others had not been seen before in human

cells, including a molecule called prostaglandin E2 (PGE2).

The MIT team found high levels of this molecule, which is also involved in zebrafish regeneration, in their liver regeneration system. By knocking out the gene for PGE2 biosynthesis in endothelial cells, the researchers were able to show that those cells are the source of PGE2, and they also demonstrated that this molecule stimulates human liver cells to enter the cell cycle.

Human-specific pathways

The researchers now plan to further explore some of the other growth factors and molecules that are produced on their chip during liver regeneration.

"We can look at the proteins that are being produced and ask, what else on this list has the same pattern as the other molecules that stimulate cell division, but is novel?" Bhatia says. "We think we can use this to discover new human-specific pathways."

In this study, the researchers focused on molecules that stimulate cells to enter cell division, but they now hope to follow the process further along and identify molecules needed to complete the cell cycle. They also hope to discover the signals that tell the liver when to stop regenerating.

Bhatia hopes that eventually, researchers will be able to harness these molecules to help treat patients with liver failure. Another possibility is that doctors could use such factors as biomarkers to determine how likely it is that a patient's liver will regrow on its own. "Right now when patients come in with liver failure, you have to transplant them because you don't know if they're going to recover on their own. But if we knew who had a robust regenerative response, and if we just needed to stabilize them for a little while, we could spare those patients from transplant," Bhatia says.

Reference: "A vascularized model of the human liver mimics regenerative responses" by Arnav Chhabra, H.-H. Greco Song, Katarzyna A. Grzelak, William J. Polacheck, Heather E. Fleming, Christopher S. Chen and Sangeeta N. Bhatia, 28 June 2022, Proceedings of the National Academy of Sciences. DOI: 10.1073/pnas.2115867119

https://bit.ly/3Pv5qJ6

Many Men Lose Y Chromosomes as They Age. Now We May Know Why It's So Deadly

mLOY triggers tissue damage that leads to heart failure in mice and is linked to cardiovascular disease.

Clare Watson

Errors in the human genome are a part of life. As we age and DNA replicates, small mistakes creep into our genes – a misplaced letter here or some erroneous repetition there – that can accumulate over time to create a 'mosaic' of cells with unique codes throughout the body. Some cells can even wind up losing whole chromosomes.

One example of this is a condition whereby white blood cells are missing their Y chromosome. Called mLOY (for mosaic Loss Of Y chromosome), it's more common than you might think, occurring in roughly 40 percent of men aged over 70.

Although the Y chromosome has long been considered a shrinking genetic wasteland full of dispensable chunks of DNA, missing a Y chromosome can have serious health consequences.

In epidemiological studies, mLOY has been associated with shorter lifespans and a greater risk of age-related diseases, such as cancer and Alzheimer's disease. Now, the condition could also be linked to impaired heart function, according to a new study mimicking the human condition in mice.

For a while it has been unclear how losing the Y chromosome from blood cells leads to organ damage and disease in other parts of the body, and ups the risk of age-related maladies, particularly cardiovascular disease and stroke.

The team of researchers led by cardiovascular researcher Soichi Sano of Osaka Metropolitan University Graduate School of Medicine in Japan, probed those questions a little deeper, and have shown how mLOY triggers tissue damage that leads to heart failure in mice and is linked to cardiovascular disease.

In the study, the researchers used the famed gene-editing tool CRISPR to engineer mice with no Y chromosomes in their white blood cells to mimic the human mLOY condition.

The CRISPR-ed mice lived shorter lives than unaffected mice, and had increased scarring of the heart, a condition known as cardiac fibrosis that stiffens heart tissues and is linked to heart failure.

"We see that mLOY [in mice] causes the fibrosis which leads to a decline in heart function," says geneticist and senior author Lars Forsberg of Uppsala University.

To test those findings against epidemiological data, the researchers then analyzed data from the UK Biobank, a decades-long study that has captured genetic and health information of some half a million typically aging adults.

They found men with mLOY in their blood at the start of the study had an increased risk of dying from heart failure and other types of cardiovascular disease during the on-average 11 years of follow-up.

"This observation is in line with the results from the mouse model and suggests that mLOY has a direct physiological effect also in humans," says Forsberg.

Of course, way more research is needed before we can map out the direct consequences of mLOY in humans. And keep in mind that losing the Y chromosome is unlikely to be the sole cause of age-related diseases which are linked to a plethora of cellular processes gone awry and a host of genetic changes that have accumulated over time.

As University of Cambridge biologist John Perry told *The Atlantic* in 2019, after publishing work showing why some are more prone to mLOY than others, "Y-chromosome loss is a manifestation of broader genome instability." Instability which is characteristic of cancer and signals that DNA has been accumulating errors faster than cells can fix them.

Chronic inflammation is another suspected culprit underlying many diseases of aging, including cancer and Alzheimer's. So, as Forsberg and colleagues note, there is more work to be done to untangle the complex interplay between inflammation and fibrosis, and the role of mLOY in both.

Returning to the mouse models for one last hoorah, Forsberg and colleagues also identified a possible treatment to ameliorate the effects of mLOY. Blocking a signaling pathway that was activated in the mice with Y chromosome-deficient immune cells, the researchers noticed the ensuing fibrotic changes were partly reversed. "The link between mLOY and fibrosis is very interesting, especially given the new treatment strategies for heart failure, pulmonary fibrosis and certain cancers that aim to counteract the onset of fibrosis," says Forsberg.

Although a potential therapy to counteract losing the Y chromosome in blood cells is still a long off, "Men with mLOY could be a patient group that responds particularly well to such treatment," Forsberg added.

But knowing what we do now, stopping smoking would be a wise move too, seeing as research also shows that men who smoke are more than three times as likely as non-smokers to show loss of the Y chromosome in their blood cells.

The study was published in *Science*.

https://bbc.in/3RDSXw2

Sore throat and cough top symptoms that could be Covid

Top symptoms that could be Covid are a sore throat or a cough, according to data from 17,500 people who said they had tested positive for the virus this week.

By Michelle Roberts Digital health editor

Other common ones reported were headache and blocked nose. A high temperature or fever and loss of smell or taste - ones which the NHS list high up as likely Covid symptoms - were far less common.

A hoarse voice, sneezing, tiredness and muscle aches scored higher. The top 20 Covid symptoms, in descending order, according to the data from the Zoe App study are:

Sore throat	***reported by 58%***	***Dizzy light-headed***	***18%***
Headache	***49%***	***Swollen neck glands***	***15%***
Blocked nose	***40%***	***Eye soreness***	***14%***
Cough no phlegm	***40%***	***Altered smell***	***13%***
Runny nose	***40%***	***Chest pain tightness***	***13%***
Cough with phlegm	***37%***	***Fever***	***13%***
Hoarse voice	***35%***	***Chills or shivers***	***12%***
Sneezing	***32%***	***Shortness of breath***	***11%***
Fatigue	***27%***	***Earache***	***11%***
Muscle pains/aches	***25%***	***Loss of smell***	***10%***

It fits with what other researchers have been seeing.

The React-1 study has, each month, been sending 150,000 randomly selected people across England swab tests to do at home.

Findings from that show the symptoms people have with Covid have changed as the pandemic has evolved.

It could be down to how the virus has been changing or mutating over time, scientists believe. Several Covid variants have emerged since the original Wuhan strain, with the latest one being Omicron.

The React-1 researchers, from Imperial College London, say loss of sense of smell and taste appears to be less common with this variant. Instead, people are reporting more cold and flu-like symptoms.

They looked at original Omicron known as BA.1 and BA.2 that was spreading in March 2022.

Since then, two fast-spreading new subvariants of Omicron called BA.4 and BA.5 have dominated, causing more new infections.

An estimated 2.7 million people in the UK, or one in 25, are thought to have Covid.

Prof Tim Spector, who runs the Zoe Health Study, said: "Covid is still rampant in the population. "Even if people have had a past infection and are fully vaccinated, people are still catching it. "Although we all want to make the most of the good weather, people will need to decide for themselves whether going to large events, working from the office or using busy public transport is worth the risk." Both the Zoe study and the React-1 study had been funded by the government until recently.

https://bit.ly/3o8fROu

How to Successfully Smash Your Face Against a Tree

A new study refutes the widespread idea that woodpeckers have shock-absorbing heads.

By Ed Yong

In my third year of reporting on the coronavirus pandemic, I find woodpeckers, which can ram their heads against hard surfaces about 20 times a second, to be incredibly relatable. But the birds' extraordinary behavior raises an obvious question: Why, as one team of scientists wrote in 1976, is the countryside "not littered with dazed and dying woodpeckers"?

The just-as-obvious answer is that woodpecker skulls have adaptations, such as spongy bone in the front of their skulls, that absorb or dissipate the shocks from their pecks, protecting their squishy brains. This explanation features in books, news articles, zoo displays, and scientific papers. "You can't avoid it," Sam Van Wassenbergh, a biologist at the University of Antwerp, told me. It's so accepted that some scientists have tried to work out exactly which parts of the skull absorb shocks, while others have designed helmets and other protective technology inspired by the birds.

There's just one problem: As Van Wassenbergh and his colleagues have now shown, woodpecker heads don't absorb shocks at all.

Although the shock-absorption idea seems superficially sound, "the more you think about it, the less sense it makes," Van Wassenbergh said. Woodpeckers peck trees to send messages, dig out hidden insects, and excavate nesting holes; many of their body parts—

strong beaks, grasping feet, and stiff, strut-like tails—have evolved to maximize the kinetic energy they deliver with each blow. If their skulls absorbed that energy, they'd just need to pound harder, which would negate any benefits from the absorption. If what you need is a hammer, why strap a cushion onto its head?

To check his suspicions, Van Wassenbergh and his colleagues filmed three woodpecker species as they hammered into wood, using high-speed cameras that could capture 4,000 frames every second. The team then analyzed every frame to see how parts of the birds' head move relative to one another. If the skull really was absorbing shocks, then upon each peck, the brain should decelerate far less than the beak—just as when a car hits a bump, its body jerks less than its wheels do. But the videos revealed that, in fact, when a woodpecker pecks wood, its entire head, including the brain, comes to a stop at the same rate. (The team used the position of the eye as a proxy for the front of the brain, because the two are jammed closely together in woodpeckers, with little room for movement.) "That really lays to rest the idea that some part of the head is acting as a shock absorber," Margaret Rubega, an ornithologist at the University of Connecticut who wasn't involved in the study, told me.

Even if woodpeckers *did* absorb shocks, it wouldn't help them. Using simulations of a black woodpecker's head, Van Wassenbergh showed that a shock-absorbing skull would force the bird to spend more energy on pecking for no benefit. As Rubega said, "You don't use a spring to hammer a nail with." Instead, you use … well … a hammer, which is what the woodpecker's head essentially is—a rigid structure that has evolved not to absorb shocks but to preserve them. "This makes intuitive sense," says Lorna Gibson, an engineer at MIT who has studied woodpeckers and was always skeptical of the shock-absorption idea. "I'm not sure why [it] was accepted."

The zoological literature is full of similarly false ideas that persisted for years or decades before being corrected: that hummingbirds drink by using their tongues as straws; that cheetahs overheat when hunting; that mantis shrimps have kaleidoscopic rainbow vision; that honey badgers follow birds to honey; or that Komodo dragons kill with bacteria-laden bites. Some of these factoids began as assumptions that somehow calcified into received wisdom without anyone checking them. Others were outright fabrications, or arose from preliminary studies that were exaggerated or overgeneralized. Many are still repeated today.

In the case of woodpeckers, few previous studies ever filmed and analyzed live birds, relying solely on digital simulations or observations of their skulls. This is typical of humans' knowledge of birds: We make a lot of assumptions but do little actual testing. "We have no idea how the stress of pecking, or biting, or anything really, is accommodated by the skull, nor how this varies between species with different skull and beak shapes, diets, and behaviors," Jen Bright at the University of Hull, in the U.K., told me.

But Van Wassenbergh also suspects that many researchers have been misled by a simple form of anthropomorphism. "It's logical to think that, if I was this bird, I'd like to have a helmet or an airbag," he said. But although we use such tools to protect us from unwanted impacts, a woodpecker is *trying* to smash its face against a tree. Its needs are completely different from ours, which means that features in its skull are probably *not* analogous to safety equipment. The spongy mass of bone at the front of the skull looks like it could be an airbag—but clearly doesn't act like one. The long tongue, which, when retracted, wraps around the back of the skull and into the bird's forehead, looks like a possible seat belt—but, again, clearly isn't one. Engineers who are looking to woodpecker skulls for inspiration might think twice, Van Wassenbergh told me: "This bird has gone through millions of years of trying to minimize shock absorption … which isn't what you want in a helmet."

But if woodpeckers lack some built-in helmet, then how *do* they peck wood without sustaining traumatic brain injuries? A human who headbutted a tree at woodpecker speed would absolutely be concussed. But we have extremely large brains—a fact that, ironically, we seem to forget. Woodpeckers have smaller and lighter brains than ours, which greatly reduces the pressure that they experience upon each peck. According to Van Wassenbergh's calculations, a woodpecker would have to hit a tree at twice its normal speed, or peck something four times stiffer than the average tree, to get a concussion. "If by accident they hit a piece of metal, I can still imagine that they'd suffer a concussion, but for their natural behavior, what they do is relatively safe," he said.

Van Wassenbergh hasn't yet checked if woodpeckers have evolved especially small brains for birds of their size, or differently shaped ones: A more spherical brain, he noted, would be better at resisting shocks than an elongated one. The birds may also have adaptations that help them cope with the damage that even subconcussive impacts can create; perhaps their brains have little fluid so that they can't slosh around too much. Whatever the case, the secret to the woodpecker's percussive powers appears to be deceptively simple: They just have small brains. Maybe I should try that the next time I'm tempted to smash my face into the nearest solid object.

https://bit.ly/3AVJWsc

Study Finds Traditional Native Indian Medicine Effective Treatment for Type 2 Diabetes

Researchers have found that several traditional medicines commonly used in South Asia are effective in maintaining blood sugar levels in patients with type 2 diabetes.

Several traditional medicines commonly used in South Asia, are effective in maintaining blood sugar levels in patients with type 2 diabetes, according to a new study led by experts at the University of Nottingham.

Many South Asian countries, including India and Nepal, have been using the Ayurvedic natural medical system for thousands of years. Some of the herbs included in this traditional medical system are also used in other parts of the world including Iran, China, and Mexico – to name a few.

It features a multi-pronged and individualized approach to managing health conditions that can include lifestyle modification (including diet), Ayurvedic detoxifying and purifying therapies (e.g. Panchakarma), and Ayurvedic medicines (containing plant, animal, or mineral-origin ingredients – single or in combination).

In this new study, published recently in the journal *Frontiers in Pharmacology*, experts conducted an in-depth review to show that these medicines are effective in blood sugar control in people with type 2 diabetes. Other beneficial effects were also demonstrated in the research, including improvements in body weight, blood pressure, cholesterol, and other diabetes-related parameters.

According to the scientists, it is the first comprehensive systematic review of any traditional medicine (including Ayurveda), which included a wide range of Ayurvedic medicines. The research was led by Dr. Kaushik Chattopadhyay, Associate Professor in Evidence Based Healthcare in the School of Medicine and the Nottingham Center for Evidence Based Healthcare (A JBI Center of Excellence) at the University. The team members have expertise in Ayurveda, diabetes, and this type of research, and are based in top institutes in the UK, India, and Nepal.

As a complex disorder, type 2 diabetes has major health, social, and economic consequences. It is also one of the main diseases for which patients consult Ayurvedic practitioners and use Ayurvedic medicines, often continuously from the point of diagnosis.

Patients often choose ayurvedic medicine because it aligns with their cultural and health views. Its acceptability, satisfaction, and perceived relief are usually high, especially among rural, poor,

older, and indigenous/minority populations. Many patients with type 2 diabetes prefer not to use Western medicines due to the associated side effects, cost, and mode of administration (e.g., injections).

Previous systematic reviews have shown the potential for managing type 2 diabetes with these medicines, however many need updating and none have provided a comprehensive summary of all the medicines evaluated for managing the condition.

As part of this review, the team searched a range of sources, including 18 electronic databases. Two hundred and nineteen articles were included in the review, which represented 199 randomized controlled trials (21,191 participants) and 98 Ayurvedic medicines.

Many Ayurvedic practitioners may view the inclusion of herb extracts and proprietary Ayurvedic medicines in this review as a deviation from the classical style of management. However, in reality, many Ayurvedic practitioners prescribe, and many people consume these types of medicines.

Dr. Chattopadhyay said: "This is the first time a thorough review has taken place looking at all these medicines on a much larger scale. The current evidence suggests the benefits of a range of Ayurvedic medicines in improving glycemic control in type 2 diabetes patients. Given the limitations of the available evidence and to strengthen the evidence base, high-quality randomized controlled trials should be conducted and reported.

"As part of the funded project, we have developed a clinical guideline for managing type 2 diabetes by Ayurvedic practitioners based on this evidence and will be evaluating it."

Reference: "Effectiveness and Safety of Ayurvedic Medicines in Type 2 Diabetes Mellitus Management: A Systematic Review and Meta-Analysis" by Kaushik Chattopadhyay, Haiquan Wang, Jaspreet Kaur, Gamze Nalbant, Abdullah Almaqhawi, Burak Kundakci, Jeemon Panniyammakal, Michael Heinrich, Sarah Anne Lewis, Sheila Margaret Greenfield, Nikhil Tandon, Tuhin Kanti Biswas, Sanjay Kinra and Jo Leonardi-Bee, 8 June 2022, Frontiers in Pharmacology. DOI: 10.3389/fphar.2022.821810

The research is funded by the UK's FCDO, MRC, NIHR, and Wellcome Trust under the prestigious Joint Global Health Trials scheme.

https://bit.ly/3uSFFSI

Scientists Discover Why Staph Vaccines Do Not Work in Humans

The sometimes-pathogenic bacteria Staphylococcus aureus has a long and intimate relationship with people, one that helps it fend off our immune response.

Staphylococcus aureus is a common bacterium that is harmless, for the most part, posing no threat to humans with whom they coexist. However, on occasion, it can develop into an opportunistic pathogen, causing food poisoning or skin and bloodstream infections.

Scientists have searched for an effective vaccine for more than a century, including at least 15 successful preclinical studies using animal models in the last 30 years. However, these vaccine candidates all failed in the subsequent human trials.

"It's a longstanding and one of the most enigmatic issues of the staphylococcal field," said George Liu, MD, PhD, professor of pediatrics at the University of California San Diego (UCSD) School of Medicine and chief of the Division of Infectious Diseases at Rady Children's Hospital-San Diego. "None of these human trials have worked and scientists have struggled to find a reason."

The issue has grown increasingly urgent with the emergence of methicillin-resistant *S. aureus* (MRSA), a type of staph bacteria that has become increasingly resistant to the antibiotics typically used to treat ordinary staph infections. MRSA has spread to become the primary source of infections acquired within hospitals and other health care settings, such as nursing homes. In fact, a study published in 2022 estimated that bacterial antimicrobial resistance resulted in tens of millions of infections and 1.2 million deaths

worldwide in 2019, with MRSA as the primary driver.

"Vaccines are the most effective way to cut down that health burden and reduce antibiotic resistance," said Liu, pointing to successes with childhood inoculations and the more recent COVID-19 vaccines.

In a new paper, published on July 7, 2022, in the journal *Cell Host & Microbe*, senior author Liu and colleagues say they may have found the answer to the conundrum of *S. aureus*, including the mechanism that explains why vaccine trials have so far failed and ways to overcome that.

Fundamentally, the difference lies in prior exposure to the pathogen, the authors write. Laboratory mice used in research are engineered (bred/raised/maintained) to be free of the specific target pathogen; they have had little or no exposure to *S. aureus* prior to vaccination.

By contrast, humans are very quickly exposed to *S. aureus* after birth. Within two months of being born, half of babies host active colonies and abundant antibodies to fend off most infections.

With first author Chih-Ming Tsai, PhD, a project scientist in his lab, and others, Liu hypothesized that while laboratory mice with no previous exposure to *S. aureus* respond well to potential vaccines because they are entirely new, human versions do not work because *S. aureus* has evolved defenses to fend off a therapeutic attack.

"Staph vaccines appear so easy to make in laboratory mice because they rarely see *S. aureus*, but humans are exposed to staph beginning in the first weeks of life and, in order to coexist, staph appears to have developed many strategies to render ineffective our immune response against them," Tsai said. "If mice had staph infections before vaccination, we think that the vaccine candidates might not work."

To test their hypothesis, Liu, Tsai, and co-authors conducted a series of experiments simulating one of the largest failed staph vaccine trials in humans, which targeted the IsdB protein used by *S. aureus* to acquire needed iron for functioning.

In mice unexposed to normal staph, the IsdB vaccine worked, generating antibodies that targeted the whole protein and disrupted bacterial functions. But in mice previously exposed to staph, the vaccine generated only antibodies against the unprotected portion of the IsdB protein, leaving bacterial functioning unimpaired. Subsequent boosters primarily amplified the ineffective antibody response and, compounding the problem, the ineffective antibodies competed with any existing, protective antibodies.

When researchers tried mixing human IsdB antibodies with protective antibodies made from the vaccine, the latter stopped working. "We surmised that if we could vaccinate only against the protective component of IsdB, we might be able to prevent suppression by bad immune response memory," said Tsai.

And, in fact, that is what the scientists found: When they vaccinated mice solely against the protective component of the IsdB protein, the animals were effectively protected, even if previously exposed to *S. aureus*. In combination with other experiments, Liu said the findings suggest that faulty memory of a pathogen and its corresponding immune response are likely explanations for the failed staph vaccine trials in humans.

"It is even possible that the same principle might also explain why many other hard-to-make vaccines have failed," he said. "If we are proven correct, an effective staph vaccine may not be too far away."

Reference: "Non-protective immune imprint underlies failure of Staphylococcus aureus IsdB vaccine" by Chih-Ming Tsai, J. R. Caldera, Irshad A. Hajam, Austin W. T. Chiang, Chih-Hsiung Tsai, Haining Li, María Lázaro Díez, Cesia Gonzalez, Desmond Trieu, Gislâine A. Martins, David M. Underhill, Moshe Arditi, Nathan E. Lewis and George Y. Liu, 7 July 2022, Cell Host & Microbe. DOI: 10.1016/j.chom.2022.06.006

Co-authors include: J.R. Caldera, UC San Diego and Cedars-Sinai Medical Center; Irshad A. Hajam, Austin W.T. Chiang, Haining Li, Maria Lazaro Diez, Cesia Gonzalez, Desmond Trieu and Nathan E. Lewis, all at UC San Diego; Chih-Hsiung Tsai, National Cheng Kung University, Taiwan; Gislaine A. Martins, David M. Underhill and Moshe Arditi, all at Cedars-Sinai Medical Center.

Funding: National Institutes of Health, Novo Nordisk Foundation through the Technical

University of Denmark

https://bit.ly/3OfHdwE

Study Finds Neighborhoods With More Dogs Have Less Crime

'Paws on the street' makes high-trust areas safer, study finds.

If you want to find a safe neighborhood to live in, choose one where the residents trust each other – and have a lot of dogs to walk.

To find a safe neighborhood to live in, choose a community where people trust one another and have plenty of dogs to walk.

Researchers discovered that neighborhoods in Columbus, Ohio with more dogs had lower rates of homicide, robbery and, to a lesser extent, aggravated assaults compared to areas with fewer dogs, at least in cases when residents also had high levels of trust in each other.

The results indicate that people walking their dogs puts more "eyes on the street," which can discourage crime, according to Nicolo Pinchak, lead author of the study and a doctoral student in sociology at The Ohio State University.

"People walking their dogs are essentially patrolling their neighborhoods," Pinchak said. "They see when things are not right, and when there are suspect outsiders in the area.

It can be a crime deterrent."

The study was recently published in the journal *Social Forces*.

Sociologists have long theorized that a combination of mutual trust and local surveillance among residents of a neighborhood can deter criminals, said study co-author Christopher Browning, a professor of sociology at Ohio State.

However, there hasn't been a good measure of how residents provide surveillance of neighborhood streets.

"We thought that dog walking probably captures that pretty well, which is one reason why we decided to do this study," Browning said.

For the study, researchers looked at crime statistics from 2014 to 2016 for 595 census block groups – the equivalent of neighborhoods – in the Columbus area.

They obtained survey data from a marketing firm that asked Columbus residents in 2013 if they had a dog in their household.

Finally, they used data from the Adolescent Health and Development in Context study (which Browning runs) to measure trust in individual neighborhoods.

As part of that study, residents were asked to rate how much they agreed that "people on the streets can be trusted" in their neighborhoods.

Research has shown that trust among neighbors is an important part of deterring crime, because it suggests residents will help each other when facing a threat and have a sense of "collective efficacy" that they can have a positive impact on their area, Pinchak said.

Results of this study showed, as expected, that neighborhoods with high levels of trust had lower levels of homicide, robbery and aggravated assaults when compared to neighborhoods with low levels of trust.

But among high-trust neighborhoods, those with high concentrations of dogs showed an additional drop in crime compared to those with low concentrations of dogs.

Among the high-trust neighborhoods, neighborhoods high in dog concentration had about two-thirds the robbery rates of those low in dog concentration and about half the homicide rates, the study found.

It really has to do with the dog walking, Pinchak said.

"Trust doesn't help neighborhoods as much if you don't have people out there on the streets noticing what is going on.

That's what dog walking does," Pinchak said.

And that's why dogs have a crime-fighting advantage over cats and other pets that don't need walking.

"When people are out walking their dogs, they have conversations, they pet each other's dogs.
Sometimes they know the dog's name and not even the owners.
They learn what's going on and can spot potential problems."
Results showed that the trust and dog-walking combination helped reduce street crimes: those crimes like homicides and robberies that tend to occur in public locations, including streets and sidewalks.
The study found that more dogs in a neighborhood was also related to fewer property crimes, like burglaries, irrespective of how much residents trust each other, Pinchak said.
That's because barking and visible dogs can keep criminals away from buildings where the dogs are found – and neighborhood trust and surveillance are not needed as a factor, as it is in street crimes.
The protective effect of dogs and trust was found even when a wide range of other factors related to crime was taken into account, including the proportion of young males in the neighborhood, residential instability and socioeconomic status.
Overall, the results suggest that it is beneficial to have a lot of trust in your neighbors to prevent crime – particularly if you add a lot of dogs and dog walkers.
"There has already been a lot of research that shows dogs are good for the health and well-being of their human companions," Pinchak said. "Our study adds another reason why dogs are good for us."

Reference: "Paws on the Street: Neighborhood-Level Concentration of Households with Dogs and Urban Crime" by Nicolo P Pinchak, Christopher R Browning, Bethany Boettner, Catherine A Calder and Jake Tarrence, 25 June 2022, Social Forces.
DOI: 10.1093/sf/soac059

Pinchak and Browning are members of Ohio State's Institute for Population Research, which supported the study.
Other co-authors of the study were Bethany Boettner of Ohio State, and Catherine Calder and Jake Tarrence of the University of Texas at Austin.
The study was based on work supported by the National Science Foundation. The Adolescent Health and Development in Context study is funded by the National Institute on Drug Abuse, the Eunice Kennedy Shriver National Institute on Child Health and Human Development, and the William T. Grant Foundation.

https://bit.ly/3AX9Col

Unidentified Bleeding Disease Kills Three in Tanzania

Thirteen people with the illness have tested negative for Ebola and Marburg. The Tanzanian government continues to investigate the source.

Andy Carstens

On July 13, the Tanzanian government's chief medical officer Aifello Sichalwe announced that a team of medical experts has been dispatched to the country's southeastern region of Lindi to investigate an as-yet unidentified disease that has infected 13 people and killed three. Although Tanzania has never officially recorded cases of either Ebola or Marburg, the people afflicted with the deadly disease—which has symptoms including fever, headaches, fatigue, and nosebleeds—were tested for both viruses, the *New Zealand Herald* reports, but the results were negative.
According to the *Herald*, Tanzanian President Samia Suluhu Hassan says that the mysterious disease may be the result of more frequent interactions between humans and animals as the region's population expands into previously undeveloped areas. While the cause of the disease is unknown, Hassan's hypothesis lines up with a World Health Organization's (WHO) statement released yesterday (July 14) that reports a 63 percent jump over the past decade in the frequency of diseases spreading from animals to humans.
"We need all hands on deck to prevent and control zoonotic diseases such as Ebola, monkeypox, and even other coronaviruses," Matshidiso Moeti, the WHO's regional director for Africa, says in the statement.
For now, officials say the Tanzanian government is working to identify the source of the current outbreak. "The government formed a team of professionals who are still investigating this unknown disease," Sichalwe says, according to the *Herald*.

https://wb.md/3zeundX

CDC Warns About Potentially Deadly Virus in Infants

The potentially fatal parechovirus is now circulating in multiple states, causing fevers, seizures, and sepsis-like symptoms, including confusion and extreme pain, according to the CDC.

Arianna Sarjoo

Human parechoviruses are common in children, and most have been infected before they start kindergarten, the CDC said. Between ages 6 months and 5 years, symptoms include an upper respiratory tract infection, fever, and rash.

But infants younger than 3 months may have more serious, and possibly fatal, infections. They may get "sepsis-like illness, seizures, and meningitis or meningoencephalitis, particularly in infants younger than 1 month," the CDC said. At least one newborn has reportedly died from the infection.

Parechovirus can spread like other common germs, from feces that are later ingested — likely due to poor hand-washing — and through droplets sent airborne by coughing or sneezing. It can be transmitted by people both with and without symptoms of the infection.

The microbe can reproduce for 1 to 3 weeks in the upper respiratory tract and up to 6 months in the gastrointestinal tract, the CDC said.

Kristina Angel Bryant, MD, a pediatric infectious disease specialist at the University of Louisville Hospital, says parechoviruses often cause rashes on the hands and feet, which some experts refer to as "mittens and booties."

The CDC is urging doctors to test for parechovirus if they recognize these symptoms in infants if there is no other explanation for what might be distressing them.

There is no specific treatment for parechovirus. And with no standard testing system in place, experts are unsure if the number of parechovirus cases is higher in 2022 than in previous years.

The message for parents, Bryant says, is: Don't panic. "This is not a new virus."

"One of the most common symptoms is fever, and in some kids, that is the only symptom," she says. "Older infants and toddlers may have only cold symptoms, and some kids have no symptoms at all."

Parents can take the usual steps to protect their child from the viral illness, including diligent handwashing and having less contact with people who are sick, Bryant says.

Sources

CDC: "Recent Reports of Human Parechovirus (PeV) in the United States— 2022."

Eyewitness News 3: "A Hamden family is heartbroken after their one-month-old baby died suddenly from a rare virus."

Kristina Angel Bryant, MD, pediatric infectious disease specialist, University of Louisville Hospital, Louisville, KY.

https://bit.ly/3uW4vko

87% Survival – New Combined Therapy Greatly Improves Prostate Cancer Survival

A Cedars-Sinai cancer study indicates improved survival following a combination of hormone therapy and pelvic lymph node treatment

A combination of androgen deprivation therapy—a common hormone injection—and pelvic lymph node radiotherapy prevented prostate cancer from therapy in nearly 90% of clinical trial participants for five years, according to a ground-breaking study from Cedars-Sinai Cancer. The results were recently published in the peer-reviewed journal *The Lancet.*

The research also demonstrates that individuals with prostate cancer who did not get pelvic lymph node radiotherapy or androgen restriction treatment had a five-year survival rate of 70%.

“We can now confirm that pelvic lymph node treatment used together with androgen deprivation therapy, or even used as a stand-alone treatment option, greatly improves outcomes in patients

with postoperative prostate cancer," said Howard Sandler, MD, chair of the Department of Radiation Oncology at Cedars-Sinai Cancer and senior author of the study. "These findings are an encouraging step forward, both for the medical community and for the patients and their loved ones seeking curative treatment options."

Between March 31, 2008, and March 30, 2015, 1,716 participants were recruited in the global Phase III clinical trial that formed the basis of The Lancet research. Three groups of participants were created. Salvage prostate bed radiotherapy was administered to Group 1; this kind of radiation is often directed towards the prostate's former location before it was surgically removed. The median five-year survival rate for these individuals was 71%.

The second group underwent androgen deprivation therapy in addition to the conventional radiation therapy. They had an 81^ median five-year survival rate. The third group received salvage prostate bed radiotherapy, androgen deprivation therapy, and pelvic lymph node radiation. These patients had a five-year freedom from progression of just over 87%.

"The combined treatment approach proved to be the most beneficial approach," said Sandler, also the Ronald H. Bloom Family Chair in Cancer Therapeutics and professor of Radiation Oncology at Cedars-Sinai.

Prostate cancer is the most common non-skin cancer in the U.S., affecting 1 in every 6 to 7 men. While there are rarely early warning signs of the disease, there is a robust screening test that can catch the disease in its earliest stages. Diagnosis usually accompanies an elevated level of PSA, an acronym for prostate-specific antigen.

Many men diagnosed with prostate cancer will undergo a prostatectomy—the surgical removal of the prostate. After surgery, a man's PSA level should be near zero. However, some men start to see their PSA levels rise several years after surgery. This is typically an indication that radiation therapy is needed.

Sandler says men with postoperative prostate cancer can have excellent outcomes, especially if radiation is given early—when PSA levels are at their lowest—and in combination with proven therapies, as suggested in this new research.

"Improving and extending lives is at the heart of all we do at Cedars-Sinai Cancer," said Dan Theodorescu, MD, Ph.D., director of Cedars-Sinai Cancer, the PHASE ONE Foundation Distinguished Chair, and professor of Surgery and Pathology and Laboratory Medicine. "These pivotal clinical findings exemplify our mission while showcasing how ideas spur leading-edge research and treatment innovations."

This study was funded by grants U10CA180868 (NRG Oncology Operations), U10CA180822 (NRG Oncology Statistical and Data Management Center), UG1CA189867 (NCORP), and U24CA180803 (Imaging and Radiation Oncology Core).

Reference: "The addition of androgen deprivation therapy and pelvic lymph node treatment to prostate bed salvage radiotherapy (NRG Oncology/RTOG 0534 SPPORT): an international, multicentre, randomised phase 3 trial" by Professor Alan Pollack, MD, Professor Theodore G Karrison, Ph.D., Alexander G Balogh, MD, Professor Leonard G Gomella, MD, Professor Daniel A Low, Ph.D., Professor Deborah W Bruner, Ph.D., Jeffrey S Wefel, Ph.D., Professor Andre-Guy Martin, MD, Professor Jeff M Michalski, MD, Steve J Angyalfi, MD, Professor Himanshu Lukka, MBChB, Sergio L Faria, MD, Professor George B Rodrigues, MD, Marie-Claude Beauchemin, MD, R Jeffrey Lee, MD, Samantha A Seaward, MD, Professor Aaron M Allen, MD, Drew C Monitto, MD, Wendy Seiferheld, MS, Professor Oliver Sartor, MD, Prof Felix Feng, MD, Professor Howard M Sandler, MD, 14 May 2022, The Lancet. DOI: 10.1016/S0140-6736(21)01790-6

https://bit.ly/3RJMkZa

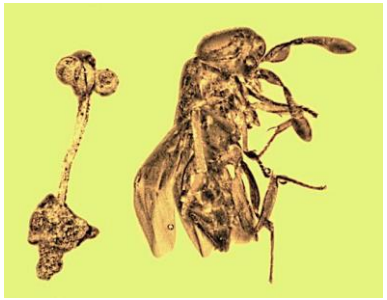
A Wasp, Flower, And Fly Trapped in Amber Reveal 30-Million-Year Old Microcosm

A newly-discovered plant, a recently-discovered wasp, and a developing fly larva have been found trapped in amber, in an exquisitely-preserved moment of prehistoric ecology.

Jess Cockerill

If the image of an insect trapped in amber seems familiar, you have

George Poinar, Jr. – the entomologist who made this discovery – to thank. His early work extracting insect DNA from Dominican amber directly inspired the premise of *Jurassic Park*. His latest study documents the first fossil record of the plant genus *Plukenetia*, and the first record of the plant genus on the Caribbean island of Hispaniola.



(George Poinar, Jr., 2022, Historical Biology)

"Fossil flowers of members of this family are quite rare," said Poinar. "I could only find one previously known fossil, from sedimentary deposits in Tennessee."

The famed Dominican amber is a fossilized form of resin from the extinct *Hymenaea protera* tree, which scientists think once grew in a moist tropical forest ecosystem, based on the variety of life forms its resin entombed. This particular specimen was mined from la Cordillera Septentrional mountain range.

There is debate over the age of Dominican amber fossils, with conflicting theories based on the microorganisms used for dating specimens. Some say that the presence of foraminifera – single-celled protists sometimes referred to as 'armored amoebae' – indicate the amber was formed roughly 20-15 million years ago.

Others suggest a date of 45-30 million years ago, based on the presence of coccoliths – plates of calcium carbonate formed by single-celled phytoplankton called coccolithophores.

Poinar notes this is further complicated because the amber was swished about and redeposited in turbulent sediment that later solidified into rock. What's more, similar amber specimens discovered in Puerto Rico and Jamaica are dated to the Oligocene (33.9-23 million years ago) and the Maastrichtian-Palaeocene (72.1-66 million years ago), respectively.

He estimates this specimen to be 30 million years old.

The fossil reveals not only a new plant species but also a whole ecological microcosm, which Poinar thinks may include pollination, predation, and even parasitism.

Modern members of the *Euphorbia* genus (the fossilized plant's living relatives) are indeed pollinated by small wasps, so it's possible this wasp played a similar ecological role.

The fossilized wasp – *Hambletonia dominicana*, discovered and named by Poinar in 2020 – is an encyrtid wasp, a group of parasites known for laying their offspring with the eggs or larvae of smaller insects, which become a meal for the developing young wasps.

Using high-resolution imaging, Poinar noticed a tiny gall gnat (Cecidomyiidae) larva within one of the flower's developing seeds and the damage to the ovary capsule the gnat inhabits.

He thinks the wasp could have been attracted to the infected flower to lay an egg that, after hatching, would have soon parasitized the gall gnat larva. Of course, the wasp's devious plot was interrupted when a blob of sticky resin abruptly froze all three organisms in the tableau they've been stuck in for millions of years.

Poinar was so taken with the beauty of this fossilized moment that he compared its appearance to 20th-century art movements, with the flower's "elegant curves" and "long lines" reminding him of Art Nouveau styles, and the wasp's "dancing", "decorative" shapes and "sharp angles" evoking Art Deco design.

"Based on interests, background, and current environment, everybody has their own way of interpreting visual images in the natural world," Poinar said. "An organism can be described, given a scientific name, and then stored away in a taxonomic hierarchy."

Fossil studies do often focus on individual organisms and their place in the timeline of the tree of life, perhaps because it is rare to come across complete specimens, let alone such a clear indication of multispecies interaction.

"In many cases, unrelated organisms become entombed together in

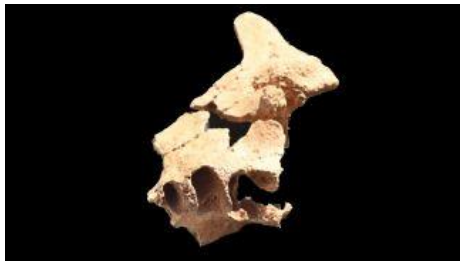
amber just by chance," Poinar said. "But I feel that in this case, the wasp was attracted to the flower, either for obtaining nectar or in attempts to deposit an egg on the capsule that contains the fly larva." The paper was published in *Historical Biology.*

https://bit.ly/3PxqSeL

1.4 million-year-old jawbone may belong to oldest known human relative in Europe

The fossil was found in Spain and included a tooth.

By Jennifer Nalewicki



An ancient upper jawbone discovered in Spain reveals the unique facial features of an individual who may be the oldest known ancient human relative in Europe.

The partial face of a hominid found at the Sima del Elefante site in Spain. **(Image credit: Susana Santamaria)**

A team of paleoanthropologists unearthed the fossil in June at Sima del Elefante (Spanish for "Pit of the Elephant"), an archeological site in the Atapuerca Mountains near the city of Burgos in northern Spain that's known for its rich fossil record. The fragmented skull is believed to be the oldest of its kind ever found in Europe and includes part of the upper jawbone (maxilla) and a tooth of a hominid who lived approximately 1.4 million years ago, the researchers said in a translated statement (opens in new tab). The hominid group includes all living and extinct members of the human and great ape family tree, including humans and our early human relatives, as well as chimpanzees and gorillas, according to The Australian Museum (opens in new tab).

Prior to this discovery, the earliest known hominid fossils unearthed in Europe (found at Sima del Elefante in 2008) were dated to 1.2 million years ago. That find included a portion of a mandible, or the lower jawbone, and several bone fragments, according to a 2012 study published in the British Dental Journal (opens in new tab).

The most recent discovery came as a surprise to researchers, who weren't expecting to find fossils that were older than those already uncovered at the site.

The upper jawbone, located approximately 6.5 feet (2 meters) deeper in the clay soil than the fossils found in 2008, was discovered by Édgar Téllez, a doctoral student at the National Center for Research on Human Evolution in Burgos, according to El País (opens in new tab), a daily newspaper in Spain.

Paleoanthropologists believe that, similar to the previous fossilized find, the upper jawbone exhibits characteristics that showcase the evolutionary pattern of the human face.

"In this maxilla there is also a vertical projection, as in the mandible found in [2008], which could indicate that this modern face was already present at this time," Téllez told El País.

In other words, Téllez and his team theorize that the bone could be that of someone who was more closely related to modern-day Europeans than more ape-like primates, such as *Homo habilis*, an extinct species of archaic humans from Africa dating to the Pleistocene epoch (2.6 million years ago to 11,700 years ago). The researchers believe that the fossil may have come from *Homo antecessor* (Latin for "pioneer man"), whose position in the human family tree is controversial (opens in new tab) but may be a close cousin of modern humans and Neanderthals, according to a 1999 study published in the Journal of Human Evolution (opens in new tab). (The first fossilized remains of *Homo antecessor* were found at Atapuerca in 1994.)

John Hawks, an anthropologist at the University of Wisconsin-Madison, who wasn't affiliated with the recent dig, said that the new discovery helps give insight into the population that initially inhabited this area.

"We don't know yet exactly where this piece of the upper jaw is going to fit, and it's going to take a lot of work and comparison for that team to determine [this]," Hawks told Live Science. "But whatever they determine, this is tied to a site with evidence of behavior. And every piece that we have that's tied to a site with evidence of behavior, such as making stone tools or hunting, tells us the behavioral capacities of ancestors and relatives of ours. For me, that's the important part."

The researchers at the site said that it will take additional study before they can determine the exact age of the upper jawbone and whether it's related to the other fossils found there.

https://bit.ly/3PDI23J

A New Antibiotic Can Kill Even Drug-Resistant Bacteria

Antibiotic-resistant pathogens could be defeated with the assistance of a synthetic antibiotic

A brand-new antibiotic that was developed at The Rockefeller University using computational models of bacterial gene products appears to kill even bacteria that are resistant to other antibiotics. According to a study published in the journal *Science*, the drug, known as cilagicin, is effective in mice and employs a novel mechanism to combat MRSA, C. diff, and numerous other dangerous infections.

The findings imply that computer models may be used to develop a new class of antibiotics. “This isn’t just a cool new molecule, it’s a validation of a novel approach to drug discovery,” says Rockefeller’s Sean F. Brady. “This study is an example of computational biology, genetic sequencing, and synthetic chemistry coming together to unlock the secrets of bacterial evolution.”

Acting on eons of bacterial warfare

Bacteria have spent billions of years inventing novel methods to kill one another, so it’s not surprising that many of our most potent antibiotics originated from bacteria. With the exception of penicillin and a few other prominent antibiotics originating from fungus, the majority of antibiotics were first used as weapons by bacteria to combat other bacteria.

“Eons of evolution have given bacteria unique ways of engaging in warfare and killing other bacteria without their foes developing resistance,” says Brady, the Evnin Professor and head of the Laboratory of Genetically Encoded Small Molecules. Antibiotic drug discovery once largely consisted of scientists growing streptomyces or bacillus in the lab and bottling their secrets to treat human diseases.

But with the rise of antibiotic-resistant bacteria, there is an urgent need for new active compounds—and we may be running out of bacteria that are easy to exploit. Untold numbers of antibiotics, however, are likely hidden within the genomes of stubborn bacteria that are tricky or impossible to study in the lab. “Many antibiotics come from bacteria, but most bacteria can’t be grown in the lab,” Brady says. “It follows that we’re probably missing out on most antibiotics.”

Finding antibacterial genes in soil and cultivating them inside more lab-friendly bacteria is an alternate strategy that has been championed by the Brady lab for the last fifteen years. But even this approach has certain drawbacks. The majority of antibiotics come from genetic sequences that are locked within bacterial gene clusters named “biosynthetic gene clusters,” which work together to collectively code for a number of proteins. But with present technology, such clusters are often inaccessible.

“Bacteria are complicated, and just because we can sequence a gene doesn’t mean we know how the bacteria would turn it on to produce proteins,” Brady says. “There are thousands and thousands of uncharacterized gene clusters, and we have only ever figured out how to activate a fraction of them.”

A new pool of antibiotics

Frustrated with their inability to unlock many bacterial gene clusters, Brady and colleagues turned to algorithms. By teasing apart the genetic instructions within a DNA sequence, modern algorithms can predict the structure of the antibiotic-like compounds that a bacterium with these sequences would produce. Organic chemists can then take that data and synthesize the predicted structure in the lab.

It may not always be a perfect prediction. "The molecule that we end up with is presumably, but not necessarily, what those genes would produce in nature," Brady says. "We aren't concerned if it is not exactly right—we only need the synthetic molecule to be close enough that it acts similarly to the compound that evolved in nature."

Postdoctoral associates Zonggiang Wang and Bimal Koirala from the Brady lab began by searching through an enormous genetic-sequence database for promising bacterial genes that were predicted to be involved in killing other bacteria and hadn't been examined previously. The "cil" gene cluster, which had not yet been explored in this context, stood out for its proximity to other genes involved in making antibiotics. The researchers duly fed its relevant sequences into an algorithm, which proposed a handful of compounds that cil likely produces. One compound, aptly dubbed cilagicin, turned out to be an active antibiotic.

Cilagicin reliably killed Gram-positive bacteria in the lab, did not harm human cells, and (once chemically optimized for use in animals) successfully treated bacterial infections in mice. Of particular interest, cilagicin was potent against several drug-resistant bacteria and, even when pitted against bacteria grown specifically to resist cilagicin, the synthetic compound prevailed.

Brady, Wang, Koirala, and colleagues determined that cilagicin works by binding two molecules, C55-P and C55-PP, both of which help maintain bacterial cell walls. Existing antibiotics such as bacitracin bind one of those two molecules but never both, and bacteria can often resist such drugs by cobbling together a cell wall with the remaining molecule. The team suspects that cilagicin's ability to take both molecules offline may present an insurmountable barrier that prevents resistance.

Cilagicin is still far from human trials. In follow-up studies, the Brady lab will perform further syntheses to optimize the compound and test it in animal models against more diverse pathogens to determine which diseases it may be most effective in treating.

Beyond the clinical implications of cilagicin, however, the study demonstrates a scalable method that researchers could use to discover and develop new antibiotics. "This work is a prime example of what could be found hidden within a gene cluster," Brady says. "We think that we can now unlock large numbers of novel natural compounds with this strategy, which we hope will provide an exciting new pool of drug candidates."

Reference: "Bioinformatic prospecting and synthesis of a bifunctional lipopeptide antibiotic that evades resistance" by Zongqiang Wang, Bimal Koirala, Yozen Hernandez, Matthew Zimmerman and Sean F. Brady, 26 May 2022, Science.
DOI: 10.1126/science.abn4213