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Methane could be the first detectable indication of life beyond Earth

If life is abundant in the universe, atmospheric methane may be the first sign of life beyond Earth detectable by astronomers.

Although nonbiological processes can generate methane, a new study by scientists at UC Santa Cruz establishes a set of circumstances in which a persuasive case could be made for biological activity as the source of methane in a rocky planet's atmosphere.

This is especially noteworthy because methane is one of the few potential signs of life, or "biosignatures," that could be readily detectable with the James Webb Space Telescope, which will begin observations later this year.

"Oxygen is often talked about as one of the best biosignatures, but it's probably going to be hard to detect with JWST," said Maggie Thompson, a graduate student in astronomy and astrophysics at UC Santa Cruz and lead author of the new study.

Despite some prior studies on methane biosignatures, there had not been an up-to-date, dedicated assessment of the planetary conditions needed for methane to be a good biosignature. "We wanted to provide a framework for interpreting observations, so if we see a rocky planet with methane, we know what other observations are needed for it to be a persuasive biosignature," Thompson said.

Published March 28 in *Proceedings of the National Academy of Sciences*, the study examines a variety of non-biological sources of methane and assesses their potential to maintain a methane-rich atmosphere. These include volcanoes; reactions in settings such as mid-ocean ridges, hydrothermal vents, and tectonic subduction zones; and comet or asteroid impacts.

The case for methane as a biosignature stems from its instability in the atmosphere. Because photochemical reactions destroy atmospheric methane, it must be steadily replenished to maintain high levels.

"If you detect a lot of methane on a rocky planet, you typically need a massive source to explain that," said coauthor Joshua Krissansen-Totton, a Sagan Fellow at UCSC. "We know biological activity creates large amounts of methane on Earth, and probably did on the early Earth as well because making methane is a fairly easy thing to do metabolically."

Nonbiological sources, however, would not be able to produce that much methane without also generating observable clues to its origins. Outgassing from volcanoes, for example, would add both methane and carbon monoxide to the atmosphere, while biological activity tends to readily consume carbon monoxide. The researchers found that nonbiological processes cannot easily produce habitable planet atmospheres rich in both methane and carbon dioxide and with little to no carbon monoxide.

The study emphasizes the need to consider the full planetary context in evaluating potential biosignatures. The researchers concluded that, for a rocky planet orbiting a sun-like star, atmospheric methane is more likely to be considered a strong indication of life if the atmosphere also has carbon dioxide, methane is more abundant than carbon monoxide, and extremely water-rich planetary compositions can be ruled out.

"One molecule is not going to give you the answer—you have to take into account the planet's full context," Thompson said. "Methane is one piece of the puzzle, but to determine if there is life on a planet you have to consider its geochemistry, how it's interacting with its star, and the many processes that can affect a planet's atmosphere on geologic timescales."

The study considers a variety of possibilities for "false positives" and provides guidelines for assessing methane biosignatures.

"There are two things that could go wrong—you could misinterpret something as a biosignature and get a false positive, or you could overlook something that's a real biosignature," Krissansen-Totton said. "With this paper, we wanted to develop a framework to help avoid both of those potential errors with methane."

He added that there is still a lot of work to be done to fully understand any future methane detections. "This study is focused on the most obvious false positives for methane as a biosignature," he said. "The atmospheres of rocky exoplanets are probably going to surprise us, and we will need to be cautious in our interpretations. Future work should try to anticipate and quantify more unusual mechanisms for nonbiological methane production."

In addition to Thompson and Krissansen-Totton, the coauthors of the paper include Jonathan Fortney, professor of astronomy and astrophysics at UCSC, Myriam Telus, assistant professor of Earth and planetary sciences at UCSC, and Nicholas Wogan at the University of Washington, Seattle.

More information: *The case and context for atmospheric methane as an exoplanet biosignature, Proceedings of the National Academy of Sciences (2022). DOI: 10.1073/pnas.2117933119*

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Common Arthritis Drug Offers New Hope For Treating Severe Alopecia

Rheumatoid arthritis and a severe form of hair loss called alopecia areata might not seem like they have much in common. One causes joint pain and swelling, while the other leads to dramatic, patchy loss of hair.

Jacinta Bowler

But in both cases, the immune system has decided that the body's own cells are a threat – in alopecia, this leads to the immune system attacking the hair follicles, while in arthritis, it's attacking tissues in the joints.

Excitingly, however, a new study of a phase three clinical trial has shown that the treatments for these two conditions could also be similar, with an arthritis drug called baricitinib effectively treating alopecia areata in one-third of patients.

This isn't a silver bullet for those with alopecia areata, but it is an exciting medical development that will hopefully soon be available for patients as a treatment option.

"Alopecia areata is a crazy journey, marked by chaos, confusion, and profound sadness for many who suffer from it," says Yale dermatology researcher Brett King.

"These large, controlled trials tell us that we can alleviate some of the suffering from this awful disease."

The reason this works is because of a protein called Janus kinase or JAKs. These enzymes are part of a signaling pathway called JAK-STAT, which is involved in a lot of areas, including the immune system. JAK-inhibitors like baricitinib are able to tone down this immune response in some patients, allowing the hair follicles to begin growing back.

The trials were double-blinded, randomized, placebo-controlled trials, making them the gold standard for analyzing how baricitinib works for those with severe alopecia.

The researchers split 1,200 patients into three groups. Participants were either given a placebo, 2 milligrams of baricitinib, or 4 milligrams of baricitinib for 36 weeks. Those who were given 4 milligrams of baricitinib had the most dramatic results, with over one-third percent of those patients experiencing significant hair growth.

The trial used something called a Severity of Alopecia Tool (SALT) to be able to evaluate the drug's effectiveness. The score goes from 0 (no hair loss) to 100 (complete scalp hair loss).

At the start of the trial, all participants had a SALT score of over 50, and by the end of the trial, around 35 percent of the patients on 4

milligrams of baricitinib had a score of 20 or less – an exciting result. Around 20 percent of patients on 2 milligrams of baricitinib also ended up with a score of 20 or less.

"The primary outcome was a SALT score of 20 or less at week 36. A SALT score of 20 or less has been identified as a meaningful treatment outcome for patients with severe alopecia areata," the team writes in their study.

"Most patients in whom the primary outcome was met had SALT scores of 10 or less at week 36."

Unfortunately, this was not free of side effects for all patients, with the researchers reporting a range of symptoms in the test groups compared to the controls, including worse acne, upper respiratory tract infections, headaches, UTIs, and elevated cholesterol levels.

In addition, due to the drug's capability to disrupt the immune system, it can also lower the immune system's capabilities to defend the body from actual threats, with increased infections previously having been seen in those using the drug for arthritis.

With that in mind, though, very few participants in the new trial dropped out due to side effects, suggesting that they were tolerable overall.

More research is currently ongoing to confirm the safety and efficacy over the long term, but this is an exciting result.

The funder for this research was Eli Lilly and Company, a pharmaceutical company that manufactures baricitinib under the brand name Olumiant, currently prescribed for treating rheumatoid arthritis.

With the phase three results from this trial now finalized, and the results looking promising, we could soon be seeing this drug remarketed to treat severe hair loss as well – hopefully providing relief for many patients.

The research was published in *The New England Journal of Medicine.*

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Japan relaunches its HPV vaccination drive. For thousands of women, it may be too late

Safety concerns led the government to stop recommending the shots in 2013

By Dennis Normile

Nine years ago, Japan's health ministry made what many scientists regarded as a terrible mistake. Pressed by antivaccine activists who claimed debilitating side effects, it stopped recommending that Japanese girls get a vaccine that helps prevent cervical cancer.

Now, in what public health officials say is a collateral benefit of the success of COVID-19 vaccines, the ministry has finally reversed its position. On 1 April, it will resume recommending that girls ages 12 to 16 get vaccinated against human papillomavirus (HPV)—"an important signal of confidence in the vaccine and its safety," says Paul Bloem, HPV vaccine strategy lead at the World Health Organization (WHO).

But part of the damage can't be undone. A modeling study published in *The Lancet* in 2020 estimated that the negligible vaccination rate between 2013 and 2019 would result in 25,000 preventable cervical cancer cases and up to 5700 deaths over time. A rapid catch-up campaign for the millions of women who missed their shots—which the government has now pledged to undertake—would only prevent 60% of that toll, the study said, because many of the women have already been infected with HPV. The disease causes nearly 3000 deaths annually in Japan, in part because cervical cancer screening rates are low.

Japan initially embraced HPV vaccines, approving GlaxoSmithKline's bivalent shot—which protects against the two HPV types carrying the greatest cancer risk—in 2009, and Merck & Co.'s quadrivalent vaccine in 2011. In April 2013, the health ministry added both to the national immunization program and

started to recommend vaccination.

But just 10 weeks later, an advisory panel suggested suspending the recommendation after a number of girls reported chronic pain, headaches, motor impairment, and other symptoms after immunization. The ministry complied, and the vaccination rate plummeted from about 70% to less than 1% of those eligible.

Such safety problems had not emerged in clinical trials, and in 2017, WHO's Global Advisory Committee on Vaccine Safety said an extensive review of studies from around the world indicated the vaccines were "extremely safe." In Japan, a nationwide survey that same year found unvaccinated girls suffer the symptoms attributed to the vaccines at similar rates as vaccine recipients.

Evidence for effectiveness grew as well. The vaccines were approved because they prevent HPV infection, but by the late 2000s, studies showed they reduced the incidence of precancerous lesions as well. Large studies in Sweden and England, reported in 2020 and 2021, respectively, showed vaccination in the early teen years cut the risk of cervical cancer by age 30 by 87% to 88%.

In other countries roiled by reports of side effects—including Denmark, the United Kingdom, and Colombia—authorities kept recommending the vaccines while investigating the claims, says Heidi Larson, head of the Vaccine Confidence Project at the London School of Hygiene & Tropical Medicine.

Vaccination rates dipped, but quickly recovered. But in Japan, the government was slow to review the evidence while antivaccine pressure "just became louder and louder," says Sharon Hanley, a cancer epidemiologist at Hokkaido University.

Opponents held press conferences, seminars, and demonstrations, and more than 100 women and girls joined lawsuits against the health ministry and vaccine manufacturers.

Still, calls to reverse the policy increased. In 2017, 17 Japanese academic societies urged the ministry to resume support for vaccination. In 2020 and 2021, a group of parliamentarians led by cervical cancer survivor Junko Mihara asked the health ministry to reconsider its position.

The COVID-19 pandemic demonstrated the power of vaccines to reduce severe illness and deaths, which eventually tipped the scales for the HPV vaccines as well, Hanley says. "Antivaccine rhetoric was also not given much space in the media" during the pandemic, she says. (About 80% of Japan's population is fully vaccinated against COVID-19.) In October 2021, the health ministry's advisory committee said there was no reason not to restart recommending HPV vaccination.

Many parents are still wary, and local governments and health care providers will have to convince them of the vaccines' benefits. The shots are in short supply globally, particularly Merck's latest, also approved in Japan, which protects against nine HPV types. And activists are not giving up. Resuming proactive recommendation "is without any scientific basis and is wrong as public health policy," says Masumi Mizuguchi, a lawyer representing plaintiffs suing the government.

The lawsuits are working their way through Japan's legal system and will continue to generate publicity.

But vaccination supporters believe the spell may have been broken. "I am confident coverage will resume to previous levels as quickly as it fell simply due to peer power," Hanley says. To her, the 9-year interlude holds an important lesson: "When the government is not supporting [a vaccine], then the people won't support it."

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I was here first! How hepatitis C inhibits hepatitis E

It is well known that co-infections with hepatitis viruses do exist.

"However, the co-infection of hepatitis C and E has not yet been systematically researched," says Thomas Burkard.

"Even though the possibility always looms that a simultaneous

infection with two viruses could perhaps be particularly dangerous."

A single protein suppresses infection

In order to find out more about simultaneous infection with the hepatitis C (HCV) and hepatitis E virus (HEV), the researchers infected liver cells in cell culture with both pathogens in the first step. It turned out that HCV is able to suppress an infection with hepatitis E. The team wanted to find out why.

"HCV consists of ten proteins," explains Thomas Burkard. "By producing individual ones in excess, we were able to study their effect."

This allowed the researchers to find that a single viral protein—called NS3/4A—successfully suppressed the replication of hepatitis E viruses in cell culture.

"It seemed that co-infection with both viruses was only possible to a very limited extent," says Burkard.

Experiments in animal models, however, presented a different pattern: genetically modified mice that have human liver cells could become infected with both viruses.

However, the infections proceeded in different ways depending on which one the mice were exposed to first. If HEV was present first, HCV could not successfully infect the animals. If HCV was present first, the infection course with HEV was often delayed.

"Here, HCV did not turn out to be as dominant as in cell culture," says Thomas Burkard. In-depth analyses of the liver cells should now shed light on the underlying causes: "Perhaps we will only find islets that are infected with one or the other virus," speculates the researcher. "In any case, it is clear that the two viruses affect each other."

More information: *Thomas Burkard et al, Viral Interference of Hepatitis C and E Virus Replication in Novel Experimental Co-Infection Systems, Cells (2022).* *DOI: 10.3390/cells11060927*

https://bit.ly/3JYm48W

There's Something Truly Unique About Pluto's Landscape, New Study Says

At the distant end of the Solar System, far from the Sun's warmth and light, a truly unique world drifts in the alien darkness.

Michelle Starr

Pluto, new research has found, has a landscape sculpted by ice volcanoes, of a type and scale seen nowhere else in the Solar System. To the south-west of the Sputnik Planitia, so much slush has erupted from below the surface of Pluto that mountains of ice stand up to 7 kilometers (4.3 miles) high.

"One of the regions with very few impact craters is dominated by enormous rises with hummocky flanks. Similar features do not exist anywhere else in the imaged Solar System," writes a team of researchers led by planetary scientist Kelsi Singer of the Southwest Research Institute.

"The existence of these massive features suggests Pluto's interior structure and evolution allows for either enhanced retention of heat or more heat overall than was anticipated before New Horizons."

As the name indicates, rather than hot molten lava, ice volcanoes erupt with slushy water slurries of volatile compounds such as ammonia and methane. Once they emerge into frigid atmospheric conditions above ground, they freeze and build up surface monuments, much like lava can create volcanic mountains and calderas, just… well, colder.

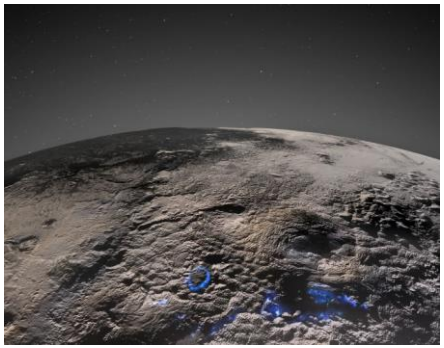
The first hint of ice volcanoes, known as cryovolcanism, was detected on Pluto in 2015, when the New Horizons probe made its epic flyby of our Solar System's erstwhile ninth planet.

Never before had scientists had access to such a wealth of data on the Kuiper Belt's largest known inhabitant; and, not far from the heart-shaped flatland of the Sputnik Planitia, some features stood out as truly interesting.

Of these, Wright Mons and Piccard Mons were tentatively identified as ice volcanoes, large mounds with what appeared to be deep holes in their centers, very similar to volcanic features elsewhere in the Solar System.

Later analysis by Singer and colleagues revealed that the elevations of the topography might appear more pronounced than they are, due to the oblique lighting at the terminator (the line that separates night and day), confusing the issue slightly.

Now, Singer and her team have conducted an in-depth analysis and found the terrain is still likely sculpted by cryovolcanism. The reason it might look different from other such terrains in the Solar System is that the processes and environment are different; "unique to Pluto", they wrote.



Cryovolcanic terrain on Pluto, with possible past activity marked in blue.
((NASA/JHU APL/SwRI/Isaac Herrera/Kelsi Singer)

Moreover, it had to have taken place fairly recently in the dwarf planet's history. That's because there's only one crater on the side of Wright Mons, suggesting that it hasn't had enough time to become pocked and scarred by multiple impacts.

Features suggestive of ice volcanoes have been spotted on multiple worlds throughout the Solar System, including dwarf planet Ceres, Saturn's moon Titan, Jupiter's moon Europa, and even Pluto's moon Charon. But cryovolcanism can be hard to positively identify, because there are no current processes on Earth of the same nature with which we can compare it.

In the cryovolcanic landscape at the edge of the Sputnik Planitia, many such mounds have proliferated, Singer and team found. The creation of such a terrain would require multiple eruption sites, and a large volume of erupted material – around 10,000 cubic kilometers, or 4 billion Olympic swimming pools' worth. The volume of Wright Mons alone is comparable to the Mauna Loa caldera in Hawaii.

It's unclear exactly what processes in the depths of Pluto might have produced such a scale of cryovolcanism. It's possible there is a deep network of fractures below the terrain, one that has since been covered up by the oozing and hardening cryomagma.

The new discovery suggests that, although it's frozen, Pluto may be very far from dead and inert. In fact, the tiny, distant dwarf planet may have a lot to teach us about cryovolcanism.

"The range of cryovolcanic features found across the Solar System is diverse. With the different conditions and surface materials present at Pluto, it is quite possible that any material movement onto the surface may not resemble that of other bodies," the team wrote.

"The extrusion of icy material onto the surface of a body with extremely low temperatures, low atmospheric pressure, low gravity, and the abundance of the volatile ices found on Pluto's surface make it unique among the visited places in the Solar System."

The research has been published in *Nature Communications*.

https://wb.md/3tYSPxq

Psychotropic Med Use Tied to 'Striking' Post-COVID Dementia Risk

Older adults taking psychotropic medication before contracting COVID-19 are at increased risk dementia in the year following the illness, new research suggests.

Megan Brooks

Results from a large study of more than 1700 patients who had been hospitalized with COVID showed a greater than twofold increased risk for post-COVID dementia in those taking antipsychotics and mood stabilizers/anticonvulsants — medications often used to treat

schizophrenia, psychosis, bipolar disorder, and seizures.

"We know that preexisting psychiatric illness is associated with poor COVID-19 outcomes, but our study is the first to show an association with certain psychiatric medications and dementia," co-investigator Liron Sinvani, MD, The Feinstein Institutes for Medical Research, Manhasset, New York, told *Medscape Medical News*.

"Our study highlights the potential interaction between baseline neuropsychiatric disease, psychotropic medications, COVID-19, and dementia," Sinvani added. The findings were published online March 18 in *Frontiers in Medicine*.

"Striking" Dementia Rate

Using electronic health records, the researchers evaluated pre-COVID psychotropic medication use and post-COVID dementia onset in 1755 adults aged 65 and older. All were hospitalized with COVID-19 at Northwell Health between March 1 and April 20, 2020. A "striking" 13% of the participants (n = 223) developed dementia within 1-year of follow-up, the investigators report.

Among the 438 patients (25%) exposed to at least one psychotropic medication before COVID-19, 105 (24%) developed dementia in the year following COVID vs 118 of 1317 (9%) patients with no pre-COVID exposure to psychotropic medication (odds ratio [OR], 3.2; 95% CI, 2.37 - 4.32).

Both pre-COVID psychotropic medication use (OR, 2.7; 95% CI, 1.8 - 4.0, $P < .001$) and delirium (OR, 3.0; 95% CI, 1.9 - 4.6, $P < .001$) were significantly associated with post-COVID dementia at 1 year.

In a sensitivity analysis in the subset of 423 patients with at least one documented neurologic or psychiatric diagnosis at the time of COVID admission, and after adjusting for confounding factors, pre-COVID psychotropic medication use remained significantly linked to post-COVID dementia onset (OR, 3.09; 95% CI, 1.5 - 6.6, $P = .002$).

Drug classes most strongly associated with 1-year post-COVID dementia onset were antipsychotics (OR, 2.8, 95% CI, 1.7 - 4.4, $P < .001$) and mood stabilizers/anticonvulsants (OR, 2.4, 95% CI, 1.39 - 4.02, $P = .001$).

In a further exploratory analysis, the psychotropics valproic acid (multiple brands) and haloperidol (Haldol) had the largest association with post-COVID dementia.

Antidepressants as a class were not associated with post-COVID dementia, but the potential effects of two commonly prescribed antidepressants in older adults, mirtazapine (Remeron) and escitalopram (Lexapro), "warrant further investigation," the researchers note.

Predictive Risk Marker?

"This research shows that psychotropic medications can be considered a predictive risk marker for post-COVID dementia. In patients taking psychotropic medications, COVID-19 could have accelerated progression of dementia after hospitalization," lead author Yun Freudenberg-Hua, MD, the Feinstein Institutes, said in a news release.

It is unclear why psychotropic medications may raise the risk for dementia onset after COVID, the investigators note

"It is intuitive that psychotropic medications indicate preexisting neuropsychiatric conditions in which COVID-19 occurs. It is possible that psychotropic medications may potentiate the neurostructural changes that have been found in the brain of those who have recovered from COVID-19," they write.

The sensitivity analysis in patients with documented neurologic and psychiatric diagnoses supports this interpretation.

COVID-19 may also accelerate the underlying brain disorders for which psychotropic medications were prescribed, leading to the greater incidence of post-COVID dementia, the researchers write.

"It is important to note that this study is no way recommending people should stop taking antipsychotics, but simply that clinicians need to factor in a patient's medication history while considering post-COVID aftereffects," Freudenberg-Hua said.

"Given that the number of patients with dementia is projected to triple in the next 30 years, these findings have significant public health implications," Sinvani added.

She noted that "care partners and healthcare professionals" should look for early signs of dementia, such as forgetfulness and depressive symptoms, in their patients. "Future studies must continue to evaluate these associations, which are key for potential future interventions to prevent dementia," Sinvani said.

The study was funded by the National Institutes of Health. Freudenberg-Hua co-owns stock and stock options from Regeneron Pharmaceuticals. Sinvani has disclosed no relevant financial relationships. Front Med. Published online March 18, 2022. Full text

https://bit.ly/36G01FW

Volcanoes, diamonds, and blobs: a billion-year history of Earth's interior shows it's more mobile than we thought

Deep in the Earth beneath us lie two blobs the size of continents. One is under Africa, the other under the Pacific Ocean.

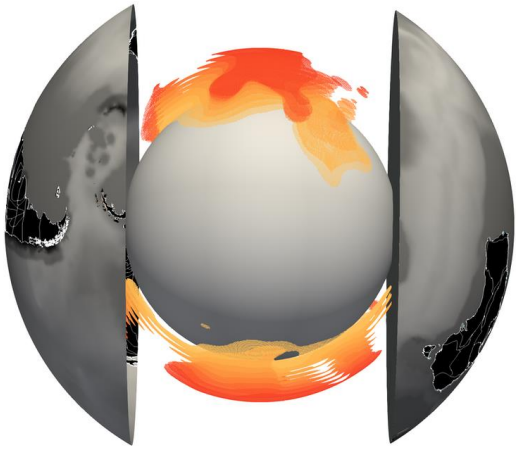
1 Nicolas Flament 2 Andrew Merdith 3 Ömer F. Bodur 4 Simon Williams

The blobs have their roots 2,900km below the surface, almost halfway to the centre of the Earth. They are thought to be the birthplace of rising columns of hot rock called "deep mantle plumes" that reach Earth's surface.

When these plumes first reach the surface, giant volcanic eruptions occur – the kind that contributed to the extinction of the dinosaurs 65.5 million years ago.

The blobs may also control the eruption of a kind of rock called kimberlite, which brings diamonds from depths 120-150km (and in some cases up to around 800km) to Earth's surface.

Scientists have known the blobs existed for a long time, but how they have behaved over Earth's history has been an open question. In new research, we modelled a billion years of geological history and discovered the blobs gather together and break apart much like continents and supercontinents.



Earth's blobs as imaged from seismic data. The African blob is at the top and the Pacific blob at the bottom. **Ömer Bodur**

A model for Earth blob evolution

The blobs are in the mantle, the thick layer of hot rock between Earth's crust and its core. The mantle is solid but slowly flows over long timescales. We know the blobs are there because they slow down waves caused by earthquakes, which suggests the blobs are hotter than their surroundings.

Scientists generally agree the blobs are linked to the movement of tectonic plates at Earth's surface. However, how the blobs have changed over the course of Earth's history has puzzled them.

One school of thought has been that the present blobs have acted as anchors, locked in place for hundreds of millions of years while other rock moves around them.

However, we know tectonic plates and mantle plumes move over time, and research suggests the shape of the blobs is changing.

Our new research shows Earth's blobs have changed shape and location far more than previously thought. In fact, over history they have assembled and broken up in the same way that continents and supercontinents have at Earth's surface.

We used Australia's National Computational Infrastructure to run

advanced computer simulations of how Earth's mantle has flowed over a billion years.

These models are based on reconstructing the movements of tectonic plates. When plates push into one another, the ocean floor is pushed down between them in a process known as subduction. The cold rock from the ocean floor sinks deeper and deeper into the mantle, and once it reaches a depth of about 2,000km it pushes the hot blobs aside.

We found that just like continents, the blobs can assemble – forming "superblobs" as in the current configuration – and break up over time.

A key aspect of our models is that although the blobs change position and shape over time, they still fit the pattern of volcanic and kimberlite eruptions recorded at Earth's surface. This pattern was previously a key argument for the blobs as unmoving "anchors".

Strikingly, our models reveal the African blob assembled as recently as 60 million years ago – in stark contrast to previous suggestions the blob could have existed in roughly its present form for nearly ten times as long.

Remaining questions about the blobs

How did the blobs originate? What exactly are they made of? We still don't know.

The blobs may be denser than the surrounding mantle, and as such they could consist of material separated out from the rest of the mantle early in Earth's history.

This could explain why the mineral composition of the Earth is different from that expected from models based on the composition of meteorites.

Alternatively, the density of the blobs could be explained by the accumulation of dense oceanic material from slabs of rock pushed down by tectonic plate movement.

Regardless of this debate, our work shows sinking slabs are more likely to transport fragments of continents to the African blob than to the Pacific blob.

Interestingly, this result is consistent with recent work suggesting the source of mantle plumes rising from the African blob contains continental material, whereas plumes rising from the Pacific blob do not.

Tracking the blobs to find minerals and diamonds

While our work addresses fundamental questions about the evolution of our planet, it also has practical applications.

Our models provide a framework to more accurately target the location of minerals associated with mantle upwelling.

This includes diamonds brought up to the surface by kimberlites that seem to be associated with the blobs.

Magmatic sulfide deposits, which are the world's primary reserve of nickel, are also associated with mantle plumes.

By helping target minerals such as nickel (an essential ingredient of lithium-ion batteries and other renewable energy technologies) our models can contribute to the transition to a low-emission economy.

1 Senior Lecturer, University of Wollongong
2 Research fellow, University of Leeds
3 Postdoctoral research fellow, University of Wollongong
4 Research Fellow, Northwest University, Xi'an

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Scientists Reveal Another Consequence of Poor Sleep: More Belly Fat

Insufficient sleep is linked with an increase in fat accumulation

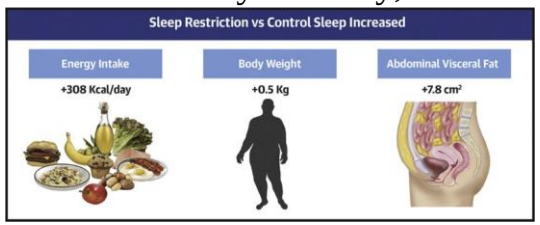
David Nield

If you need another reason to make sure you're getting a decent amount of shut-eye each night, a new study found insufficient sleep is linked with an increase in fat accumulation – especially unhealthy abdominal fat in the belly.

The randomized experiment involved 12 healthy, non-obese volunteers over a period of 21 days, finding that a lack of sufficient sleep in sleep-restricted participants was linked to a 9 percent increase in total abdominal fat area and an 11 percent increase in abdominal visceral fat.

This kind of visceral fat builds up deep inside the abdomen around internal organs, and has previously been linked to an increased risk of cardiac and metabolic diseases.

While fat is normally deposited under the skin by the body, not getting enough sleep seems to move it deeper to the visceral areas around the organs, the researchers say, where it can potentially cause more damage.



Above: A breakdown of the consequences of insufficient sleep in the experiment. **(Covassin et al., Journal of the American College of Cardiology, 2022)**

"Inadequate sleep appears to redirect fat to the more dangerous visceral compartment," says cardiologist Virend Somers from the Mayo Clinic in Minnesota.

"Importantly, although during recovery sleep there was a decrease in calorie intake and weight, visceral fat continued to increase. This suggests that inadequate sleep is a previously unrecognized trigger for visceral fat deposition, and that catch-up sleep, at least in the short term, does not reverse the visceral fat accumulation."

The volunteers were split into two groups over the course of the experiment, with one group getting nine hours of sleep per night, and the other group having to get by with just four hours of sleep, over the course of two weeks. Three months later, the tests were repeated with the participants swapping groups.

As well as the differences in visceral fat build-up, the researchers noticed that the participants who were getting less sleep were also consuming an average of more than 300 extra calories per day, taking in around 13 percent more protein and 17 percent more fat. Energy expenditure stayed mostly the same.

Throughout the study, the team monitored energy intake and expenditure, body weight, body composition, fat distribution (including visceral fat inside the belly), and circulating appetite biomarkers – and some of the apparent biological changes wouldn't have been noticed outside of a full scientific evaluation, the researchers say.

"The visceral fat accumulation was only detected by CT scan and would otherwise have been missed, especially since the increase in weight was quite modest – only about a pound," says first author of the study Naima Covassin, a cardiovascular medicine researcher at the Mayo Clinic. "Measures of weight alone would be falsely reassuring in terms of the health consequences of inadequate sleep."

That the belly fat build-up is difficult to spot makes it even more dangerous. Around one-third of adults in the US don't get enough sleep on a regular basis, with factors such as shift work and late-night use of screens both contributing to the problem.

We know that getting enough sleep is important for brain functions such as memory, and for keeping the body well hydrated, and for protecting against dementia, and for a host of other mental and physical health reasons.

What this study helps to show is that there can be a lot of knock-on effects in terms of other health risks too.

As well as making sure our periods of sleep are regular and for long enough durations, the researchers recommend increased exercise and healthy food choices as ways of preventing belly fat accumulation.

"In the long term, these findings implicate inadequate sleep as a contributor to the epidemics of obesity, cardiovascular, and metabolic diseases," says Somers. The research has been published in the *Journal of the American College of Cardiology*.

https://bit.ly/378iB9d

The human fingertip can sense single atom substitutions in a surface

The human fingertip can not only perceive subtle differences as small as single atom substitutions in silane monolayers, but can also detect differences in a polymer's crystallinity.

By Rebecca Trager

The research out of the University of Delaware was presented at the American Chemical Society's (ACS) spring conference held virtually and in-person in San Diego, US.

These discoveries could help recreate human tactile sense in a way that has applications for areas like virtual reality (VR), human machine interfaces, soft robotics and rehabilitation following an accident.

During touch, the friction generated between the finger and an object produces different types of mechanical vibrations that together form a tactile perception, explained Charles Dhong, a material scientist at the University of Delaware who led the research.

Most haptic devices, also known as touch-based interfaces, rely on reconfigurable bumps or electrical stimulations that buzz the user, but he is working on creating tactile sensations through materials chemistry.

'When you touch an object, you're feeling its surface, and you can change how it feels by changing the friction between that surface and your finger. That's where the chemistry comes in,' Dhong said. 'We think materials chemistry could open the door to recreating more nuanced sensations, whether you're designing a surface to feel a certain way, or creating feedback devices for VR.'

Touching chemistry

The structure of the molecules within a substance and the properties of its surface influence the sensation of touching an object. Consequently, the University of Delaware team theorised that by altering only chemistry-related features, the surface of an object would feel different.

Dhong's previous work had study participants touch single-molecule-thick layers of silanes – compounds containing only silicon and hydrogen – and it turned out that they could differentiate them based on slight changes in friction caused by chemical differences, including the substitution of one atom within each silane molecule with an amine.

ut his new study demonstrates that our sense of touch can also identify chemical changes as small as swapping a nitrogen atom for a carbon atom.

'Even though we show that it is a single atom substitution, we are really talking about multiple length scales of phenomenon here,' Dhong explained. 'That small change in the chemical structure gives rise to the difference in molecular forces, which gives rise to these changes in friction, which you ultimately perceive.'

Dhong's team also performed experiments that focused on the perceived texture of thin layers of polymers with identical formulas and molecular weights, but different degrees of crystallinity. As in silanes, the study subjects were able to differentiate between the polymers based only on variations in the friction resulting from

slight changes to the crystallinity of the molecules.

'Even these subtle changes in crystallinity – so we are talking about molecules that have the same molecular weight, same structure, but they have different stereochemistry and we are using different processing conditions – we found that people can actually tell differences in crystallinity in polymer films,' Dhong recounted.

In terms of future applications, he hopes that these findings can be combined with existing tactile aids to make them higher contrast. 'If we think about VR applications, there is still this limitation of the number of different tactile sensations that these bumps or buzzers can make,' Dhong said.

He envisions a scenario where some of his discoveries can be adapted to a new system, for example an electronic glove, that can allow greater tactile sense through electrical control.

Dhong pointed out that the technologies currently available to people with low vision and blindness, for example, don't have the same kind of information density as a visual graphic. 'Also, if you have low vision and blindness, can we develop better technologies to close the gap between Stem education, making abstract concepts a little more accessible.'

Roberta Klatzky, a professor of psychology and human-computer interaction at Carnegie Mellon University in Pennsylvania, US, finds it fascinating that such tiny modifications to a surface can yield changes in the perception of touch. 'It is a surprise how little you have to change a surface in order to get detectable effects, and it is very interesting that people can pick up chemical composition by virtue of the frictional changes,' adds Klatzky, who has studied the human perception of touch for decades but was not involved in the research.

She suggests that beyond friction, thermal changes may also play a role in the phenomenon reported by Dhong and colleagues.

https://bit.ly/3wSPZM3

Common Coronavirus Infections Don't Generate Effective Antibodies Against COVID

Prior infection with HCoVs is unlikely to protect against COVID-19

Although SARS-CoV-2 (the virus that causes COVID-19) has taken the world by storm, it's not the only coronavirus that can infect humans. But unlike SARS-CoV-2, common human coronaviruses (HCoVs) generally cause only mild disease. Now, researchers reporting in *ACS Infectious Diseases* have shown that infections with two different HCoVs don't generate antibodies that effectively cross-react with SARS-CoV-2. So, prior infection with HCoVs is unlikely to protect against COVID-19 or worsen a SARS-CoV-2 infection through antibody-dependent enhancement (ADE), the researchers say.

Because SARS-CoV-2 shares significant sequence similarity with its HCoV cousins, researchers have wondered if the immune system might recognize the new coronavirus from prior bouts with HCoVs. This could re-activate memory B cells, causing them to produce antibodies that helped the person overcome previous HCoV infections, and might also help fight COVID-19. On the other hand, if the antibodies against HCoVs recognize SARS-CoV-2, but not strongly enough to generate an immune response, they could cause ADE. In this rare condition, sub-optimal antibodies actually help some viruses attach to and enter host cells, making the infection worse. Sebastien Fiedler, Tuomas Knowles and colleagues wanted to compare the strength and concentration of antibodies against HCoVs and SARS-CoV-2 in the sera of nine recovered COVID-19 patients and in three pre-pandemic sera.

The researchers used a technique called microfluidic antibody-affinity profiling, which unlike the traditionally used enzyme-linked immunosorbent assay (known as ELISA), can measure both

antibody affinity and concentration independently. They found that all nine recovered COVID-19 sera samples contained moderate amounts of antibodies with high affinity to the SARS-CoV-2 spike protein. In contrast, none of the pre-pandemic sera contained high-affinity antibodies for SARS-CoV-2. All 12 sera contained low amounts of very high-affinity antibodies against two common HCoVs, indicating previous infections. Other experiments showed that these antibodies did not bind to SARS-CoV-2. The results suggest that there is no significant cross-reactivity of antibodies against common HCoVs and SARS-CoV-2, and therefore, no expected protective or adverse effects of antibody cross-reactivity for these coronaviruses, the researchers say.

Reference: "Microfluidic Antibody Affinity Profiling Reveals the Role of Memory Reactivation and Cross-Reactivity in the Defense Against SARS-CoV-2" by Viola Denninger, Catherine K. Xu, Georg Meisl, Alexey S. Morgunov, Sebastian Fiedler, Alison Ilsley, Marc Emmenegger, Anisa Y. Malik, Monika A. Piziorska, Matthias M. Schneider, Sean R. A. Devenish, Vasilis Kosmoliaptsis, Adriano Aguzzi, Heike Fiegler and Tuomas P. J. Knowles, 30 March 2022, ACS Infectious Diseases. DOI: 10.1021/acsinfecdis.1c00486

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https://bit.ly/3uLlJAa

We finally have a fully complete human genome

About 8 percent of the genome was missing from earlier versions of the genetic instruction book

By Tina Hesman Saey

Researchers have finally deciphered a complete human genetic instruction book from cover to cover.

The completion of the human genome has been announced a couple of times in the past, but those were actually incomplete drafts. "We really mean it this time," says Evan Eichler, a human geneticist and Howard Hughes Medical Institute investigator at the University of Washington in Seattle.

The completed genome is presented in a series of papers published online March 31 in *Science* and *Nature Methods*.

An international team of researchers, including Eichler, used new DNA sequencing technology to untangle repetitive stretches of DNA that were redacted from an earlier version of the genome, widely used as a reference for guiding biomedical research.

Deciphering those tricky stretches adds about 200 million DNA bases, about 8 percent of the genome, to the instruction book, researchers report in *Science*. That's essentially an entire chapter. And it's a juicy one, containing the first-ever looks at the short arms of some chromosomes, long-lost genes and important parts of chromosomes called centromeres — where machinery responsible for divvying up DNA grips the chromosome.

"Some of the regions that were missing actually turn out to be the most interesting," says Rajiv McCoy, a human geneticist at Johns Hopkins University, who was part of the team known as the Telomere-to-Telomere (T2T) Consortium assembling the complete genome. "It's exciting because we get to take the first look inside these regions and see what we can find." Telomeres are repetitive stretches of DNA found at the ends of chromosomes. Like aglets on shoelaces, they may help keep chromosomes from unraveling.

Data from the effort are already available for other researchers to explore. And some, like geneticist Ting Wang of Washington University School of Medicine in St. Louis, have already delved in. "Having a complete genome reference definitely improves biomedical studies.… It's an extremely useful resource," he says. "There's no question that this is an important achievement."

But, Wang says, "the human genome isn't quite complete yet."

To understand why and what this new volume of the human genetic encyclopedia tells us, here's a closer look at the milestone.

What did the researchers do?

Eichler is careful to point out that "this is the completion of *a*

human genome. There is no such thing as *the* human genome." Any two people will have large portions of their genomes that range from very similar to virtually identical and "smaller portions that are wildly different." A reference genome can help researchers see where people differ, which can point to genes that may be involved in diseases. Having a view of the entire genome, with no gaps or hidden DNA, may give scientists a better understanding of human health, disease and evolution.

The newly complete genome doesn't have gaps like the previous human reference genome. But it still has limitations, Wang says. The old reference genome is a conglomerate of more than 60 people's DNA (*SN: 3/4/21*). "Not a single individual, or single cell on this planet, has that genome." That goes for the new, complete genome, too. "It's a quote-unquote fake genome," says Wang, who was not involved with the project.

The new genome doesn't come from a person either. It's the genome of a complete hydatidiform mole, a sort of tumor that arises when a sperm fertilizes an empty egg and the father's chromosomes are duplicated. The researchers chose to decipher the complete genome from a cell line called CHM13 made from one of these unusual tumors.

That decision was made for a technical reason, says geneticist Karen Miga of the University of California, Santa Cruz. Usually, people get one set of chromosomes from their mother and another set from their father. So "we all have two genomes in every cell."

If putting together a genome is like assembling a puzzle, "you essentially have two puzzles in the same box that look very similar to each other," says Miga, borrowing an analogy from a colleague. Researchers would have to sort the two puzzles before piecing them together. "Genomes from hydatidiform moles don't present that same challenge. It's just one puzzle in the box."

The researchers did have to add the Y chromosome from another person, because the sperm that created the hydatidiform mole carried an X chromosome.

Even putting one puzzle together is a Herculean task. But new technologies that allow researchers to put DNA bases — represented by the letters A, T, C and G — in order, can spit out stretches up to more than 100,000 bases long. Just as children's puzzles are easier to solve because of larger and fewer pieces, these "long reads" made assembling the bits of the genome easier, especially in repetitive parts where just a few bases might distinguish one copy from another. The bigger pieces also allowed researchers to correct some mistakes in the old reference genome.

What did they find?

For starters, the newly deciphered DNA contains the short arms of chromosomes 13, 14, 15, 21 and 22. These "acrocentric chromosomes" don't resemble nice, neat X's the way the rest of the chromosomes do. Instead, they have a set of long arms and one of nubby short arms.

The length of the short arms belies their importance. These arms are home to rDNA genes, which encode rRNAs, which are key components of complex molecular machines called ribosomes. Ribosomes read genetic instructions and build all the proteins needed to make cells and bodies work. There are hundreds of copies of these rDNA regions in every person's genome, an average of 315, but some people have more and some fewer. They're important for making sure cells have protein-building factories at the ready.

"We didn't know what to expect in these regions," Miga says. "We found that every acrocentric chromosome, and every rDNA on that acrocentric chromosome, had variants, changes to the repeat unit that was private to that particular chromosome."

By using fluorescent tags, Eichler and colleagues discovered that repetitive DNA next to the rDNA regions — and perhaps the rDNA

too — sometimes switches places to land on another chromosome, the team reports in *Science*. "It's like musical chairs," he says. Why and how that happens is still a mystery.

The complete genome also contains 3,604 genes, including 104 that encode proteins, that weren't present in the old, incomplete genome. Many of those genes are slightly different copies of previously known genes, including some that have been implicated in brain evolution and development, autism, immune responses, cancer and cardiovascular disease. Having a map of where all these genes lie may lead to a better understanding of what they do, and perhaps even of what makes humans human.

One of the biggest finds may be the structure of all of the human centromeres. Centromeres, the pinched portions which give most chromosomes their characteristic X shape, are the assembly points for kinetochores, the cellular machinery that divvies up DNA during cell division. That's one of the most important jobs in a cell. When it goes wrong, birth defects, cancer or death can result. Researchers had already deciphered the centromeres of fruit flies and the human 8, X and Y chromosomes (*SN: 5/17/19*), but this is the first time that researchers got a glimpse of the rest of the human centromeres.

The structures are mostly head-to-tail repeats of about 171 base pairs of DNA known as alpha satellites. But those repeats are nestled within other repeats, creating complex patterns that distinguish each chromosome's individual centromere, Miga and colleagues describe in *Science*. Knowing the structures will help researchers learn more about how chromosomes are divvied up and what sometimes throws off the process.

Researchers also now have a more complete map of epigenetic marks — chemical tags on DNA or associated proteins that may change how genes are regulated. One type of epigenetic mark, known as DNA methylation, is fairly abundant across the centromeres, except for one spot in each chromosome called the centromeric dip region, Winston Timp, a biomedical engineer at Johns Hopkins University and colleagues report in *Science*.

Those dips are where kinetochores grab the DNA, the researchers discovered. But it's not yet clear whether the dip in methylation causes the cellular machinery to assemble in that spot or if assembly of the machinery leads to lower levels of methylation.

Examining DNA methylation patterns in multiple people's DNA and comparing them with the new reference revealed that the dips occur at different spots in each person's centromeres, though the consequences of that aren't known.

About half of genes implicated in the evolution of humans' large, wrinkly brains are found in multiple copies in the newly uncovered repetitive parts of the genome (*SN: 2/26/15*). Overlaying the epigenetic maps on the reference allowed researchers to figure out which of many copies of those genes were turned on and off, says Ariel Gershman, a geneticist at Johns Hopkins University School of Medicine.

"That gives us a little bit more insight into which of them are actually important and playing a functional role in the development of the human brain," Gershman says. "That was exciting for us, because there's never been a reference that was accurate enough in these [repetitive] regions to tell which gene was which, and which ones are turned on or off."

What is next?

One criticism of genetics research is that it has relied too heavily on DNA from people of European descent. CHM13 also has European heritage. But researchers have used the new reference to discover new patterns of genetic diversity. Using DNA data collected from thousands of people of diverse backgrounds who participated in earlier research projects compared with the T2T reference, researchers more easily and accurately found places where people

differ, McCoy and colleagues report in *Science*.

The Telomere-to-Telomere Consortium has now teamed up with Wang and his colleagues to make complete genomes of 350 people from diverse backgrounds (*SN: 2/22/21*). That effort, known as the pangenome project, is poised to reveal some of its first findings later this year, Wang says.

McCoy and Timp say that it may take some time, but eventually, researchers may switch from using the old reference genome to the more complete and accurate T2T reference. “It’s like upgrading to a new version of software,” Timp says. “Not everyone is going to want to do it right away.”

The completed human genome will also be useful for researchers studying other organisms, says Amanda Larracuente, an evolutionary geneticist at the University of Rochester in New York who was not involved in the project. “What I’m excited about is the techniques and tools this team has developed, and being able to apply those to study other species.”

Eichler and others already have plans to make complete genomes of chimpanzees, bonobos and other great apes to learn more about how humans evolved differently than apes did. “No one should see this as the end,” Eichler says, “but a transformation, not only for genomic research but for clinical medicine, though that will take years to achieve.”

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https://bit.ly/3x0ISBA

Monkeys often eat fruit containing alcohol, shedding light on our taste for booze

New study supports the "drunken monkey" hypothesis, which proposes the scent of alcohol led monkeys to ripe, fermenting and nutritious fruit

For 25 years, UC Berkeley biologist Robert Dudley has been intrigued by humans' love of alcohol. In 2014, he wrote a book proposing that our attraction to booze arose millions of years ago, when our ape and monkey ancestors discovered that the scent of alcohol led them to ripe, fermenting and nutritious fruit.

A new study now supports this idea, which Dudley calls the "drunken monkey" hypothesis.

The study was led by primatologist Christina Campbell of California State University, Northridge (CSUN), and her graduate student Victoria Weaver, who collected fruit eaten and discarded by black-handed spider monkeys (Ateles geoffroyi) in Panama. They found that the alcohol concentration in the fruit was typically between 1% and 2% by volume, a by-product of natural fermentation by yeasts that eat sugar in ripening fruit.

Moreover, the researchers collected urine from these free-ranging monkeys and found that the urine contained secondary metabolites of alcohol. This result shows that the animals were actually utilizing the alcohol for energy—it wasn't just passing through their bodies.

"For the first time, we have been able to show, without a shadow of a doubt, that wild primates, with no human interference, consume fruit-containing ethanol," said Campbell, a CUSN professor of anthropology who obtained her Ph.D. in anthropology from Berkeley in 2000. "This is just one study, and more need to be done, but it looks like there may be some truth to that 'drunken monkey' hypothesis—that the proclivity of humans to consume alcohol stems from a deep-rooted affinity of frugivorous (fruit-eating) primates for naturally-occurring ethanol within ripe fruit."

Dudley laid out evidence for his idea eight years ago in the book, "The Drunken Monkey: Why We Drink and Abuse Alcohol." Measurements showed that some fruits known to be eaten by primates have a naturally high alcohol content of up to 7%. But at the time, he did not have data showing that monkeys or apes preferentially sought out and ate fermented fruits, or that they digested the alcohol in the fruit.

For the newly reported study, the CSUN researchers teamed up with Dudley and UC Berkeley graduate student Aleksey Maro to analyze the alcohol content in the fruits. Maro is conducting a parallel study of the alcohol content in the fruit-based diet of chimpanzees in Uganda and the Ivory Coast.

"It (the study) is a direct test of the drunken monkey hypothesis," said Dudley, UC Berkeley professor of integrative biology. "Part one, there is ethanol in the food they're eating, and they're eating a lot of fruit. Then, part two, they're actually metabolizing alcohol—secondary metabolites, ethyl glucuronide and ethyl sulfate are coming out in the urine. What we don't know is how much of it they're eating and what the effects are behaviorally and physiologically. But it's confirmatory."

The study, which appeared this month in the journal *Royal Society Open Science*, was conducted at a field site, Barro Colorado Island in Panama, where Dudley has often conducted research and where he first began thinking about the role of ethanol in animal diets and how that might play into our enjoyment and abuse of alcohol.

In this 2014 video, Robert Dudley explains his ‘drunken monkey’ hypothesis and his reasons for writing a book about the primate origins of our love of alcohol. Credit: Roxanne Makasdjian and Stephen McNalley

The researchers found that the fruit that spider monkeys sniffed and took a bite out of routinely had alcohol concentrations of between 1% and 2%, about half the concentration of low-alcohol brews The ripe fruits they collected were from the jobo tree, Spondias mombin, and were a major component of the spider monkey diet. But the fruit also has been used for millennia by Indigenous human populations throughout Central and South America to make chicha, a fermented alcoholic beverage.

The researchers also collected urine from six spider monkeys. Five of the samples contained secondary metabolites of ethanol.

"The monkeys were likely eating the fruit with ethanol for the calories," Campbell said. "They would get more calories from fermented fruit than they would from unfermented fruit. The higher calories mean more energy."

Dudley said that he doubts that the monkeys feel the inebriating effects of alcohol that humans appreciate.

"They're probably not getting drunk, because their guts are filling before they reach inebriating levels," he said. "But it is providing some physiological benefit. Maybe, also, there's an anti-microbial benefit within the food that they're consuming, or the activity of the yeast and the microbes may be predigesting the fruit. You can't rule

that out."

The need for the monkeys' high caloric intake may similarly have influenced human ancestors' decisions when choosing which fruit to eat, Campbell said.

"Human ancestors may also have preferentially selected ethanol-laden fruit for consumption, given that it has more calories," she said. "Psychoactive and hedonic effects of ethanol may similarly result in increased consumption rates and caloric gain."

Today, the availability of alcohol in liquid form, without the gut-filling pulp of fermenting fruit, means it's easy to overindulge. The idea that humans' natural affinity for alcohol is inherited from our primate ancestors could help society deal with the adverse consequences of alcohol abuse.

"Excessive consumption of alcohol, as with diabetes and obesity, can then be viewed conceptually as a disease of nutritional excess," Campbell said.

More information: *Christina J. Campbell et al, Dietary ethanol ingestion by free-ranging spider monkeys (Ateles geoffroyi), Royal Society Open Science (2022). DOI: 10.1098/rsos.211729*

https://bit.ly/3u4L09y

Distinct Gut Bacterial Communities are Associated with Personality Traits: Study

New research provides evidence that four traits may have unique yet overlapping gut bacteria profiles

New research provides evidence that the four traits (i.e., mental energy and fatigue, physical energy and fatigue) may have unique yet overlapping gut bacteria profiles; for example, the bacteria most often correlated with feelings of energy perform metabolic functions, while bacteria most often correlated with feelings of fatigue are associated with inflammation.

About 45% of the U.S. population experiences elevated and persistent fatigue, a common, costly, and poorly understood problem. It has been estimated that fatigue costs employers over $136 billion per year in lost productivity.

However, these estimates do not account for fatigue-related driving and other accidents, poor medical performance, school absences, and declines in school performance and negative health outcomes.

Fatigue is underreported in medical care and linked to many diseases and disorders.

Despite fatigue's high financial and social costs, it is a poorly understood problem despite there being over 250 different instruments and no consensus about how best to measure fatigue.

One challenge for fatigue researchers is articulating the conceptual relationship between fatigue and energy.

"Our findings reinforce many of the public health concepts related to nutrition and health," said Dr. Matthew Lee Smith, a researcher in the Department of Environmental and Occupational Health and the Center for Population Health and Aging at Texas A&M University.

"Gut microbiome may be influencing the way you are, not just the way you are today," he added. "The findings are more suggestive than definitive, but they have contributed to our understanding of what gut health can do and how it makes people feel."

In the study, Dr. Smith and colleagues studied the correlation between mental energy (ME), mental fatigue (MF), physical energy (PE), physical fatigue (PF) and the gut microbiome. "Twenty subjects who were 31 years old, physically active, and not obese participated," they said.

Bacteroidetes (45%), the most prominent bacterial phyla, was only negatively correlated with PF. The second most predominant phyla, Firmicutes (43%), had members that correlated with each trait. However, the bacteria Anaerostipes was positively correlated with ME and negatively with MF and PF, respectively. Diet influences the gut microbiota composition, and only one food group,

processed meat, was correlated with the four moods: positively with MF and PF and negatively with ME and PE. Only the Firmicutes genus *Holdemania* was correlated with processed meat.

"What you eat determines the bacteria and the microbiome in your gut," said Dr. Ali Boolani, a researcher in the Department of Physical Therapy and the Department of Biology at Clarkson University. "With this study, we have made an exploratory link between a person's microbiome and their mood."

"We know that energy and fatigue can be influenced by so many things like what you eat, your physical activity, your sleep, your chronic conditions or the medications you take for these conditions," Dr. Smith said.

"Understanding how nutrition and malnutrition are linked to fatigue and energy is important because falls, chronic fatigue and low-energy can diminish the health and quality of life for older adults living with chronic conditions." "I think part of the fun here is looking at some of these relationships and being able to better see this interplay and how what you eat can influence these things."

The study appears in the journal *Nutrients*.

Ali Boolani et al. 2022. Trait Energy and Fatigue May Be Connected to Gut Bacteria among Young Physically Active Adults: An Exploratory Study. Nutrients 14 (3): 466; doi: 10.3390/nu14030466

https://bit.ly/3NIuSSI

Some Types of Asthma Protect Against Severe COVID-19, And We May Finally Know Why

People with some types of asthma are doing better than expected – we might at last understand why

Carly Cassella

When the COVID-19 pandemic first began, those with chronic lung conditions like asthma were anxious about the disease being particularly severe for them. However, it appears that people with some types of asthma are faring better than expected – and we might finally understand why. Population-based studies in Australia, the UK and Europe, and the United States, have so far found no evidence that asthma drives severe symptoms of COVID-19.

In fact, it's just the opposite. Generally, people with allergic asthma are less likely to get really sick after catching SARS-CoV-2; this is in contrast to people with other lung conditions like emphysema, who are more likely to get severe symptoms.

So what sets asthma patients apart? Researchers at the University of North Carolina at Chapel Hill think they've finally figured it out.

To research this, the team used cell cultures from the human respiratory tract. To mimic the airways of asthmatic people, they treated some of the samples with a small protein known to be more prevalent in asthma, called interleukin-13 (IL-13). One of the things its presence causes in asthmatics is ramping up mucus production beyond healthy levels.

Then, they infected the cell cultures with SARS-CoV-2. In the IL-13-treated cells, the coronavirus showed trouble invading the cell to replicate and spread copies of itself. In untreated cells, meanwhile, there were many more infections.

"We knew there had to be a bio-mechanistic reason why people with allergic asthma seemed more protected from severe disease," says biochemist Camille Ehre from UNC.

"Our research team discovered a number of significant cellular changes, particularly due to IL-13, leading us to conclude that IL-13 plays a unique role in defense against SARS-CoV-2 infection in certain patient populations."

When watching the respiratory cells and the virus interact under an electron microscope, Ehre and her colleagues noticed IL-13 treatments significantly diminished the number of infected cells, while increasing the mucus these cells produced.

Even when the mucus was removed, however, the cells still showed a degree of protection against the invading coronavirus.

RNA-sequencing further confirmed that the presence of IL-13 in the cell culture was upregulating genes linked to antiviral properties, while downregulating the expression of cell receptors that coronaviruses are known to attach to, like ACE2.

In untreated respiratory cells, these receptors allow a coronavirus to invade relatively easily. If a cell was really infected, researchers noticed it was more likely to shed away from the airway surface, allowing it to drop deeper into the lungs, thereby spreading the infection. "In conclusion, intense viral and cell shedding caused by SARS-CoV-2 infection was attenuated by IL-13, which affected viral entry, replication, and spread," the authors conclude.

Unfortunately IL-13 can't be used as a treatment by itself. It is part of the immune response, which means it can trigger inflammation in a patient's airways. But understanding the finer points of what's going on in the lungs is crucial nevertheless. By comparing cells that mimic asthmatic airways to healthy airway cells, scientists have highlighted some of the underlying mechanisms behind severe COVID-19 cases.

In the future, therapeutic drugs could help target certain sites that appear more involved in severe symptoms. "We think this research further shows how important it is to treat SARS-CoV-2 infection as early as possible," says Ehre. "And it shows just how important specific mechanisms involving ACE2 and IL-13 are, as we try our best to protect patients from developing severe infections."

The study was published in *PNAS*.

https://bit.ly/3NDd7UZ

Who Moved My Seed?

A rare animal found a rare plant. Then, it seems, the two teamed up.

By Katherine J. Wu

Zamia pseudoparasitica is a paradox packaged into a Panamanian plant. Its sticky yellow seeds are absolute chonksters, each about the size of a Sour Patch Kid—perfectly designed, it would seem, to pop off the plant and drop straight into the soil. And yet, that's exactly the fate the plant *doesn't* want to befall its progeny. The real estate the plants seek is in the cloud-forest canopy, some 25 to 70 feet off the ground. Among the world's known gymnosperms, a group of more than 1,000 types of flowerless plants, *pseudoparasitica* is the only species that refuses to root properly in soil. It prefers instead to grow *on top of other plants*, draping itself across tree branches, or nestling into the crooks of trunks at four-story-building height, its roots dangling like dreadlocks. Knobby cones and frondlike leaves give it the look of a stunted palm uncannily "growing in a tree," says Lilisbeth Rodríguez Castro of the Smithsonian Tropical Research Institute. But for years, scientists couldn't explain how *pseudoparasitica* was nabbing its penthouse perch—or who or what might be helping it along.

The stakes for the seeds are high. Should they fall to the forest floor, "they basically have no future," says Michael Calonje, a *Zamia* expert at the Montgomery Botanical Center, in Florida. But seeds don't tend to do much moseying about on their own, especially ones this chubby. The guilty party can't be wind: The seeds are far too heavy to be easily buffeted about. That means "something else, something big, should be responsible," says Claudio Monteza, of the Max Planck Institute of Animal Behavior, in Germany—perhaps a winged or tree-climbing animal accomplice that snacks on the seeds and stashes them, or scatters them as scat. Only, no one had ever caught a potential seed chauffeur in the act.

A couple of years ago, Monteza, Rodríguez Castro, and their colleagues decided to change that by getting on the plants' level. In October 2019, the team located three cone-laden *pseudoparasitica* specimens in forests across western Panama, and fit the branches of nearby trees with camera traps. Over the next four or so months, the devices captured 271 days' worth of photos, the final shots taken in

March 2020, right before the COVID-19 pandemic sent the country into mandatory quarantine.

Then the search for the seed bandit began. Monteza, the team's resident camera-trap expert, analyzed thousands of images. He remembers wondering whether he'd see a bat or a toucan, two creatures that had been posited as *pseudoparasitica*-seed dispersers. But neither ever appeared on film—just seven totally flightless mammals. One was a dwarf squirrel, only a few inches in length; two were opossums known to nosh on insects and fruit; another was a tamandua, a type of anteater with a vestlike patch of black fur. Also spotted was a white-faced capuchin monkey, a reputed seed-pooper, and two similar-looking cousins of raccoons—a kinkajou and a northern olingo, both limber, springy, and sharp-clawed.

Round one of elimination was easy. Three of the candidates—the dwarf squirrel, the tamandua, and the Robinson's mouse opossum—made mere cameos, flashing across the screen without interacting with the *pseudoparasitica* cones. Of the remaining four, Monteza spied one character who seemed like an obvious suspect: the capuchin, a species that's been documented nibbling on other forest seeds, then redistributing them through its other end. "As soon as I saw the first photo, I was like, *Yes, that makes total sense*," he told me. But the footage kept rolling, and he quickly saw that the capuchin cared … not at all for *Zamia pseudoparasitica*. It inspected the cone briefly, lost interest, then peaced out. "It was just one individual, doing nothing," Monteza said. "I was like, *You are disappointing me*." The Central American woolly opossum and the kinkajou, too, were a bit blasé. Both prodded the cone, flicked their tongues around its base—and left without lifting any seeds.

And then there was one: the northern olingo, a nocturnal, stern-faced tree-climber known for its intense yen for fruit. It blew into Monteza's data set and suddenly, spectacularly, began implicating itself. The team's traps, he realized, had captured *dozens* of instances of olingos patronizing the plants at all three study sites. Unlike the other creatures, who showed little enthusiasm for the cones, the olingos strutted up as if greeting old friends, and diligently sniffed, rubbed, nibbled, and poked. Early in Panama's dry season, when the cones were still young and sealed shut, the animals seemed to be scouting their prospects, yanking unsuccessfully at the seeds before flitting away, as if "waiting for those suckers to ripen," says Roland Kays, an olingo expert at North Carolina State University who watched the team's footage.

In January, the cones began to crack, allowing the olingos to excavate the now-mature, rank-smelling seeds with their teeth and claws. They stuffed their winnings into their mouth, two or four or even eight at a time, and leaped away into the dark.

Credit: Courtesy of Claudio Monteza, Max Planck Institute of Animal Behavior

Clearly, the olingos looked to be the guiltiest members of the camera-trap lineup—"they were the only ones that came back repeatedly, the only ones seen going in and taking seeds out," says Kristin Saltonstall, of the Smithsonian Tropical Research Institute, who helped supervise the team's work. The olingo's culpability "seems pretty solid to me," says Calonje, who wasn't involved in the study.

But no one is quite ready to call the case *closed*. The olingos captured on film didn't seem to be immediately consuming the seeds they pilfered—they just jammed them into their cheeks like hamsters and ran. "We don't know where the olingo goes next," says Ann Marie Gawel, a seed-dispersal researcher at Iowa State University who wasn't involved with the STRI project. Maybe the seeds get swallowed whole, then serendipitously pooped out to germinate in the trees. Or maybe they're chewed up and irreparably

damaged, making the olingo a predator, rather than a reproductive ally in arms. Even if the seeds survive the sojourn, that doesn't mean olingos get to take all the credit; other animals may still be involved. (During the study, a researcher on the forest floor managed to snap a non-trap photo of a yellow-eared toucanet harvesting a *pseudoparasitica* seed—but it appeared to destroy its prize shortly thereafter.)

To really clinch the story, Rodríguez Castro told me, "we would have to track the animal and track the seeds," maybe with some sort of collar for the olingo, and luminescent paint for the plant. It also wouldn't hurt, Gawel says, to sift through some olingo scat, to see if any gulped-down seeds emerge out the other end.

For now, Monteza is keen on another explanation that doesn't necessarily require a trip through a digestive tract. Perhaps the olingos are absentmindedly *caching* seeds in tree nooks and crannies; the ones the animals forget to collect then get the chance to grow. The olingos, after all, weren't feasting on the cones at their source, but amassing facefuls and skedaddling, as if scared they would be detained and frisked. If that's the case, Kays, the olingo expert, wouldn't be surprised. Olingos must share their habitat with their bigger, buffer kinkajou cousins, which will sometimes bully smaller mammals out of their meals. Hastily hoarding food for later might be olingos' best bet at outsmarting their rivals. Kays also notes that a collect-and-hide seed-dispersal strategy might be more sensible than a feces-based one, considering where a lot of olingo waste ends up. "I've sat under them, while they do that," he told me, referring to the act of defecating. The scat, like seeds, cannot defy gravity: "It lands on my head."

I asked Kays, who has respectfully chased many northern olingos through the tropics, if "*pseudoparasitica*-seed disperser" might be a title befitting of the species and its antics. "Who the hell knows," he said. (Though he does find the STRI team's data compelling.) "We don't know much about what olingos do." But should the dynamics of this duo be cemented in the future, it'll be a neat narrative—the teaming-up of a "rare animal and a rare plant," Saltonstall says. The perfect partners in arboreal crime.

https://bit.ly/35A8fP7

Combination of Biomarkers Discovered That Can Identify Common Cognitive Disease

It is possible to identify patients with subcortical small-vessel disease by combining two biomarkers that are measured in spinal fluid and blood

In recent years, subcortical small-vessel disease has become an increasingly common cognitive diagnosis. Researchers at University of Gothenburg have now shown that it is possible to identify patients with the disease by combining two biomarkers that are measured in spinal fluid and blood, increasing the potential for both treatment and development of medication.

Subcortical small-vessel disease is one of the most common cognitive diseases, along with Alzheimer's disease and mixed dementia, which is a form in which Alzheimer's disease occurs together with vascular damage in the brain.

Petronella Kettunen, associate professor in neurobiology at the University of Gothenburg and project manager for the Gothenburg Mild Cognitive Impairment study, is the article's lead author:

"Up to now, we have had no markers for subcortical small-vessel disease, which means that the disease could not be easily identified by testing samples of spinal fluid or blood. We have now opened up an opportunity to identify the disease, enabling help for this patient group in the form of lifestyle changes and blood pressure-reducing medication," she says.

In the study, researchers at the University of Gothenburg examined several biomarkers, measured in samples of both spinal fluid and blood, to see whether they could be used to distinguish between

these three common cognitive diseases. A total of 170 patients are included in the study, including control subjects.

Identifies subcortical small-vessel disease

The study confirms that a biomarker for vascular injury, based on the ratio of the protein albumin in spinal fluid and blood, was significantly higher in patients with subcortical small-vessel disease. The study also presents a new biomarker, a fragment of the amyloid precursor protein (APP) in spinal fluid, which was lower in patients with subcortical small-vessel disease.

"When we combined the biomarker for vascular injury with the protein fragment we identified, the potential for separating patients with subcortical small-vessel disease from control subjects, patients with Alzheimer's disease and patients with mixed dementia was improved," says Kettunen.

Well-defined research basis

The findings also improve the possibilities for refining patient cohorts during clinical trials for new drugs. Diagnosing patients with these diseases is important for identifying the correct patient groups for each disease that in turn enable future treatment studies.

"For a treatment study for Alzheimer's disease, for example, you need to know that all of the patients are suffering from Alzheimer's and not from another cognitive disease, otherwise the result will not be accurate."

Facts Alzheimer's & Subcortical Small-Vessel Disease

* *Alzheimer's disease progresses gradually. Early in its development, the disease usually causes memory loss because the brain regions responsible for this function are broken down.*

* *In contrast, subcortical small-vascular disease affects vessels deep within the brain, below the cerebral cortex, so that the cognitive symptoms are different. Patients often suffer sudden personality changes and slowed mental acuity before memory becomes noticeably diminished.*

* *Small-vessel disease can be associated with high blood pressure, and patients often exhibit small cerebral infarcts and other vascular injury in white brain matter. Patients with subcortical small-vessel disease constitute a large proportion of cases in the vascular cognitive disease group.*

The results have been published in the US Alzheimer's Association scientific journal *Alzheimer's & Dementia*: *Diagnosis, Assessment & Disease Monitoring*.

Reference: "Blood-brain barrier dysfunction and reduced cerebrospinal fluid levels of soluble amyloid precursor protein-β in patients with subcortical small-vessel disease" by Petronella Kettunen, Maria Bjerke, Carl Eckerström, Michael Jonsson, Henrik Zetterberg, Kaj Blennow, Johan Svensson and Anders Wallin, 25 March 2022, Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring. DOI: 10.1002/dad2.12296

https://wb.md/3wYH5wy

Low-Sodium Diet Did Not Cut Clinical Events in Heart Failure Trial

A low-sodium diet was not associated with a reduction in future clinical events in a new study in ambulatory patients with heart failure.

Sue Hughes

But there was a moderate benefit on quality of life and New York Heart Association (NYHA) functional class. The results of the SODIUM-HF trial were presented today at the American College of Cardiology (ACC) 2022 Scientific Session, conducted virtually and in-person in Washington, DC. They were also simultaneously published online in *The Lancet*. The study found that a strategy to reduce dietary sodium intake to less than 1500 mg daily was not more effective than usual care in reducing the primary endpoint of risk for hospitalization or emergency department visits due to cardiovascular causes or all-cause death at 12 months.

"This is the largest and longest trial to look at the question of reducing dietary sodium in heart failure patients," lead author, Justin Ezekowitz, MBBCh, from the Canadian VIGOUR Center at

the University of Alberta, Edmonton, Canada, told *theheart.org |Medscape Cardiology*.

But he pointed out that there were fewer events than expected in the study, which was stopped early because of a combination of futility and practical difficulties caused by the COVID pandemic, so it could have been underpowered. Ezekowitz also suggested that a greater reduction in sodium than achieved in this study or a longer follow-up may be required to show an effect on clinical events.

"We hope others will do additional studies of sodium as well as other dietary recommendations as part of a comprehensive diet for heart failure patients," he commented.

Ezekowitz said that the study results did not allow blanket recommendations to be made on reducing sodium intake in heart failure. But he added: "I don't think we should write off sodium reduction in this population. I think we can tell patients that reducing dietary sodium may potentially improve symptoms and quality of life, and I will continue to recommend reducing sodium as part of an overall healthy diet. We don't want to throw the baby out with the bathwater."

Ezekowitz noted that heart failure is associated with neurohormonal activation and abnormalities in autonomic control that lead to sodium and water retention; thus, dietary restriction of sodium has been historically endorsed as a mechanism to prevent fluid overload and subsequent clinical outcomes; however, clinical trials so far have shown mixed results. "The guidelines used to strongly recommend a reduction in sodium intake in heart failure patients, but this advice has backed off in recent years because of the lack of data. Most heart failure guidelines now do not make any recommendations on dietary sodium," he said.

SODIUM-HF was a pragmatic, multinational, open-label, randomized trial conducted in six countries (Australia, Canada, Chile, Colombia, Mexico, and New Zealand), which included 809 patients (median age, 67 years) with chronic heart failure (NYHA functional class II–III) who were receiving optimally tolerated guideline-directed medical treatment. They were randomly assigned to usual care according to local guidelines or a low-sodium diet of less than 100 mmol (<1500 mg/day). Patients with a baseline sodium intake of less than 1500 mg/day were excluded.

In the intervention group, patients were asked to follow low-sodium menus developed by dietitians localized to each region. They also received behavioral counseling by trained dietitians or physicians or nurses.

Dietary sodium intake was assessed by using a 3-day food record (including 1 weekend day) at baseline, 6 months, and 12 months in both groups and, for the intervention group, also at 3 and 9 months to monitor and support dietary adherence.

Ezekowitz explained that although the best method for measuring sodium levels would normally be a 24-hour urine sodium, this would be impractical in a large clinical trial. In addition, he pointed out that urinary sodium is not an accurate measure of actual sodium levels in patients taking diuretics, so it is not a good measure to use in a heart failure population. "The food record method of assessing sodium levels has been well validated; I think we measured it as accurately as we could have done," he added.

Results showed that between baseline and 12 months, the median sodium intake decreased from 2286 mg/day to 1658 mg/day in the low-sodium group and from 2119 mg/day to 2073 mg/day in the usual care group. The median difference between groups was 415 mg/day at 12 months.

By 12 months, events comprising the primary outcome (hospitalization or emergency department visits due to cardiovascular causes or all-cause death) had occurred in 15% of patients in the low-sodium diet group and 17% of those in the usual care group (hazard ratio [HR], 0.89 [95% CI, 0.63 - 1.26]; P = .53).

All-cause death occurred in 6% of patients in the low-sodium diet group and 4% of those in the usual care group (HR, 1.38; *P* = .32). Cardiovascular-related hospitalization occurred in 10% of the low-sodium group and 12% of the usual care group (HR, 0.82; *P* = .36), and cardiovascular-related emergency department visits occurred in 4% of both groups (HR, 1.21; *P* = .60).

The absence of treatment effect for the primary outcome was consistent across most prespecified subgroups, including those with higher vs lower baseline sodium intake. But there was a suggestion of a greater reduction in the primary outcome in individuals younger than age 65 years than in those age 65 years and older.

Quality-of-life measures on the Kansas City Cardiomyopathy Questionnaire (KCCQ) suggested a benefit in the low-sodium group, with mean between-group differences in the change from baseline to 12 months of 3.38 points in the overall summary score, 3.29 points in the clinical summary score, and 3.77 points in the physical limitation score (all differences were statistically significant). There was no significant difference in 6-minute-walk distance at 12 months between the low-sodium diet group and the usual care group.

NYHA functional class at 12 months differed significantly between groups; the low-sodium diet group had a greater likelihood of improving by one NYHA class than the usual care group (odds ratio, 0.59; *P* = .0061). No safety events related to the study treatment were reported in either group. Ezekowitz said that to investigate whether longer follow-up may show a difference in events, further analyses are planned at 2 years and 5 years.

Questions on Food Recall and Blinding

Commenting on the findings at the late-breaking clinical trials session at the ACC meeting, Biykem Bozkurt, MD, professor of medicine at Baylor College of Medicine, Houston, Texas, congratulated Ezekowitz on conducting this trial. "We have been chasing the holy grail of sodium reduction in heart failure for a very long time, so I have to commend you and your team for taking on this challenge, especially during the pandemic," she said.

But Bozkurt questioned whether the intervention group actually had a meaningful sodium reduction given that this was measured by food recall and this may have been accounted for by under-reporting of certain food intakes.

Ezekowitz responded that patients acted as their own controls in that calorie intake, fluid intake, and weight were also assessed and did not change. "So I think we did have a meaningful reduction in sodium," he said.

Bozkurt also queried whether the improvements in quality of life and functional status were reliable given that this was an unblinded study. To this point, Ezekowitz pointed out that the KCCQ quality-of-life measure was a highly validated instrument and that improvements were seen in these measures at 3, 6, and 12 months. "It is not like these were spurious findings, so I think we have to look at this as a real result," he argued.

Commenting on the study at an ACC press conference, Mary Norine Walsh, MD, director of the heart failure and cardiac transplantation programs at St Vincent Heart Center in Indianapolis, Indiana, said the trial had answered two important questions: that sodium reduction in heart failure may not reduce heart failure hospitalization/death but that patients feel better.

"I think we can safety tell patients that if they slip up a bit they may not end up in hospital," she added.

This study was funded by the Canadian Institutes of Health Research and the University Hospital Foundation (Edmonton, Alberta, Canada) and the Health Research Council of New Zealand. Ezekowitz reports research grants from American Regent, Amgen, AstraZeneca, Bayer, Bristol-Myers Squibb/Pfizer, eko.ai, US2.ai, Merck, Novartis, Otsuka, Sanofi, and Servier and consulting fees from American Regent, Amgen, AstraZeneca, Bayer, Bristol-Myers Squibb/Pfizer, Merck, Novartis, Otsuka, Sanofi, and Servier.

American College of Cardiology (ACC) 2022 Scientific Session. Presented April 2, 2022. Lancet. Published online April 2, 2022. Abstract

https://bit.ly/3DJrqLF

Compound From Cardamom Spice Can Kill Aggressive Triple-Negative Breast Cancer Cells

Study shows that compound from cardamom shows promise for treating aggressive breast cancer.

Cardamonin — a natural compound found in the spice cardamom and other plants — could have therapeutic potential for triple-negative breast cancer, according to a new study using human cancer cells. The findings also show that the compound targets a gene that helps cancer cells elude the immune system.

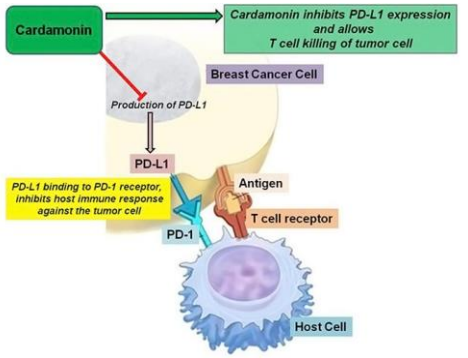
About 10-15% of breast cancers are triple-negative, which means they don't have receptors for estrogen or progesterone and don't make excess amounts of a protein called HER2. These tumors are difficult to treat because they don't respond to the hormone-based therapies used for other types of breast cancer. They also tend to be more aggressive and have a higher mortality rate than other breast cancers.

"It has been challenging to develop a targeted therapy for triple-negative breast cancer that is safe and effective at the same time," said Patricia Mendonca, PhD, assistant professor and research analyst at Florida A&M University in Tallahassee. "Because of this, there is a critical need to investigate medicinal plants as a new way to combat this cancer."

Mendonca will present the new research at the American Society for Investigative Pathology annual meeting during the Experimental Biology (EB) 2022 meeting, to be held April 2–5 in Philadelphia.

"The fact that cardamonin has been used for centuries as a spice and, more recently, as a supplement shows that its intake is safe and may bring health benefits," said Mendonca. "Our research shows that cardamonin holds potential for improving cancer therapy without as many side effects as other chemotherapeutic agents."

For the new study, the researchers investigated how cardamonin affected the expression of the programmed cell death ligand 1 (PD-L1) gene, which is found in tumor cells. PD-L1 is overexpressed during breast cancer progression and plays a critical role in helping breast cancer cells evade the body's immune system.



The production of PD-LI helps breast cancer cells escape the immune system, but cardamonin may block this process by inhibiting PD-L1 expression, leading to tumor cell death. **Credit: Patricia Mendonca, Florida A&M University**

The researchers used two genetically different triple-negative breast cancer cell lines — one derived from women with African American ancestry and the other from women of European origin (Caucasian). They found that cardamonin treatment caused a dose-dependent decrease in cell viability in both cell lines. It also reduced PD-L1 expression in the Caucasian cell line but not the African American cell line, indicating that cells from different races may respond differently to cardamonin because of genetic variations among races.

"This is the first study to describe cardamonin's inhibitory effect on the expression of PD-L1, which is relevant for the treatment of triple-negative breast cancer," said Mendonca. "These findings add support to other research that has shown differences in the tumor microenvironment between African and non-African Americans."

The researchers caution that this research is still in progress. They plan to perform more studies in both cells and animals to confirm the efficacy of this compound before it is tested in people. They also want to explore other mechanisms that may be involved in cardamonin's anti-cancer properties.

Patricia Mendonca will present this research on from 2:15– 2:30 p.m., Sunday, April 3, in

Room 118 A, Pennsylvania Convention Center (abstract). Contact the media team for more information or to obtain a free press pass to attend the meeting.
Meeting: Experimental Biology 2022

https://bit.ly/3j4mrmw

Wild New Paper Suggests T. Rex Had Short Arms So Friends Wouldn't Bite Them Off

The teeny tiny arms of Tyrannosaurus rex have been the butt of jokes for many scientists and non-scientists alike.

Jacinta Bowler

We have various hypotheses: perhaps its arms were vicious slashing machines or a way to help grasp on during sex, but it's hard to work out these sorts of evolutionary questions from a pile of 66 million-year-old bones.

A new paper now presents a wild hypothesis – that these dinosaurs evolved short arms to lower the risk of accidental bites by other *T. rex* while engaging in feeding frenzies. Put simply, short arms are less likely to be chomped on by friends.

"What if several adult tyrannosaurs converged on a carcass? You have a bunch of massive skulls, with incredibly powerful jaws and teeth, ripping and chomping down flesh and bone right next to you. What if your friend there thinks you're getting a little too close? They might warn you away by severing your arm," says Kevin Padian, integrative biologist at the University of California, Berkeley and the author of the new paper.

"So, it could be a benefit to reduce the forelimbs, since you're not using them in predation anyway."

Paleontologists are getting ever better at understanding what dinosaurs looked like, thanks to fossil finds of skin and feathers (or buttholes), and we can make some assumptions on what dinosaurs did because of how the bones are placed, or footprints that provide more information about their habits.

But complex evolutionary questions are still difficult to determine even for species whose behaviors we can watch, or have access to the genomes of their ancestors. Get to an ancient animal like *T. rex*, and it's all the more frustrating to figure stuff out.

While *T. rex* arms look laughably small, proportionally speaking they're even more ludicrous when compared to other animals. Let's imagine a 14-meter (45 feet) long *T. rex*. They might have a 1.5-meter-long skull, but their arms would only be a meter long. This is the equivalent of a 6-foot human with 12-centimeter (5 inch) arms.

To try and work out if this new 'friend arm biting' hypothesis had any legs (ha ha), Padian took measurements of a mostly complete fossil specimen called MOR 555. Using these measurements, he suggests that some of the previous hypotheses – including both the sexual aid and slashing arms hypothesis – are unlikely, as *T. rex* arms are just too small and weak to be of use.

He instead posits it could have been evolutionarily advantageous to have tiny arms, to get them out of the way for group feeding.

"Longer arms, especially in their natural, somewhat anteriorly extended orientation, would have brought them into the ambit of the deadliest jaws ever recorded on land. The danger of wounds, amputations, infections, disease and ultimate death .. would have been a selective force for reduction, irrespective of relict functionality of the limbs," explains Padian in his paper.

"Let us hypothesize, therefore, that the reduction of forelimb size was a secondary function of selection for something else. As such, we should not look for functionality in these reduced limbs, but for how that reduction served a larger purpose."

Of course, like the other suggestions above, this is a hypothesis. In the paper Padian suggests some ways that other researchers might be able to test it: for example, if we found relatively fewer bite marks on their arm bones than other parts of their bodies.

"What I first wanted to do was to establish that the prevailing functional ideas simply don't work," he said.

"That gets us back to square one. Then, we can take an integrative approach, thinking about social organization, feeding behavior and ecological factors apart from purely mechanical considerations."

The research has been published in *Acta Palaeontologica Polonica*.