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Non-Viral COVID-19 Nasal Vaccine Candidate Effective at Preventing Disease Transmission

Non-viral vaccine elicits immunity in respiratory tract.

Breathe in, breathe out. That's how easy it is for SARS-CoV-2, the virus that causes COVID-19, to enter your nose. And though remarkable progress has been made in developing intramuscular vaccines against SARS-CoV- 2, such as the readily available Pfizer, Moderna and Johnson & Johnson vaccines, nothing yet – like a nasal vaccine – has been approved to provide mucosal immunity in the nose, the first barrier against the virus before it travels down to the lungs. But now, we're one step closer.

Navin Varadarajan, University of Houston M.D. Anderson Professor of Chemical and Biomolecular Engineering, and his colleagues, are reporting in *iScience* the development of an intranasal subunit vaccine that provides durable local immunity against inhaled pathogens.

"Mucosal vaccination can stimulate both systemic and mucosal immunity and has the advantage of being a non-invasive procedure suitable for immunization of large populations," said Varadarajan. "However, mucosal vaccination has been hampered by the lack of efficient delivery of the antigen and the need for appropriate adjuvants that can stimulate a robust immune response without toxicity."

To solve those problems, Varadarajan collaborated with Xinli Liu, associate professor of pharmaceutics at the UH College of Pharmacy, and an expert in nanoparticle delivery. Liu's team was able to encapsulate the agonist of the stimulator of interferon genes (STING) within liposomal particles to yield the adjuvant named NanoSTING. The function of the adjuvant is to promote the body's immune response. "NanoSTING has a small particle size around 100 nanometers which exhibits significantly different physical and chemical properties to the conventional adjuvant," said Liu.

"We used NanoSTING as the adjuvant for intranasal vaccination and single-cell RNA-sequencing to confirm the nasal-associated lymphoid tissue as an inductive site upon vaccination. Our results show that the candidate vaccine formulation is safe, produces rapid immune responses — within seven days — and elicits comprehensive immunity against SARS-CoV-2," said Varadarajan.

A fundamental limitation of intramuscular vaccines is that they are not designed to elicit mucosal immunity. As prior work with other respiratory pathogens like influenza has shown, sterilizing immunity to virus re-infection requires adaptive immune responses in the respiratory tract and the lung.

The nasal vaccine will also serve to equitably distribute vaccines worldwide, according to the researchers. It is estimated that first world countries have already secured and vaccinated multiple intramuscular doses for each citizen while billions of people in countries like India, South Africa, and Brazil with large outbreaks are currently not immunized. These outbreaks and viral spread are known to facilitate viral evolution leading to decreased efficacy of all vaccines.

"Equitable distribution requires vaccines that are stable and that can be shipped easily. As we have shown, each of our components, the protein (lyophilized) and the adjuvant (NanoSTING) are stable for over 11 months and can be stored and shipped without the need for freezing," said Varadarajan.

Varadarajan is co-founder of AuraVax Therapeutics Inc., a pioneering biotech company developing novel intranasal vaccines and therapies to help patients defeat debilitating diseases, including COVID-19. The company has an exclusive license agreement with UH with respect to the intellectual property covering intranasal vaccines and STING agonist technologies. They have initiated the manufacturing process and plan to engage the FDA later this year.

Reference: "Single-dose intranasal vaccination elicits systemic and mucosal immunity against SARS-CoV-2" by Xingyue An, Melisa Martinez-Paniagua, Ali Rezvan, Samiur Rahman Sefat, Mohsen Fathi, Shailbala Singh, Sujit Biswas, Melissa Pourpak, Cassian Yee, Xinli Liu and Navin Varadarajan, 24 September 2021, iScience.
DOI: 10.1016/j.isci.2021.103037
Along with Liu, Varadarajan's team includes postdoctoral researchers Xingyue An, Melisa Martinez-Paniagua; research assistants Ali Rezvan, Mohsen Fathi and Sujit Biswas; doctoral student Samiur Rahman Sefat, all from the University of Houston; and Shailbala Sing, postdoctoral researcher at University of Texas M. D. Anderson Cancer Center; Melissa Pourpak, BD; and Cassian Yee, M.D., University of Texas M. D. Anderson Cancer Center.

https://bit.ly/3AFXncX

Salty Diet Helps Gut Bugs Fight Cancer in Mice: Study

A high-salt diet suppressed the growth of tumors in a mouse model of melanoma, apparently because of an interplay between the gut microbiome and natural killer cells.

Sophie Fessl

In mice, a diet high in salt suppresses tumor growth—but only when gut microbes are there to stimulate immune cells, a September 10 study in *Science Advances* reports. The findings raise tantalizing questions about the role of diet and gut microbes in human cancers, and may point to new avenues for therapeutic development.

While the study isn't the first to connect a high-salt diet to shrinking tumors, "[the authors] have shown a unique mechanistic role of high salt induced gut microbiome changes as the central phenomenon behind their observed anti-cancer effect," writes Venkataswarup Tiriveedhi, a biologist at Tennessee State University who has studied the effect of salt on cancer progression but was not involved in the study, in an email to *The Scientist*.

Amit Awasthi, an immunologist with the Translational Health Science and Technology Institute in India and corresponding author of the study, says he and his colleagues pursued this line of inquiry because previous research had linked high salt intake with autoimmune diseases, suggesting that increased salt stimulates immune cells. Meanwhile, tumors are well known to grow in immune-suppressive environments. Awasthi recalls wondering with his team: "If we put salt in the mice's diet, maybe [the immune system in] the tumor environment becomes activated," suppressing cancerous growth.

Indeed, a 2019 *Frontiers in Immunology* study from a European team led by Hasselt University immunologist Markus Kleinewietfeld reported that high-salt diets inhibited tumor growth in mice. When Awasthi and his colleagues carried out similar experiments, implanting mice with B16F10 skin melanoma cells and then feeding the tumor transplant mice diets with different salt levels, they got similar results: tumors grew slower in mice who were fed a high-salt diet.

That led to what Awasthi calls an "obvious question": How does the immune system respond to dietary salt? To answer that, the team dissected the tumor sites and found that immune cells known as natural killer (NK) cells were enriched in the mice fed the high-salt diet compared with mice fed diets with normal or slightly elevated salt levels. When the NK cells were removed, the high-salt diet no longer led to tumor regression—an effect that wasn't seen after depleting both T and B cells.

To drill into why salt had this effect on NK cells, Awasthi and his colleagues looked in the literature and found studies reporting that high-salt diets alter the gut microbiome, as well as others that found the gut microbiome modulates patients' response to cancer immunotherapy. To test for a role of the resident gut bacteria in the effects of a high-salt diet on cancer growth, the researchers gave the mice antibiotics before feeding them the different diets. Sure enough, a high-salt diet no longer suppressed tumor growth. But that wasn't all: when the team transplanted fecal material from mice fed a high-salt diet into microbe-free mice, they were surprised to find that tumors shrank, Awasthi recalls.

The researchers looked at the diversity of species in the mice's gut and saw an increased abundance of *Bifidobacterium* species in mice fed a high-salt diet. Moreover, the tumors of these mice showed a sixfold increase in *Bifidobacterium* abundance compared with the tumors of mice on a normal diet. According to Awasthi, that suggests "*Bifidobacterium* is leaking out from the gut and actually reaching the tumor site," likely the result of salt-induced gut permeability.

In mice fed a normal diet, injection of *Bifidobacterium* into tumors led to tumor regression, an effect that disappeared if the researchers removed the animals' NK cells, they reported. Awasthi says that might mean there's a way to capitalize on the tumor-fighting qualities of a high-salt diet while avoiding the potential downsides, such as autoimmune issues or hypertension: "we can replace the salt with the *Bifidobacterium*."

Kleinewietfeld says the new study is in line with his 2019 study and previous work showing that salt can affect the gut microbiota. Still, he writes in an email to *The Scientist*, "The microbiome part of this paper seems a bit preliminary . . . and some data are yet hard to interpret with the information provided in the manuscript."

A perplexing problem, writes Tiriveedhi, "is the dual nature of the impact of salt on solid tumors." While salt may suppress cancer by enhancing antitumor immune responses, Tiriveedhi points to studies by his group that find salt can also induce cancer progression and proliferation. According to Tiriveedhi, these results "suggest a temporal role of salt on cancer progression." In the short term, salt might trigger anticancer mechanisms, he says, but "over a prolonged chronic period of time, salt might switch sides and exert a pro-cancer effect."

Even with such questions outstanding, Awasthi says that his group's results could provide the basis of a new form of cancer therapy, and the team is already planning clinical trials in collaboration with oncologists. Whether those trials will validate the antitumor activities of salt or *Bifidobacterium* remains to be seen.

"[I]t's an exciting field of research, though still in its infancy," writes Kleinewietfeld, adding "more studies [are] needed to understand the complex interactions of nutrition, microbiome and immunity in the context of cancer. Thus, future studies will show if new findings could indeed lead to novel treatment options for patients."

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There Could Be an Extremely Simple Reason Why Mars Isn't as Suitable For Life

Mars' diameter is just 53 percent that of Earth's, which would make it impossible for Mars to hang onto volatiles such as water

Michelle Starr

We often talk about the strong similarities between Earth and Mars, but it's the differences that are likely behind why one planet has life and the other doesn't – at least, no life we've found so far.

Specifically, new research suggests it could be down to the size discrepancy. The diameter of Mars is just 53 percent that of Earth's (just over half the size), and that would make it impossible for Mars to hang onto volatiles that we know are vital for life – such as water.

"Mars's fate was decided from the beginning," says planetary scientist Kun Wang of Washington University in St. Louis.

"There is likely a threshold on the size requirements of rocky planets to retain enough water to enable habitability and plate tectonics, with mass exceeding that of Mars."

Although there are many differences between Earth and other terrestrial planets in the Solar System, it can be difficult to ascertain which factors are conducive to the emergence of life, and which factors hinder it. But we can look at some of the things life on Earth needs in order to exist, and work from there.

One thing that life on Earth requires is liquid water, so conditions that enable the presence of liquid water is one of the key items on the planet habitability checklist. We know that Mars used to have surface water – we've seen evidence of it in Martian meteorites that have made their way from Earth, excavated from the red planet when the Solar System was still young. Today, however, Mars is dusty, dry and desolate, and any water on its surface is frozen.

The transition from a relatively wet planet to arid dustbowl is sometimes attributed to Mars's lost magnetic field. But it's possible that other factors play a role in the retention of volatiles, such as the surface gravity of a cosmic body; Earth's gravity, for reference, is 2.66 times that of Mars's. So Wang and his team set about investigating.

Specifically, they started looking at the abundances of the moderately volatile element potassium on various Solar System objects, using it as a tracer for other volatile elements and compounds. That's because potassium isotope ratios are a strong proxy for volatile depletion in planetary interiors, because they are insensitive to igneous processes and impact-induced vaporization.

"Martian meteorites are the only samples available to us to study the chemical makeup of the bulk Mars," Wang says.

"Those Martian meteorites have ages varying from several hundred millions to 4 billion years and recorded Mars's volatile evolution history. Through measuring the isotopes of moderately volatile elements, such as potassium, we can infer the degree of volatile depletion of bulk planets and make comparisons between different Solar System bodies."

The team studied the isotope compositions of potassium in 20 Mars meteorites, chosen because they seem to be representative of Mars's bulk silicate composition. These compositions were then compared to the known bulk silicate compositions of three other inner Solar System objects of varying masses – Earth, the Moon, and the asteroid Vesta.

The results showed that Mars lost more volatiles than Earth did during its formation, but retained more than the Moon and Vesta, both of which are significantly smaller and drier than Mars.

"The reason for far lower abundances of volatile elements and their compounds in differentiated planets than in primitive undifferentiated meteorites has been a longstanding question," says planetary scientist Katharina Lodders of Washington University.

"The finding of the correlation of potassium isotopic compositions with planet gravity is a novel discovery with important quantitative implications for when and how the differentiated planets received and lost their volatiles."

This has implications for our understanding of the planet's history, the researchers said. Previous research has found that Mars was once very soggy indeed. This new correlation between gravity and volatile retention might help place constraints on just how much water Mars once had.

Additionally, the finding has implications for our search for habitable worlds outside the Solar System. One factor that influences the presence of liquid water on a planetary surface is its temperature, related to its proximity to the host star. Too close and water evaporates; too far, and it freezes.

We can also measure the sizes and masses of exoplanets, based on how much starlight they block when they move between us and the star, and how much the star moves in its mutual orbit with the exoplanet. So the team's work could help us rule out exoplanets that are too small for liquid water.

"The size of an exoplanet is one of the parameters that is easiest to determine," Wang said. "Based on size and mass, we now know whether an exoplanet is a candidate for life, because a first-order determining factor for volatile retention is size."

The research has been published in *PNAS*.

https://bit.ly/3lSW83L

Dangerous Paradox: Physical Activity May Hasten Build-Up of Heart Attack Risk Factor

Linked to calcium deposits in coronary arteries, used to measure cardiovascular disease risk

Physical activity may paradoxically hasten the build-up of calcium deposits (plaque) in the coronary arteries, the amount of which is used to assess future cardiovascular disease risk, finds research published online in the journal *Heart.* But the findings don't outweigh the numerous health benefits of exercise, emphasize the researchers.

The coronary artery calcium score, or CAC score for short, is used to guide treatment to ward off a heart attack or stroke. Statins are indicated for most people with a CAC score of 100 or above.

Regular physical activity is associated with a dose-dependent reduction in the risk of obesity, diabetes, heart attack/stroke, and death, among other things.

But the research shows that despite these important health benefits people who are very physically active seem to have high levels of calcium deposits in their coronary arteries. So it's not clear if exercise may itself be associated with calcification (artery hardening).

In a bid to explore this further, the researchers studied healthy adults who underwent regular comprehensive check-ups at two major health centers in Seoul and Suwon, South Korea, between March 2011 and December 2017, as part of the Kangbuk Samsung Health Study.

At each health check, participants filled out a questionnaire, which included questions on medical and family history, lifestyle, and educational attainment. Weight (BMI), blood pressure, and blood fats were also assessed.

Physical activity was formally categorized at the first check-up as either inactive, moderately active, or 'health-enhancing' (intensely) physically active, using a validated questionnaire.

Scans tracked the development and/or progression of coronary artery calcification which was then scored (CAC score) over an average period of 3 years.

Some 25,485 people (22,741 men and 2744 women), aged at least 30, and with at least two CAC scores, were included in the final analysis. Some 47% (11,920), 38% (9683), and 15% (3882) of them were, respectively, inactive, moderately active, and intensely physically active–equivalent to running 6.5 km/day.

Those who were more physically active tended to be older and less likely to smoke than less physically active participants. They also had lower total cholesterol, more high blood pressure, and existing evidence of calcium deposits in their coronary arteries.

A graded association between physical activity level and the prevalence and progression of coronary artery calcification emerged over time, irrespective of CAC scores at the start of the monitoring period. The estimated adjusted average CAC scores in all three groups at the start of the monitoring period were 9.45, 10.20, and 12.04, respectively.

But higher physical activity was associated with faster progression of CAC scores both in those with no calcium deposits and in those who already had a CAC score at the start of the monitoring period.

Compared with those who were inactive, the estimated adjusted 5-year average increases in CAC scores in moderately and intensely active participants were 3.20 and 8.16, respectively, even after accounting for potentially influential factors, including BMI, blood pressure, and blood fats.

This is an observational study, and as such, can't establish cause. The researchers also acknowledge several study limitations, including the absence of an objective assessment of physical activity; and no data on incident heart attacks/stroke or on CAC

density or volume.

Physical activity may increase coronary atherosclerosis (artery narrowing) through mechanical stress and vessel wall injury and through the physiological responses it prompts, such as increases in blood pressure and parathyroid hormone, they explain. Physical activity may also modify the effect of diet, vitamins, and minerals, they suggest.

"The second possibility is that physical activity may increase CAC scores without increasing [cardiovascular disease] risk," they write.

"The cardiovascular benefits of physical activity are unquestionable," they emphasize, reiterating national guidelines recommending at least 150–300 minutes/week of moderate intensity or 75–150 minutes/week of vigorous intensity aerobic physical activity. "Patients and physicians, however, need to consider that engaging in physical activity may accelerate the progression of coronary calcium, possibly due to plaque healing, stabilization and calcification," they conclude.

In a linked editorial, Drs Gaurav Gulsin and Alastair James Moss, of the Department of Cardiovascular Science, University of Leicester, ask: "Do these findings mean that we should stop using coronary artery calcium scores to assess coronary artery disease?"

The study highlights the complexity of interpreting CAC scores in patients who have upped their physical activity or started taking statins – also associated with higher scores, they point out.

"While proponents would argue that it is an effective tool to screen for subclinical atherosclerosis in asymptomatic individuals, clinicians should be cautious regarding the overuse of this test in otherwise healthy individuals," they caution.

In a linked podcast, Dr. Moss explains that non-calcified plaque, which is more unstable and more likely to rupture, may be more important and should be scored to assess a person's future risk of a heart attack or stroke. "It may be the target we need to look for is non-calcified plaque rather than calcified plaque," he suggests. This wasn't visible on the scans used in this study.

"Increasing rates of coronary artery calcification is a phenomenon that is observed both in response to effective treatment like statin therapy and exercise. But it shouldn't necessarily be regarded that serial imaging with calcium scans is the best way to accurately assess [cardiovascular disease] risk in these individuals.

But he reiterates: "Clearly, exercise is one of the best ways of trying to control cardiovascular risk in [people without symptoms]."

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"Physical activity and the progression of coronary artery calcification" by Ki-Chul Sung, Yun Soo Hong, Jong-Young Lee, Seung-Jae Lee, Yoosoo Chang, Seungho Ryu, Di Zhao, Juhee Cho, Eliseo Guallar and Joao A C Lima, 20 September 2021, Heart. DOI: 10.1136/heartjnl-2021-319346

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https://bit.ly/3zE2qBK

Sodom and Gomorrah? Evidence That a Cosmic Impact Destroyed a Biblical City in the Jordan Valley

As the inhabitants of Tall el-Hammam went about their business about 3,600 years ago, they had no idea an unseen icy space rock was speeding toward them

An Ancient Disaster

In the Middle Bronze Age (about 3,600 years ago or roughly 1650 BCE), the city of Tall el-Hammam was ascendant.

Located on high ground in the southern Jordan Valley, northeast of the Dead Sea, the settlement in its time had become the largest continuously occupied Bronze Age city in the southern Levant, having hosted early civilization for a few thousand years. At that time, it was 10 times larger than Jerusalem and 5 times larger than Jericho.

"It's an incredibly culturally important area," said James Kennett, emeritus professor of earth science at UC Santa Barbara. "Much of

where the early cultural complexity of humans developed is in this general area."

A favorite site for archaeologists and biblical scholars, the mound hosts evidence of culture all the way from the Chalcolithic, or Copper Age, all compacted into layers as the highly strategic settlement was built, destroyed, and rebuilt over millennia.

But there is a 1.5-meter interval in the Middle Bronze Age II stratum that caught the interest of some researchers for its "highly unusual" materials.

In addition to the debris one would expect from destruction via warfare and earthquakes, they found pottery shards with outer surfaces melted into glass, "bubbled" mudbrick and partially melted building material, all indications of an anomalously high-temperature event, much hotter than anything the technology of the time could produce.

"We saw evidence for temperatures greater than 2,000 degrees Celsius," said Kennett, whose research group at the time happened to have been building the case for an older cosmic airburst about 12,800 years ago that triggered major widespread burning, climatic changes and animal extinctions.

The charred and melted materials at Tall el-Hammam looked familiar, and a group of researchers including impact scientist Allen West and Kennett joined Trinity Southwest University biblical scholar Philip J. Silvia's research effort to determine what happened at this city 3,650 years ago. Their results are published in the journal *Nature Scientific Reports*.

Salt and Bone

"There's evidence of a large cosmic airburst, close to this city called Tall el-Hammam," Kennett said of an explosion similar to the Tunguska Event, a roughly 12-megaton airburst that occurred in 1908, when a 56-60-meter meteor pierced the Earth's atmosphere over the Eastern Siberian Taiga.

The shock of the explosion over Tall el-Hammam was enough to level the city, flattening the palace and surrounding walls and mudbrick structures, according to the paper.

The distribution of bones indicated "extreme disarticulation and skeletal fragmentation in nearby humans."

For Kennett, further proof of the airburst was found by conducting many different kinds of analyses on soil and sediments from the critical layer. Tiny iron- and silica-rich spherules turned up in their analysis, as did melted metals.

"I think one of the main discoveries is shocked quartz.

These are sand grains containing cracks that form only under very high pressure," Kennett said of one of many lines of evidence that point to a large airburst near Tall el-Hammam.

"We have shocked quartz from this layer, and that means there were incredible pressures involved to shock the quartz crystals — quartz is one of the hardest minerals; it's very hard to shock."

The airburst, according to the paper, may also explain the "anomalously high concentrations of salt" found in the destruction layer — an average of 4% in the sediment and as high as 25% in some samples.

"The salt was thrown up due to the high impact pressures," Kennett said of the meteor that likely fragmented upon contact with the Earth's atmosphere.

"And it may be that the impact partially hit the Dead Sea, which is rich in salt." The local shores of the Dead Sea are also salt-rich, so the impact may have redistributed those salt crystals far and wide — not just at Tall el-Hammam, but also nearby Tell es-Sultan (proposed as the biblical Jericho, which also underwent violent destruction at the same time) and Tall-Nimrin (also then destroyed).

The high-salinity soil could have been responsible for the so-called "Late Bronze Age Gap," the researchers say, in which cities along the lower Jordan Valley were abandoned, dropping the population

from tens of thousands to maybe a few hundred nomads.

Nothing could grow in these formerly fertile grounds, forcing people to leave the area for centuries.

Evidence for resettlement of Tall el-Hammam and nearby communities appears again in the Iron Age, roughly 600 years after the cities' sudden devastation in the Bronze Age.

Fire and Brimstone

Tall el-Hamman has been the focus of an ongoing debate as to whether it could be the biblical city of Sodom, one of the two cities in the Old Testament Book of Genesis that were destroyed by God for how wicked they and their inhabitants had become.

One denizen, Lot, is saved by two angels who instruct him not to look behind as they flee.

Lot's wife, however, lingers and is turned into a pillar of salt.

Meanwhile, fire and brimstone fell from the sky; multiple cities were destroyed; thick smoke rose from the fires; city inhabitants were killed and area crops were destroyed in what sounds like an eyewitness account of a cosmic impact event.

It's a satisfying connection to make.

"All the observations stated in Genesis are consistent with a cosmic airburst," Kennett said, "but there's no scientific proof that this destroyed city is indeed the Sodom of the Old Testament." However, the researchers said, the disaster could have generated an oral tradition that may have served as the inspiration for the written account in the book of Genesis, as well as the biblical account of the burning of Jericho in the Old Testament Book of Joshua.

Reference: "A Tunguska sized airburst destroyed Tall el-Hammam a Middle Bronze Age city in the Jordan Valley near the Dead Sea" by Ted E. Bunch, Malcolm A. LeCompte, A. Victor Adedeji, James H. Wittke, T. David Burleigh, Robert E. Hermes, Charles Mooney, Dale Batchelor, Wendy S. Wolbach, Joel Kathan, Gunther Kletetschka, Mark C. L. Patterson, Edward C. Swindel, Timothy Witwer, George A. Howard, Siddhartha Mitra, Christopher R. Moore, Kurt Langworthy, James P. Kennett, Allen West and Phillip J. Silvia, 20 September 2021, Scientific Reports.
DOI: 10.1038/s41598-021-97778-3

https://bit.ly/3i5tVWj

Futuristic Solar Electric Thrusters Makes NASA's Psyche Spacecraft Go

Futuristic electric thrusters emitting a cool blue glow will guide the Psyche spacecraft through deep space to a metal-rich asteroid.

When it comes time for NASA's Psyche spacecraft to power itself through deep space, it'll be more brain than brawn that does the work. Once the stuff of science fiction, the efficient and quiet power of electric propulsion will provide the force that propels the Psyche spacecraft all the way to the main asteroid belt between Mars and Jupiter. The orbiter's target: a metal-rich asteroid also called Psyche.

The spacecraft will launch in August 2022 and travel about 1.5 billion miles (2.4 billion kilometers) over three and a half years to get to the asteroid, which scientists believe may be part of the core of a planetesimal, the building block of an early rocky planet. Once in orbit, the mission team will use the payload of science instruments to investigate what this unique target can reveal about the formation of rocky planets like Earth.

The spacecraft will rely on the large chemical rocket engines of the Falcon Heavy launch vehicle to blast off the launchpad and to escape Earth's gravity. But the rest of the journey, once Psyche separates from the launch vehicle, will rely on solar electric propulsion. This form of propulsion starts with large solar arrays that convert sunlight into electricity, providing the power source for the spacecraft's thrusters. They're known as Hall thrusters, and the Psyche spacecraft will be the first to use them beyond the orbit of our Moon.

For propellant, Psyche will carry tanks full of xenon, the same neutral gas used in car headlights and plasma TVs. The spacecraft's four thrusters will use electromagnetic fields to accelerate and expel charged atoms, or ions, of that xenon. As those ions are expelled,

they create thrust that gently propels Psyche through space, emitting blue beams of ionized xenon.

In fact, the thrust is so gentle, it exerts about the same amount of pressure you'd feel holding three quarters in your hand. But it's enough to accelerate Psyche through deep space. With no atmospheric drag to hold it back, the spacecraft eventually will accelerate to speeds of up to 200,000 miles per hour (320,000 kilometers per hour).

Because they're so efficient, Psyche's Hall thrusters could operate nearly nonstop for years without running out of fuel. Psyche will carry 2,030 pounds (922 kilograms) of xenon in its tanks; engineers estimate that the mission would burn through about five times that amount of propellant if it had to use traditional chemical thrusters.

"Even in the beginning, when we were first designing the mission in 2012, we were talking about solar electric propulsion as part of the plan. Without it, we wouldn't have the Psyche mission," said Arizona State University's Lindy Elkins-Tanton, who as principal investigator leads the mission. "And it's become part of the character of the mission. It takes a specialized team to calculate trajectories and orbits using solar electric propulsion."

Psyche will launch from the historic Pad 39A at NASA's Kennedy Space Center. The Falcon Heavy will place the spacecraft on a trajectory to fly by Mars for a gravity assist seven months later, in May 2023. In early 2026, the thrusters will do the delicate work of getting the spacecraft into orbit around asteroid Psyche, using a bit of ballet to back into orbit around its target.

That task will be especially tricky because of how little scientists know about the asteroid, which appears as only a tiny dot of light in telescopes. Ground-based radar suggests it's about 140 miles (226 kilometers) wide and potato-shaped, which means that scientists won't know until they get there how exactly its gravity field works. As the mission conducts its science investigation over 21 months, navigation engineers will use the electric propulsion thrusters to fly the spacecraft through a progression of orbits that gradually bring the spacecraft closer and closer to Psyche.

NASA's Jet Propulsion Laboratory in Southern California, which manages the mission, used a similar propulsion system with the agency's Deep Space 1, which launched in 1998 and flew by an asteroid and a comet before the mission ended in 2001. Next came Dawn, which used solar electric propulsion to travel to and orbit the asteroid Vesta and then the protoplanet Ceres. The first spacecraft ever to orbit two extraterrestrial targets, the Dawn mission lasted 11 years, ending in 2018 when it used up the last of the hydrazine propellant used to maintain its orientation.

Partners in Propulsion

Maxar Technologies has been using solar electric propulsion to power commercial communications satellites for decades. But for Psyche, they needed to adapt the superefficient Hall thrusters to fly in deep space, and that's where JPL engineers came in. Both teams hope that Psyche, by using Hall thrusters for the first time beyond lunar orbit, will help push the limits of solar electric propulsion.

"Solar electric propulsion technology delivers the right mix of cost savings, efficiency, and power and could play an important role in supporting future science missions to Mars and beyond," said Steven Scott, Maxar's Psyche program manager.

Along with supplying the thrusters, Maxar's team in Palo Alto, California, was responsible for building the spacecraft's van-size chassis, which houses the electrical system, the propulsion systems, the thermal system, and the guidance and navigation system. When fully assembled, Psyche will move into JPL's huge thermal vacuum chamber for testing that simulates the environment of deep space. By next spring, the spacecraft will ship from JPL to Cape Canaveral for launch.

More About the Mission

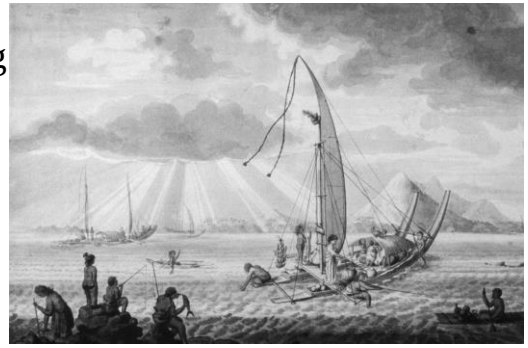
ASU leads the mission. JPL is responsible for the mission's overall management, system engineering, integration and testing, and mission operations. Psyche is the 14th mission selected as part of NASA's Discovery Program.

https://bit.ly/3kFNNRz

'No one could have predicted.' DNA offers surprises on how Polynesia was settled

Early explorers island hopped to discover islands thousands of kilometers apart

By Andrew Curry



The peopling of Polynesia was a stunning achievement: Beginning around 800 C.E., audacious Polynesian navigators in double-hulled sailing canoes used the stars and their knowledge of the waves to discover specks of land separated by thousands of kilometers of open ocean.

Polynesian explorers crossed thousands of kilometers of open oceans in double-hulled canoes like this one in Tahiti, painted by a European artist in 1768. **Universal History Archive/Universal Images Group via Getty Images**

Within just a few centuries, they had populated most of the Pacific Ocean's far-flung islands. Now, researchers have used modern DNA samples to trace the exploration in detail, working out what order the islands were settled in and dating each new landfall to within a few decades.

"The whole question of the settlement of Polynesia has been going on for 200 years," says University of Hawaii, Manoa, archaeologist Patrick Kirch, who was not involved in the research. "This is a really great paper, and I'm happy to see it."

Archaeologists already had hints of how this great exploration took place. Studying the styles of stone tools and carvings, as well as languages, of the people on the various islands had suggested the original ancestors traced back to Samoa and that the expansion ended halfway across the ocean in Rapa Nui, or Easter Island. But they disagreed on whether it happened in a few centuries, beginning around 900 C.E., or started much earlier and lasted 1 millennium or more.

To learn more, Stanford University computational geneticist Alexander Ioannidis and Andrés Moreno Estrada, a population geneticist at Mexico's National Laboratory of Genetics for Biodiversity, compared the DNA of 430 modern individuals from all across Polynesia (most collected for previous studies), and then eliminated later genetic input from European people. Because the researchers knew Polynesians had journeyed stepwise from island to island, their genetic analysis utilized a genetic phenomenon known as a population bottleneck. When a few dozen to a few hundred individuals from already-isolated island populations settled a new island, and then a subset of that group left to settle an additional island, and so forth, their genetic diversity would have shrunk with each voyage—like a telescope in reverse.

"It's a mode of dispersal that's different from any other place in the world," Moreno Estrada says. "We can tell who comes from which island."

In a paper published today in *Nature*, Ioannidis, Moreno Estrada, and colleagues identified genetic patterns specific to the founder population on each island. By analyzing the DNA, the team could trace the sequential journeys to each subsequent island, "like pearls on a string," says University of Tübingen geneticist Cosimo Posth, who was not involved in the study.

To estimate how many generations went by between each island discovery, the scientists measured the length of shared genomic sequences between founder populations. Together, the data showed

who descended from whom. That made it possible to not only show that two populations were related, but which came first.

"Getting deep-grained details on direction? That was impossible before," says University of California (UC), Santa Cruz, population geneticist Lars Fehren-Schmitz, who was not involved with the work.

The analysis suggests canoes set sail from the shores of Samoa—more than 2000 kilometers north of New Zealand—around 800 CE. The explorers arrived first on Rarotonga, the largest island in a chain now called the Cook Islands. Successive explorers moved in all directions, island hopping over the course of centuries and eventually reaching all the way to Rapa Nui, 6500 kilometers from Samoa and 3700 kilometers off the coast of Chile, by 1210 C.E.

And because the genetic evidence allowed the researchers to reconstruct the order in which the islands were settled, they could spot connections between islands that might not seem intuitive based on the geography.

For example, they argue that three island cultures known for carving massive stone statues—Rapa Nui, Raivavae, and the North and South Marquesas—shared a common founder population in the Tuamotu Islands, even though they are thousands of kilometers apart and geographically closer to other parts of the Pacific.

***Geneticists showed the people who carved the enigmatic moai statues of Rapa Nui were related to far-flung islanders with similar megalithic traditions.*Carlos Aranguiz/iStock**

Those three islands also hold the earliest genetic traces of Native American ancestry among Polynesians. That suggests ancient Polynesians first contacted the Americas around 1100 C.E., when the seafarers were beginning their last, and longest, expeditions. "That's something no one could have predicted through archaeology or oral history," Moreno Estrada says.

The vast distances and difficult journeys meant less of the back-and-forth that comes with typical migrations across continents, Moreno Estrada says. Instead, islands were settled by small groups who lived more or less in isolation until the next group of explorers set sail bearing their genetic legacy. "In most situations you get gradients of genetic difference, with everyone moving around. You don't see that here," he says.

But Kirch says that may be too simplistic: Tools and other archaeological evidence suggest ancient voyages weren't simple one-way trips, and that intermarriage and contact between populations continued after islands were settled. "Their analysis makes it seem like there's a discrete set of migratory movements," he says. "The archaeology suggests there's a lot of back and forth, with continued interaction … between islands."

By mapping out the genetic variations specific to each island's isolated population, the data might help guide research into medical conditions that disproportionately affect Polynesians, or even people on specific Pacific islands—knowledge that massive genetic data sets based mainly on European and Asian populations would miss. In a recent preprint, for example, Ioannidis found that Polynesian ancestry is associated with higher risk for severe cases of COVID-19.

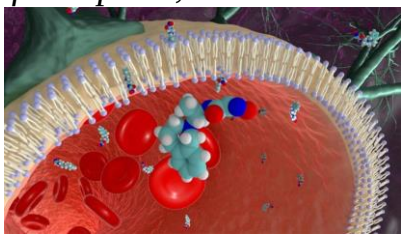
A bit like the Polynesian navigators who used the stars and waves to guide their voyages centuries ago, the researchers hope the new knowledge can chart a course to better health for people living in Polynesia today. "In Hawaiian we say '*I ka wā ma mua, ka wā ma hope*," says study co-author Keolu Fox, a Kānaka Maoli, or Native Hawaiian, and a geneticist at UC San Diego. "It means we're 'walking backwards into the future.'"

https://bit.ly/3i1PqjB

Antidote Developed for Nerve Agent Poisoning

Scientists at Lawrence Livermore National Laboratory (LLNL) have developed a new, versatile antidote to counteract exposure to nerve agent poisoning.

The work, appearing in the journal *Scientific Reports*, was the result of a highly iterative process built in collaboration between LLNL's Global Security Directorate, its Forensic Science Center and the U.S. Army Medical Research Institute of Chemical Defense (USAMRICD).



LLNL-02 can pass through the blood-brain barrier (pictured), making it more effective in protecting the central nervous system. **Credit: Liam Krauss/LLNL**

Chemical weapon nerve agents like Sarin or Novichok typically function by blocking the transmission of messages from the central nervous system (CNS), composed of the brain and the spinal cord, to the peripheral nervous system (PNS), which controls many processes, including respiration. The brain's natural protection — the blood-brain barrier (BBB) — has long been a major obstacle to the development of effective nerve agent antidotes, which historically only protect against damage to the PNS because they cannot cross the BBB.

After the most promising compounds were identified using a parallel effort involving computational modeling and medicinal chemistry, the best candidates were evaluated in several biochemical assays, resulting in the discovery of LLNL-02. LLNL-02 was found to protect both the CNS and the PNS against the effects of the nerve agent Sarin. LLNL-02 is the first antidote of its kind, as it does cross the BBB to confer protection to the brain.

"The process was extremely challenging — most of the synthesized compounds, upon biochemical evaluation, were found to either effectively cross the BBB models but were not effective, or vice-versa," said corresponding author Carlos Valdez and LLNL lead chemist of the project. "I will go so far as calling [LLNL-02] a needle in a haystack and we were ecstatic to find it when we did. It was quite an accomplishment by our team."

After two years of laboratory and computational testing, LLNL-02 was shown to be nontoxic to human cell lines in biochemical assays conducted at the USAMRICD. The next step was to evaluate LLNL-02 in an animal model. "It worked as well as the 'gold standard' antidote that the U.S. Army currently uses," Valdez said.

Research continues into LLNL-02's effectiveness against VX and newer agents like the Novichoks, most notably used in the assassination attempts of Sergei Skripal and his daughter in 2018 in the U.K., and of Alexei Navalny in 2020.

"These people were lucky they were able to be rushed to a hospital and kept alive until their bodies were able to properly deal with the agent," Valdez said. "This is what we're looking forward to seeing now — if LLNL-02 has some protective activity that goes beyond Sarin."

"The results show that LLNL's unique collection of facilities and scientific talent is pushing the boundaries of what's possible," said Audrey Williams, director of LLNL's Forensic Science Center. "LLNL-02 is a promising and versatile compound built by a unique process that demonstrates a path forward for protecting victims of bioterrorism and chemical weapons."

Reference: "Development of a CNS-permeable reactivator for nerve agent exposure: an iterative, multi-disciplinary approach" by Brian J. Bennion, Michael A. Malfatti, Nicholas A. Be, Heather A. Enright, Saphon Hok, C. Linn Cadieux, Timothy S. Carpenter, Victoria Lao, Edward A. Kuhn, M. Windy McNerney, Felice C. Lightstone, Tuan H. Nguyen and Carlos A. Valdez, 30 July 2021, Scientific Reports. DOI: 10.1038/s41598-021-94963-2

Additional LLNL coauthors include Brian Bennion, Michael Malfatti, Nicholas Be, Heather Enright, Saphon Hok, Timothy Carpenter, Victoria Lao, Edward Kuhn, Windy McNerney, Felice Lightstone and Tuan Nguyen.

The work was funded by the Defense Threat Reduction Agency Chemical and Biological Technologies Department.

https://bit.ly/39RobLD

World's oldest known beads found in Morocco

Perforated shells may have signaled identity, attracted mates

The human penchant for bling is ancient—and a new study suggests it may go back as far as 142,000 years. That's when hunter-gatherers in what is now Morocco collected tiny seashells, bored them with holes, and strung them up to adorn their hair, bodies, or clothing. The look must have been bedazzling, because the same type of perforated shells spread quickly throughout northern Africa and into the Middle East. The beads—the world's oldest if new dates hold up—suggest modern humans were engaged in fully symbolic behavior 10,000 to 20,000 years earlier than previously known.

"Shells are special wherever you find them, because when you wear a shell on a string around some part of your body, you're using your body to send messages to strangers about your identity," says paleoanthropologist Alison Brooks of George Washington University, who was not part of the new study. "Everyone's arguing that when you have symbolic behavior, you have fully capable modern humans."

Previously, the earliest known shell beads came from the Contrebandiers and El Mnasra caves in Morocco, dating to between 103,000 and 122,000 years ago, and from Israel's Skhul Cave. But the "iffy" dates at Skhul come from only two shell beads from a layer dated roughly to between 100,000 and 135,000 years ago, Brooks says.

The new beads were found in Bizmoune Cave, a stunning gallery in the flank of an 800-meter limestone mountain in western Morocco, just 12 kilometers east of the Atlantic Ocean. Between 2014 and 2018, researchers excavated 33 oval-shaped, perforated shells of the mollusk *Tritia gibbosula*. All but one of the thumbnail-size oval shells were found in a single layer of ashy silt as stone blades and scrapers, charcoal from ancient campfires, and fragments of wildebeest, gazelle, and zebra bone.

The researchers next dated carbonate mineral deposits such as stalagmites and flowstones that had formed in the cave, including one near the cave's mouth that was in the same layer as the beads—and likely formed around the same time. They measured the radioactive decay of uranium into thorium in that flowstone to date it to 142,000 years ago.

Given the large margins of error on the date, the researchers say there is a 95% chance the bead-bearing layer is between 120,000 and 171,000 years old—and propose an age of at least 142,000 years for the beads, they report today in *Science Advances*.

Among modern humans, these ancient shell beads may have been the height of Stone Age style. **Sehasseh et al., Science Advances**

But dating experts expressed concern that the age of the bead-bearing layer relies on just one sample. University of Wollongong, Wollongong, geochronologist Richard "Bert" Roberts, who is not part of the study but has dated other bead sites in North Africa, says he would like to see the date replicated by other methods, "before accepting it at face value." Based on the data in the new study, he suggests the beads are between 100,000 and 120,000 years, right in the ballpark of beads at other sites in North Africa and Israel.

Regardless of their antiquity, the beads from Bizmoune Cave show humans across North Africa were using the same types of shells to make beads before such ornaments appeared widely elsewhere in Africa or Asia. "North Africa has played a major role in the origins of symbolic behavior," says archeologist Abdeljalil Bouzouggar of

Morocco's National Institute of Archaeology and Heritage and the Max Planck Institute for Evolutionary Anthropology, who led the excavations at Bizmoune Cave. And, he adds, the same type of shell beads' appearance at a half-dozen sites across the region suggests making shell beads was a widespread practice.

The abundance of shell beads first in North Africa suggests modern humans there may have been strengthening ties with other groups. The beads could have been strung in different ways to signal clan identity, or indicate whether an individual had a partner. "Wearing beads has to do with meeting strangers, expanding social networks," says archaeologist Steven Kuhn of the University of Arizona. "You don't have to signal your identity to your mother or whether you're married to your husband or wife."

But these early beads are quite similar across sites and hard to see at a distance, points out anthropologist Polly Wiessner of Arizona State University, Tempe, and the University of Utah. She doubts they were used to signal to strangers. Instead, she suggests they were used as gifts within established social networks to solidify bonds, or as an offering to boost the odds of food sharing in future times of need. Mainly, she thinks these Stone Age baubles were used primarily for "personal adornment to enhance beauty in the pursuit of mates, or increase social esteem." Some things never change. *doi: 10.1126/science.acx9173*

https://bit.ly/3uf9nQi

Greenery May Be the Secret to Slowing the Biological Aging Process – At Least for Women

We all know being surrounded by greenery is good for the mind and soul, but can it be good for the body, too?

Planetary health researchers at Monash University's School of Public Health and Preventive Medicine have found that may indeed be the case, at least for women.

In a world first, they've shown a link between the amount of plant life in a person's immediate environment and slower biological aging, based on changes to DNA methylation.

"We searched the medical literature prior to embarking on this project," says PhD candidate and first author Rongbin Xu, "and could only find a single abstract, presented at a conference but never written up and published in a peer-reviewed journal, that touched on this subject.

"It focused on infants, and compared their biological gestational age with the greenness surrounding the mother during pregnancy, so it was quite a different application to our current study."

Their study was recently published in *Environmental Health Perspectives*.

With an aging global population driven by increased longevity and falling birth rates, understanding how to prolong good health and functioning into old age is a priority.

One of the most robust markers of biological aging is the aging-related methylation changes found in an individual's DNA. This is where some sections of DNA become covered by methyl molecules.

The role of methylation

Some sections of DNA have CpG sites that are particularly prone to increased methylation with age, and this restricts the functionality of affected genes. Conversely, aging can also reduce methylation in other areas, leading to over-expression of genes, which can be equally as harmful.

DNAmAge is a measure of a person's biological age as measured by methylation, and there are four main algorithms in popular use to calculate it: Horvath's Age, Hannum's Age, PhenoAge, and GrimAge. There's a growing body of research that indicates GrimAge may be the most robust DNAmAge estimator, given its strong predictive power of future health, such as time to death, cancer, and heart diseases.

By comparing an individual's DNAmAge to their chronological age

in years, researchers can calculate the acceleration of biological aging (DNAmAgeAC). Increased acceleration is associated with early death and numerous diseases of aging, such as cancer and heart disease.

While some methylation changes are inevitable, we actually do have some influence over it. Research shows that interventions such as dietary adjustments and environmental factors may reverse adverse methylation changes.

"We speculated that the amount of greenery in a person's immediate environment may play a role in reducing accelerated biological aging," says Rongbin.

"A high degree of local vegetation density – gardens, parkland, bush – can reduce mental stress, provide a space for social interaction, encourage physical activity and reduce harm from air pollution and heat. Given these are all determinants for good health, it made sense that there may be a connection."

The researchers leveraged existing data from the Australian Mammographic Density Twins and Sisters Study, which had previously explored the links between environmental, genetic and lifestyle factors and breast tissue density, a known risk factor for breast cancer.

Initial trial participants included female twins aged 40-70 years in Perth, Sydney, and Melbourne, and the cohort was later expanded to include their non-twin sisters. Blood samples were collected and stored as Guthrie cards, much like is done for newborn babies.

These cards formed the source for the DNA methylation analysis performed as part of this current study. Methylation levels were analyzed in a laboratory, and four DNAmAges were calculated for each of 479 women from 130 different families, using the four algorithms mentioned above.

The second part of the project involved mapping vegetation levels near participants' homes. Those taking part had provided residential addresses for the study, which were converted to longitude-latitude coordinates using a Google Maps interface.

While there's a risk some participants may have moved house during that time, a national Australian survey in 2008 showed 80% in this age group hadn't moved house for more than five years.

The team used infrared and visible light readings from a NASA satellite to estimate local vegetation mass in the 12 months leading up to each participant's blood draw.

Plant life absorbs visible red light for photosynthesis, but strongly reflects infrared and near-infrared light. The researchers used this – and some fairly complex mathematical formulas that accounted for atmospheric distortion in light readings – to estimate greenness density up to 2km from their homes.

"We found that using the most robust of the algorithms, GrimAge, increased surrounding greenness was associated with slower biological aging," says Rongbin. "Our study shows that a 0.1-unit increase in the Normalised Difference Vegetation Index within 500 meters of home is associated with a 0.31-years reduction in biological aging as measured by GrimAge.

"Previous cohort studies tell us this is equivalent to a 3% reduction in all-cause mortality. The association remained stable when measuring greenness at 300 meters, one kilometer and two kilometers from home."

Three components of GrimAge showed particularly strong association with slowed biological aging:

- ***Greenness is associated with a reversal of DNA methylation changes arising from exposure to cigarette smoke***
- ***Greenness may be associated with improved immune function and metabolic health as indicated by the biomarker GDF-15***
- ***Greenness may be associated with a reduction in fatty tissues seen in obesity, and improved kidney health as indicated by the biomarker cystatin.***

"More research is needed to confirm our results in larger studies," says Rongbin, "and to look at the process in men, but it's an exciting foray into this field."

Reference: "Surrounding Greenness and Biological Aging Based on DNA Methylation: A Twin and Family Study in Australia" by Rongbin Xu, Shuai Li, Shanshan Li, Ee Ming Wong, Melissa C. Southey, John L. Hopper, Michael J. Abramson and Yuming Guo, 30 August 2021, Environmental Health Perspectives.
DOI: 10.1289/EHP8793

https://wb.md/3i74BiF

Remdesivir Sharply Cuts COVID Hospitalization Risk, Gilead Says

Remdesivir (Veklury, Gilead) was found to reduce some COVID-19 patients' risk of hospitalization by 87% in a phase 3 trial, the drug's manufacturer announced Wednesday in a press release.

Marcia Frellick

The randomized, double-blind, placebo-controlled trial evaluated the efficacy and safety of a 3-day course of intravenous remdesivir in an analysis of 562 nonhospitalized patients at high risk for disease progression.

Remdesivir demonstrated a statistically significant 87% reduction in risk for COVID-19-related hospitalization or all-cause death by Day 28 (0.7% [2/279]) compared with placebo (5.3% [15/283]) *P* = .008. Participants were assigned 1:1 to remdesivir or the placebo group.

Researchers also found an 81% reduction in risk for the composite secondary endpoint — medical visits due to COVID-19 or all-cause death by Day 28. Only 1.6% had COVID-19 medical visits [4/246]) compared with those in the placebo group (8.3% [21/252]) *P* = .002. No deaths were observed in either arm by Day 28.

"These latest data show remdesivir's potential to help high-risk patients recover before they get sicker and stay out of the hospital altogether," coauthor Robert L. Gottlieb, MD, PhD, from Baylor University Medical Center in Houston, Texas, said in the press release.

Remdesivir is the only drug approved by the US Food and Drug Administration for hospitalized COVID-19 patients at least 12 years old. Its treatment of nonhospitalized patients with 3 days of dosing is investigational, and the safety and efficacy for this use and dosing duration have not been established or approved by any regulatory agency, the Gilead press release notes.

The patients in this study were considered high-risk for disease progression based on comorbidities — commonly obesity, hypertension, and diabetes — and age, but had not recently been hospitalized due to COVID-19.

A third of the participants were at least 60 years old. Participants in the study must have received a positive diagnosis within 4 days of starting treatment and experienced symptoms for 7 days or less.

Use of Remdesivir Controversial

Results from the Adaptive COVID-19 Treatment Trial (ACTT-1) showed remdesivir was superior to placebo in shortening time to recovery in adults hospitalized with COVID-19 with evidence of lower respiratory tract infection.

However, a large trial of more than 11,000 people in 30 countries, sponsored by the World Health Organization (WHO), did not show any benefit for the drug in reducing COVID deaths.

The WHO has conditionally recommended against using remdesivir in hospitalized patients, regardless of disease severity, "as there is currently no evidence that remdesivir improves survival and other outcomes in these patients."

The drug also is given intravenously and this study tested three infusions over 3 days, a difficult treatment for nonhospitalized patients.

The study results were released ahead of IDWeek, where the late-breaking abstract will be presented at the virtual conference in full at the end of next week.

https://bit.ly/39IThEN

Hospital Reports a Scary Effect of Severe COVID-19 Is Far More Common Than Thought

Patients with COVID-19 who have been admitted to the intensive care unit are very likely to experience unusually persistent delirium, according to emerging research.

Carly Cassella

Delirium is a medical term used to describe confused thinking and reduced awareness of surroundings - a not uncommon state of mind for the sickest hospitalized patients.

As it turns out, severe cases of COVID-19 are enough to trigger something similar.

In fact, initial investigations have suggested delirium occurs in up to 80 percent of ICU patients with COVID-19, possibly as a result of loss of oxygen to the brain or widespread inflammation.

Now a new analysis of critically ill COVID-19 patients at a single hospital in Michigan has found even more evidence that delirium is a very common symptom of the disease - one that could possibly slow patient recovery if it's not addressed.

Using medical records and discharge surveys from 148 patients checked into the ICU between March and May 2020, researchers have found more than 70 percent of the cohort experienced a prolonged disturbance in their mental abilities.

In most cases, the delirium lasted for days.

But nearly a third of participants left hospital without demonstrating they'd fully recovered from their delirium.

Of those who were discharged with signs of cognitive impairment, nearly half required skilled nursing care to get by at home.

Their persistent confusion reduced their ability to look after themselves, according to follow-up phone surveys conducted between month one and month two of being discharged.

"These results align with previous data demonstrating a high incidence of delirium in critically ill patients with COVID-19," the authors conclude.

"Moreover, the median duration of delirium (10 days) is relatively long compared with other critically ill populations."

It's not yet clear whether these severe impairments are a result of the SARS-CoV-2 virus itself, which seems to cause an unusual number of neurological symptoms that can persist for six months or more, or if it's a sign of critical illness more broadly.

Generally, cognitive impairment is seen in about 20 percent of patients in acute care facilities, so it's expected to a certain extent.

But the current pandemic seems to have at least tripled that number.

While the mechanism behind COVID-19 delirium remains a mystery, researchers in Michigan say it is clear that ICU patients infected with the coronavirus are experiencing "considerable neuropsychological burden" both during their hospital stay and after being discharged.

"Overall, this study highlights another reason why getting vaccinated and preventing severe illness is so important," says anesthesiologist Phillip Vlisides from Michigan Medicine.

"There can be long term neurological complications that perhaps we don't talk about as much as we should."

Early on in the pandemic, for instance, checking patients for symptoms of delirium was not commonplace.

Even when delirium was observed, exercise regimes and other novel strategies for improving cognitive performance, like face-to-face time with family or breathing trials, were rarely introduced, possibly because protective equipment was not easily available at the time.

The likely result is that many patients with severe cases of COVID-19 have been discharged from hospital with serious cognitive impairments, which were not addressed properly.

And that's a big problem.

Delirium is generally associated with prolonged hospitalization and illness recovery.

In the new Michigan study, for instance, those patients experiencing delirium had longer stays at the hospital and ICU.

They also spent more time relying on mechanical ventilation.

"Whatever creative ways we can implement delirium prevention protocols is likely to be very helpful," says Vlisides.

"That includes consistent communication with family members, bringing in pictures and objects from home, and video visits if family cannot safely visit."

As it turns out, those patients disproportionately vulnerable to severe forms of COVID-19, like those from racial and ethnic minority communities, are also the most likely to experience delirium while hospitalized.

In fact, researchers in Michigan found half the patients in the delirium group were African American - a damning reflection of ongoing disparities in US healthcare.

Further research at more acute care facilities and among larger and more diverse cohorts will be needed before we can say with any certainty who is most at risk of experiencing delirium when hospitalized with COVID-19.

While the study in Michigan found female patients are more likely to fall in the delirium group, other initial studies suggest male patients in the ICU are more susceptible to cognitive impairment.

If it turns out that delirium really is such a common experience for those with severe COVID-19, we need to start to recognize and treat the symptoms as early as possible.

Otherwise, it could prove much harder for the sickest COVID-19 patients to get back on their feet.

The study was published in *BMJ Open*.

https://bit.ly/3ESLQcB

Potential Remnants of Original Dinosaur DNA Discovered in Exquisitely Preserved Dinosaur Cells

Organic molecule remnants found in nuclei of 125-million-year-old dinosaur cells.

A team of scientists from the Institute of Vertebrate Paleontology and Paleoanthropology (IVPP) of the Chinese Academy of Sciences and from the Shandong Tianyu Museum of Nature (STM) has isolated exquisitely preserved cartilage cells in a 125-million-year-old dinosaur from Northeast China that contain nuclei with remnants of organic molecules and chromatin. The study was published in *Communications Biology* on September 24, 2021.

The dinosaur, called *Caudipteryx*, was a small peacock-sized omnivore with long tail feathers. It roamed the shores of the shallow lakes of the Jehol Biota in Liaoning province during the Early Cretaceous.

“Geological data has accumulated over the years and shown that fossil preservation in the Jehol Biota was exceptional due to fine volcanic ashes that entombed the carcasses and preserved them down to the cellular level,” said LI Zhiheng, Associate Professor at IVPP and a co-author of this study.

The scientists extracted a piece of distal articular cartilage from the right femur of this specimen, decalcified it, and used different microscopy and chemical methods to analyze it. They realized that all the cells had been mineralized by silicification after the death of the animal. This silicification is most likely what allowed the excellent preservation of these cells.

They also discovered two main types of cells: cells that were healthy at the time of fossilization, and not-so-healthy cells that were porous and fossilized while in the process of dying. “It is possible that these cells were already dying even before the animal died,” said Alida Bailleul, Associate Professor at IVPP and the

corresponding author of this study.

Cell death is a process that occurs naturally throughout the lives of all animals. But being able to place a fossilized cell into a specific spot within the cell cycle is quite new in paleontology. This is one of the objectives of the IVPP scientists: to improve cellular imagery in fossils.

Furthermore, the team isolated some cells and stained them with a chemical used in biological laboratories worldwide. This purple chemical, called hematoxylin, is known to bind to the nuclei of cells. After staining the dinosaur material, one dinosaur cell showed a purple nucleus with some darker purple threads. This means the 125-million-year-old dinosaur cell has a nucleus so well-preserved that it retains some original biomolecules and threads of chromatin.

Chromatin within the cells of all living organisms on Earth is made of tightly packed DNA molecules. The results of this study thus provide preliminary data suggesting that remnants of original dinosaur DNA may still be preserved. But to precisely test this, the team needs to do a lot more work and use chemical methods that are much more refined than the staining they used here.

"Let's be honest, we are obviously interested in fossilized cell nuclei because this is where most of the DNA should be if DNA was preserved," said Alida Bailleul. Last year she published another study reporting exceptional nuclear and biomolecule preservation in the cartilage cells of a dinosaur from Montana." So, we have good preliminary data, very exciting data, but we are just starting to understand cellular biochemistry in very old fossils. At this point, we need to work more."

The team insists they need to do many more analyses and even develop new methods to understand the processes that may allow biomolecule preservation in dinosaur cells, because no one has ever successfully sequenced any dinosaur DNA. In the ancient DNA community, sequencing methods are used to confirm if ancient DNA is preserved in fossils. So far, these methods have only worked for young fossils (not much older than about one million years), but they have never worked for dinosaur material. Dinosaurs are considered way too old to retain any DNA. However, the chemical data collected by the scientists from IVPP and STM suggest otherwise.

Even though more data must be collected, this study definitely shows that 125-million-year old fossil dinosaur cells cannot be considered 100% rock. They are not completely "stonified." Instead, they still contain remnants of organic molecules. Now, it is vital to figure out precisely what these molecules are, whether they retain any biological information and remnants of DNA.

Reference: "Nuclear preservation in the cartilage of the Jehol dinosaur Caudipteryx" by Xiaoting Zheng, Alida M. Bailleul, Zhiheng Li, Xiaoli Wang and Zhonghe Zhou, 24 September 2021, Communications Biology. DOI: 10.1038/s42003-021-02627-8

https://bit.ly/3lV1Zpm

Could Future COVID Variants Fully Dodge Our Immune System?

With every new variant of SARS-CoV-2 that emerges to cause a surge in cases, a worrisome question also arises: Could the virus eventually arrive at a set of mutations that would enable it to fully evade our immune response?

A new study, published in *Nature*, suggests that it will be hard for the virus to get there. Studying dozens of naturally occurring and laboratory-selected mutations, including those found in Delta and other concerning variants, researchers found that a future SARS-CoV-2 variant will need to pack about 20 of the right mutations to become fully resistant to the antibodies that an average person generates in response to a coronavirus infection or vaccination.

But even if the virus pulls off this genetic feat, it still remains vulnerable to an improved set of antibodies: those arising after natural infection and further boosted through mRNA vaccines.

The findings suggest that our immune system, if properly stimulated, is capable of dealing with the worst that the coronavirus may have to offer for the foreseeable future. "Immunity in people who fought off COVID last year and later received mRNA vaccines is impressively broad," says Paul Bieniasz, head of the Laboratory of Retrovirology at Rockefeller. "This tells us that although natural infection or the vaccines lead to immunity, they have in no way come close to exhausting the capacity of the human immune system to mount defense against this virus."

Polymutant viruses

Just as the coronavirus comes in many variants, so do our antibodies. That's why even the Delta variant, the most contagious version of SARS-CoV-2 so far, doesn't entirely escape our immune response. It may be dodging some of the antibodies we produce, but not all of them. But Delta is not the last version of SARS-CoV-2 that we are going to see. The virus is still replicating at a high rate in large populations—new mutations are popping up, and new variants are continuously arising.

Postdocs Fabian Schmidt and Yiska Weisblum set out to identify which kinds of mutations give SARS-CoV-2 the edge over antibodies. For the study, they first created a safe stand-in for the coronavirus by tweaking a different, harmless virus to express SARS-CoV-2 spike protein on its surface. As the faux coronaviruses replicated, some picked up mutations as they made mistakes copying themselves. The team then bathed the faux coronaviruses in plasma samples from people who had recovered from COVID, and selected the mutants that escaped neutralization by antibodies. A few rounds of this and the team found many mutations that were in the same locations as those occurring naturally in SARS-CoV-2 variants, including those found in Delta or other variants of concern.

The researchers then created a "polymutant" virus: a faux coronavirus sporting a spike protein featuring 20 of the worst of those mutations all at once. This polymutant showed near-complete resistance to antibodies generated by individuals who have been infected by or vaccinated against SARS-CoV-2. "So it is possible for the virus to evolve and evade the majority of our antibodies, but the genetic barrier to that occurring is quite high," Bieniasz says.

Extra immunity

Findings from one group of people suggest that in the long run, our immune system will win the race against the mutating coronavirus. People who have experienced both natural infection and vaccination produce remarkably effective antibodies. Previously, the Rockefeller team that includes Michel Nussenzweig, Paul Bieniasz, and Theodora Hatziioannou, a research associate professor at Rockefeller, found that after the infection subsides, antibodies continue to evolve over several months, becoming better at binding tighter to the spike protein. Receiving mRNA vaccines strongly boosts those antibodies even more, increasing them in numbers and improving their ability to cope with many of the variants simply by binding tighter and tighter to the original sequence.

In the current study, plasma from those who had been both infected and vaccinated neutralized the polymutant spike. It also neutralized the six SARS-CoV-2 variants tested, as well as the original SARS coronavirus and SARS-like viruses found in bats and pangolins. "Antibodies from this group of people are incredibly potent and flexible," says Hatziioannou, who co-directed the study. "It's likely that they offer protection against any SARS-CoV-2 variants in the future and possibly against future coronavirus pandemics."

More studies would show whether booster shots could lead to a similar improvement of antibodies in vaccinated people who have never been infected with the coronavirus.

Reference: "High genetic barrier to SARS-CoV-2 polyclonal neutralizing antibody

escape" by Fabian Schmidt, Yiska Weisblum, Magdalena Rutkowska, Daniel Poston, Justin Da Silva, Fengwen Zhang, Eva Bednarski, Alice Cho, Dennis J. Schaefer-Babajew, Christian Gaebler, Marina Caskey, Michel C. Nussenzweig, Theodora Hatziioannou and Paul D. Bieniasz, 20 September 2021, Nature. DOI: 10.1038/s41586-021-04005-0

https://bit.ly/3kQeKSZ

The Common Kitchen Ingredient That Could Help if Your Child Swallows a Battery

Every day, and thousands of times a year in the US, a kid swallows a battery.

Peter Dockrill

In the last 20 years or so, this dangerous and sometimes fatal accident has actually become significantly more common in children, and severe injuries caused by button battery ingestion (BBI) have led to a marked increase in hospitalizations.

Thankfully, in most such cases the item ends up passing harmlessly through the patient's digestive tract. However, even tiny batteries can cause tremendous damage if they get stuck in the esophagus.

Young children up to six years of age are most at risk of BBI complications due to their smaller body size, which increases the chance that a swallowed battery might get lodged in their esophagus – especially larger button batteries such as the ubiquitous 20-millimeter CR2032, used in a vast range of small electronics.

Within just two hours, a stuck battery can cause severe burns as its negatively charged surface makes prolonged contact with the conductive tissue of the esophagus; this contact produces an electrical current and breaks nearby water down into a highly corrosive fluid.

If this happens to your child – or you suspect your young, non-verbal child might have swallowed a battery – do not delay. **Seek immediate medical attention**, as a lodged battery could require urgent endoscopic removal.

However, while you're waiting for medical assistance, researchers now say there is something you can do yourself to mitigate the risk of tissue injury – and it makes use of a condiment many of us have in our kitchens.

According to a newly published research summary on BBI events and complications, honey may help when administered before the patient reaches the hospital, given at 10 milliliters every 10 minutes for children older than one year (up to six doses).

That recommendation is based on a study published in 2018, which explored injury mitigation from button battery blockages in the esophagus using an animal model of young pigs.

In the experiment, researchers tested a range of different household liquids (including honey, maple syrup, Gatorade, and fruit juices) to see whether any of them helped minimize tissue injury resulting from battery lodgment in the animal's esophagus.

Ultimately, two liquids produced the most clinically optimal results: honey, and a product called Carafate, (brand-name version of the medication sucralfate), which is used to treat ulcers and other stomach conditions.

"In the crucial period between button battery ingestion and endoscopic removal, early and frequent ingestion of honey in the household setting and Carafate in the clinical setting has the potential to reduce injury severity and improve patient outcomes," the authors explained.

"Esophageal BB impactions are serious, conferring a high risk of debilitating complications and even death. Our cadaveric and live animal studies support that early intervention with honey or Carafate suspension is clearly better than doing nothing."

It's worth noting, of course, that the animal model used here isn't solid proof that honey or sucralfate work to minimize esophageal injuries in human patients with batteries stuck in the esophagus.

Furthermore, at least some in the medical community have raised concerns about the honey technique, fearing parents might delay

seeking urgent medical care, wasting critical time to try this home remedy first.

Additionally, in the piglet model, the various test solutions were injected near the site of the battery to ensure it would be adequately coated. If a kid ingests the honey, it would get diluted with saliva, and may not properly reach the battery to effectively coat it.

In response, the researchers behind the experiment clarified that their study was only seeking to illustrate a potential treatment option that might elongate the very short time period before tissue injury occurs.

"We are up against a severe hazard, a caustic BB that rapidly generates hydroxide ions, and the clock begins ticking from the moment it becomes lodged in the esophagus," the researchers wrote in a response to criticisms of their original study.

While the jury's out on just how *effective* honey administration might be in human children who have swallowed batteries, it's clear what the most important thing to do is in this scenario: Seek medical help right away, because in rare circumstances where the battery becomes stuck, you're looking at an emergency.

The new research summary on BBI complications is reported in the *Canadian Medical Association Journal*, and the 2018 study on honey as a mitigation strategy is available here.