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Little Foot Fossil Sheds New Light on Hominin Brain Evolution

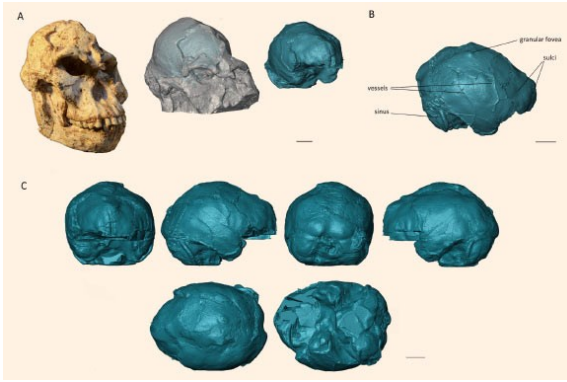
Brain of this ancient human relative is a mosaic of ape-like and human-like features

by News Staff / Source

The first detailed comparative description of the external neuroanatomy of the 3.67-million-year-old *Australopithecus prometheus* fossil known as the Little Foot reveals that the brain of this ancient human relative is a mosaic of ape-like (an expanded visual cortex and reduced parietal association cortex) and human-like (an asymmetrical structure and pattern of middle meningeal vessels) features.

"Our ability to reconstruct features of early hominin brains has been limited by the very fragmentary nature of the fossil record," said Dr. Amélie Beaudet, a researcher at the University of the Witwatersrand, South Africa.

"The Little Foot endocast is exceptionally well preserved and relatively complete, allowing us to explore our own origins better than ever before." The endocast showed that Little Foot's brain was asymmetrical, with a distinct left occipital petalia.



Original skull (left), virtual skull (light gray) showing the endocast in semi-transparency (middle) and virtual endocast (dark blue, right) of the Little Foot: (A) oblique view of the virtual endocast of the Little Foot showing the main cerebral imprints; (B) standard views (anterior, right, posterior, left, superior and inferior) of the Little Foot endocast; (C) photo of the original Little Foot skull. Scale bars – 2 cm. **Beaudet *et al*, doi: 10.1016/j.jhevol.2018.11.009.**

"Brain asymmetry is essential for lateralization of brain function. Asymmetry occurs in humans and living apes, as well as in other younger hominin endocasts," Dr. Beaudet and co-authors said.

"Little Foot now shows us that this brain asymmetry was present at a very early date, and supports suggestions that it was probably present in the last common ancestor of hominins and other great apes."

Other brain structures, such as an expanded visual cortex, suggest that the brain of Little Foot probably had some features that are closer to the ancestor we share with living chimpanzees.

"In human evolution, when know that a reduced visual cortex, as we can see in our own brain, is related to a more expanded parietal cortex — which is a critical cerebral area responsible for several aspects of sensory processing and sensorimotor integration," Dr. Beaudet said.

"On the contrary, Little Foot has a large visual cortex, which is more similar to chimpanzees than to humans."

The scientists compared the endocast of the Little Foot with those of ten southern African hominin specimens from Makapansgat, Malapa, Sterkfontein and Swartkrans attributed to *Australopithecus* sp. and *Paranthropus* sp. (between 3 and 1.5 million years old).

"Little Foot's endocranial volume was at the low end of the range for *Australopithecus*, which is in keeping with its great age and its place among other very early fossils of *Australopithecus* from East Africa," they said.

The team also found that the vascular system in *Australopithecus* was more complex than previously thought, which raises new questions on the metabolism of the brain at this time.

This might be consistent with a previous hypothesis suggesting that the endocranial vascular system in *Australopithecus* was closer to modern humans than it was in the geologically younger genus *Paranthropus*.

"This would mean that even if Little Foot's brain was different from us, the vascular system that allows for blood flow (which brings

oxygen) and may control temperature in the brain — both essential aspects for evolving a large and complex brain — were possibly already present at that time," Dr. Beaudet said.

"Given its geological age of over 3 million years, Little Foot's brain suggests that younger hominins evolved greater complexity in certain brain structures over time, perhaps in response to increasing environmental pressures experienced after 2.6 million years ago with continuing reduction in closed habitats."

"Such environmental changes could also potentially have encouraged more complex social interaction, which is driven by structures in the brain."

The findings are published in the *Journal of Human Evolution*.

Amélie Beaudet et al. *2019. The endocast of StW 573 ("Little Foot") and hominin brain evolution.* Journal of Human Evolution *126: 112-123; doi: 10.1016/j.jhevol.2018.11.009*

https://wb.md/2BKZjUh

FDA Approves New Enzyme Product for ALL

The US Food and Drug Administration (FDA) has approved a new drug for the treatment of acute lymphoblastic leukemia (ALL), a cancer of the blood and bone marrow.

Roxanne Nelson, RN, BSN

The agency has granted approval for calaspargase pegol-mknl (*Asparlas*, Servier Pharmaceuticals), an asparagine-specific enzyme, to be used as part of a multi-agent chemotherapeutic regimen in pediatric and young adult patients (age 1 month to 21 years). This new product differs from other available pegaspargase products, such as pegaspargase (*Oncaspar*, Sigma-Tau Pharmaceuticals) and asparaginase (*Erwinaze*, Jazz Pharmaceuticals), in that it provides for a longer interval between doses. It also has an extended shelf-life beyond that of the current pegylated asparaginase treatment, which helps ensure availability to patients.

Calaspargase contains an asparagine-specific enzyme derived from *Escherichia coli* and depletes plasma asparagine, selectively killing leukemic cells that are unable to synthesize asparagine because of a lack of asparagine synthetase. Leukemic cells with low expression of asparagine synthetase have a reduced ability to synthesize L-asparagine, and therefore depend on an exogenous source of L-asparagine for survival.

The approval was based on demonstration of the achievement and maintenance of nadir serum asparaginase activity (NSAA) above 0.1 U/mL when using a dose of 2500 U/m^2 given intravenously every 3 weeks. The pharmacokinetics were studied in a cohort of 124 patients with B cell lineage ALL who were a median age of 11.5 years (range, 1-26). Within this group, 62 (50%) were male, 102 (82%) white, six (5%) Asian, five (4%) Black or African American, two (2%) Native Hawaiian or Pacific Islander, and nine (7%) other or unknown.

When calaspargase was administered with multi-agent chemotherapy, the results showed that 123 of the 124 patients (99%, 95% CI, 96 - 100) maintained NSAA > 0.1 U/mL at weeks 6, 12, 18, 24, and 30.

The recommended dosage is 2500 units/m^2 intravenously administered no more frequently than every 21 days.

The most common (incidence ≥ 10%) grade ≥ 3 adverse reactions associated with this agent were elevated transaminase, increased bilirubin, pancreatitis, and abnormal clotting studies. In a randomized trial, the safety profile of calaspargase pegol-mknl administered every 3 weeks was similar to that of pegaspargase administered every 2 weeks, according to the FDA.

Calaspargase pegol-mknl has received FDA orphan drug designation.

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Catheter ablation superior to standard drug

1. Catheter ablation superior to standard drug therapy for heart failure

Abstract: http://annals.org/aim/article/doi/10.7326/M18-0992

A meta-analysis of randomized controlled trials found that catheter ablation was superior to conventional drug therapy alone for patients

with atrial fibrillation and heart failure. Findings are published in *Annals of Internal Medicine*.

Atrial fibrillation is associated with thromboembolic stroke, systemic embolism, and decompensated heart failure. Catheter ablation is an established therapeutic strategy for atrial fibrillation, but guidelines recommend caution in certain patients. The benefits and harms of catheter ablation versus drug therapy for patients with atrial fibrillation have not been firmly established.

Researchers from Icahn School of Medicine at Mount Sinai reviewed six published randomized controlled trials to compare the benefits and harms between catheter ablation and standard drug therapy (rate or rhythm control medications) in adult patients with atrial fibrillation and heart failure. Their analysis showed that compared to medication, catheter ablation was associated with reductions in all-cause mortality and heart failure hospitalizations and improvements in left ventricular ejection fraction; quality of life; cardiopulmonary exercise capacity; and 6-minute walk test distance, with no statistically significant increase in serious adverse events.

The major adverse events rates observed in the pooled analysis were 7.2 percent in the ablation group and 3.8 percent in the standard therapy group. Despite the complications associated with catheter ablation, the authors explain that the long-term benefits in all-cause mortality, heart failure hospitalizations, and overall clinical outcomes must be weighed in clinical decision making.

2. Proposed technique prevents confused patients from dislodging central line

Abstract: ***http://annals.org/aim/article/doi/10.7326/L18-0439***

A proposed technique for placing a central venous catheter that may prevent confused patients from pulling it out or dislodging it easily. Findings from a case report are published in *Annals of Internal Medicine*.

Sometimes patients, particularly confused patients, dislodge or pull out central venous catheters inadvertently or intentionally. Although this occurrence is uncommon, it is not rare, and it may have negative consequences.

Physicians from Beth Israel Deaconess Medical Center and Harvard Medical School saw a 77-year-old patient with waxing and waning mental status who required dialysis for chronic kidney failure. The patient became confused and repeatedly pulled out his hemodialysis catheters. Since he was unsuitable for an arteriovenous access and the medical literature offered no solution, the physicians developed a novel technique. They placed a right external jugular vein catheter, tunneling subcutaneously to exit from the patient's upper back, near the midline, just below his neck. It was out of reach to the patient, but not in an area where it would cause pressure on his skin when he was lying on his back. It worked well enough that the authors suggest clinicians consider this placement when caring for patients at risk for central line dislodgement.

Also in this issue:

Testing Novel payment and Delivery Approaches Through the Veterans Health Administration's New Center for Innovation

Steven D. Pizer, PhD; Austin B. Frakt, PhD; Kyle Sheetz, MD, MS; Carolyn Clancy, MD

Ideas and Opinions

Abstract: http://annals.org/aim/article/doi/10.7326/M18-2225

http://bit.ly/2BImfDE

Later School Start Times Increase Sleep, Attendance and Grades: Study

Later start time led to increased sleep, associated with a 4.5% increased grades of the students and an improvement in attendance

News Staff / Source

In 2017, the Seattle School District decided to delay the start time for secondary schools from 7:50 a.m. to 8:45 a.m. This change allowed a team of researchers from the University of Washington

and the Salk Institute for Biological Studies to conduct a pre-/post-study in which they measured sleep-wake cycles. Published in the journal *Science Advances*, the results show that there was a median increase of 34 minutes of sleep each night, associated with a 4.5% increase in the median grades of the students and an improvement in attendance.

Teenagers tend to stay up late at night; they usually do not get the recommended eight to ten hours of sleep.

With many teenagers being chronically sleep-deprived, some experts and organizations like the American Academy of Pediatrics have suggested delaying school start times, which would allow students to wake up later without shifting their natural bedtimes (the latter being biologically determined by the circadian clock).

However, quantitative data showing that delaying school start times would increase daily sleep and academic performance is lacking.

Taking advantage of a natural pre/post study setup, created after the Seattle School District delayed high school start time by 55 minutes in 2017, University of Washington's Professor Horacio de la Iglesia and co-authors measured sleep-wake cycles of sophomore students enrolled in two public high schools — Roosevelt High School and Franklin High School — in Seattle for two weeks using wrist activity devices.

"School start time has serious implications for how students learn and perform in their education," Professor de la Iglesia said.

"Adolescents are on one schedule. The question is: what schedule will their schools be on?"

The delay had several measurable benefits for students — notably, the median sleep duration increased by 34 minutes in 2017 compared to 2016.

This increase in amount of sleep was associated with a 4.5% increase in the median grades of students at both schools.

Roosevelt High School showed no difference in improved attendance and punctuality between years, but students in Franklin High School, an economically disadvantaged school, had significantly fewer instances of late arrival and absenteeism after the delayed school start time was implemented.

"Our study shows a significant improvement in the sleep duration of students — all by delaying school start times so that they're more in line with the natural wake-up times of adolescents," Professor de la Iglesia said.

Gideon P. Dunster et al. *2018. Sleepmore in Seattle: Later school start times are associated with more sleep and better performance in high school students.* Science Advances *4 (12): eaau6200; doi: 10.1126/sciadv.aau6200*

https://wb.md/2QRLugY

Million-Strong Study Supports CRC Screening Every 10 Years

Clinicians following guideline recommendations to screen for colorectal cancer once every 10 years can reassure their patients that the time interval is effective and does not put them at increased risk, conclude US investigators.

Liam Davenport

Researchers evaluated more than 1.2 million Californians aged 50 to 75 years who were enrolled in a health plan. They compared unscreened individuals with those who had a negative colonoscopy result over a 10-year period.

The results showed that the relative risk of developing colorectal cancer in people with a negative result at 10 years was 46% lower than that for unscreened individuals; the relative risk of colorectal cancer death was 88% lower. The research was published online December 17 in *JAMA Internal Medicine*.

Lead author Jeffrey K. Lee, MD, Division of Research, Kaiser Permanente Northern California, Oakland, said in a press release: "Our study shows that, following a colonoscopy with normal

findings, there is a reduced risk of developing and dying from colorectal cancer for at least 10 years."

These findings suggest, said Lee, that physicians "can feel confident" about the guideline-recommended 10-year rescreening interval after a negative colonoscopy in which no colorectal cancer or polyps were found. "There is now solid evidence supporting that recommendation," he said.

Senior author Douglas A. Corley, MD, PhD, MPH, also of Kaiser Permanente Northern California, added: "This large study is the first with a high enough number of average-risk individuals to evaluate cancer risks after colonoscopy examinations, compared with no screening."

The study provides "greater certainty regarding the appropriate timing for rescreening after a negative colonoscopy," he said.

Asked for comment, Robert A. Smith, PhD, vice president of cancer screening, American Cancer Society in Atlanta, Georgia, said that "the new data show that a 10-year interval is pretty effective."

Approximately 63% of eligible individuals in the United States undergo colorectal cancer screening, Smith told *Medscape Medical News*. In the majority of cases, screening is opportunistic, with patients referred as a result of another encounter, he explained.

The current study, said Smith, "probably reinforces in people's minds the importance of screening.... It's widely accepted that colorectal cancer screening is a good thing."

On the other hand, some patients either do not undergo colonoscopy or do not prepare for the procedure properly and end up having to cancel. "A concern is raised that we have uneven quality of colonoscopy in this country," he said.

"Just because you've had a normal examination doesn't mean that there aren't some lesions in there that were overlooked but could potentially grow to become malignancies in the interval before your next examination is due," Smith continued.

Echoing previous suggestions that "a reasonable and safe thing to do is a fecal immunochemical test, say, at 5 years," Smith argued that "a high-sensitivity stool test would have the opportunity to pick those [malignancies] up."

Study Details

Although current guidelines recommend that individuals with a negative colonoscopy result be rescreened after 10 years, the California investigators say the evidence supporting this is "modest" and that that recommendation is based on estimates of colonoscopy sensitivity and the time it takes for adenoma to progress.

Colorectal cancer is, however, a heterogeneous disease, and the few studies that have been conducted on long-term risk for colorectal cancer have suggested that a 10-year screening interval might either be too short or too long.

To investigate further, the team conducted a retrospective cohort study of members of Kaiser Permanente Northern California, an integrated healthcare delivery organization serving approximately 4 million individuals.

They included health plan members enrolled between 1998 and 2015 who were aged 50 to 75 years, had been continuously enrolled ≥1 years, and were at average risk for colorectal cancer.

This yielded a total of 1,251,318 eligible participants, for whom 9,339,354 person-years of follow-up information was available. The mean age of the participants was 55.6 years at entry, and 50.9% were men.

During 4,639,809 person-years of unscreened follow-up, 5743 colorectal cancer cases were diagnosed, of which 1821 (31.7%) were proximal and 2588 (45.1%) were of advanced stage.

Among 99,166 individuals who contributed 417,987 person-years of negative colonoscopy follow-up, 184 colorectal cancer cases were diagnosed, of which 94 (51.1%) were proximal and 91 (49.5%) were of advanced stage.

In the unscreened cohort, colorectal cancer incidence rates increased from 62.9 per 100,000 person-years in year 1 to 224.8 per 100,000 person-years in year 12. The mortality rate increased from 10.5 per 100,000 person-years to 192.0 per 100,000 person-years over the same period.

Among individuals with a negative colonoscopy result, the incidence of colorectal cancer increased from 16.6 per 100,000 person-years to 133.2 per 100,000 person-years from year 1 to year 10. The mortality rate increased from 6.8 per 100,000 person-years in year 1 to 92.2 per 100,000 person-years in year 12.

A negative colonoscopy result was associated with a marked reduction in the risk for colorectal cancer compared with not undergoing screening, at an adjusted hazard ratio of 0.05 at year 1 or less and 0.54 at year 10, with all reductions significant.

The team also calculated that there was significant reduction in colorectal cancer mortality with a negative screening result vs not undergoing screening, at an adjusted hazard ratio of 0.04 at year 1 or less and 0.12 at year 10. All reductions were significant.

Looking more widely at the research program conducted by Lee and colleagues, Smith said: "This group has now had a series of articles that are providing us with some outstanding data on the protective effects of colorectal cancer screening, but also explaining what accounts for the deaths that we still see.

"For example, there was a recent one that showed that failure to follow up adults who have a positive stool test accounts for a significant fraction of the deaths from colorectal cancer.... They are a completely avoidable cause of death, if people had just been properly followed up after a positive test."

Moreover, he believes that more is to come from the dataset.

"For example, if they were to examine individual characteristics for what factors are associated with a colorectal cancer appearing before the next colonoscopy, that means that you could potentially at some point refer some patients to a wider screening interval and some patients to a narrower one," Smith said.

"Another question that's on everybody's mind is, let's say you start screening at the age of 50, and your first colonoscopy shows that you don't have any polyps, you have a normal examination."

He explained that, if results of the second examination 10 years later are identical to the first, "that tells us you've just not the kind of person that grows polyps. "At that point, could we safely say you're done with screening? That would be great if we could."

Smith added: "I don't think anyone would be sad about not having to have another colonoscopy."

The study was conducted within the National Cancer Institute–funded Population-Based Research Optimizing Screening Through Personalized Regimens consortium and was supported by the National Cancer Institute, an American Gastroenterological Association Research Scholar Award, and the Sylvia Allison Kaplan Foundation. One study author is a member of the US Preventive Services Task Force. The other authors have disclosed no relevant financial relationships.

JAMA Intern Med. Published online December 17, 2018. Full text

https://bbc.in/2BId7Pf

Why are more boys than girls born every single year?

Every year, there are always more baby boys than girls born in England and Wales. Fact. Why?

By Philippa Roxby Health reporter, BBC News

Since records began in 1838, the cries of babies born every year have been predominately male.

In not one year, stretching back to the start of Queen Victoria's reign, have girls outnumbered boys at birth.

In 2017, in England and Wales, for example, there were 348,071 live male births and 331,035 live female births - a difference of roughly 17,000.

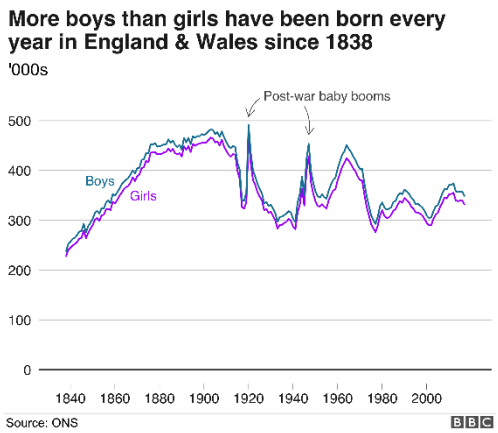
And that higher tally of males compared to females born each year is a pattern that has repeated itself for nearly 180 years.

In fact, a ratio of roughly 105 male births for every 100 female ones is generally seen as natural and normal.

It is fairly consistent around the world, although in some countries like China and India the gap is wider because male offspring are more desirable.

More surprisingly, it is a ratio that has been known about since the 17th Century.

But why this ratio exists is not yet completely understood - although there are several theories.



It's all about evolution

The first theory is an evolutionary one which says that in order to have an equal number of males and female in adulthood, there have to be slightly more males born.

That is because being a male is a dangerous thing. Males are more likely than females to die in childhood and at all stages of life - from accidents, taking risks, suicide and from health problems.

"At every age, in almost every time and place, a man is more likely to die than a woman," says Prof David Steinsaltz, associate professor of statistics at the University of Oxford.

So more males than females at the start of life should mean equal numbers of men and women in adulthood, so the theory goes.

In fact, adult women always end up slightly outnumbering adult men in the UK, according to Office for National Statistics figures - and living longer.

Sperm and timing

There are lots of different factors that could determine whether a male sperm (carrying a Y chromosome) or a female sperm (carrying an X chromosome) is first in the race to fertilise the woman's egg.

These include the ages of the parents, the woman's ovulation cycle, levels of stress, diet and sexual position.

One popular theory is that the odds of having a girl increase by having sex several days before ovulation and then abstaining so that the female sperm, which live longer, but swim more slowly than male sperm, outlast their counterparts.

Image copyright Getty Images Image caption Male sperm are the best swimmers but female sperm live longer

Conversely, if sex happens closer to ovulation or after it, the best swimmers get to the egg first and boys are produced.

Parents may swear by these techniques, but scientists say there is little evidence they make any difference.

There is also some research which suggests parental stress could lead to the birth of more girls, while living through wars and conflicts may give rise to more male conceptions.

Survival in the womb

If planning that sexual encounter does not have an impact on gender, then could something else be happening during pregnancy?

If there are equal numbers of female and male-producing sperm and roughly equal numbers of conceptions, then more female foetuses must perish to give males the upper hand.

Some research suggests females are more likely to be lost in the womb during early pregnancy, but other studies have shown males foetuses are more fragile later in pregnancy and lead to more stillbirths.

Scientists say it is hard to pin down what actually happens and the reasons why. What we do know is that more male conceptions reach term and more boys are born.

http://bit.ly/2TeqfK0

Losing neurons can sometimes not be that bad

New results could lead to a complete rethinking of therapeutical approaches to Alzheimer's

For the first time, scientists at the Champalimaud Centre for the Unknown (CCU), in Lisbon, Portugal, have shown that neuronal cell

death in Alzheimer's disease (AD) may actually not be a bad thing - on the contrary, it may be the result of a cell quality control mechanism trying to protect the brain from the accumulation of malfunctioning neurons. Their results, which were obtained using fruit flies that had been genetically modified to mimic the symptoms of human AD, were published in the journal *Cell Reports*.

The cell quality control mechanism at play is called cell competition. It leads to the selection of the fittest cells in a tissue by enabling a "fitness comparison" between each cell and its neighbors - with the fitter cells then triggering the suicide of less fit ones.

It has been recently shown that cell competition is a normal, powerful anti-aging mechanism in the body in general and in the brain in particular. "In 2015, we discovered that clearing unfit cells from a tissue was a very important anti-aging mechanism to preserve organ function, says Eduardo Moreno, principal investigator of the Cell Fitness lab at the CCU.

His team reasoned that, if these fitness comparisons happened in normal aging, they could also be involved in neurodegenerative diseases associated with accelerated aging, such as Alzheimer's, Parkinson's disease or Huntington's disease, Moreno explains. "This had never been tested", he says. In collaboration with Christa Rhiner's Stem Cells and Regeneration lab at the CCU, they started by testing AD hallmarks in fruit fly models of the disease.

For this, they bred fruit flies that had been genetically manipulated to express in their brain the human amyloid-beta protein, that forms aggregates in the brains of AD patients. The formation of amyloid-β aggregates in the brain is a crucial step in the development of AD.

The transgenic flies displayed symptoms and pathologies similar to those of AD patients: "they showed loss of long-term memory, accelerated aging of the brain and motor coordination problems, all of which got worse with age", specifies Christa Rhiner, whose team studied the cognitive and motor functions of the flies.

The first thing the scientists wanted to do was to see whether in these flies, neuronal death was indeed activated by the process of fitness comparison - in other words, "that the neurons were not dying on their own but being killed by fitter neighbors", Moreno points out.

"When we started, the current view was that neuronal death must be always detrimental. And much to our surprise, we found that neuronal death actually counteracts the disease", says Dina Coelho, first author of the study. What happened was that when she blocked neuronal death in the flies' brain, the insects developed even worse memory problems, worse motor coordination problems, died earlier and their brain degenerated faster.

However, when she boosted the fitness comparison process, thus accelerating the death of unfit neurons, the flies expressing the AD-associated amyloid-beta proteins showed an impressive recovery. "The flies almost behaved like normal flies with regard to memory formation, locomotive behavior and learning", says Rhiner, and this at a time point where the AD flies were already strongly affected.

This means that the anti-aging mechanism in question keeps working well in Alzheimer's disease and shows that, in fact, "the neuronal death protects the brain from more widespread damage and therefore the neuronal loss is not what is bad, it is worse not to let those neurons die", Moreno emphasizes. "Our most important finding is that we have probably been thinking the wrong way about Alzheimer's disease. Our results suggest that neuronal death is beneficial because it removes neurons that are affected by noxious beta-amyloid aggregates from brain circuits, and having those dysfunctional neurons is worse than losing them" Moreno concludes.

The results could have crucial therapeutical implications. "Some molecules have already been identified as potential inhibitors of cell suicide, and some experimental drugs exist, and are being tested which inhibit those inhibitors of cell death, therefore accelerating neuronal death", says Moreno.

But he cautions: "this work has been done in fruit flies". It will be necessary to see, whether these results on neuronal death in Alzheimer's also hold true for humans.

http://bit.ly/2BIfrpr

Yale experts treat severe, disfiguring sarcoidosis with novel therapy

Successful treatment of a patient with disfiguring sarcoidosis with a drug approved for rheumatoid arthritis

New Haven, Conn. -- An all-Yale team of researchers successfully treated a patient with disfiguring sarcoidosis, a chronic disease that can affect multiple organs, with a drug approved for rheumatoid arthritis. Successful treatment of two other patients with similarly severe disease suggests an effective treatment for an incurable, sometimes life-threatening illness is within reach, the scientists said.

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

Sarcoidosis is an inflammatory disease that affects multiple organs in the body. While some sarcoidosis patients recover without treatment, others suffer damage to the lungs, heart, lymph nodes, skin, and other organs. Current treatments, including steroids, are not reliably effective for the skin and can cause serious side effects.

Based on clues gleaned from prior studies, the Yale team decided to try the arthritis medication tofacitinib. The drug, a Jak inhibitor, blocks a pathway known as Jak-STAT. The lead author, Brett King, M.D., has pioneered the use of Jak inhibitors to treat other intractable skin diseases, including vitiligo, alopecia areata, and eczema.

For several months, a 48-year-old female patient was treated with the drug, a twice-daily pill. The researchers observed that her skin lesions nearly disappeared. They also performed RNA sequencing on biopsied skin from the patient before and during treatment. "Before treatment, we were able to show that the Jak-STAT pathway is activated," King said. "During treatment, not only does her skin disease go away, but there is no activation of the pathway."

"We plan to evaluate the activation of the Jak-STAT pathway in the lung fluid and blood of over 200 patients with pulmonary and multiorgan sarcoidosis," said co-author Nkiruka Emeagwali. These are big steps toward understanding a disease that has been a mystery for years, the researchers said.

The findings are being tested further by the Yale team in a clinical trial. If confirmed, they could represent a breakthrough for sarcoidosis patients, King noted.

"A frequently awful disease, which to date has no reliably effective therapy, may now be targeted with Jak inhibitors," he said. "We have a relatively safe medicine that works."

Other Yale authors are William Damsky, Durga Thakral, and Anjela Galan.

This work was funded in part by the Ranjini and Ajay Poddar Resource Fund for Dermatologic Diseases Research, the National Institutes of Health, and The Dermatology Foundation.

King is a consultant to and a clinical trials investigator for Pfizer, the maker of tofacitinib.

Citation: New England Journal of Medicine

http://bit.ly/2Q8ZoX0

Rerouting nerves during amputation reduces phantom limb pain before it starts

Researchers find life-altering benefits to surgery developed for advanced prosthetics

Doctors at The Ohio State University Wexner Medical Center and College of Medicine are pioneering the use of primary targeted muscle reinnervation (TMR) to prevent or reduce debilitating phantom limb and stump pain in amputees.

Losing a limb due to trauma, cancer, or poor circulation can result in phantom limb and stump pain in upwards of 75 percent of amputees in the United States. Primary TMR - the rerouting of nerves cut during amputation into surrounding muscle - greatly reduces phantom limb and residual limb pain, as reported in recent publications by Dr. Ian Valerio, division chief of Burn, Wound and

Trauma in Ohio State's Department of Plastic and Reconstructive Surgery, and Dr. J. Byers Bowen, a former resident who is now in private practice. Their latest work featured in the January 2019 issue of *Plastic and Reconstructive Surgery* describes how to perform this technique in below-the-knee amputations.

TMR was first developed to allow amputees better control of upper limb prosthetics. Traditionally doctors perform the surgery months or years after the initial amputation. When surgeons discovered the procedure also improves certain causes of pain, they started using it to treat disorganized nerve endings called symptomatic neuromas and/or phantom limb pain.

In this paper, Valerio and Bowen provide a detailed description of TMR in below-the-knee amputees and document the benefits of primary TMR for preventing pain.

"This paper provides a blueprint for improving patient outcomes and quality of life following amputation," said Dr. K. Craig Kent, dean of The Ohio State University College of Medicine.

Over the course of three years, the surgeons performed 22 TMR surgeries on below-the-knee amputees, 18 primary and four secondary. None of the patients have developed symptomatic neuromas and only 13 percent of patients who received primary TMR reported having pain six months later.

"A significant amount of pain in amputees is caused by disorganized nerve endings, i.e. symptomatic neuromas, in the residual limb. They form when nerves are severed and not addressed, thus they have nowhere to go," Valerio said. "Attaching those cut nerve endings to motor nerves in a nearby muscle allows the body to re-establish its neural circuitry. This alleviates phantom and residual limb pain by giving those severed nerves somewhere to go and something to do."

Valerio said patients who've had TMR significantly reduce or sometimes stop using narcotics and other nerve pain related medications, which can greatly improve their quality of life.

"TMR has been shown to reduce pain scores and multiple types of pain via a variety of validated pain surveys. These findings are the first to show that surgery can greatly reduce phantom and other types of limb pain directly," Valerio said.

Bowen added that upper extremity amputees are better able to use and control their prosthetics in addition to their improved pain outcomes. He said, "TMR allows for more individual muscle unit firings through the patient's thoughts. It provides for better intuitive control resulting in more refined functional movements and more degrees of motion by an advanced prosthetic."

The researchers believe primary TMR is a reliable technique to prevent the development of disorganized nerve endings and to reduce phantom and other limb pain in all types of amputations. When done at the time of initial amputation, there is minimal health risk and recovery is similar to that of traditional amputation surgery.

Surgeons perform TMR routinely at Ohio State, with primary TMR as the standard of care for most orthopedic-based traumatic and oncologic amputations. Valerio lectures and trains surgeons around the world on the primary TMR technique in an effort to make it a global best practice.

http://bit.ly/2EVAARa

Phytochemistry, traditional uses and pharmacological profile of rose hip

This article by Dr. Amirhossein Sahebkar et al. is published in Current Pharmaceutical Design, 2018

The genus *Rosa* from family Rosaceae is one of the most widespread species from the family. One species, rose hip (rose haw), is known as a good source of different types of micronutrients and phytochemicals such as phenolic acids, tannins, and flavonoids. It is known as a traditional treatment in folk medicine. It has been used for the treatment of several illness including ear, nose, and throat problems since old times. In European folk medicine, it has been

used a laxative, diuretic, anti-gout, and anti-rheumatism medication. rose hip has also been used to treat kidney stones, gastroenteric ailments, hypertension, and respiratory problems like bronchitis, cough, and cold. To discover more of its abilities, researchers have reviewed its traditional applications, its clinical properties, and pharmacological potentials in various ethnomedical systems.

It was found that the rose hip fruit contained approximately 129 chemical compounds. All the compounds have successfully been isolated and identified. Some major bioactive compounds include flavonoids, tannins, anthocyanin, phenolic compounds, fatty oil, organic acids and some inorganic compounds. Further research on these compound suggests that the fruit can be used for as antioxidant, anti-inflammatory, anti-obesity, anti-cancer, hepatoprotective, nephroprotective, cardioprotective, and antiaging, anti H. pylori, neuroprotective and antinociceptive medicines. Therapeutic effects against arthritis have also been reported.

Some of the effects of rose hip studied from ethnomedical practices, such as nephroprotective and gastroproetctive actions, have been confirmed by preclinical pharmacological studies. Further investigations on these effects as well as evidence from randomized controlled trials are essential to assess the therapeutic values of the natural products in rose hip.

The article is Open Access till 31st December, 2018. To obtain the article, please visit: http://www.eurekaselect.com/166136

http://bit.ly/2CEOZyG

Bacteria found in ancient Irish soil halts growth of superbugs -- new hope for tackling antibiotic resistance

Soil from Ireland thought to have medicinal properties discovered to contain previously unknown strain of bacteria effective against four of the top six superbugs

Researchers analysing soil from Ireland long thought to have medicinal properties have discovered that it contains a previously unknown strain of bacteria which is effective against four of the top six superbugs that are resistant to antibiotics, including MRSA.

Antibiotic resistant superbugs could kill up to 1.3 million people in Europe by 2050, according to recent research.

The World Health Organisation (WHO) describes the problem as "one of the biggest threats to global health, food security, and development today".

The new strain of bacteria was discovered by a team based in Swansea University Medical School, made up of researchers from Wales, Brazil, Iraq and Northern Ireland.

They have named the new strain *Streptomyces sp. myrophorea*.

The soil they analysed originated from an area of Fermanagh, Northern Ireland, which is known as the Boho Highlands. It is an area of alkaline grassland and the soil is reputed to have healing properties.

The search for replacement antibiotics to combat multi-resistance has prompted researchers to explore new sources, including folk medicines: a field of study known as ethnopharmacology. They are also focusing on environments where well-known antibiotic producers like *Streptomyces* can be found.

One of the research team, Dr Gerry Quinn, a previous resident of Boho, County Fermanagh, had been aware of the healing traditions of the area for many years.

Traditionally a small amount of soil was wrapped up in cotton cloth and used to heal many ailments including toothache, throat and neck infections. Interestingly, this area was previously occupied by the Druids, around 1500 years ago, and Neolithic people 4000 years ago.

The main findings of the research were that the newly-identified strain of Streptomyces:

- ***Inhibited the growth of four of the top six multi-resistant pathogens identified by the WHO as being responsible for healthcare-associated infections: Vancomycin resistant*** **Enterococcus faecium** ***(VRE),***

***methicillin-resistant* Staphylococcus aureus *(MRSA),* Klebsiella pneumonia*, and Carbenepenem-resistant* Acinetobacter baumanii**

Inhibited both gram positive and gram negative bacteria, which differ in the structure of their cell wall; usually gram negative bacteria are more resistant to antibiotics

It is not yet clear which component of the new strain prevents the growth of the pathogens, but the team are already investigating this.

Professor Paul Dyson of Swansea University Medical School said:

"This new strain of bacteria is effective against 4 of the top 6 pathogens that are resistant to antibiotics, including MRSA. Our discovery is an important step forward in the fight against antibiotic resistance.

Our results show that folklore and traditional medicines are worth investigating in the search for new antibiotics. Scientists, historians and archaeologists can all have something to contribute to this task. It seems that part of the answer to this very modern problem might lie in the wisdom of the past."

Dr Gerry Quinn from the research team said:

"The discovery of antimicrobial substances from *Streptomyces sp.myrophorea* will help in our search for new drugs to treat multi-resistant bacteria, the cause of many dangerous and lethal infections. We will now concentrate on the purification and identification of these antibiotics. We have also discovered additional antibacterial organisms from the same soil cure which may cover a broader spectrum of multi-resistant pathogens."

The research was published in *Frontiers in Microbiology*.

Notes to Editors:

Read the research paper

https://www.frontiersin.org/articles/10.3389/fmicb.2018.02458/full

Research team/authors: Luciana Terra, Paul Dyson, Matthew Hitchings, Liam Thomas, Alyaa Abdelhameed, Ibrahim Banat, Salvatore Gazze, Dusica Vujaklija, Paul Facey, Lewis Francis, Gerry Quinn.

http://bit.ly/2Tf1Z3r

A tilt of the head facilitates social engagement, researchers say

New findings of potential value for people with autism

Every time we look at a face, we take in a flood of information effortlessly: age, gender, race, expression, the direction of our subject's gaze, perhaps even their mood. Faces draw us in and help us navigate relationships and the world around us.

***A tilt of the head leads people to look more at the eyes, perhaps because it makes them more approachable and less threatening. "When the head is tilted, we look at the upper eye more than either or both eyes when the head is upright," said Nicolas Davidenko. "I think this finding could be used therapeutically."* Courtesy of Nicolas Davidenko**

How the brain does this is a mystery. Understanding how facial recognition works has great value--perhaps particularly for those whose brains process information in ways that make eye contact challenging, including people with autism. Helping people tap into this flow of social cues could be transformational.

A new study of facial "fixation" led by Nicolas Davidenko, an assistant professor of psychology at the University of California, Santa Cruz, boosts our insights considerably.

"Looking at the eyes allows you to gather much more information," said Davidenko. "It's a real advantage."

By contrast, the inability to make eye contact has causal effects. "It impairs your facial processing abilities and puts you at a real social disadvantage," he said. People who are reluctant to make eye contact may also be misperceived as disinterested, distracted, or aloof, he noted.

Scientists have known for decades that when we look at a face, we tend to focus on the left side of the face we're viewing, from the viewer's perspective. Called the "left-gaze bias," this phenomenon is thought to be rooted in the brain, the right hemisphere of which dominates the face-processing task.

Researchers also know that we have a terrible time "reading" a face that's upside down. It's as if our neural circuits become scrambled, and we are challenged to grasp the most basic information. Much less is known about the middle ground, how we take in faces that are rotated or slightly tilted.

"We take in faces holistically, all at once--not feature by feature," said Davidenko. "But no one had studied where we look on rotated faces."

Davidenko used eye-tracking technology to get the answers, and what he found surprised him: The left-gaze bias completely vanished and an "upper eye bias" emerged, even with a tilt as minor as 11 degrees off center.

"People tend to look first at whichever eye is higher," he said. "A slight tilt kills the left-gaze bias that has been known for so long. That's what's so interesting. I was surprised how strong it was."

Perhaps more importantly for people with autism, Davidenko found that the tilt leads people to look more at the eyes, perhaps because it makes them more approachable and less threatening. "Across species, direct eye contact can be threatening," he said. "When the head is tilted, we look at the upper eye more than either or both eyes when the head is upright. I think this finding could be used therapeutically."

Davidenko is eager to explore two aspects of these findings: whether people with autism are more comfortable engaging with images of rotated faces, and whether tilts help facilitate comprehension during conversation.

The findings may also be of value for people with amblyopia, or "lazy eye," which can be disconcerting to others. "In conversation, they may want to tilt their head so their dominant eye is up," he said. "That taps into our natural tendency to fix our gaze on that eye."

The effect is strongest when the rotation is 45 degrees. The upper-eye bias is much weaker at a 90-degree rotation. "Ninety degrees is too weird," said Davidenko. "People don't know where to look, and it changes their behavior totally."

Davidenko's findings appear in the latest edition of the journal *Perception*, in an article titled "The Upper Eye Bias: Rotated Faces Draw Fixations to the Upper." His coauthors are Hema Kopalle, a graduate student in the Department of Neurosciences at UC San Diego who was an undergraduate researcher on the project, and the late Bruce Bridgeman, professor emeritus of psychology at UCSC.

http://bit.ly/2GIIv68

Man Gets Black Widow Spider Bite. Then He Can't Pee.

There's a whole range of reasons you don't want to be bitten by a black widow spider, but you probably wouldn't think that losing the ability to pee is one of them.

By Cari Nierenberg, Live Science Contributor

But that's what may have happened to a man in Canada. After he got a suspected black widow bite on his foot, he developed a condition called acute urinary retention, meaning he couldn't pee despite having a very full bladder, according to a recent report of his case.

The 50-year-old encountered the spider while he was walking through tall grass at his cottage in southern Ontario, the report said. Black widow spiders are rare in Canada because the arachnids are

typically found in warmer climates; however, climate change may be driving the spiders farther north, Live Science reported in August.

The man didn't think much about the bite when it happened: When he felt it, he quickly brushed away what he believed to be a black spider, said lead case report author Dr. Matthew Carere, who treated the man while he was an emergency room physician at The Ottawa Hospital (Carere is currently an emergency room physician in Victoria, Canada.)

A female black widow spider. **Credit: James Gathany, CDC**

But two hours later, the man felt excruciating pain in his foot. And by the next morning, the pain was so severe — and he had also developed cramps in his abdomen — that he went to the emergency room. Doctors there thought his abdominal pain was caused by kidney stones and suspected the spider bite was just a coincidental occurrence, Carere told Live Science, and the man was sent home.

However, he returned later that day because his abdominal pain had worsened, so doctors sent him to a larger hospital for additional testing.

Range of symptoms

By the time the man arrived at the emergency room where Carere treated him, he was in a lot of pain and sweating heavily, and both of his eyelids were swollen. His blood pressure was extremely high and a CT scan revealed that his bladder was massively distended, according to the case report.

The man also told doctors about the spider bite, but after carefully examining his skin, they found no evidence of a bite or rash. However, despite the lack of a mark, doctors suspect the man was bitten by a northern black widow spider, a species found in southern Ontario.

The venom from a black widow spider contains a variety of toxins that may have been responsible for the man's range of symptoms following the bite. Black widow venom causes a medical syndrome known as "latrodectism," which can include symptoms such as high blood pressure, heavy sweating and muscle pain, Carere said. The toxins found in the venom contain enzymes that cause a flood of neurotransmitters, which are chemicals that transmit signals from one neuron to the next, as well as vasodilators, which are substances that widen blood vessels and increase blood flow.

The release of one such neurotransmitter, called acetylcholine, may be one reason why the man developed urinary retention and had difficulty peeing after the spider bite, Carere said. He also noted that another factor may have been the man's age: The 50-year-old likely had some sort of underlying benign prostatic hyperplasia, or enlarged prostate.

Carere noted that the doctors can't definitively prove that the spider bite was the cause of the man's urinary retention. Indeed, they couldn't find any previous cases of this happening in the medical literature.

The man was hospitalized for two days so that doctors could insert a catheter to drain urine from his full bladder and get his elevated blood pressure and pain under control. By the time he went home, he was able to pee without any problems. The case was published in July in the Canadian Journal of Emergency Medicine.

http://bit.ly/2TfsKVp

Simple Sugars Wipe Out Beneficial Gut Bugs

Fructose and sucrose can make it all the way to the colon, where they spell a sugary death sentence for beneficial bacteria.

Karen Hopkin reports.

We all know that stuffing our faces with sweet treats is not good for us. In part because it’s bad for the health-promoting bacteria that

inhabit our intestines. Now, researchers have figured out how simple sugars wipe out a particular strain of beneficial gut microbes.

"The underlying assumption that existed in the literature was that simple sugars such as fructose and sucrose which are prevalent in Western diet are not good for humans."

Yale professor of Microbial Pathogenesis Eduardo Groisman, who led the study.

Simple sugars…like those in high fructose corn syrup or the table sugar formally known as sucrose…were thought to be absorbed in the small intestine, so a lot of our gut bacteria would never actually be exposed to them.

Because fiber and complex carbs, made of long chains of sugar molecules, are harder to digest…they make it all the way to the large intestine, where they promote the growth of good bugs like *Bacteroides thetaiotaomicron*…a microbe found in individuals who are healthy and lean.

"But now what our work actually shows is that both fructose and sucrose do make it to the colon where the microbiota exist. And second that these sugars impact a good bacterium even though nutrition is not involved."

In other words, the bacteria are not using fructose and sucrose as food. Instead, the sugars serve as signals that shut down production of a protein that beneficial *Bacteroides* need to colonize the intestine.

The findings appear in the *Proceedings of the National Academy of Sciences*. [Guy E. Townsend II et al., Dietary sugar silences a colonization factor in a mammalian gut symbiont]

Groisman says he'd like to explore whether complex polysaccharides can save Bacteroides from this sugary death sentence. Because then maybe we can eat cake and have our gut bugs too.

https://wapo.st/2GMmZx5

A Chinese alternative medicine empire is under fire after doctors say it gave jujube tea to a 4-year old cancer patient

For 15 years, Quanjian Group touted all kinds of miraculous products, growing into a $3 billion-a-year behemoth

By Gerry Shih and Lyric Li

"Negative ion" tampons for women. High-tech shoe pads for improving sleep. Jujube tea for curing cancer.

Over the last 15 years, China's Quanjian Group grew from obscurity into a $3 billion-a-year alternative medicine empire by peddling products that were as incredible as the company's meteoric rise. Years of doubts voiced by medical professionals — and even a tough investigation by China's influential state broadcaster — failed to slow the company's growth. The story of Zhou Yang might.

A group of Chinese doctors this week sparked a national sensation after they posted an account of how they dug into Quanjian's ad campaigns and found a cancer-stricken 4-year-old girl in northern China who was taken off chemotherapy in 2012 on the advice of executives from Quanjian, who gave her jujube powder and gromwell root oil aromatherapy. The executives plastered Zhou Yang's face on a countrywide ad campaign for their cancer therapy, the doctors said. Zhou Yang's parents eventually put her back on chemo, but she died in 2015.

The story of little Yang — and other accounts collected by the doctors of Quanjian's alleged quackery — went viral this week as soon as it hit a Reddit-like Chinese forum called DXY.cn, getting hundreds of thousands of shares and dominating Chinese social chatter.

The online allegations against Quanjian, which spurred blanket media coverage and a government investigation, touched a sore spot in China, where outrage is building among citizens over bogus

health-care products and misleading ads that take advantage of poor consumer education, particularly among the elderly and poor.

The story also raised the question of whether a group of citizens can take down a corporate giant in a country where whistleblowers face huge risks and retaliation, as seen in other recent cases.

Quanjian has flatly denied the doctors' account and said it would sue to protect its reputation. But it has already taken a massive hit. Major Chinese e-commerce platforms — including JD.com, Suning and Vipshop — removed all Quanjian products on Thursday. Regulators in Tianjin, where Quanjian's headquarters is located, launched an investigation and said they would try to verify the allegations in DXY's post.

"We have demanded that Quanjian make a comprehensive and honest clarification on this issue," the government investigators said Thursday.

In their initial blog post on DXY.cn, the doctors said Quanjian first talked in 2012 to the family of Zhou Yang, who had been diagnosed with a rare type of cancer, persuading them to suspend the girl's chemotherapy and switch to alternative treatment.

The DXY article claimed that Yang's father — a farmer with little education — made the decision after meeting at Quanjian's headquarters with its chairman, who allegedly vouched for the efficacy of his company's homeopathy.

"We talked for about 40 minutes, and he told us Quanjian is China's largest base for the research and development of traditional Chinese medicine, and that it had a secret anti-cancer drug that could cure my daughter," the father, who goes by the pseudonym Zhou Erli, told the Shanghai-based news portal ThePaper.com this week.

Quanjian's anti-cancer remedies, which included sachets of jujube powder for oral intake and gromwell-root oil for aromatherapy, did not stop malignant germ-cell tumor growths in Yang, the father said. In March 2013, the girl had to be sent back to the hospital for regular treatment. But Yang's family found that Quanjian had started using the girl's photos without permission in its online advertising to tout its "miraculous" anti-cancer therapies.

Zhou Erli sued the company in early 2015 over misleading marketing but lost due to insufficient evidence. His daughter died in December that year. "It was an outright lie, and my daughter had to take those medications for four whole months," the father said this week.

DXY's "in-depth" report cited a dozen court judgments and previous media reports.

In response, Quanjian released a statement Wednesday saying it never claimed that the company's therapies cured Zhou Yang. In addition, the company accused DXY of libel and threatened legal action if it did not issue a retraction and apology.

But the doctors on DXY, who signed their real names in posts, did not back down. They said they stand by their allegations and accused Quanjian of also running pyramid schemes and failing to disclose its products' safety data.

"We are responsible for every single word we have said, and even welcome a lawsuit from Quanjian," the doctors said in their latest post.

Many Chinese say they believe the doctors who were going after the medical behemoth. In fact, the risks of going up against powerful companies in China are well known. Earlier this year, a Chinese physician was arrested for criticizing a traditional medicinal liquor brand called Hongmao, which claimed that it could cure ailments for the elderly.

The doctor was released after spending almost 100 days in jail, but the case prompted widespread fears that it could set a precedent and silence scientific debate about traditional remedies.

Sean Tan, a 28-year-old office worker in the southern city of Guangzhou, expressed concerns over the ability of big companies to use criminal law to punish critics.

“DXY will find itself facing pressure from all around,” Tan said. “After all, Quanjian has got powerful supporters and could do anything to protect its own interests.”

Quanjian also owns the Chinese Super League soccer team Tianjin Quanjian, as well as more than 600 hospitals and 7,000 health-care clubs across China. Quanjian’s founder, Shu Yuhui, who has described himself as a “gentleman merchant” and purveyor of time-honored recipes, is said to be worth $1.5 billion. “It is not impossible for Quanjian to seek retaliation against whistleblowers in the same way Hongmao Liquor is doing,” Tan added.

Zhou Erli, the father, said he plans to file another lawsuit against the company in the coming weeks, given the renewed attention to his case.

“Now I have enough evidence to prove that they had tricked us,” Zhou said. “I want to live to see the day when Quanjian gets the punishment it deserves.”

http://bit.ly/2Qci73U

This May Be Life's 'Missing Ingredient'

Early RNA may have had one nucleobase that isn't part of the modern form

By Yasemin Saplakoglu, Staff Writer

Billions of years ago, molecules on a lifeless and tumultuous Earth mixed, forming the first life-forms. Eons later, a larger, smarter form of life is huddling over lab experiments trying to understand its own beginnings.

While some say life emerged from simple chains of molecules, others say early chemical reactions formed self-replicating RNA. A relative of DNA, RNA acts as a decoder or messenger of genetic information.

A new study provides evidence for the RNA idea, which is known as the "RNA world hypothesis." But at least one ingredient in early RNA may differ from what's found in the modern form, a group of scientists reported on Dec. 3 in the journal Proceedings of the National Academy of Sciences.

Modern RNA, alongside its sugar and phosphate backbone, is made of four main building blocks: nucleobases called adenine (A), cytosine (C), guanine (G), and uracil (U).

But it turns out that early RNA may have had one nucleobase that isn't part of the modern form.

In tiny plastic tubes, the researchers put water, a little bit of salt, buffer to keep the pH basic and magnesium ions to speed up reactions. These conditions are similar to those found in a freshwater lake or pond, a crater lake, or the kind of lake or pool found in volcanic regions such as Yellowstone National Park — all places that life could have started.

The researchers then added a small piece of RNA called a primer attached to a longer piece of RNA called a template. New RNA is made when a primer copies template RNA, through base pairing . The nucleobases uniquely match up with one another; C binds only with G, and A binds only with U.

The researchers added the nucleobases (A, C, G and U) so they could bind to the template and thereby extend the shorter piece, the primer. Results showed that, with ingredients from modern RNA, the reaction didn't work fast enough for the RNA to form and replicate without errors.

But then, the researchers added another chemical, called inosine, into the mix, instead of the guanine-based molecule. After that, the researchers were surprised to find that RNA could form and replicate slightly more accurately than it does in a mix with guanine.

This mix didn't cause what's called an "error catastrophe," meaning that mutations or random mistakes in replications stayed below a threshold, ensuring they could be eliminated before accumulating.

"The fact that [the addition of inosine] surmounts the problem of error catastrophe is an important test of [the molecule's] significance," said David Deamer, a biologist at the University of California, Santa Cruz, who was not part of the study. His only quibble is the claim that inosine is more plausible in the making of primitive RNA than other alternative bases, Deamer said. He doesn't yet think the other bases should be excluded, since "this is a fairly broad claim … based on a highly specific chemical reaction," Deamer told Live Science

But because inosine can be easily derived from another base pair, adenine, it makes the process of originating life "easier" than if you had to make guanine from scratch, said John Sutherland, a researcher into the chemical origins of molecular biology at the MRC Laboratory of Molecular Biology in the U.K., who was not part of the study either.

The findings break "the conventional wisdom that inosine couldn't have been useful," Sutherland told Live Science. Inosine had earned this reputation because it works a very specific job in a form of RNA called transfer RNA, which decodes genetic information.

Inosine was thought to "wobble," or bind to various base pairs rather than a single one. That would have made it a poor molecule for giving unique instructions to form new RNA, because there wouldn't have been clear direction for what inosine could bind with. And so, "a lot of us had wrongly thought that [wobble] was an inherent property of inosine," Sutherland said. But this study showed that inosine, in the early world context where RNA first emerged, doesn't wobble, but instead pairs reliably with cytosine, he added.

"It all makes sense now, but based on the older results, we didn't expect inosine to work as well as it did," said study senior author Jack Szostak, a professor of chemistry and chemical biology at Harvard University, who is also a Nobel laureate.

Szostak and his team are now trying to figure out how else that primitive RNA might have been different from modern RNA — and how it eventually turned into modern RNA. Also, much of their lab is focused on how RNA molecules replicated before enzymes evolved. (Enzymes are proteins that speed up chemical reactions.)

"This is a big challenge," Szostak told Live Science. "We've made a lot of progress, but there are still unsolved puzzles."

Sutherland also noted that the field is generally moving on from a pure "RNA world hypothesis" into one that sees more components mixed into the cauldron that created life. Those include lipids, peptides, proteins and energy sources. He added that in researchers' minds, "It's a less purist RNA world than it used to be."

http://bit.ly/2GLS2JA

Scientists model Mercury's glaciers

The processes that led to glaciation at the cratered poles of Mercury, the planet closest to the sun, have been modeled by a University of Maine-led research team.

by Margaret Nagle

James Fastook, a UMaine professor of computer science and Climate Change Institute researcher, and James Head and Ariel Deutsch of Brown University, studied the accumulation and flow of ice on Mercury, and how the glacial deposits on the smallest planet in our solar system compare to those on Earth and Mars.

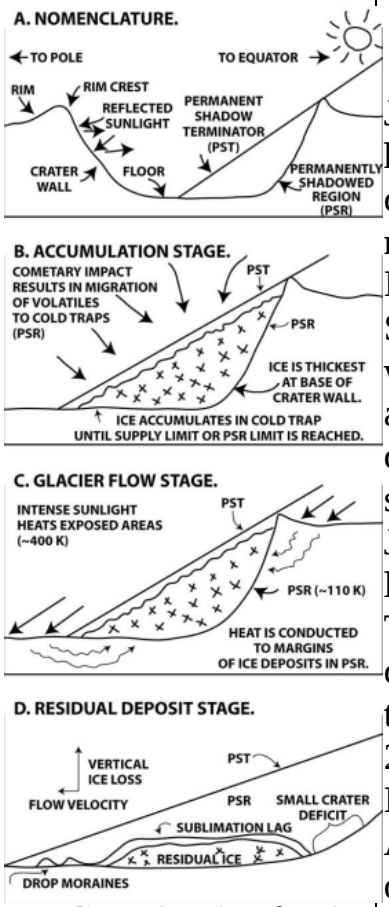
Their findings, published in the journal *Icarus*, add to our understanding of how Mercury's ice accumulations—estimated to be less than 50 million years old and up to 50 meters thick in places—may have changed over time. Changes in ice sheets serve as climatic indicators.

Analysis of Mercury's cold-based glaciers, located in the permanently shadowed craters near the poles and visible by Earth-

based radar, was funded by a NASA Solar System Exploration Research Virtual Institute grant for Evolution and Environment of Exploration Destinations, and is part of a study of volatile deposits on the moon.

Like the moon, Mercury does not have an atmosphere that produces snow or ice that could account for glaciers at the poles. Simulations by Fastook's team suggest that the planet's ice was deposited—likely the result of a water-rich comet or other impact event—and has remained stable, with little or no flow velocity. That's despite the extreme temperature difference between the permanently shadowed locations of the glaciers on Mercury and the adjacent regions illuminated by the sun.

One of the team's primary scientific tools was the University of Maine Ice Sheet Model (UMISM), developed by Fastook with National Science Foundation funding. Fastook has used UMISM to reconstruct the shape and outline of past and present ice sheets on Earth and Mars, with findings published in 2002 and 2008, respectively.



Credit: University of Maine

"We expect the deposits (on Mercury) are supply limited, and that they are basically stagnant unmoving deposits, reflecting the extreme efficiency of the cold-trapping mechanism" of the polar terrain, according to the researchers.

More information: *James L. Fastook et al. Glaciation on Mercury: Accumulation and flow of ice in permanently shadowed circum-polar crater interiors, Icarus (2018).* [DOI: 10.1016/j.icarus.2018.07.004]

http://bit.ly/2QU3TtD

Entering a crowded market, Japan's new rocket scores an early win

Mitsubishi's new H3 rocket is now deep into development.

Eric Berger - 12/21/2018, 10:00 PM

Japan's largest rocket company, Mitsubishi Heavy Industries (MHI), has received a vote of confidence as it seeks to compete for commercial launches in an increasingly crowded market. Earlier this month, the company announced an agreement with satellite operator Inmarsat for a launch in 2022 or later.

Significantly, the flight will take place on Mitsubishi's new H3 rocket, which was designed and developed to fly at a lower cost in order to attract more commercial business. It was the first commercial contract for the rocket, which is set to debut in 2020 by launching a satellite payload for Japan's space agency, JAXA.

JAXA and MHI want to increase the country's number of orbital launches annually from the current average of four to about eight. The only realistic way to do this is to increase launch orders from commercial companies. And as MHI has sought to do this, it seems to have found a good partner in Inmarsat. Already, in September 2017, Inmarsat selected MHI's H-2A rocket for the launch of its Inmarsat-6 F1 satellite in 2020.

And now, the company has returned to MHI for a second consecutive order. This is a big win for the Japanese firm, as Inmarsat could have picked almost any number of competitors. Since it began launching satellites in 1990, the London-based satellite operator has flown on US Delta, Atlas, and Falcon 9 rockets, multiple variations of Europe's Ariane launcher, and Russia's Proton and Ukraine's Zenit vehicles.

"We've always maintained a portfolio of launchers to account for unforeseen events," Mark Dickinson, Inmarsat's deputy chief technology officer and vice president of satellite operations, told Ars

in an interview. The two recent launch contracts with the Japanese company reflect confidence in the reliability of its service, Dickinson said.

"We have a very good working relationship with them," he said. MHI has afforded Inmarsat good visibility into the technical development of the H3 rocket, both the successes and challenges. This raises confidence that the H3 rocket will be ready in 2020, Dickinson said. He added that the insurance market is favorable toward the H3 and that the vehicle is seen as an "important and significant incremental step forward" to lower costs and improve launch cadence.

***Enlarge / Four configurations of the H3 rocket, with and without boosters, and a larger second stage.* JAXA**

H3 under development

In a separate interview, Ko Ogasawara, the vice president of MHI's space system division, said development of the H3 rocket is coming along well. The company has been conducting multiple firings of the LE-9 rocket engine that will power the first stage and has also begun successfully testing the solid fuel rocket boosters designed for the H3 launcher.

Next year, he said, MHI will move into testing the first and second stages, with a hold-down test of the launch system at the very end of 2019 or early in 2020 at the Tanegashima Space Center in southern Japan.

The Japanese government has funded the H3 rocket with the goal of launching it for the first time in 2020, although a month has not yet been determined, Ogasawara said. He is mindful that Tokyo is hosting the 2020 Summer Olympics from late July to early August and that a launch around that event would capture some of the world's attention. But a lot would have to go right to meet such a target. (Ogasawara just laughed when asked if he was targeting a launch during the Olympics).

Ogasawara did acknowledge that Japan is coming to the commercial satellite launch market at a difficult time. Not only have orders for large geostationary satellites fallen by about half, to less than 10 per year, but he must compete against other emerging, cost-competitive rockets. Aside from SpaceX's existing Falcon 9 and Falcon Heavy rockets, United Launch Alliance (Vulcan), Blue Origin (New Glenn), and Arianespace (Ariane 6) are all developing rockets for debut in 2020 or 2021 that will go after the commercial market.

"Yeah, we have many competitors," Ogasawara said. "We should compete anyway. Our market is now changing. Big satellites for geostationary orbit, the number is diminishing. At the same time, small satellite programs, such as constellations, are spinning up all over the world. That is good news for launchers."

Like the recent SSO-A launch on a Falcon 9 rocket, coordinated by Spaceflight, MHI will work to develop a dispenser that can fly two or perhaps many more satellites into space at a time.

http://bit.ly/2BLje5m

A desert explosion helps scientists plan earthquake-detecting balloons on Venus

Could provide important clues about the interior of our sister planet and why it evolved so differently from our own

By Adam Mann

This week, in the still, silent desert near Pahrump, Nevada, researchers set off an artificial earthquake. It shook the ground and, less obviously, the air, allowing NASA scientists to listen for the vibrations with balloons floating overhead. If the technology can be shifted to Venus, it could be the first to detect earthquakes there,

which could provide important clues about the interior of our sister planet and why it evolved so differently from our own.

"We've never made a direct seismic measurement on Venus," says Siddharth Krishnamoorthy, an experiment team member at NASA's Jet Propulsion Laboratory (JPL) in Pasadena, California. "There is a lot balloons can offer in terms of unlocking some major questions about the planet."

For the 19 December test, U.S. Department of Energy researchers set off a 50-ton chemical explosion roughly 300 meters underground to generate a magnitude-3 or -4 tremor—partly to verify the agency's ability to detect underground nuclear explosions. But researchers also lofted two helium-filled balloons over the site, one tethered and another free floating, each a few hundred meters above the ground. The balloons carried barometers to measure changes in atmospheric pressure and detect the earthquake's infrasound waves, low-frequency acoustic vibrations below the threshold of human hearing. A similar setup could one day float high in the atmosphere of Venus.

At the planet's surface, conditions are infernal: Temperatures are high enough to melt lead, and pressures are so overwhelming that they would crush a submarine. It would be hard for any lander to survive long enough to detect a tremor. But 50 kilometers above the surface, temperatures and pressures are remarkably clement, perfect for a long-lived balloon (aside from a touch of sulfuric acid in the greenhouse atmosphere, which is 96% carbon dioxide). In 1985, the Soviet Union showed it could be done, flying two balloons for 2.5 days in this layer. They only stopped recording data when their batteries ran out.

Balloons could detect tremors from such as high perch because Venus's atmosphere is so much thicker than Earth's: Waves would transfer better from the ground into the air and travel more readily. Based on preliminary calculations, the team believes it could detect venusian quakes as small as magnitude 2 from that height. That goal was advanced by an initial desert test last year—dropping 13-ton weights onto the desert floor from a height of 1.5 meters—that proved instruments could pick up infrasound waves from the shaking and infer the direction of the quake.

Krishnamoorthy says he and colleagues are now trying to detect stronger seismic sources at larger distances, as they did this week, to better tease out the quake's signature from the environmental noise. The team next plans to loft balloons over Oklahoma, where thousands of earthquakes have occurred in recent years, triggered by oil and gas activity. That could allow the group to detect shaking coming from much deeper underground.

Translating the tests to Venus could be somewhat tricky, however, says planetary scientist Ralph Lorenz of the University of Arizona in Tucson. The timing and character of the test quakes were known to the experimenters, and it might be a challenge to separate a signal from the background clatter on blustery Venus, where winds are supersonic.

It could be that Venus is seismically quiet, an important negative result that would force researchers to reevaluate their models of the planet's interior. But many scientists think heat is still trying to escape the planet, potentially in ways that shake the surface. Scuff marks across its surface today point to stretching and strain that could be causing tremors, although many scientists think the planet has not had plate tectonics for a long time, if ever—one reason why the planet has ended up with a runaway greenhouse effect. On Earth, tectonic plate motion is responsible for most earthquakes and it also helps bury carbon deep within the mantle, buffering the planet from global warming.

This makes Venus our sister, but not our twin, says geologist Paul Byrne of North Carolina State University in Raleigh. He says a gauge of tectonic activity would provide clues to Venus's interior structure and past history, perhaps explaining why it lacks a magnetic field

like Earth's or at what point its water disappeared. Knowing why Venus went down such a different path than our own could also help in understanding the glut of rocky exoplanets now being found around other stars. Byrne points out that alien astronomers peering at our solar system from far away would be hard pressed to say whether Earth or Venus hold life.