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We May Have Finally Found a Chunk of Theia Buried Deep Inside The Moon

For the first time, scientists believe they've found traces of Theia in the Moon.

Michelle Starr

Around 4.5 billion years ago, something the size of Mars collided with a newly formed Earth, to colossal effect. This object is not only thought to have fused with Earth and primed it for life, it also broke off a large chunk that went on to become the Moon.

This story is known as the giant-impact hypothesis; the Mars-sized object is called Theia; and now, for the first time, scientists believe they've found traces of Theia in the Moon.

The giant-impact hypothesis has been the favoured model for explaining the formation of the Moon for years.

"This model was capable of accounting for the then-recent observations from samples returned by the Apollo missions, which included the Moon's low iron content relative to Earth, depletion in volatiles and enrichment in refractory elements, while avoiding most of the pitfalls of previous lunar origin theories," researchers from the University of New Mexico wrote in their paper.

But there was one big spanner stuck in the works.

Models predicted that around 70 to 90 percent of the Moon should have been made up of mooshed and reformed Theia. However, oxygen isotopes in lunar samples collected by Apollo astronauts were very similar to terrestrial oxygen isotopes - and very different from oxygen isotopes on other Solar System objects.

One possible explanation is that Earth and Theia had similar compositions to start with. Another is that everything got completely mixed during the impact, which, according to simulations, isn't very likely.

Furthermore, the odds of Theia having a similar composition to Earth - as far as oxygen isotopes go - are actually extremely small. Which means that, if the Moon is mostly Theia, its oxygen isotopes should be different from Earth's oxygen isotopes.

This close similarity has been a major pain in the proverbial butt for the giant-impactor hypothesis. Over the years, researchers have published several papers trying to explain it.

That's where the idea that Theia fused with Earth originated. Another paper proposed that the impact created a cloud of dust that went on to become Earth and Moon. Another suggested that perhaps Theia and Earth formed really close to each other. And others have sought to rewrite the history entirely.

Planetary scientist Erick Cano and colleagues went a different route: a careful reanalysis of the lunar samples.

They acquired a range of samples from different rock types gathered on the Moon - both high- and low-titanium basalts from the lunar maria; anorthosites from the highlands, and norites from the depths, brought upwards during a process called lunar mantle overturn; and volcanic glass.

For the new analysis, the research team modified a standard isotope analysis technique to produce high-precision oxygen isotope measurements. And they found something new indeed: that oxygen isotopic composition varied depending on the type of rock tested.

"We show," they wrote in their paper, "that the method of averaging together lunar isotope data while ignoring lithological differences does not give an accurate picture of the differences between the Earth and Moon."

In fact, the deeper the rock sample's origins, the researchers found, the heavier the oxygen isotopes, compared to Earth's.

This difference could be explained if only the outer surface of the Moon was pulverised and mixed during the impact, resulting in the similarity with Earth. But deep inside the Moon, the Theia chunk

remained relatively intact, and its oxygen isotopes were left closer to their original state.

The study claims that this is a pretty neat bit of evidence showing Theia could have formed farther out in the Solar System, and moved inwards before the big bada-Moon-making-boom.

Importantly, these results could also tidily clean up that messy problem with the giant-impactor hypothesis.

"Clearly, Theia's distinct oxygen isotope composition was not completely lost through homogenisation during the giant impact," the researchers concluded.

"This result thereby eliminates the necessity for giant-impact models to include a mechanism for complete oxygen isotope homogenisation between the two bodies and provides a foundation for future modelling of the impact and lunar formation."

Humans have not set foot on the Moon since 1972, thus precious Moon rocks available for analysis are in short supply, and replicating these results may be a little tricky for now.

However, within the next few years we might finally see crewed missions execute a long-awaited return to the lunar surface, and can hope for a real boom in Moon science - including further research around the giant-impact hypothesis.

The research has been published in *Nature Geoscience*.

http://bit.ly/2TWGl6q

Scientists may be 'on the cusp' of a universal flu vaccine

We may be one step closer to a universal flu vaccine, according to a new study.

By Joshua A. Krisch - Live Science Contributor

In the study, published Monday (March 9) in the journal Annals of Internal Medicine, researchers found that a single dose of the vaccine, called Flu-v, elicited greater immune responses than placebo in a small trial involving 175 volunteers. These results suggest that the vaccine is safe and potentially effective, and the research will usher Flu-v into the final stages of clinical testing.

"We're on the cusp of a universal flu vaccine," said Dr. Amesh Adalja, an infectious-diseases specialist and senior scholar at Johns Hopkins Center for Health Security in Baltimore, who was not involved in the new study. "It's long been a joke that a universal flu vaccine is always five years away. But I think, this time, it really is coming within the next five years."

While the seasonal flu vaccine certainly saves lives, "it is suboptimal," Adalja told Live Science. Indeed, each flu season begins with a race to predict the characteristics of burgeoning flu strains and develop vaccines that will prevent widespread infection. The process is lengthy and expensive, because vaccines are manufactured painstakingly using eggs or cell cultures, and the World Health Organization releases data on likely strains only months before the incoming flu season. This can result in frequent vaccine shortages, and even when there is ample supply, the virus can throw a curveball, mutating midseason and rendering the hard-earned dose impotent.

"Seasonal flu vaccine manufacturing is laborious, and this limits the number of doses available every year," said study co-author Olga Pleguezuelos, chief scientific officer at Seek, the drug discovery company that's developing Flu-v. "The schedule is very tight in order for the vaccine to be available before the flu season starts, which puts a huge strain on health services as they must make sure that patients are vaccinated within a two- or three-month window."

Flu-v is a promising alternative — a candidate for the long-awaited universal flu vaccine — because it is designed to target areas of the virus that are common to multiple strains of flu virus and unlikely to mutate. "Flu-v can be manufactured all year round," Pleguezuelos added. "The manufacturing is synthetic, so there are

no limitations on the scale of production," which there are for flu vaccines that are grown using eggs or cell cultures, she said.

The trick is demonstrating that Flu-v is safe and effective. No fewer than four prior trials have demonstrated safety for the vaccine. The new study, called a "Phase 2" study, was the first human trial to suggest that Flu-v increases the body's production of antibodies that prevent flu infection. What remains to be determined is whether the vaccine in fact prevents flu, a question reserved for a final round of "Phase 3" clinical trials.

"This is a hugely successful study in a prestigious journal," Adalja said. "But the next step is to see whether these antibodies are effective and how the vaccine works against real-life flu."

Pleguezuelos and her colleagues are currently planning a large study to address this very question, but they are cautiously optimistic about their current results, she said. The vaccine "has the potential to change how countries protect their citizens against flu, and its burden on health services and the economy," Pleguezuelos said. The new study was funded in part by Seek.

There are several other candidates for universal flu vaccine in the works. For example, the U.S. National Institute of Allergy and Infectious Diseases (NIAID) began its first in-human trial of a different universal flu vaccine in 2019, Live Science previously reported. And the Israeli company BiondVax is in Phase 3 trials of its universal flu vaccine, known simply as M-001. That study has already enrolled more than 12,000 people, and results are expected at the end of 2020, according to the company.

http://bit.ly/39KrdiP

Higher concentrations of IGF-1 are a probable cause of breast cancer

Insulin-like growth factor-1 is likely to play a role in the development of breast cancer

A growth hormone called insulin-like growth factor-1 (IGF-1) is likely to play a role in the development of breast cancer, according to new research published in the leading cancer journal *Annals of Oncology* [1] today (Wednesday).

IGF-1 is already known to encourage the growth and proliferation of cancer cells. Now, two analyses of information from several hundred thousand women enrolled in the UK Biobank study have shown that not only is there an association between higher levels of IGF-1 circulating in the blood and the development of breast cancer, but also, for the first time, that IGF-1 is likely to be a cause of the disease.

Researchers from the International Agency for Research on Cancer (IARC), Lyon, France, and the Cancer Epidemiology Unit at the University of Oxford, UK, carried out two, complementary studies to investigate the role of IGF-1 in breast cancer development. The first looked at the associations between levels of IGF-1 in the blood and the chances of the disease developing in 206,263 women.

The second study used a technique called Mendelian randomisation to analyse data from 265 variants of genes (single nucleotide polymorphisms or "SNPs") known to be associated with IGF-1 concentrations in 122,977 cases of breast cancer and 105,974 women without cancer (the controls). In this analysis, the researchers also looked at four SNPs for insulin-like growth factor-binding protein-3 (IGFBP-3), which may modulate the availability of IGF-1.

Mendelian randomisation uses complex statistical analysis of data from large population studies, such as UK Biobank, to provide evidence for cause and effect, rather than just the existence of an association. Randomly inherited genetic variations that alter levels of IGF-1 and IGFBP-3 mimic the effect of a randomised trial and are unaffected by the disease process, so the researchers were able

to use them to see whether people with a different genetic make-up had a different risk of breast cancer.

During an average of seven years of follow-up, 4,360 cases of breast cancer occurred. Among the 206,263 women included in the observational analysis, levels of IGF-1 ranged between an average of around 14 nanomoles per litre of blood (nmol/L) among participants with levels in the lowest 20% and 29 nmol/L in the top 20%.

In the observational study, the researchers found that women with IGF-1 concentrations in the top 20% had 1.24-fold increased chance of developing breast cancer compared to those in the bottom 20%, after adjustments for various factors that could affect the results, such as age, physical activity, body mass index, alcohol consumption, smoking, educational level and concentrations of other hormones and proteins in the blood, such as C-reactive protein, and testosterone. For every 1,000 women in the study who had the lowest IGF-1 concentrations, 21 were diagnosed with breast cancer over the study period, while 26 were diagnosed among those who had the highest concentrations. Every additional 5 nmol/L of IGF-1 concentrations was associated with a 1.11-fold increased risk. The results were consistent for both pre- and post-menopausal women.

Results from the Mendelian randomisation study were similar. For every additional genetically predicted 5 nmol/L of IGF-1, the risk of breast cancer increased by 1.05. However, when the researchers looked at oestrogen receptor positive (ER+) and negative (ER-) breast cancers [2] separately, IGF-1 was only associated with an increased risk of ER+ breast cancer. For every additional 5 nmol/L of IGF-1, there was a 1.06-fold increased risk of ER+ breast cancer. No association was found for IGFBP-3 concentrations and breast cancer risk.

Dr Neil Murphy, a scientist at IARC, said: "We found that higher levels of IGF-1 circulating in the blood, as determined by blood measurements and genetic markers, were related to higher breast cancer risk. These results support a probable causal role of the IGF pathway in breast cancer development."

Dr Marc Gunter, scientist and head of the nutrition and metabolism section at IARC, said: "To our knowledge, this is largest single study and the first Mendelian randomisation study to examine the relationship between IGF-1 and breast cancer. Importantly, our Mendelian randomisation analyses yielded strikingly similar positive associations between IGF-1 and breast cancer as those found in our observational analyses. Taken together, these results provide the strongest evidence to date for a causal role of the IGF-pathway in breast cancer development, and suggest that altering IGF-1 levels through diet and lifestyle or pharmacological means may be an effective strategy in the primary prevention of breast cancer. Our next step is to gain a fuller understanding of which lifestyle practices can alter IGF-1 concentrations and, in turn, the chances of breast cancer developing."

Dr Anika Knüppel, a nutritional epidemiologist at the University of Oxford, said: "The association between IGF-1 and breast cancer was first investigated in the 1980s and our findings are in line with various studies since then. But clarifying the direction of the association using Mendelian randomisation in our study leads the way for research into how the IGF-1 pathway can be harnessed in breast cancer prevention."

It may be possible to modify IGF-1 concentrations in the blood through changes to the amount and types of protein in a person's diet. In addition, drugs that target the IGF-1 system have been developed. There may be other, as yet unknown factors that can affect IGF-1 concentrations too.

Dr Murphy said: "Although levels of IGF-1 in the blood are potentially modifiable it is currently unknown how long an intervention aimed at altering IGF-1 concentrations would have to be applied in order to have a measurable effect or whether there could be other adverse impacts of such an intervention."

Limitations of the study include the possibility that a different biological pathway may be involved in the effect of IGF-1 on breast cancer, although the researchers conducted various analyses to test this.

Notes:

[1] "Insulin-like growth factor-1 (IGF-1), insulin growth factor-binding protein-3 (IGFBP-3) and breast cancer risk: observational and Mendelian randomization analyses with ~430,000 women", by Neil Murphy et al. Annals of Oncology. *doi:10.1016/j.annonc.2020.01.066*

[2] The hormone oestrogen can often be involved in driving the development of breast cancer. Breast cancers that are driven by oestrogen are called ER positive because they have receptors for oestrogen on the surface of cancer cells; while those that do not, are ER negative. In the UK, for example, about 70% of breast cancers are receptor positive and receptor status affects the treatment options.

http://bit.ly/38IuAWl

Low-dose chest CT leaves DNA intact

Low-dose chest CT scans used in lung cancer screening do not appear to damage human DNA

Oak Brook, Ill. - The low-dose chest CT scans used in lung cancer screening do not appear to damage human DNA, according to a study appearing in the journal *Radiology*. The results could help allay fears that such screenings will lead to an increase in radiation-induced cancer.

Low-dose CT screening for lung cancer in high-risk patients such as longtime smokers gained favor after the National Lung Screening Trial. The trial reported that use of low-dose chest CT scans could significantly reduce deaths from lung cancer compared to screening with chest X-rays. CT was able to identify cancers at an earlier, more treatable stage.

Along with the promise of CT screening came worries over the effects of radiation exposure on patients, as even the low-dose exam delivers more radiation than an X-ray--radiation that could affect DNA and potentially lead to cancer. Studies of these potential effects that rely on epidemiology, or the analysis of diseases in the population at large, have limitations, according to study senior author Satoshi Tashiro, M.D., Ph.D., director of the Research Institute for Radiation Biology and Medicine at Hiroshima University in Hiroshima, Japan. A biological approach that looks at the effects of exposure on DNA has more power, he said.

"The National Lung Screening Trial suggested the value of low-dose CT screening in high-risk population for developing lung cancer," he said. "There were, however, no studies investigating the biological effect of low-dose CT scans on large numbers of patients. These findings led us to investigate these effects."

Dr. Tashiro and colleagues developed a system to look for damage and abnormalities in chromosomes, strands of DNA wound into a double helix structure inside the cell. In a previous study, the technology showed increases in chromosomal aberrations after standard CT scans.

For the new study, the researchers compared the DNA in 107 patients who underwent low-dose chest CT with that of 102 who had standard-dose chest CT. They obtained blood samples before and 15 minutes after CT. The median effective radiation dose of low-dose CT was 1.5 millisieverts (mSv). The standard CT dose was 5.0 mSv.

Analysis of the DNA found significant differences between the group that had a standard-dose chest CT scan and those who had a low-dose chest CT. "We could clearly detect the increase of DNA damage and chromosome aberrations after standard chest CT," Dr. Tashiro said. "In contrast, no significant differences were observed in these biological effects before and after low-dose CT."

Although low-dose CT is now commonly used for screening exams, standard CT is an effective diagnostic tool that is appropriate when the benefits outweigh any potential risk.

While the study did not endorse lung cancer screening with low-dose CT, its results appear to ease concerns over a potential increase in radiation-related cancer risk related to screening programs. "Even using these sensitive analyses, we could not detect the biological effects of low-dose CT scans," Dr. Tashiro said. "This suggests that application of low-dose CT for lung cancer screening is justified from a biological point of view." Beyond lung cancer screening, Dr. Tashiro said the DNA analysis could be used to study the biological effects of other types of imaging.

"We are interested in the biological effects of various types of radiological diagnosis, including PET/CT, to establish a better system for the management of medical radiation exposure," he said.

"Biological Effects of Low-Dose Chest CT on Chromosomal DNA." Collaborating with Dr. Tashiro were Hiroaki Sakane, M.D., Mari Ishida, M.D., Ph.D., Lin Shi, Ph.D., Wataru Fukumoto, M.D., Ph.D., Chiemi Sakai, Ph.D., Yoshihiro Miyata, M.D., Ph.D., Takafumi Ishida, M.D., Ph.D., Tomoyuki Akita, Ph.D., Morihito Okada, M.D., Ph.D., and Kazuo Awai, M.D., Ph.D.

http://bit.ly/3aSQPKr

The Lancet HIV: Study suggests a second patient has been cured of HIV

Long-term follow-up of the London patient suggests no detectable active HIV virus remains in the patient.

- ***Long-term follow-up of the London patient suggests no detectable active HIV virus remains in the patient.***
- ***Although the treatment is high-risk and only suitable for certain patients, the results provide evidence that this patient is the second to be cured of the virus - replicating the finding that HIV cure is possible through stem cell transplantation.*** [1]

A study of the second HIV patient to undergo successful stem cell transplantation from donors with a HIV-resistant gene, finds that there was no active viral infection in the patient's blood 30 months after they stopped anti-retroviral therapy, according to a case report published in The Lancet HIV journal and presented at CROI (Conference on Retroviruses and Opportunistic Infections).

Although there was no active viral infection in the patient's body, remnants of integrated HIV-1 DNA remained in tissue samples, which were also found in the first patient to be cured of HIV. The authors suggest that these can be regarded as so-called 'fossils', as they are unlikely to be capable of reproducing the virus.

Lead author on the study, Professor Ravindra Kumar Gupta, University of Cambridge, UK, says: "We propose that these results represent the second ever case of a patient to be cured of HIV. Our findings show that the success of stem cell transplantation as a cure for HIV, first reported nine years ago in the Berlin patient, can be replicated." [1,2]

He cautions: "It is important to note that this curative treatment is high-risk, and only used as a last resort for patients with HIV who also have life-threatening haematological malignancies. Therefore, this is not a treatment that would be offered widely to patients with HIV who are on successful antiretroviral treatment. [2]

While most HIV patients can manage the virus with current treatment options and have the possibility of living a long and healthy life, experimental research of this kind following patients who have undergone high-risk, last-resort curative treatments, can provide insight into how a more widely applicable cure might be developed in the future.

In 2011, another patient based in Berlin (the 'Berlin patient') was the first HIV patient to be reported cured of the virus three and half years after undergoing similar treatment. Their treatment included total body irradiation, two rounds of stem cell transplant from a donor who carried a gene (CCR5Δ32/Δ32) that is resistant to HIV, and a chemotherapy drug regimen. [2] The transplant aims to make

the virus unable to replicate in the patient's body by replacing the patient's immune cells with those of the donors, whilst the body irradiation and chemotherapy targets any residual HIV virus.

The patient reported in this study (the 'London patient'), underwent one stem-cell transplantation, a reduced-intensity chemotherapy drug regimen, without whole body irradiation. In 2019, it was reported that their HIV was in remission, and this study provides follow-up viral load blood test results at 30-months and a modelling analysis to predict the chances of viral re-emergence.

Ultrasensitive viral load sampling from the London patient's cerebrospinal fluid, intestinal tissue, or lymphoid tissue was taken at 29 months after interruption of ART and viral load sampling of their blood at 30 months. At 29 months, CD4 cell count (indicators of immune system health and stem cell transplantation success) was measured, and the extent to which the patient's immune cells have been replaced by those derived from the transplant.

Results showed no active viral infection was detected in samples of the patient's blood at 30 months, or in their cerebrospinal fluid, semen, intestinal tissue, and lymphoid tissue 29 months after stopping ART.

The patient had a healthy CD4 cell count, suggesting they have recovered well from the transplant, with their CD4 cells replaced by cells derived from the HIV-resistant transplanted stem cells.

Furthermore, 99% of the patient's immune cells were derived from the donor's stem cells, indicating the stem-cell transplant had been successful.

Since it was not possible to measure proportion of cells derived from the donor's stem cells in all parts of the patient's body (i.e. measurement was not possible in some tissue cells like lymph nodes), the authors used a modelling analysis to predict the probability of cure based on two possible scenarios. If 80% of patient's cells are derived from the transplant, the probability of cure is predicted at 98%; whereas if they have 90% donor derived cells, they predict a 99% probability of cure.

Comparing to the treatment used on the Berlin patient, the authors highlight that their case study of the London patient represents a step towards a less intensive treatment approach, showing that the long-term remission of HIV can be achieved using reduced intensity drug regimens, with one stem cell transplant (rather than two) and without total body irradiation.

However, being only the second reported patient to undergo this experimental treatment successfully, the authors note that that the London patient will need continued, but much less frequent, monitoring for re-emergence of the virus.

Speculating on what their results might mean for future developments of HIV cures that utilise the CCR5 (HIV resistant) gene, co-author on the study, Dr Dimitra Peppa, University of Oxford, UK, says: "Gene editing using the CCR5 has received a lot of attention recently. The London and Berlin patient are examples of using the CCR5 gene in curative therapies outside of gene editing. There are still many ethical and technical barriers - e.g. gene editing, efficiency and robust safety data - to overcome before any approach using CCR5 gene editing can be considered as a scalable cure strategy for HIV." [2]

Writing in a linked Comment, lead author Professor Sharon R Lewin, University of Melbourne, Australia, (who was not involved in the study), says, "The finding of no intact virus can be reassuring for a patient who might face significant anxiety and uncertainty about whether and when viral rebound off ART might occur, which in other settings has been completely unpredictable. Given the large number of cells sampled here and the absence of any intact virus, is the London patient truly cured? The additional data provided in this follow up case report is certainly encouraging but unfortunately in the end, only time will tell."

NOTES TO EDITORS

This study was funded by The Wellcome Trust and amfAR. It was conducted by researchers from University of Cambridge, UK; Africa Health Research Institute, South Africa; University of Oxford, UK; Harvard University, USA; IrsiCaixa AIDS Research Institute, Spain; Autonomous University of Barcelona, Spain; University College London, UK; Imperial College London, UK; University Medical Center, Utrecht, Netherlands; Mortimer Market

Centre, Department of HIV, Central and North West London NHS Trust, London, UK; Imperial College NHS Healthcare Trust, Hammersmith Hospital, London, UK; Oxford National Institute for Health Research Biomedical Research Centre, Oxford, UK; University of Vic Central University of Catalonia, Spain;

Catalan Institution for Research and Advanced Studies, Barcelona, Spain

The labels have been added to this press release as part of a project run by the Academy of Medical Sciences seeking to improve the communication of evidence. For more information, please see: http://www.sciencemediacentre.org/wp-content/uploads/2018/01/AMS-press-release-labelling-system-GUIDANCE.pdf if you have any questions or feedback, please contact The Lancet press office pressoffice@lancet.com

[1] Evidence for first patient reported cured of HIV (known as the 'Berlin patient')- https://www.ncbi.nlm.nih.gov/pubmed/21148083

[2] Quote direct from author and cannot be found in the text of the Article.

[3] https://www.nature.com/articles/s41586-019-1027-4

http://bit.ly/38F0OSq

Science continues to suggest a link between autism and the gut. Here's why that's important

Newer research is showing gastrointestinal symptoms in autism may be due to differences in the gut itself.

Elisa Hill[*] **Ashley Frank**[**] **Sonja McKeown**[***]

Many people will associate autism with traits including atypical social interactions, repetitive behaviours, and difficulties with speech and communication.

But perhaps lesser known is the fact people with autism are more likely to experience gastrointestinal disorders than the general population.

One review found children with autism were four times more likely to report gastrointestinal symptoms than children without a diagnosis. A number of studies in the review reported the prevalence of gut problems was the same among boys and girls.

These symptoms can include constipation, diarrhoea, abdominal pain, bloating, reflux and vomiting.

Gut problems like these hinder quality of life for people with autism and their families, further affecting sleep, concentration and behavioural issues.

For a long time we thought this was due to the way the brain controls the gut. Think of the "butterflies" you get in your stomach, or the need to rush to the toilet when you're really nervous.

While the brain does influence gut function, this is only part of the story. Newer research is showing gastrointestinal symptoms in autism may be due to differences in the gut itself.

The mini brain of the gut

The gut contains its own dedicated nervous system, called the enteric nervous system, which co-ordinates digestion and the absorption of food and nutrients.

The enteric nervous system is a complex integrated network of neurons that extends along the gastrointestinal tract.

While structurally quite different, it contains about the same number of cells as the spinal cord and uses many of the same neurochemical messengers, receptors and proteins as the brain.

Autism has a strong genetic component. More than 1,000 gene mutations are associated with the disorder. Many of these gene mutations alter how neurons communicate in the brain.

We hypothesised some of these gene mutations may also cause neuron wiring to go awry in the gut, resulting in gastrointestinal issues in some people with autism.

Our research

To test this theory, we studied patient records of two brothers with autism, who have a single gene mutation associated with autism that affects neuron communication. We also studied mice.

Mouse models with this specific mutation, called neuroligin-3, have previously shown behaviours relevant to autism, such as altered

social interactions, reduced communication and repetitive behaviours.

We found this mutation also affects the enteric nervous system of the gut in mice. Mutant mice exhibited altered gut contractions, and the speed at which food moved through their small intestine was faster than the speed for mice without the mutation.

Meanwhile, both brothers have gut issues including esophagitis (inflammation of the esophagus) and diarrhoea.

So our work shows a gene mutation associated with autism, previously only studied in the brain, could affect the gut too.

The gut microbiota

We also found mice with the mutation had differences in their gut microbiota compared to normally developing mice.

The gut microbiota is the community of microorganisms (including bacteria, fungi and viruses) that live within the gastrointestinal tract. The largest amount of microbiota are found in the large intestine, where they digest some of the food we eat.

The mice we studied with the neuroligin-3 mutation had what's called an altered Firmicutes:Bacteroidetes ratio.

Scientists have found this ratio is altered in people with a range of conditions including type 2 diabetes, obesity and inflammatory bowel disease.

Why is all this important?

Now that we're beginning to understand more about the link between autism and the gut, scientists are investigating whether changing the gut microbiota could affect autism behaviours. One way we can alter the gut microbiota is using faecal transplants.

One recent study took faeces (microbiota) from boys with or without autism and transplanted the faeces into mice. The researchers then studied how the offspring of these mice behaved.

The offspring of mice that received microbes from boys with autism showed behaviours that could be relevant to autism (they buried more marbles in their cage bedding, potentially an indication of repetitive behaviour), compared to mice who were transplanted with microbes from typically developing children.

Another recent study assessed gut problems and behavioural traits for two years in people with autism after they received a faecal transplant. This study reported improvements in gut symptoms and behaviour. But the researchers only studied a small number of people, and didn't control for placebo effects.

Other studies have tested if changing gut microbes by treating patients with prebiotics (food for the bacteria in your gut) or probiotics (helpful bacteria) can affect autism behaviours. But a review of these studies showed no consensus – in other words, some studies showed an effect, while others didn't.

What does this mean for people with autism?

Many of the studies looking at the gut in autism so far have been conducted using mice. We need more research in humans to confirm the results can be extrapolated.

We need to continue to build our understanding of how gene mutations in the nervous system influence gut microbes. In the future, tweaking the gut microbiota might be one way to manage behaviours in people with autism.

This would not reverse gene mutations leading to autism, but it might tone down the effects, and improve quality of life for people with autism and their families.

In the meantime, clinicians treating people with autism should consider assessing and treating gut problems alongside behavioural issues.

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http://bit.ly/3aNRAEF

Studies Estimate Incubation Time, Infectious Period of SARS-CoV-2

It takes a median of five days after infection to get sick, and patients shed the most coronavirus particles early in the illness, according to two new reports.

Shawna Williams

Patients have tested positive for SARS-CoV-2 genetic material after apparently recovering from infection with the virus and being discharged from the hospital, according to media reports and a study published in *JAMA* last month.

The phenomenon has sparked concerns that people could continue to infect others long after their illness had passed. But a preprint posted to *medRxiv* yesterday (March 9) suggests that patients with mild symptoms shed viable viral particles for 10 days or less after the onset of illness.

"This is a very important contribution to understanding both the natural history of Covid-19 clinical disease as well as the public health implications of viral shedding," says Michael Osterholm, the director of the University of Minnesota's Center for Infectious Diseases Research and Policy, in remarks to *STAT*. Osterholm was not involved in the study.

The work was conducted on nine patients in Germany. The authors found a high load of infectious viral particles in samples from the patients' throats and lungs early in the illness, peaking four days after symptoms started. But while viral RNA could still be observed in the samples once symptoms had cleared, there were no detectable infectious particles after day eight from the onset of symptoms in those patients who'd had mild symptoms. No infectious particles were detected in stool, blood, or urine.

"Based on the present findings, early discharge with ensuing home isolation could be chosen for patients who are beyond day 10 of symptoms with less than 100,000 viral RNA copies per ml of sputum," the authors write in their report. The results have not undergone peer review.

In another study, published today in the *Annals of Internal Medicine*, researchers analyzed news reports and press releases mentioning exposure and symptom onset dates for patients with COVID-19, the illness caused by SARS-CoV-2. Among the 181 cases the authors found, the median time between exposure and symptom onset was 5.1 days, and 97.5 percent of people who became ill did so within 11.5 days of exposure.

"Based on our analysis of publicly available data, the current recommendation of 14 days for active monitoring or quarantine is reasonable, although with that period some cases would be missed over the long term," says study coauthor Justin Lessler, an epidemiologist at the Johns Hopkins Bloomberg School of Public Health, in a news release.

"It's very reassuring that by 14 days, while it might not be 100%, it will be close," Graham Cooke, an infectious disease expert at Imperial College London, tells *The Guardian*. Cooke cautions that people who've been exposed shouldn't assume they're in the clear if they haven't developed symptoms after five days. "That's absolutely the wrong interpretation," he says. "At five days, half of people won't yet have developed symptoms."

Clarification (March 10): The wording of this article's subheading has been adjusted to make it clear that five days after infection was the median time it took for people to get sick in the study.

https://go.nature.com/2W2Qilf

Tiny bird fossil might be the world's smallest dinosaur

A tiny skull trapped in 99-million-year-old amber suggests that some of the earliest birds evolved to become miniature. The fossil illustrates how ancient amber can act as a window into the distant past.

Roger B. J. Benson

Dinosaurs were big, whereas birds — which evolved from dinosaurs — are small. This variation is of great importance, because body size affects lifespan, food requirements, sensory capabilities and many other fundamental aspects of biology. The smallest dinosaurs[1] weighed hundreds of grams, but the smallest living bird, the bee hummingbird (*Mellisuga helenae*)[2], weighs only 2 grams. How did this difference come about, and why?

In a paper in *Nature*, Xing *et al*.[3] describe the tiny, fossilized, bird-like skull of a previously unknown species, which they name *Oculudentavis khaungraae*. The discovery suggests that miniature body sizes in birds evolved earlier than previously recognized, and might provide insights into the evolutionary process of miniaturization.

Read the paper: Hummingbird-sized dinosaur from the Cretaceous period of Myanmar

Fossilization of bones in sediments such as clay, silt and sand can crush and destroy the remains of small animals, and can flatten and decay soft parts such as skin, scales and feathers. By contrast, preservation of small animals in Burmese amber (which formed from the resin flows of coniferous trees about 99 million years ago) helps to protect their soft parts. A wide range of invertebrates[4] and small vertebrates, including lizards[5] and birds[6], have been found in Burmese amber. Specimens preserved in this material are rapidly emerging as an exceptional way to study tiny vertebrates from the age of dinosaurs[5,6].

It is in Burmese amber that the single known fossil skull of *Oculudentavis* has been preserved (see Fig. 1a of the paper[3]). *Oculudentavis* means eye tooth bird, a name that Xing *et al*. chose because of two unusual features of the skull, each of which provides evidence about the likely lifestyle of this 99-million-year-old species. First, the skull is dominated by two enormous eye sockets containing scleral ossicles — rings of bone that form the eye skeletons of birds (Fig. 1).

The opening at the centre of these ossicles is narrow, restricting access for light into the eye and providing strong evidence that *Oculudentavis* was active in well-lit, daytime environments.

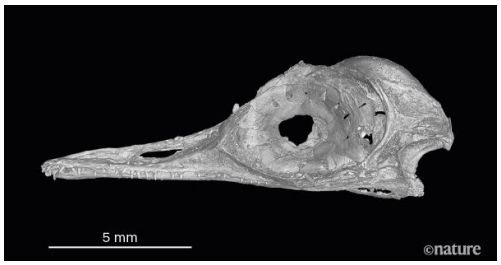

Fig 1 | ***Computed tomography scan of the skull of Oculudentavis khaungraae. Xing et al.[3] have characterized this 99-million-year-old fossil bird.***

Second, the jaws of *Oculudentavis* have many small teeth. This might seem odd, given the absence of teeth in today's birds, but teeth are in fact common among early fossil birds[7]. However, *Oculudentavis* has more teeth than other birds of the period, and these extend unusually far back in the jaws to a point just under the eye. On the basis of these facts, along with observations of the fossilized tongue, the authors suggest that *Oculudentavis* was a predator that mainly ate invertebrates. This diet differs considerably from the nectar-based diet of the smallest living birds, and suggests that extinct and living birds took different paths to miniaturization (although how diet might be involved in this process remains unknown).

Oculudentavis is just one fossil species. However, even single fossils can contribute greatly to our understanding of the history of

life on Earth. In this case, weighing perhaps 2 grams, *Oculudentavis* is about one-sixth of the size of the smallest known early fossil bird[1]. This indicates that, only shortly after their origins late in the Jurassic period (which lasted from about 201 million to 145 million years ago), birds had already attained their minimum body sizes. By contrast, the smallest dinosaurs weighed hundreds of times more[1] (Fig. 2). Understanding when, how and why the lower limits of body size shifted in this way requires greater knowledge of the earliest fossil birds. But *Oculudentavis* is a stepping stone towards this.

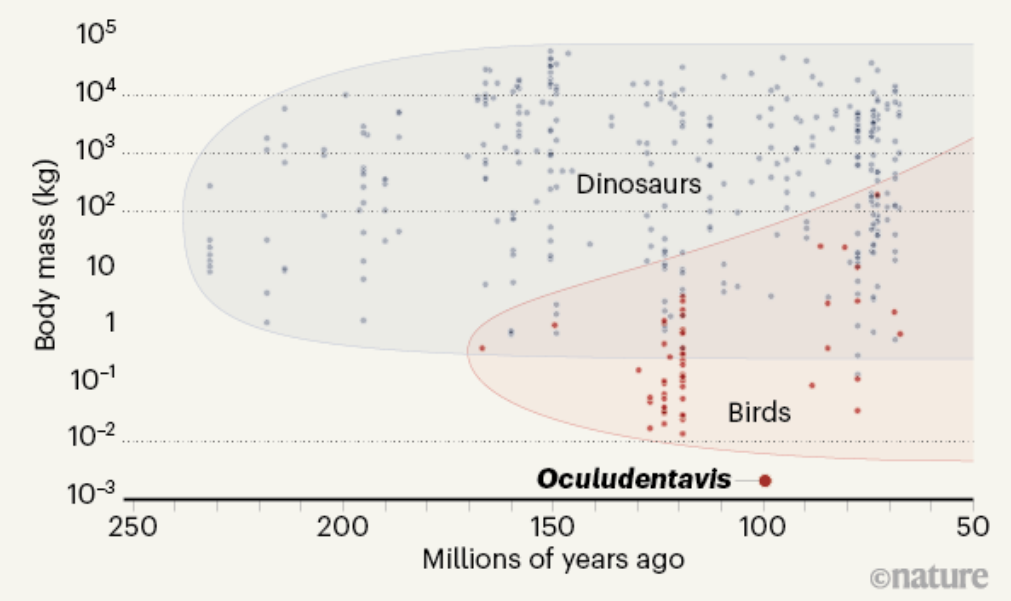

Figure 2 | Different size ranges of dinosaurs and birds. Dinosaurs varied from about 500 grams to many tonnes in weight. By contrast, the first birds were much smaller. The smallest fossil bird found so far from the Cretaceous period weighs in at about 12 grams (data taken from ref. 9). Xing et al.[3] report that the tiny Oculudentavis weighed just 2 grams. This discovery provides new insight into the lower limits of vertebrate body size in the age of dinosaurs.

The evolutionary relationships between *Oculudentavis* and other dinosaurs and birds are difficult to determine, but are central to clarifying the evolutionary implications of this discovery. Xing and colleagues' analysis suggests two possibilities. *Oculudentavis* could belong to the most common group of birds of the Cretaceous period (about 145 million to 66 million years ago), the enantiornithines. Alternatively, it could be much more closely related to dinsosaurs, lying almost midway on the evolutionary tree between the Cretaceous birds and *Archaeopteryx*, the iconic winged dinosaur from the Jurassic.

This confusion is a result of the bizarre features seen in *Oculudentavis*. These include many characteristics that differ from those of other birds, such as more-robust, fused bones, and proportionally enlarged sensory organs relative to the overall body size. The authors suggest that these features could have arisen from the constraints of evolutionary miniaturization or from ecological specialization. Both of these might have required *Oculudentavis* to have a strengthened skull and proportionally large eyes to maintain sensory capacity at such a tiny size. In addition, *Oculudentavis* has features that are not seen in dinosaurs or birds, but are present in lizards — these include the spoon shape of its scleral ossicles and the fact that its teeth are attached to the jaw bone by their sides, rather than being implanted in sockets. The challenge of determining how *Oculudentavis* is related to other early birds and bird-like dinosaurs would be greatly assisted by knowing more about its skeleton.

The past decade has generated much data on the dinosaur–bird transition, greatly advancing our understanding of this major evolutionary event[7,8]. In the past few years, Burmese amber has yielded surprising insights, including previously unseen feather and skeletal structures in other extinct birds[6]. The study of small vertebrates preserved in amber, their ecosystems and their

evolutionary relationships with one another is in a nascent phase. But *Oculudentavis* suggests that the potential for continued discovery remains large — especially for animals of diminutive sizes. *Nature* ***579****, 199-200 (2020) doi: 10.1038/d41586-020-00576-6*

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http://bit.ly/2IJGhS4

Magnolia bark compound could someday help treat drug-resistant epilepsy

Potential new treatment for epilepsy by turning to traditional Chinese medicine

In patients with epilepsy, normal neurological activity becomes disrupted, causing debilitating seizures. Now, researchers report in *ACS Chemical Neuroscience* that they have found a potential new treatment for this disorder by turning to traditional Chinese medicine. Tests of extracts from plants used in these ancient remedies led the team to one compound, derived from a magnolia tree, that could quell drug-resistant seizures in both fish and mice.

Epilepsy is one of the most common neurological diseases worldwide, and the World Health Organization estimates that about 50 million people have the disorder. Medications are available, but they don't help everyone. Research suggests that about 70% of patients with epilepsy can control it well with medication, leaving many patients without effective treatment. But even when they work, the drugs can cause a range of side effects, from dizziness to mood disruptions. To look for new drug leads that could help even those patients who don't respond to conventional anti-seizure medications, Peter de Witte and colleagues set their sights on plants used in traditional Chinese medicine.

The team collected 14 plants used in traditional Chinese medicine anti-seizure remedies. They then tested the plants' extracts in two types of zebrafish with epileptic-like seizures, one of which could respond to conventional anti-seizure medications, whereas the other type could not. Only extracts from the bark of *Magnolia officinalis*, a tree native to China, reduced seizure-like behavior in both types of fish. In tests with mice, the researchers found that the magnolia bark's most potent anti-seizure compound, magnolol, reduced the rodents' otherwise drug-resistant seizures. It and similar compounds in magnolia bark could provide a starting point for the development of treatments for resistant epilepsy, according to the researchers.

The authors acknowledge funding from the China Scholarship Council, the KU Leuven Internal Funds and the Fund for Scientific Research Flanders.

The abstract that accompanies this study is available here.

http://bit.ly/2U5Hf04

University of Minnesota first to prove new method to grow human blood vessels

Early studies show further applications that could impact donor transplant system

Minneapolis, MN - A team of researchers at the University of Minnesota Medical School recently proved the ability to grow human-derived blood vessels in a pig--a novel approach that has the potential for providing unlimited human vessels for transplant purposes. Because

these vessels were made with patient-derived skin cells, they are less likely to be rejected by the recipient, helping patients potentially avoid the need for life-long, anti-rejection drugs.

Daniel Garry, MD, PhD, and Mary Garry, PhD, both professors in the Department of Medicine at the U of M Medical School, co-led the research team and published their findings in *Nature Biotechnology* last week.

"There's so many chronic and terminal diseases, and many people are not able to participate in organ transplantation," said Daniel, who is also a heart failure and transplant cardiologist. "About 98 percent of people are not going to be eligible for a heart transplant, so there's been a huge effort in trying to come up with strategies to increase the donor pool. Our approach looked at a pig."

Because of similarities between human and pig physiology, scientists have historically studied pigs to discover treatments for health issues, including diabetes. Before researchers engineered human insulin, doctors treated patients with pig insulin.

"Our discovery has made a platform for making human blood vessels in a pig," said Daniel. "This could allow us to make organs with human blood vessels that would be less apt to be rejected and could be used in patients in need of a transplant. That's what typically causes rejection--the lining of the blood vessels in the organs."

The blood vessels created by the Garry duo will avoid rejection because of the method by which they are made. The team injects human-induced pluripotent stem cells--taken from mature cells scraped from a patient's skin and reprogrammed to a stem cell state--into a pig embryo, which is then placed into a surrogate pig. In the future, viable piglets, with blood vessels that will be an exact match to the patient, will ensure a successful transplant and the ability to live without the need for immunosuppression, or anti-rejection, drugs.

"There's hundreds of thousands of patients that have peripheral artery disease, either because of smoking or diabetes or any number of causes, and they have limb amputations," Mary said. "These blood vessels would be engineered and could be utilized in these patients to prevent those kinds of life-long handicaps, if you will."

The first phase of their study, approved by the U of M's Stem Cell Research Oversight committee, brought the first embryo to a 27-day term. Because of the success of this phase, Daniel and Mary are currently seeking the committee's approval to advance the research further into the later gestational period.

"We're trying to take it in a phased approach," Daniel said. "We want to be sure we address all of the possible issues--whether human cells go where we want them to go."

"While it is a first phase, there's pretty solid proof of concept," Mary said. "We believe that we've proven that there's no off-target effects of these cells, so we're ready to move forward to later gestational stages."

Current U of M investigators who participated in this study include Satya Das, Naoko Koyano-Nakagawa, PhD, Geunho Maeng, Bhairab Singh, Daniel Mickelson, Wuming Gong, PhD, Cyprian Weaver, PhD, Stefan Kren and Demetris Yannopoulos, MD.

http://bit.ly/2QcEBVk

Astronomers Observe a Nightmarish Exoplanet So Hot That It Rains Iron at Night

In the constellation of Pisces, 640 light-years from Earth, sits a hell-planet.

Michelle Starr

The gas giant WASP-76b whips around its star at a breakneck orbit of just 1.8 days, and those days are brutal, with temperatures in excess of 2,400 degrees Celsius (4,350 Fahrenheit) - hot enough to vaporise iron.

But where day turns to night, the temperature cools enough for the iron vapour to condense again into scorching liquid that then rains

down towards the planet's interior, according to a new study. "One could say that this planet gets rainy in the evening, except it rains iron," said astrophysicist David Ehrenreich of the University of Geneva in Switzerland.

WASP-76b, whose discovery was announced back in 2016, is a type of planet known as a hot Jupiter. It's a smidge less than the mass of Jupiter, but more bloated and fluffy, around 1.8 times Jupiter's size.

It's also only about 5 million kilometres from its star, which is both larger and hotter than our Sun - 1.5 times the Sun's mass, 1.8 times the size, and with a temperature of around 6,329 Kelvin (the Sun is 5,778 Kelvin).

So, not only is the exoplanet subject to scorching radiation thousands of times greater than Earth's irradiation from the Sun, it's also tidally locked. This is when one side of an orbiting body always faces the object it is orbiting - for a nearby example, the Moon is tidally locked with Earth.

In the case of WASP-76b, this means one side is in perpetual day, and the other in perpetual night, with a significant temperature difference between the two. The day side is around 2,400 degrees Celsius (4,350 Fahrenheit), and the night around 1,500 degrees Celsius (2,730 Fahrenheit).

This isn't the hottest exoplanet ever discovered - that crown is being worn by KELT-9b, an exoplanet so hot it's literally evaporating - but it's definitely more on the extreme end of the scale.

Modelling has suggested that, on planets like WASP-76b, the extreme temperature difference between the two sides should generate strong winds. This, and the planet's rotation, should push iron vapour around the planet, and atoms on the day side should recombine into molecules on the night side.

However, evidence supporting this expectation - a chemical gradient, for instance - has not been acquired. So Ehrenreich and his team decided to take a closer look. Specifically, they wanted to study the terminators - the lines between night and day - to see if these displayed asymmetrical chemistry. This, too, would support the metal rain theory.

They used high-dispersion spectroscopy to analyse the light around the edge of the planet, looking for signatures in the spectrum that indicated an element was blocking some of the light. And they found it. On the evening terminator - where day turns into night - they found a strong signature of iron vapour.

On the morning terminator - where night turns to day - this signature was absent. This is pretty strong evidence in support of iron rain, since liquid iron is the most stable high-temperature iron-bearing condensate.

"The observations show that iron vapour is abundant in the atmosphere of the hot day side of WASP-76b," said astrophysicist María Rosa Zapatero Osorio of the Centre for Astrobiology in Spain.

"A fraction of this iron is injected into the night side owing to the planet's rotation and atmospheric winds. There, the iron encounters much cooler environments, condenses, and rains down."

Then, because the iron has rained out of the upper atmosphere, it does not reappear as vapour on the morning terminator.

Now that the team's observations have returned a result, it may be possible to take similar observations of other hot Jupiters, looking for signs of metal rain. And, of course, everyone has high hopes for the high-tech James Webb Space Telescope's ability to peer into the atmospheres of different exoplanets. It's due to launch next year.

Astronomers have already identified exoplanets with clouds of corundum - the building block of rubies and sapphires - and another that has iron clouds. We can't wait to see what other wacky weather is out there in the Universe.

The research has been published in *Nature*.

http://bit.ly/2Wb1DQm

Astronomers Discover 139 New Trans-Neptunian Objects

Minor planets located in the far reaches of the Solar System

Astronomers have released a catalog of 316 **trans-Neptunian objects** (TNOs) — minor planets located in the far reaches of the Solar System — detected from the first four years of the **Dark Energy Survey** (DES). The new catalog includes 245 discoveries by DES, 139 not previously published.

The goal of DES, which completed six years of data collection in January 2020, is to understand the nature of dark energy by collecting high-precision images of the southern sky.

While the survey wasn't specifically designed with TNOs in mind, its breadth and depth of coverage made it particularly adept at finding new objects beyond Neptune.

"The number of TNOs you can find depends on how much of the sky you look at and what's the faintest thing you can find," said University of Pennsylvania's Professor Gary Bernstein.

Because DES was designed to study galaxies and supernovas, the astronomers had to develop a new way to track movement.

Dedicated TNO surveys take measurements as frequently as every hour or two, which allows researchers to more easily track their movements. "Dedicated TNO surveys have a way of seeing the object move, and it's easy to track them down," said Pedro Bernardinelli, a graduate student at the University of Pennsylvania. "One of the key things we did in this paper was figure out a way to recover those movements."

The team analyzed data from the first four years of DES and found 316 TNOs, including 245 discoveries made by the survey and 139 new objects that were not previously published.

With only 3,000 objects currently known, this DES catalog represents 10% of all known TNOs. Pluto, the best-known TNO, is 40 times farther away from the Sun than Earth is, and the TNOs found using the DES data range from 30 to 90 times Earth's distance from the Sun. Some of these objects are on extremely long-distance orbits that will carry them far beyond Pluto.

The new catalog will be a useful scientific tool for research about the Solar System. Because DES collects a wide spectrum of data on each detected object, astronomers can attempt to figure out where the TNO originated from, since objects that form more closely to the Sun have are expected to have different colors than those that originated in more distant and colder locations.

And, by studying the orbits of these objects, they might be one step closer to finding Planet Nine, a hypothesized Neptune-sized planet that's thought to exist beyond Pluto.

"There are lots of ideas about giant planets that used to be in the Solar System and aren't there anymore, or planets that are far away and massive but too faint for us to have noticed yet," Professor Bernstein said. "Making the catalog is the fun discovery part. Then when you create this resource; you can compare what you did find to what somebody's theory said you should find." The team's paper was published in the *Astrophysical Journal Supplement Series*.

Pedro H. Bernardinelli et al. *2020. Trans-Neptunian Objects Found in the First Four Years of the Dark Energy Survey.* ApJS *247, 32; doi: 10.3847/1538-4365/ab6bd8*

http://bit.ly/2QbJIVU

Like patching a flat tire: New fix heals herniated discs

A new two-step technique to repair herniated discs uses hyaluronic acid gel to re-inflate the disc and collagen gel to seal the hole, essentially repairing ruptured discs like you'd repair a flat tire.

Ithaca, N.Y. - After a rupture, a jelly-like material leaks out of a herniated disc, causing inflammation and pain.

The injury is usually treated one of two ways: a surgeon sews up the hole, leaving the disc deflated; or the disc is refilled with a

replacement material, which doesn't prevent repeat leakages. Each approach on its own isn't always effective.

A collaboration led by Cornell University professor Lawrence Bonassar combined these two methods into a new two-step technique that results in a "patched" disc that maintains mechanical function and won't collapse or deteriorate.

"This is really a new avenue and a whole new approach to treating people who have herniated discs," Bonassar said.

"We now have potentially a new option for them, other than walking around with a big hole in their intervertebral disc and hoping that it doesn't re-herniate or continue to degenerate.

And we can fully restore the mechanical competence of the disc."

Bonassar's research group seeks engineering-based solutions for degenerative disc disease.

Over the last decade, the group has developed a collagen gel that incorporates riboflavin, a photoactive vitamin B derivative.

Instead of sewing up a ruptured disc, the researchers can patch it by applying their gel and shining light on it to activate the riboflavin.

The resulting chemical reaction causes fibers in the collagen to bond together and the thick gel stiffens into a solid.

Most importantly, the gel provides a more fertile ground for cells to grow new tissue, sealing the defect better than any suture could.

The technique only takes five or 10 minutes and can be applied in conjunction with a discectomy, the hourlong procedure by which the leaked nucleus pulposus is removed from the nerve root.

The technique could be used to address other types of disc degeneration, or integrated into other spinal procedures and therapies.

The paper, "Combined Nucleus Pulposus Augmentation and Annulus Fibrosus Repair Prevents Acute Intervertebral Disc Degeneration after Discectomy," published in Science Translational Medicine.

http://bit.ly/2U0A1dY

Coronavirus may be most infectious when symptoms are mildest, small study finds

Those with mild COVID-19 infections may not be infectious after about 10 days of symptoms.

By Nicoletta Lanese - Staff Writer

People infected with the novel coronavirus shed large quantities of the virus early in their illness and likely become less infectious as the disease wears on, according to a small study.

The research, posted Sunday (March 8) to the preprint database medRxiv, is still preliminary, because it has not yet been peer-reviewed and because it included only nine participants. Still, it may hint at why the new virus spreads so easily: Many people may be at their most infectious when exhibiting only mild, cold-like symptoms.

"This is in stark contrast to SARS," a related disease caused by a different coronavirus, the authors noted. In SARS patients, viral shedding peaked about seven to 10 days into the illness, as the infection spread from the upper respiratory tract into deep lung tissue. In seven patients with COVID-19, the disease caused by the new virus, "peak concentrations were reached before Day 5 and were more than 1,000 times higher" than those seen in SARS patients, the authors wrote.

This peak appeared later in two patients whose infections had progressed into their lungs, sparking the first signs of pneumonia. In these severe cases, viral shedding reached maximum levels around Day 10 or 11. In the mild cases, viral shedding dipped steadily after Day 5, and by Day 10, patients likely weren't contagious anymore, the authors noted.

"Based on the present findings, early discharge with ensuing home isolation could be chosen for patients who are beyond Day 10 of symptoms," provided that swab samples from their throat

contain fewer than 100,000 copies of viral genetic material per milliliter, the authors wrote. "This is a very important contribution to understanding both the natural history of COVID-19 clinical disease as well as the public health implications of viral shedding," Michael Osterholm, director of the University of Minnesota's Center for Infectious Disease Research and Policy, told Stat News.

The researchers conducted their analysis by taking swabs from the patients' noses and throats, also examining their blood, urine, stool and sputum — a mixture of saliva and mucus that builds up in the respiratory tract during infection. The team examined each sample for bits of viral genetic material called RNA to determine how much of the virus was present at different stages of the disease.

Researchers tracked the rise and fall of the virus over time. However, viral load can't reveal whether patients remained infectious, as RNA from the virus may be present in human tissue but not functional. To find out who was infectious and when, the researchers isolated samples of the virus throughout the study and attempted to grow them in the lab.

The researchers found that they could grow virus from the throat, nose and sputum samples gathered early in the course of illness, but after Day 8, samples taken from patients with mild cases did not yield any viral growth. That change indicates that those patients had become less infectious. Despite their improvement, they still tested "positive" for the virus, however. The finding may help explain reports from China suggesting that the virus can persist in the body for at least two weeks after COVID-19 symptoms clear up.

The team in the new study could not grow virus from any blood or urine samples collected during the study, nor could they grow virus from stool. The stool analysis was based on 13 samples collected between Day 6 and Day 12 from four patients, as these contained the largest quantities of viral RNA and enabled the researchers to isolate samples. A previous report from China and the World Health Organization suggested that "viable virus" could be recovered from infected people's stool, but it was unclear whether these fragments contributed to disease transmission.

As the new study is based on a select number of relatively mild cases, more research is needed to determine how stool might contribute to COVID-19 transmission, the authors noted.

Notably, the team detected antibodies in each of the patients between Day 6 and Day 12, suggesting that the immune system begins building a defense against the pathogen soon after exposure. Scientists don't yet know whether this rapid immune response appears in most patients, particularly those with more-severe infections.

http://bit.ly/2U8k59q

Metabolic fossils from the origin of life

An international team of researchers has investigated metabolic networks of primitive microbes and identified autocatalytic sets that are older than genes.

Life converts food into cells via dense networks involving thousands of reactions. New research uncovers insights as to how such networks could have arisen from scratch at life's origin. An international team of researchers in Germany, New Zealand and the U.S.A. has investigated metabolic networks of primitive microbes and identified autocatalytic sets (interconnected collections of self-reinforcing reactions) that are older than genes.

Living cells are the end product of metabolic networks. Food molecules that enter the cell are converted to central intermediates that are then channeled into the pathways that produce the molecules of which cells are made. These networks typically entail more than 1000 reactions, almost all of which are performed by enzymes (proteins), which are encoded by genes (nucleic acids). The link between genes and proteins is, in turn, the universal genetic code that instructs ribosomes to make proteins according to

the information stored in genes. These components are all interlinked: the ribosome is 50% protein and 50% RNA by weight, the proteins are made of amino acids, the RNA is made of nucleic acid bases, and the amino acids and bases are made by the roughly 1000 reactions in metabolism, which are catalyzed by the enzymes that the genes encode. With so many layers of mutual interdependence, it is no wonder that scientists have been flatly stumped for over a century when it comes to the question of how such a complex system of interactions could arise at the origin of life.

As with the evolution of all complex systems, it had to start from something simpler. But what? New findings by Joana C. Xavier and colleagues reported in *Proceedings of the Royal Society B* in London provide new inroads into this longstanding question.

The new clues come from the least expected of all places: mathematics. Almost 50 years ago the American polymath Stuart Kauffman suggested that theoretical constructs called autocatalytic sets might have been intermediates in the origin of molecular complexity of the kind that we find in metabolism and cells. Such autocatalytic sets consist of elements (members of the set) that are both products and catalysts such that they can make more of themselves given suitable starting material.

The analogy to metabolism and enzymes is evident. The existence and properties of such autocatalytic sets remained the subject of much speculation and decades of fierce debate until the mathematician Mike Steel from the University of Canterbury in New Zealand and Wim Hordijk, a computer scientist from The Netherlands, both coauthors on the study, found ways of harnessing them in the computer. They found that a particular class of autocatalytic sets called RAFs (for reflexively autocatalytic food generated networks), which are very similar in design to cellular metabolism, have the unexpected property of being downright likely to arise from scratch. "The surprise is that the elements only need to add a tiny amount of catalysis to the system before they start to make more of themselves" says Steel. "This is what physicists call self organization, a kind of holy grail in origin of life research" adds Hordijk.

With a background in the metabolic networks of real cells, Joana C. Xavier in the Institute for Molecular Evolution at the University of Düsseldorf asked whether RAFs could be detected in the metabolic networks of the most primitive microbes, strict anaerobes that live from H2 and CO2. Indeed, she found that RAFs were there in the metabolism of ancient anaerobes, but they were substantially smaller than the whole metabolic map, comprising only 394 reactions in the case of an ancient microbe that converts H2 and CO2 to acetate for a living and 209 reactions in the case of an ancient microbe that converts H2 and CO2 to methane. "This intermediate size is interesting" says Xavier, "because it points to an intermediate state in the evolution of metabolism, something more complex than individual reactions but less complex than a cell."

The two kinds of unicellular organisms at the focus of the study, called acetogens and methanogens, have long been in the sights of microbiologists interested in the origin of life. They have been linked to the last universal common ancestor, LUCA, and to geochemical reactions at hydrothermal vents. Xavier found that the acetogen and methanogen sets overlap to form an ancient core network of 172 reactions.

This ancient conserved core predates the divergence of bacteria and archaea and has intriguing properties. It can generate amino acids and nucleic acid bases from a simple starting food set, but if provided only the bases as food, no network at all emerges. "Not only have autocatalytic networks left fossils in real metabolism, they preceded both RNA and protein polymers in evolution, that is

a step forward in my book," says Kauffman, coauthor of the study and autocatalysis pioneer.

William Martin at the University of Düsseldorf and coauthor of the study says "The networks that trace to LUCA's metabolism are older than genes, they point to natural order in the chemical reactions of life." Acetogens and methanogens grow under the kinds of conditions that are encountered today at hydrothermal vents. Did life arise at hydrothermal vents? "The closer we look, the more signs keep pointing in that direction" says Xavier, "the idea keeps uncovering findings that converge. These vents were probably the first bioreactors on Earth."

The identification of autocatalytic networks as components of modern metabolism takes them off the drawing board and into the real world of microbial life. That they uncover fossils from the earliest stages of chemical evolution was unexpected, and opens up new routes for the study of our deepest evolutionary past, probing the time 4 billion years ago, when life was just starting from a small set of naturally-occurring chemical reactions that took place somewhere, perhaps at a hydrothermal vent.

http://bit.ly/38WdDYI

Thriving 'Neuron Nurseries' Have Been Found Inside The Adult Human Nose

Our noses appear to be home to thriving 'neuron nurseries', according to new research.

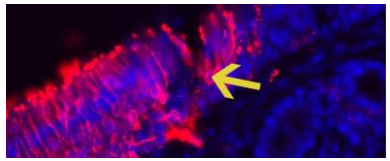
DAVID NIELD

It's a curious finding, given recent investigations on whether our brains keep making new neurons as we become adults; some evidence points to us growing these nerve cells well into old age.

But we don't really know whether such neurogenesis could be found in other busy nerve bundles - such as the nose.

This latest study suggests the olfactory neuroepithelium in the human nose seems to carry on producing neurons in our adulthood, based on an analysis of human tissue taken from seven middle-aged human donors.

Not only does this result give scientists a fresh insight into our body's intricate neuron-producing processes, it also hints at new ways to treat conditions when these neurons may be badly damaged, or die off due to old age.



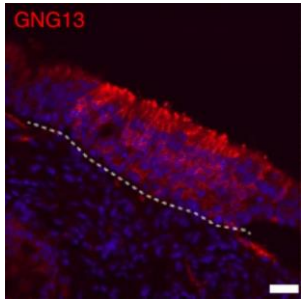
Tissue section from a human nasal biopsy. Red staining outlines olfactory neurons. **(Brad Goldstein)**

"We do not fully understand why people lose their sense of smell, which can occur for many reasons, and our data sets provide a wealth of information about the cell populations present in adult olfactory tissue," says ear, nose and throat doctor Brad Goldstein from the Duke University Medical Center.

"This is an important step in developing treatment strategies for conditions when this tissue may be damaged."

Using single-cell RNA sequencing, the researchers looked at 28,726 different cells in total, finding that more than half were 'baby' or immature neurons produced by neural stem cells – and their youthfulness suggests the neurons were produced inside the tissue itself.

In fact, the team found neurons at several stages of life in the nose tissue. While mouse studies have suggested some nerve regrowth in the nose was possible, the proportion of new cells in human noses was still surprising.



Neurons shown in red in human nasal tissue. **(Durante, etal., Nature Neuroscience, 2020)**

As neurons are responsible for transmitting information to other cells and muscles, when something goes wrong with these cells it can cause big problems – as seen with diseases such as Alzheimer's.

"It will be very useful to use this window to analyse samples from people with conditions in which the nervous system has degeneration, such as Alzheimer's disease," says Goldstein.

"Alzheimer's is of particular interest, since these patients lose their sense of smell quite early in the disease process, and we have few treatments for Alzheimer's disease. So, it may make sense to look carefully at regions of the olfactory system in these patients."

While the new study supports the idea that this nasal nursery is capable of churning out new neurons as we get older, further research will be needed to make sure – we haven't yet actually observed them being made. Scientists are continuing to make strides forward in their understanding of how neurons operate and communicate with each other, offering insight into the workings of the complex biological computer that is the human body.

This new study does align with findings from last year, which showed neurons at different stages of maturity deep within the human brain. It seems we can keep producing these cells as we get older – the next question is how.

"Because the nose is exposed to the external environment, it might be possible we could one day collect these neuronal stem cells from patients and use them to treat their own brain disorders," says microbiologist Hiroaki Matsunami from Duke University Medical Center. "It is not outside of the realm of possibility."

The research has been published in *Nature Neuroscience*.

http://bit.ly/2U4vzLc

Arrival delayed! Water, carbon and nitrogen were not immediately supplied to Earth

Evidence that a large proportion of the elements that are important for the formation of oceans and life were delivered to Earth very late in its history

Spearheaded by earth scientists of the University of Cologne, an international team of geologists has found evidence that a large proportion of the elements that are important for the formation of oceans and life, such as water, carbon and nitrogen, were delivered to Earth very late in its history. Previously, many scientists believed that these elements were already present when the Earth began to form. However, geological investigations have now shown that most of the water in fact was only delivered to Earth when its formation was almost complete.

3.8 billion-year-old rocks at the Earth's surface in southwestern Greenland.
Credit: Kristoffer Szilas, University of Copenhagen

The new findings, which are a result of collaboration among scientists from Germany, Denmark, Wales, Australia and Japan, will be published in Nature under the title 'Ruthenium isotope vestige of Earth's pre-late veneer mantle preserved in Archean rocks' on 11 March 2020.

It is a generally accepted fact that volatile elements such as water originate from asteroids, the 'planetary building blocks' that formed in the outer solar system. However, there is ongoing discussion among experts as to when precisely they came to Earth. 'We have now been able to narrow down the timeframe much more precisely', said first author Dr. Mario Fischer-Gödde from the Institute of Geology and Mineralogy at the University of Cologne. 'To do so, we compared the composition of the oldest, approximately 3.8 billion-year-old mantle rocks from the Archean Eon with the composition of the asteroids from which they may have formed, and with the present-day composition of the Earth's mantle.'

To constrain the delivery of the so-called 'volatile' elements to Earth, the researchers measured the isotope abundances of a very rare platinum metal called ruthenium, which was already present in Earth's mantle by Archean time. Like a genetic fingerprint, this rare

platinum metal is an indicator for the late growth phase of the Earth. 'Platinum group metals like ruthenium have an extremely high tendency to combine with iron. Therefore, when the Earth formed all ruthenium must have been completely sequestered into the Earth's metallic core', said Fischer-Gödde.

Professor Dr. Carsten Münker added: 'If we still find traces of the rare platinum metals in the Earth's mantle, we can assume that they were only added after the formation of the core was completed. They were certainly added during later collisions of the Earth with asteroids or smaller protoplanets, so called planetesimals.'

Scientists refer to these very late building blocks of the Earth, which were delivered by these collisions, as the 'late veneer'. If ruthenium was added during this stage, it is distributed and well mixed into Earth's mantle by now. The old Archean mantle relics in Greenland, on the other hand, have still preserved Earth's pristine composition.

'The up to 3.8 billion-year-old rocks from Greenland are the oldest preserved mantle rocks. They allow us a glimpse into the early history of the Earth as if through a window', Fischer-Gödde said. Interestingly, Earth's oldest mantle is openly accessible in surface outcrops in southwest Greenland, allowing the geologists to easily collect rock samples.

The pristine ruthenium preserved in the old mantle rocks most likely originates from the inner part of the solar system, the two Cologne-based geologists report. It is presumably the same material that - for the most part - also formed Mercury and Venus. The reference values for the asteroidal ruthenium were previously obtained from meteorites found on Earth.

'Our findings suggest that water and other volatile elements such as carbon and nitrogen did indeed arrive on Earth very late, during the "late veneer" phase', Fischer-Gödde concluded. This result is surprising because the scientific community had previously assumed that water-bearing planetary building blocks were already delivered to Earth during the early stages of its formation.

The scientists are planning further field trips to India and Greenland to investigate more rock samples. Their work is being supported by the German Research Foundation's Priority Programme 1833 'Building a Habitable Earth', which is coordinated in Cologne, as well as Professor Münker's ERC grant 'Infant Earth' by the European Union.

http://bit.ly/2vXiBXJ

Statins starve cancer cells to death

Uncovering clues to how statins kill cancer cells

More than 35 million Americans take statin drugs daily to lower their blood cholesterol levels. Now, in experiments with human cells in the laboratory, researchers at Johns Hopkins Medicine have added to growing evidence that the ubiquitous drug may kill cancer cells and have uncovered clues to how they do it.

The findings, say the researchers, enhance previous evidence that statins could be valuable in combating some forms of cancer. In unrelated studies, other Johns Hopkins Medicine researchers have studied how statins may cut the risk for aggressive prostate cancer.

"There have been epidemiological indications that people who take statins long term have fewer and less aggressive cancers, and that statins can kill cancer cells in the laboratory, but our research was not initially designed to investigate possible biological causes of these observations," says Peter Devreotes, Ph.D., Issac Morris and Lucille Elizabeth Hay Professor of Cell Biology.

Results of the new research appeared Feb. 12 in the *Proceedings of the National Academy of Sciences*.

Devreotes and his team began the new study with an unbiased screen of about 2,500 drugs approved by the U.S. Food and Drug Administration (FDA) to see which ones had the best kill rate of cells genetically engineered to have a mutation in a cancer gene

called PTEN. The gene codes for an enzyme that suppresses tumor growth. Among the thousands of drugs, statins and in particular pitavastatin, emerged as a top contender in cancer-killing ability. Most of the other drugs had no effect or killed normal and engineered cells at the same rate. Equal concentrations of pitavastatin caused cell death in nearly all of the engineered cells, but very in few normal cells.

Devreotes and his team then looked at the molecular pathways that statins were likely to affect. It's well known, for example, that statins block a liver enzyme that makes cholesterol, but the drug also blocks the creation of a small molecule called geranylgeranyl pyrophosphate, or GGPP, which is responsible for connecting cellular proteins to cellular membranes.

When the researchers added pitavastatin and GGPP to human cancer cells with PTEN mutations, the researchers found that GGPP prevented the statin's killing effects and the cancer cells survived, suggesting that GGPP may be a key ingredient to cancer cell survival.

Next, looking under a microscope at cells engineered to lack the enzyme that makes GGPP, Devreotes and his team saw that as the cells began to die, they stopped moving. Under normal circumstances, cancer cells are a bundle of moving energy, consuming massive amounts of nutrients to maintain their unchecked growth. They maintain this breakneck pace by creating straw-like protrusions from their surface to drink up nutrients from the surrounding environment.

Suspecting that the non-moving cancer cells were literally "starving to death," Devreotes says, the scientists then measured the statin-treated cells' intake by adding a fluorescent tag to proteins in the cells' environment.

Normal human cells glowed brightly with the fluorescent tag, suggesting that these cells ingested protein from their surroundings regardless of whether the scientists added statins to the mix of nutrients and cells. However, human cancer cells with PTEN mutations took in almost no glowing proteins after the scientists added statins. The inability of the statin-treated cancer cells to make the protrusions needed take up proteins leads to their starvation.

Devreotes says his team plans further research on the effects of statins in people with cancer and compounds that block GGPP.

Other researchers involved in this study include Zhihua Jiao, Yu Long, Orit Katarina Sirka, Veena Padmanaban and Andrew Ewald of the Johns Hopkins University School of Medicine; and Huaqing Cai of the Chinese Academy of Sciences.

This work was supported by the National Institute of General Medical Sciences (R35 GM118177), the Air Force Office of Scientific Research Multidisciplinary Research Program of the University Research Initiative (FA95501610052), Defense Advanced Research Projects Agency (Q:9HR0011-16-C-0139), the Office of the Director, Centers for Disease Control and Prevention (S10 OD016374), the Breast Cancer Research Foundation (BCRF-18-048) and the National Cancer Institute (U01CA217846, 3P30CA006973).

The authors declare no competing interest.

http://bit.ly/2Ucs0m2

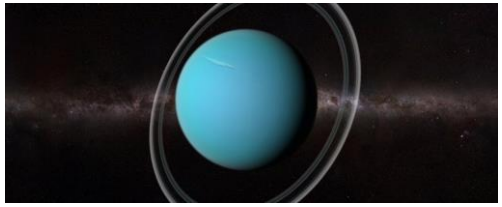
There's a New Hypothesis For How Uranus Ended Up Tipped on Its Side

Uranus's rotation axis is oriented 98° relative to its orbit, and it's whirling around in a clockwise direction.

Michelle Starr

Uranus is quite the individual. Most of the planets in our Solar System have their poles more or less oriented in the same direction. And most of them are spinning anticlockwise, when viewed from above.

But Uranus? Its rotation axis is oriented 98 degrees relative to its orbit, and it's whirling around in a clockwise direction.



(SCIEPRO/Science Photo Library/Getty Images)

The leading hypothesis for this weirdness is that something large smacked into Uranus a long time ago, knocking it arse over

teakettle. Although that scenario is not impossible, there are some pretty significant holes in this model.

Never fear, though. Astronomers at the University of Maryland have come up with a new scenario that neatly solves those issues. No, Uranus didn't get drunk on comet booze and fall over. But it could have been tilted sideways by a giant ring system.

"Wait a second," you are no doubt thinking, "Uranus doesn't have a giant ring system." And that's correct. Right now, it doesn't - its rings are faint and wispy things compared to Saturn's glorious spread.

But recent evidence from Cassini suggests rings could be temporary and short-lived - so it's possible Uranus had a much more extensive system sometime over its 4.5 billion-year past.

The problems with the smacked-upside model have mainly to do with the stuff around the planet. Neptune, for instance. If you look at the excellent video below, you'll see that Neptune and Uranus have a similar spin period.

The similarity of these spin periods implies that - as with Jupiter and Saturn - the two planets were born together. The probability of similar spin periods becomes much lower if you factor in one or more impacts large enough to tip Uranus sideways.

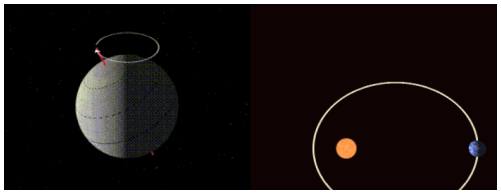
Uranus' moons are a problem too. A sudden tilting resulting from impact would likely disrupt and destabilise its satellite system, yet the ice planet's moons are similar in relative size and spacing to the Galilean moons.

And those moons are icy, too. Impacts large enough to tip the planet should have generated enough heat to vaporise any ice on these moons, making them mostly rocky, yet all of the planet's major moons have at least equal parts rock and ice.

According to astronomers Zeeve Rogoszinski and Douglas Hamilton of the University of Maryland, these problems are solved if Uranus had a ring system large enough to cause it to wobble on its axis like a spinning top - a phenomenon called precession - and if that precession aligned with the planet's orbital precession, where the ellipse slowly shifts position around the Sun.

You can see these two concepts animated below.

This alignment of motion is called resonance, and it has occurred a few times in the Solar System - usually between the orbits of two or more bodies.



***Spin precession (left) and orbital precession (right)*. (Robert Simmon/NASA; WillowW/Wikimedia Commons)**

For example, Pluto and Neptune have a 2:3 orbital resonance, which means that for every two of Pluto's orbits around the Sun, Neptune orbits three times.

The resonance between a planet's precession and its orbital precession is known as a secular spin-orbital resonance, and it can generate a large axial tilt. It's thought that a resonance of this type could have introduced an axial tilt in Saturn greater than that of Jupiter, for example.

The secular spin orbit resonance has been explored in relation to Uranus' tilt before, but with the resonance induced by the hypothetical Planet Nine. It was ultimately discarded as extremely unlikely.

But, Rogoszinski and Hamilton propose, a large disc could be a better fit. They modelled both Uranus and Neptune with large discs to see how they interact with the planets. And they found that a large disc of material accreting onto the planet - which we know is part of the formation process of giant planets - was the best fit.

But even though it produced the best result of all their models, it still couldn't get Uranus all the way prone. Over a period of a million years, it only produced a 70-degree tilt. Which means there's life in the big boom theory yet.

However, any impacting rocks required to push Uranus the rest of the way over would be much smaller - and therefore more likely.

"Although we can generate tilts greater than 70 degrees only rarely and cannot drive tilts beyond 90 degrees, a subsequent collision with an object about half the mass of Earth could tilt Uranus from 70 to 98 degrees," the researchers wrote in their paper.

"Minimising the masses and number of giant impactors from two or more to just one increases the likelihood of producing Uranus's spin states by about an order of magnitude." These are just hypotheses for now, and it's still very much up in the air, but one thing seems certain: that must have been a wild time for Uranus, comet booze or no. The research has been published in *The Astrophysical Journal*.

http://bit.ly/39Rq3C9

Surprising research: Prehistoric hyenas and humans share migration patterns

Prehistoric humans left Africa for the first time about 2 million years ago. The research community has been aware of this for some time. Now, novel research reveals that hyenas apparently did the same thing.

'Our new study shows that prehistoric humans and hyenas left Africa at approximately the same time. And like humans, spotted hyenas have had extensive and complex migration between continents. We can observe repeated gene flow events between Africa and Eurasia', says Michael Westbury, corresponding author and postdoc at GLOBE Institute at the University of Copenhagen.

The researchers collaborated with researchers at the University of Potsdam and sequenced complete genomes from both modern spotted hyenas in Africa and subfossils of the extinct cave hyena from Europe and Asia.

Separate lineages

The two kinds of hyena - spotted and cave - were previously believed to form a closely related evolutionary lineage. DNA analyses published 15 years ago showed that the two types of hyena were genetically intermingled. Today, however, thanks to technological advances, the researchers have been able to obtain a lot more genetic data and show that this genetic intermingling is limited. The new study thus reveals an ancient separation.

'The results nicely illustrate the power of palaeogenome analyses. The relationship of spotted and cave hyenas could not be resolved using morphological or short mitochondrial DNA sequence data and was actually discussed quite controversially for decades', says Michael Hofreiter Professor at the University of Potsdam.

While prehistoric hyenas show some similarities with humans in their trans-continental migration patterns, the researchers also found signs that modern humans of the species *Homo sapiens* had a detrimental impact on hyenas.

'Historical population sizes of spotted hyenas seem to correlate negatively with that of humans after about 100,000 years ago, echoing similar results we found for herbivores', says Rasmus Heller, Assistant Professor at the Department of Biology at the University of Copenhagen.

In addition, he explains that humans are believed to have played a role in the extinction of cave hyenas around the end of the last ice age. That means that coexistence between humans and hyenas - like that between humans and other large mammals - may have changed from being relatively benign to detrimental as humans became more advanced.

The researchers argue that their study reveals new aspects of when and how animals moved across continents in prehistory. "Our results conforms with the hypothesis that animal migration may have occurred in pulses during which several species migrated more or less at the same time, possibly as a response to climate change. More comparative work is needed to confirm this hypothesis", says postdoc Michael Westbury, postdoc at GLOBE Institute.

http://bit.ly/39OgvrO

One drug, three action modes

Chemotherapy and photodynamic therapy combined in a single drug to fight resistant cancers

Clinicians combat the drug resistances of some cancer types by using a combination of different drugs. To make this approach more effective, chemists have designed a chemical conjugate that can simultaneously attack several cellular targets using different modes of action. Such a single-drug therapy would increase the chances of killing all cancer cells, the authors state in the journal Angewandte Chemie.

The most frequently clinically applied chemotherapeutic drug is cisplatin, a metal complex based on the platinum(II) ion. The drug's mode of action is binding to the DNA in the tumor cells, where it distorts the DNA structure and ultimately triggers cell death. Other chemicals facilitate the interaction of cisplatin with DNA, and they are often combined with cisplatin for chemotherapy. The photodynamic therapy (PDT) approach, in contrast, relies on the activation of a metal complex by laser light. A reactive form of oxygen is formed, which interferes with cell metabolism, triggering cell death.

"In clinical protocols, each drug is administered separately and may not reach the tumor at the same time or at a fixed ratio," says Prof. Gilles Gasser from the Paris Sciences et Lettres (PSL) University in Paris, France, who is one of the leading authors of the study. His group, in collaboration with Prof. Dan Gibson's group from Hebrew University, Jerusalem, Israel, combined cisplatin, phenylbutyrate, which is a chemical enhancer for cisplatin, and a PDT drug, which is a metal complex based on ruthenium(II), into a single compound called Ru-Pt. The idea was that the three drugs in conjunction could travel the bloodstream intact and enter their target tumor cells, which would reduce side effects and the need to adjust the dosages.

The scientists have designed the phototherapeutic Ru(II) half of Ru-Pt so that it can be excited with laser light in the deep red section of the wavelength spectrum, which penetrates deeply in the biological tissue. The cisplatin and phenylbutyrate containing half of Ru-Pt was designed as a prodrug, which would be activated by cellular components inside the cell. Both therapeutic components were attached to each other by a molecular spacer. "The correct spacer length was critical to ensure that both drug compounds will not interfere with each other, but the molecule remains small, water-soluble, and able to travel across membranes," Gasser says.

The researchers added Ru-Pt to some normal and cancer cell lines and found that Ru-Pt was significantly more efficient in killing cancer cells than the single compounds Ru(II) and Pt(IV). The authors also reported that the irradiated samples had significantly higher tumor-killing rates, which means that the specific drug activation in tumor tissue is possible. And finally, Ru-Pt had a ten times higher efficiency for drug-resistant cell lines than the single reagents. These results demonstrate the high potential of multimodal drugs for developing more selective and effective drugs that have fewer side effects and allow for a simple handling for an effective cancer treatment.

http://bit.ly/2TQsY8y

Resolving inflammation: Could it prevent memory loss in Down syndrome and Alzheimer's?

Researchers at the Medical University of South Carolina and elsewhere discover the therapeutic potential for a class of lipids to prevent progressive memory loss in a preclinical model of Down syndrome

Individuals with Down syndrome are at a much greater risk of developing Alzheimer's disease, with inflammation of the brain starting early in life and the risk of Alzheimer's reaching nearly 80% by the age of 60.

The root cause of Alzheimer's disease is unknown. However, its frequency in patients with Down syndrome suggests that targeting inflammation in preclinical models of that syndrome could be an attractive strategy for designing therapies to promote healthier aging.

In one such preclinical model of Down syndrome, administering specialized lipids, known as resolvins, reduced inflammation and prevented memory loss, according to a recent article in Glia.

The findings were reported by researchers at the Medical University of South Carolina (MUSC), the Center for Alzheimer's Research at the Karolinska Institute in Sweden and the Knoebel Institute for Healthy Aging at the University of Denver.

"We have an ancient pathway that helps us return our damaged bodies to normal, which is known as the resolution response," said lead author Eric D. Hamlett, Ph.D., assistant professor in the Department of Pathology and Laboratory Medicine at MUSC. "In our model, we can now engage this response with the specialized lipids and, in a more natural way, calm down long-term inflammation."

While the Down syndrome model does not produce the same brain 'tangles' that normally would be observed with Alzheimer's disease, constant brain inflammation begins early in life and leads to similar neuronal damage. In humans, long-term inflammation is often seen alongside other indicators of Alzheimer's in the brain, but it is not yet known how these conditions get started.

Chronic brain inflammation typically leads to progressive memory loss. Surprisingly, a sustained treatment regime with the lipid reversed memory loss in the Down syndrome model without having any adverse effects, reinforcing its role as a potential therapeutic.

The tragic progression of memory loss and dementia due to Alzheimer's represents a breakdown of the brain's ability to self-maintain and to limit wild fluctuations in condition. However, self-maintenance can be disrupted by injuries, pathogens and sometimes by aging.

The disruption of self-maintenance can manifest as prolonged inflammation, which can result in devastating effects if left unchecked. Down syndrome is one such condition that can result in this sustained inflammation response.

Typically, the inflammation caused by a disease is resolved by the body naturally. However, when the body cannot do so, long-term inflammation can result. With the body on high-alert but unable to rectify the problem, progressive damage can occur as our normal tissues are caught in the crossfire.

"Our bodies first need to be able to respond to a problem and then have a separate and equally important response to resolve the inflammation mechanism," explained Hamlett.

Gaining insights into the role of inflammation in a healthy brain could bring us closer to identifying key mechanisms in our body that are activated in response to damage and age. Understanding how these mechanisms are activated could allow us to control the balances our bodies must achieve every day, leading to breakthroughs in regenerative medicine and potential new therapies that halt the progression of dementia.

Brevity of inflammation is crucial to healthy healing, and using these naturally produced lipids may be the first step in understanding our body's most ancient system of recovery.

Disclaimer: The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

http://bit.ly/2UbInzi

Researchers fast-track coronavirus vaccine by skipping key animal testing first

Animal tests normally constitute a critical step in vaccine development.

By Nicoletta Lanese - Staff Writer

A clinical trial for an experimental coronavirus vaccine has begun recruiting participants in Seattle, but researchers did not first show that the vaccine triggered an immune response in animals, as is normally required.

Now, biomedical ethicists are calling the shortcut into question, according to Stat News.

"Outbreaks and national emergencies often create pressure to suspend rights, standards and/or normal rules of ethical conduct," Jonathan Kimmelman, director of McGill University's biomedical ethics unit, wrote in an email to Stat News. "Often our decision to do so seems unwise in retrospect."

Typically, vaccine development can take 15 to 20 years, start to finish, Mark Feinberg, president and CEO of the International AIDS Vaccine Initiative, told Stat News. The lengthy process requires that scientists first give the vaccine to animals to determine whether it's safe and effective at preventing the disease in question. Only after passing through iterative tests in animal models, and being adjusted along the way, can a formulation be tested in human trials.

"When you hear predictions about it taking at best a year or a year and a half to have a vaccine available … there's no way to come close to those timelines unless we take new approaches," Feinberg said.

In this context, these new approaches include skipping over some animal testing, although virologists at the National Institute of Allergy and Infectious Diseases did give the experimental vaccine to lab mice on the same day that the human trial began recruiting participants, according to Stat News. These mice showed a similar immune response to mice given an experimental vaccine for MERS-CoV, a related coronavirus, Barney Graham, director of NIAID's vaccine research center, told Stat News.

However, standard lab mice can't catch the novel coronavirus SARS-CoV-2 as humans do, and efforts to breed susceptible rodents are not yet complete, he added. He said that those mice should be available "within the next few weeks," but until then, researchers can run safety tests only on standard mice.

If even these preliminary animal experiments appear harmful or don't prevent infection, the conductors of the clinical trial should be prepared to stop testing the vaccine in humans, Karen Maschke, a scholar in bioethics at the Hastings Center and the editor of the journal Ethics & Human Research, told Stat News. "You don't burden people to be in a study if the intervention is not going to help," although animal studies aren't always reliable indicators of how a drug will work in people, she said.

The new vaccine, developed by the biotechnology company Moderna Therapeutics, does not contain the virus that triggers COVID-19, as a conventional vaccine might. Instead, Moderna researchers used a new technique to make messenger RNA (mRNA), which is similar to mRNA found in SARS-CoV-2. In theory, the artificial mRNA will act as instructions that prompt human cells to build a protein found on the surface of the virus. That protein would theoretically trigger a protective immune response. Standard vaccines work similarly but use a dead or weak virus as their base, forgoing the process of constructing viral proteins from scratch.

Designing the vaccine to work in this way allowed Moderna to fast-track the development process, as the company did not need to isolate and modify live samples of SARS-CoV-2 as it would for a more conventional vaccine, according to a report by Kaiser Permanente. But Moderna has not put this technology to the test before; the company has yet to bring such a vaccine to market.

"We have not previously tested our rapid response capability and may be unable to produce a vaccine that successfully treats the

virus in a timely manner, if at all," the company wrote in a document filed with the Securities and Exchange Commission. Assuming the method works, though, speeding through animal testing may prove to be a good decision, especially in the context of the current pandemic, Feinberg said. While taking shortcuts may speed up the vaccine development process, but it's uncertain how much time it will save in the long run.

If this research meant a vaccine might be ready by this June, people would probably be all for it in spite of the cut corners, Holly Fernandez Lynch, assistant professor of medical ethics at the University of Pennsylvania, told Stat News. "If we're talking about us getting a vaccine in June of 2021 rather than March of 2021, that's a much more uncertain scenario. We shouldn't delude ourselves into thinking that skipping over steps is going to get a vaccine into our hands by next week or next month."

http://bit.ly/2xHiaRL

Transplant Method Avoids Rejection of Donor Leg for Months in Rats

A proof-of-concept study uses a strategy similar to the way tumors evade immune detection. The new limbs survive for more than 200 days.

Abby Olena

Getting any kind of transplant typically means taking multiple immune-suppressing drugs forever after to avoid rejection of the donor organ or tissue.

This white rat received a donor leg from a brown rat along with microparticles that release a protein that trains the immune system to accept the foreign tissue. **UPMC**

A study published today (March 13) in *Science Advances* demonstrates a way around long-term immune suppression. The researchers injected microparticles that release a protein that recruits regulatory T cells to train the immune system of rats receiving a donor limb to recognize the foreign tissue as self instead of non-self.

The conventional immunosuppression strategy after transplantation comes with "a lot of side effects and complications down the line, but I think we've now realized that we need to shift this and this [study] is one testimony to this," says Gerald Brandacher, a surgeon who specializes in upper extremity and face transplantation at Johns Hopkins University School of Medicine and was not involved in the work. "In these first small animal models, we see proof of concept that [immune regulation] strategies can work, and hopefully down the road will lead to a much better way to actually navigate the immune system in the setting of transplantation."

The concept of training the immune system to ignore tissue came from tumors, says Steven Little, a bioengineer at the University of Pittsburgh. He points to previous work from the last couple of decades showing that tumors can recruit the body's own regulatory T cells by releasing the protein CCL22, which then leads to a decrease in immune recognition of the tumor. He says he thought that it would be possible to engineer a therapeutic that would release CCL22 synthetically and "create something that's not a tumor, but still tricks the body into accepting something that would otherwise be rejected, like a transplant."

Years of work led to the current study in rats. Little and colleagues transplanted hindlimbs from brown rats onto the bodies of white rats. They treated all the rats with an immunosuppression drug for 21 days, and some of them also got one of three possible doses of biodegradable microparticles containing synthetic mouse CCL22, CCL22 protein alone, or empty microparticles, each injected under the skin of the donor limb. There was also a control group that

received an injection of microparticles containing CCL22 in the unaffected hindlimb.

Within the first 50 days, all the donor limbs had been rejected, except in the rats that received either the medium or high dose of CCL22-loaded microparticles. The researchers gave another microparticle injection 21 days after the transplant and confirmed that CCL22 was released for 40 days. In six of the eight rats that received the medium dose of these microparticles, the donor limbs survived for much longer—more than the 200 days of the experiment. The medium dose worked better than the high dose: only two of those animals had a surviving graft by day 60 and only one had a surviving graft for the duration of the experiment.

The authors found that there was a higher percentage of regulatory T cells among all the T cells in the grafts that survived compared to the ones that didn't. Plus, the accepted donor limbs had a lower abundance of pro-inflammatory genes than the ones that were rejected. The recipients' immune systems not only accepted the transplanted limbs, but also accepted a skin graft from a donor of the same strain as their limb donor. The acceptance of the skin graft happened in the absence of immunosuppression, and the recipients completely rejected a skin graft from another rat strain. This indicates that the recognition of that particular set of foreign antigens as self is ongoing.

"Through the transplantation procedure we have effectively reeducated the rat's immune system to now accept this donor's whole host or repertoire of antigens," says Little. "We've convinced that immune system that that [donor] is now self too, but the immune system is still competent so if you give it a third animal's antigen, it rejects that."

"The graft survival data with the hindlimb transplant in the rat is quite impressive," both in this study and another one the authors published last year in *PNAS*, says Christene Huang, who studies alternatives to prolonged immunosuppression after transplants at the University of Colorado Anschutz Medical Campus and did not participate in the work.

She cautions that some strategies that work to induce tolerance of foreign tissue when that tissue comes from a living donor fail when the tissue comes instead from a brain-dead donor, as is the case in human limb and face transplants. It's not well understood why there's a difference, but that's an open question that could influence this strategy's efficacy going forward. Another question, she says, is how well the microparticles will work in larger animals.

Testing the approach in pigs is next, according to coauthor Jim Fisher, a graduate student in Little's lab. If it makes sense, they'll then move toward studies of safety and efficacy in people. "We're releasing a protein from the microparticles, but that's not really the medicine," he says. The protein is then recruiting the body's "own cells that are actually acting as the medicine, which is fundamentally different than anything that is used right now in transplants."

J.D. Fisher et al., "In situ recruitment of regulatory T cells promotes donor-specific tolerance in vascularized composite allotransplantation," **Science Advances**, *doi:10.1126/sciadv.aax8429, 2020.*

https://wb.md/2QiRoFI

So You Have a COVID-19 Patient, How Do You Treat Them?

Clinicians are working out how to manage patients with or suspected of having COVID-19. Here's what several physicians have told* Medscape Medical News *about how they're treating COVID-19 cases now.

Ricki Lewis, PhD

Editor's note: Find the latest COVID-19 news and guidance in Medscape's Coronavirus Resource Center.

"Over the past couple of weeks, we've been preparing for the oncoming onslaught of patients," said Lillian Wu, MD, of the

HealthPoint network in the Seattle area of greater King County and president elect of the Washington Academy of Family Physicians.

Step One: Triage

The first step, Wu says, is careful triage.

When patients call one of the 17 clinics in the HealthPoint system, nurses gauge how sick they are. High fever? Shortness of breath? Do they have a chronic illness, such as diabetes, cardiovascular disease, or a lung condition, that increases risk for infection and complications?

"If a patient has mild symptoms, we ask them to stay home or to check back in 24 hours, or we'll reach out to them. For moderate symptoms, we ask them to come in, and [we] clearly mark on the schedule that it is a respiratory patient, who will be sent to a separate area. If the patient is severe, we don't even see them and send them directly to the hospital to the ER," Wu told *Medscape Medical News*.

These categories parallel the World Health Organization's designations of uncomplicated illness, mild pneumonia, severe pneumonia, acute respiratory distress syndrome, sepsis, and septic shock. The Centers for Disease Control and Prevention (CDC) advises case by case regarding decisions as to outpatient or inpatient assignment.

"Patients who pass the initial phone triage are given masks, separated, and sent to different parts of the clinic or are required to wait in their cars until it's time to be seen," Wu said.

Step 2: Hospital Arrival

Once at the hospital, the CDC's interim guidance kicks in.

"Any patient with fever, cough, and shortness of breath presenting with a history of travel to countries with high ongoing transmission or a credible history of exposure should be promptly evaluated for COVID-19," said Raghavendra Tirupathi, MD, medical director, Keystone Infectious Diseases/HIV; chair in infection prevention, Summit Health; and clinical assistant professor of medicine, Penn State School of Medicine, Hershey, Pennsylvania.

"We recommend obtaining baseline CBC with differential, basic metabolic panel, liver function tests, and procalcitonin. Clues for COVID-19 include leukopenia, seen in 30% to 45% of patients, and lymphocytopenia, seen in 85% of the patients in the case series from China," Tirupathi said. He uses a respiratory virus polymerase chain reaction panel to rule out other pathogens.

Wu concurs. "This is the one time we are grateful when someone tests positive for the flu! If flu is negative and other common respiratory infections are negative, then we do a COVID-19 test," she said.

But test results may be delayed. "At the University of Washington, it takes 8 hours, but commercial labs take up to 4 days," Wu said. All patients with respiratory symptoms are treated as persons under investigation, for whom isolation precautions are required. In addition, for these patients, use of personal protective equipment by caregivers is required.

For suspected pneumonia, the American College of Radiography recommends chest CT to identify peripheral basal ground-glass opacities characteristic of COVID-19.

However, diagnosis should be based on detection of SARS-CoV-2, because chest images for COVID-19 are nonspecific — associated signs can also be seen in H1N1 influenza, SARS, and MERS.

Step 3: Supportive Care

Once a patient is admitted, supportive care entails "maintaining fluid status and nutrition and supporting physiological functions until we heal. It's treating complications and organ support, whether that means providing supplementary oxygen all the way to ventilator support, and just waiting it out. If a patient progresses to acute respiratory distress syndrome, it becomes tougher," said

David Liebers, MD, chief medical officer and an infectious disease specialist at Ellis Medicine in Schenectady, New York.

Efforts are ramping up to develop therapeutics. Remdesivir, an investigational antiviral drug developed to treat Ebola and Marburg hemorrhagic fevers, shows activity against SARS-CoV-2 in vitro.

Remdesivir has been used in a few patients on a compassionate-use basis outside of a clinical trial setting. "It's a nucleotide analogue, and like other drugs of that class, it disrupts nucleic acid production. Some data suggest that it might have some efficacy," Liebers said.

Antibiotics are reserved for patients suspected of having concomitant bacterial or fungal infections. Liebers said clinicians should be alerted to "the big three" signs of secondary infection — fever, elevated white blood cell count, and lactic acidosis. Immunosuppressed patients are at elevated risk for secondary infection.

Step 4: Managing Complications

Patients do die of COVID-19, mostly through an inability to ventilate, even when supported with oxygen, Liebers told *Medscape Medical News*. (According to Tirupathi, "The studies from China indicate that from 6% to 10% of patients needed ventilators.")

Liebers continued, "Others may develop sepsis or a syndrome of multisystem organ failure with renal and endothelial collapse, making it difficult to maintain blood pressure. Like with so many pathologies, it is a vicious circle in which everything gets overworked. Off-and-on treatments can sometimes break the cycle: supplementary oxygen, giving red blood cells, dialysis. We support those functions while waiting for healing to occur."

A facility's airborne-infection isolation rooms may become filled to capacity, but that isn't critical, Liebers said. "Airborne precautions are standard to contain measles, tuberculosis, chickenpox, and herpes zoster, in which very small particles spread in the air," he said.

Consensus is growing that SARS-CoV-2 spreads in large droplets, he added. Private rooms and closed doors may suffice.

Step 5: Discharge

Liebers said that as of now, the million-dollar question regards criteria for discharge. Patients who clinically improve are sent home with instructions to remain in isolation. They may be tested again for virus before or after discharge.

Liebers and Wu pointed to the experience at EvergreenHealth Medical Center, in Kirkland, Washington, as guidance from the trenches. "They're the ones who are learning firsthand and passing the experience along to everyone else," Wu said.

"The situation is unprecedented," said Liebers, who, like many others, has barely slept these past weeks. "We're swimming in murky water right now."

The epidemic in the United States is still months from peaking, Wu emphasized. "There is no vaccine, and many cases are subclinical. COVID-19 has to spread through the country before it infects a critical mass of people who will develop immunity. It's too late to contain." Added Liebers, "It's a constantly changing situation, and we are still being surprised — not that this wasn't predicted."

http://bit.ly/38X0JcK

Coronavirus: China's first confirmed Covid-19 case traced back to November 17

Government records suggest first person infected with new disease may have been a Hubei resident aged 55, but 'patient zero' has yet to be confirmed

Documents seen by the Post could help scientists track the spread of the disease and perhaps determine its source

Josephine Ma

The first case of someone in China suffering from Covid-19, the disease caused by the novel coronavirus, can be traced back to

November 17, according to government data seen by the *South China Morning Post*.

Chinese authorities have so far identified at least 266 people who were infected last year, all of whom came under medical surveillance at some point.

Some of the cases were likely backdated after health authorities had tested specimens taken from suspected patients.

Interviews with whistle-blowers from the medical community suggest Chinese doctors only realised they were dealing with a new disease in late December.

Scientists have been trying to map the pattern of the early transmission of Covid-19 since an epidemic was reported in the central China city of Wuhan in January, two months before the outbreak became a global health crisis.

Understanding how the disease spread and determining how undetected and undocumented cases contributed to its transmission will greatly improve their understanding of the size of that threat.

According to the government data seen by the *Post*, a 55 year-old from Hubei province could have been the first person to have contracted Covid-19 on November 17.

From that date onwards, one to five new cases were reported each day. By December 15, the total number of infections stood at 27 – the first double-digit daily rise was reported on December 17 – and by December 20, the total number of confirmed cases had reached 60.

On December 27, Zhang Jixian, a doctor from Hubei Provincial Hospital of Integrated Chinese and Western Medicine, told China's health authorities that the disease was caused by a new coronavirus. By that date, more than 180 people had been infected, though doctors might not have been aware of all of them at the time.

By the final day of 2019, the number of confirmed cases had risen to 266, On the first day of 2020 it stood at 381.

While the government records have not been released to the public, they provide valuable clues about how the disease spread in its early days and the speed of its transmission, as well as how many confirmed cases Beijing has recorded.

Scientists are now keen to identify the so-called patient zero, which could help them to trace the source of the coronavirus, which is generally thought to have jumped to humans from a wild animal, possibly a bat.

Of the first nine cases to be reported in November – four men and five women – none has been confirmed as being "patient zero". They were all aged between 39 and 79, but it is unknown how many were residents of Wuhan, the capital of Hubei and the epicentre of the outbreak.

It is possible that there were reported cases dating back even earlier than those seen by the *Post*.

According to the World Health Organisation's website, the first confirmed Covid-19 case in China was on December 8, but the global body does not track the disease itself but relies on nations to provide such information.

A report published in medical journal *The Lancet* by Chinese doctors from Jinyintan Hospital in Wuhan, which treated some of the earliest patients, put the date of the first known infection at December 1.

Dr Ai Fen, the first known whistle-blower, told *People* magazine in an interview that was later censored, that tests showed that a patient at Wuhan Central Hospital was diagnosed on December 16 as having contracted an unknown coronavirus.

Accounts by other doctors seem to suggest the medical community in Wuhan became aware of the disease in late December.

Previous reports said that although doctors in the city collected samples from suspected cases in late December, they could not confirm their findings because they were bogged down by

bureaucracy, such as having to get approval from the Chinese Centre for Disease Control and Prevention, which could take days. They were also ordered not to disclose any information about the new disease to the public.

As late as January 11, Wuhan's health authorities were still claiming there were just 41 confirmed cases.

http://bit.ly/2wanFYK

Earth's mantle, not its core, may have generated planet's Early magnetic field

Scripps Oceanography researcher's assertion bolstered by series of new studies

New research lends credence to an unorthodox retelling of the story of early Earth first proposed by a geophysicist at Scripps Institution of Oceanography at UC San Diego.

In a study appearing March 15 in the journal Earth and Planetary Science Letters, Scripps Oceanography researchers Dave Stegman, Leah Ziegler, and Nicolas Blanc provide new estimates for the thermodynamics of magnetic field generation within the liquid portion of the early Earth's mantle and show how long that field was available.

The paper provides a "door-opening opportunity" to resolve inconsistencies in the narrative of the planet's early days. Significantly, it coincides with two new studies from UCLA and Arizona State University geophysicists that expand on Stegman's concept and apply it in new ways.

"Currently we have no grand unifying theory for how Earth has evolved thermally," Stegman said. "We don't have this conceptual framework for understanding the planet's evolution. This is one viable hypothesis."

The trio of studies are the latest developments in a paradigm shift that could change how Earth history is understood.

It has been a bedrock tenet of geophysics that Earth's liquid outer core has always been the source of the dynamo that generates its magnetic field. Magnetic fields form on Earth and other planets that have liquid, metallic cores, rotate rapidly, and experience conditions that make the convection of heat possible.

In 2007, researchers in France proposed a radical departure from the long-held assumption that the Earth's mantle has remained entirely solid since the very beginnings of the planet. They argued that during the first half of the planet's 4.5-billion-year history, the bottom third of Earth's mantle would have had to have been molten, which they call "the basal magma ocean." Six years later, Stegman and Ziegler expanded upon that idea, publishing the first work showing how this once-liquid portion of the lower mantle, rather than the core, could have exceeded the thresholds needed to create Earth's magnetic field during that time.

The Earth's mantle is made of silicate material that is normally a very poor electrical conductor. Therefore, even if the lowermost mantle were liquid for billions of years, rapid fluid motions inside it wouldn't produce large electrical currents needed for magnetic field generation, similar to how Earth's dynamo currently works in the core. Stegman's team asserted the liquid silicate might actually be more electrically conductive than what was generally believed.

"Ziegler and Stegman first proposed the idea of a silicate dynamo for the early Earth," said UCLA geophysicist Lars Stixrude. The idea was met with skepticism because their early results "showed that a silicate dynamo was only possible if the electrical conductivity of silicate liquid was remarkably high, much higher than had been measured in silicate liquids at low pressure and temperature."

A team led by Stixrude used quantum-mechanical computations to predict the conductivity of silicate liquid at basal magma ocean conditions for the first time.

According to Stixrude, "we found very large values of the electrical conductivity, large enough to sustain a silicate dynamo." The UCLA study appeared in the Feb. 25 issue of Nature Communications.

In another paper, Arizona State geophysicist Joseph O'Rourke applied Stegman's concept to consider whether it's possible that Venus might have at one point generated a magnetic field within a molten mantle.

These new studies are signs that the premise is starting to take hold, but is still far from being widely accepted.

"No one is going to believe it until they do it themselves and now two other highly esteemed scientists have done it themselves," said Stegman.

"The pioneering studies of Dave Stegman and his collaborators directly inspired my work on Venus," said O'Rourke. "Their recent paper helps answer a question that vexed scientists for many years: How has Earth's magnetic field survived for billions of years?"

If Stegman's premise is correct, it would mean the mantle could have provided the young planet's first magnetic shield against cosmic radiation. It could also underpin studies of how tectonics evolved on the planet later in history.

"If the magnetic field was generated in the molten lower mantle above the core, then Earth had protection from the very beginning and that might have made life on Earth possible sooner," Stegman said.

"Ultimately, our papers are complementary because they demonstrate that basal magma oceans are important to the evolution of terrestrial planets," said O'Rourke. "Earth's basal magma ocean has solidified but was key to the longevity of our magnetic field."

The Scripps Oceanography study was funded by the National Science Foundation, the U.S. Department of Energy, and a UC San Diego SEED Fellowship.