http://bit.ly/2Pk6VEP

Oldest reconstructed bacterial genomes link farming, herding with emergence of new disease

Scientists present the first ancient DNA that links the spread of farming culture in ancient Eurasia to the emergence of human-adapted pathogens

The Neolithic revolution, and the corresponding transition to agricultural and pastoralist lifestyles, represents one of the greatest cultural shifts in human history, and it has long been hypothesized that this might have also provided the opportunity for the emergence of human-adapted diseases.

A new study published in Nature Ecology & Evolution led by Felix M. Key, Alexander Herbig, and Johannes Krause of the Max Planck Institute for the Science of Human History studied human remains excavated across Western Eurasia and reconstructed eight ancient *Salmonella enterica* genomes - all part of a related group within the much larger diversity of modern *S. enterica*. These results illuminate what was likely a serious health concern in the past and reveal how this bacterial pathogen evolved over a period of 6,500 years.

Searching for ancient pathogens

Most pathogens do not cause any lasting impact on the skeleton, which can make identifying affected archeological remains difficult for scientists. In order to identify past diseases and reconstruct their histories, researchers have turned to genetic techniques. Using a newly developed bacterial screening pipeline called HOPS, Key and colleagues were able to overcome many of the challenges of finding ancient pathogens in metagenomics data.

"With our newly developed methodologies we were able to screen thousands of archaeological samples for traces of *Salmonella* DNA," says Herbig. The researchers screened 2,739 ancient human remains in total, eventually reconstructing eight *Salmonella* genomes up to 6,500 years old - the oldest reconstructed bacterial genomes to date. This highlights an inherent difficulty in the field of ancient pathogen research, as hundreds of human samples are often required to recover just a single microbial genome. The genomes in the current study were recovered by taking samples from the teeth of the deceased. The presence of *S. enterica* in the teeth of these ancient individuals suggests they were suffering from systemic disease at their time of death.

The individuals whose remains were studied came from sites located from Russia to Switzerland, representing different cultural groups, from late hunter-gatherers to nomadic herders to early farmers. "This broad spectrum in time, geography and culture allowed us, for the first time, to apply molecular genetics to link the evolution of a pathogen to the development of a new human lifestyle," explained Herbig.

"Neolithization process" provided opportunities for pathogen evolution

With the introduction of domesticated animals, increased contact with both human and animal excrement, and a dramatic change in mobility, it has long been hypothesized that "Neolithization" - the transition to a sedentary, agricultural lifestyle - enabled more constant and recurrent exposure to pathogens and thus the emergence of new diseases. However, prior to the current study, there was no direct molecular evidence.

"Ancient metagenomics provides an unprecedented window into the past of human diseases," says lead author Felix M. Key, formerly of the Max Planck Institute for the Science of Human History and now at the Massachusetts Institute of Technology. "We now have molecular data to understand the emergence and spread of pathogens thousands of years ago, and it is exciting how we can utilize high-throughput technology to address long standing questions about microbial evolution."

Humans, Pigs, and the Origin of Paratyphi C

The researchers were able to determine that all six *Salmonella* genomes recovered from herders and farmers are progenitors to a strain that specifically infects humans but is rare today, Paratyphi C. Those ancient *Salmonella*, however, were probably not yet adapted to humans, and instead infected humans and animals alike, which suggests the cultural practices uniquely associated with the Neolithization process facilitated the emergence of those progenitors and subsequently human-specific disease. It was previously suggested that this strain of *Salmonella* spread from domesticated pigs to humans around 4000 years ago, but the discovery of progenitor strains in humans more than 5000 years ago suggests they might have spread from humans to pigs. However, the authors argue for a more moderate hypothesis, where both human and pig specific *Salmonella* evolved independently from unspecific progenitors within the permissive environment of close human-animal contact.

"The fascinating possibilities of ancient DNA allow us to examine infectious microbes in the past, which sometimes puts the spotlight on diseases that today most people don't consider to be a major health concern," says Johannes Krause, director at the Max Planck Institute for the Science of Human History.

The current study allows the scientists to gain a perspective on the changes in the disease over time and in different human cultural contexts. "We're beginning to understand the genetics of host adaptation in *Salmonella*," says Key, "and we can translate that knowledge into mechanistic understanding about the emergence of human and animal adapted diseases."

The scientists hope that the current study will illuminate the possibilities of these methods and that future research will further examine the ways that human cultural evolution has impacted and driven the evolution of human-adapted diseases.

Publication information:

Title: Emergence of human-adapted Salmonella enterica *is linked to the Neolithization process*

Authors: Felix M. Key, Cosimo Posth, Luis R. Esquivel-Gomez, Ron Hübler, Maria A. Spyrou, Gunnar U. Neumann, Anja Furtwängler, Susanna Sabin, Marta Burri, Antje Wissgott, Aditya Kumar Lankapalli, Åshild J. Vågene, Matthias Meyer, Sarah Nagel, Rezeda Tukhbatova, Aleksandr Khokhlov, Andrey Chizhevsky, Svend Hansen, Andrey B. Belinsky, Alexey Kalmykov, Anatoly R. Kantorovich, Vladimir E. Maslov, Philipp W. Stockhammer, Stefania Vai, Monica Zavattaro, Alessandro Riga, David Caramelli, Robin Skeates, Jessica Beckett, Maria Giuseppina Gradoli, Noah Steuri, Albert Hafner, Marianne Ramstein, Inga Siebke, Sandra Lösch, Yilmaz Selim Erdal, Nabil-Fareed Alikhan, Zhemin Zhou, Mark Achtman, Kirsten Bos, Sabine Reinhold, Wolfgang Haak, Denise Kühnert, Alexander Herbig, Johannes Krause

Publication: Nature Ecology and Evolution DOI: 10.1038/s41559-020-1106-9

http://bit.ly/3911hiG

Supplementing diet with amino acid successfully staves off signs of ALS in pre-clinical study

The addition of dietary L-serine, a naturally occurring amino acid necessary for formation of proteins and nerve cells, delayed signs of amyotrophic lateral sclerosis (ALS) in an animal study.

The research also represents a significant advance in animal modeling of ALS, a debilitating neurodegenerative disease, said David A. Davis, Ph.D., lead author and research assistant professor of neurology and associate director of the Brain Endowment Bank at the University of Miami Miller School of Medicine.

The new research protocol using vervets appears more analogous to how ALS develops in humans, Dr. Davis said, compared to historic models using rodents.

When he and colleagues gave the vervets a toxin produced by blue-green algae known as β-N-methylamino-L-alanine or BMAA, they developed pathology that closely resembles how ALS affects the spinal cords in humans.

When a group of these animals were fed L-serine together with BMAA for 140 days, the strategy was protective - the vervets

showed significantly reduced signs of protein inclusions in spinal cord neurons and a decrease in pro-inflammatory microglia.

The results were published on Thursday, February 20 at 5 a.m. EST in the prestigious Journal of Neuropathology & Experimental Neurology.

"The big message is that dietary exposure to this cyanobacterial toxin triggers ALS-type pathology, and if you include L-serine in the diet, it could slow the progression of these pathological changes," Dr. Davis said.

"I was surprised at how close the model mirrored ALS in humans," he added. Beyond looking at changes in the brain, "When we looked at the spinal cord, that was really surprising." The investigators observed changes specific to ALS seen in patients, including presence of intracellular occlusion such as TDP-43 and other protein aggregates.

Walter G. Bradley D.M., F.R.C.P., founder of the ALS Clinical and Research Center at the University of Miami Miller School of Medicine, said: "ALS is a progressive neurological disease, also known as Lou Gehrig's disease, causing progressive limb paralysis and respiratory failure.

There is a great unmet need for effective therapies in this disease. After clinical trials of more than 30 potential drugs to treat ALS, we still have only two that slow the disease progression."

ALS can rapidly progress in some people, leading to death in 6 months to 2 years after diagnosis. For this reason, it is difficult to enroll people in clinical trials, a reality that supports development of a corresponding animal model, Dr. Davis said.

In addition, prevention remains essential. "This is a pre-clinical model, which is really the most important type of model, because once people have full-blown disease, it's hard to reverse or slow its progression," he added.

The research builds on earlier findings from Dr. Davis and colleagues in a 2016 study that demonstrated cyanotoxin BMAA can cause changes in the brain that resemble Alzheimer's disease in humans, including neurofibrillary tangles and amyloid deposits.

Even with the promise of L-serine, the researchers note there is a bigger picture to their new ALS animal model. "Other drugs can also be tested, making this very valuable for clinical affirmation," Davis said.

The research also has implications for Florida, as BMAA comes from harmful blue-green algae blooms, which have become more common in the summer months in Florida.

According to Larry Brand, Ph.D., professor of marine biology at the Rosenstiel School at the University of Miami, "We have found that the BMAA from these blooms has biomagnified to high concentrations in South Florida aquatic food chains, thus our seafood."

"We are very curious about how BMAA affects individuals in South Florida," Davis said. "That's our next step."

Future research could attempt to answer multiple questions, including: How common is BMAA in local seafood? What are the risks of exposure through exposure to aerosolized cyanotoxins? Is there a specific group of people who are more vulnerable from this exposure to developing diseases like Alzheimer's and ALS?

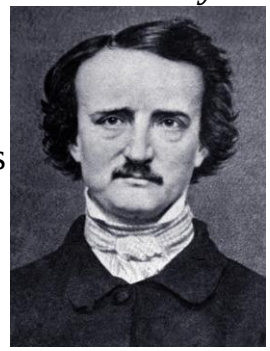
The current research would not have been possible, Dr. Davis said, without interdisciplinary collaboration both inside and outside the University of Miami. Another essential factor is the "very unique research environment" in the UM Department of Neurology. For example, the Brain Endowment Bank allows Miller School researchers access to other investigators and to essential research material.

The study was supported by funding from Josephine P. and John J. Louis Foundation, the William Stamps Farish Fund and Patrick and Heather Henry and the Brain Research Fund, which was funded by a generous donation from Dr. Rita Eisenberg.

http://bit.ly/32pqc3K

Why Edgar Allan Poe probably did not kill himself

A computational analysis of language used by the writer Edgar Allan Poe has revealed that his mysterious death was unlikely to have been suicide.



The author, poet, editor, and literary critic died in 1849 after spending several days in hospital while in a state of delirium. To date, Poe's death remains an unsolved enigma, with his contemporary, poet Charles Baudelaire even speculating that the incident was "almost a suicide, a suicide prepared for a long time".

The writer died in 1849 after spending several days in hospital while in a state of delirium. Credit: Lancaster University

But psychologist Dr Ryan Boyd from Lancaster University and his colleague -- Hannah Dean from the University of Texas at Austin -- have found that Poe's psychological markers of depression are not consistent with suicide. This research has now been published in the Journal of Affective Disorders.

Dr Boyd said: "My hunch is that he was indeed spiralling into a depression toward the end of his life, but that he didn't kill himself."

Using computerized language analysis, they analysed 309 of Poe's personal letters, 49 poems, and 63 short stories and investigated whether a pattern of linguistic cues consistent with depression and suicidal cognition were discernible throughout the writer's life, particularly in his final years. They focused on five measures which have been established as diagnostic of depression and/or suicidality;

- **Increased use of first-person singular pronouns (e.g., words like I, me, and my)**
- **Increased use of negative emotion words (bad, sad, angry)**
- **More cognitive processing words (think, understand, know)**
- **Fewer positive emotion words (happy, good, terrific)**
- **Fewer first-person plural pronouns (we, us, our).**

These linguistic markers of depression spiked during negative events in Poe's life, like the death of his wife. Past research has shown that depressive language patterns tend to dramatically rise leading up to one's death by suicide, however, this pattern did not consistently emerge in the last year of Poe's life.

Poe was known to have suffered from regular bouts of severe depression and also had drug and alcohol problems. He lost his parents as a two year old and was devastated first by the death of his foster mother and then by that of his own wife Virginia Clemm Poe in 1847.

The researchers concluded: "Significant, consistent patterns of depression were not found and do not support suicide as a cause of death. However, linguistic evidence was found suggesting the presence of several potential depressive episodes over the course of Poe's life - these episodes were the most pronounced during years of Poe's greatest success, as well as those following the death of his late wife."

"Our analyses suggest that he struggled deeply with success, with linguistic markers of depression peaking during the times of his greatest fame and popularity in 1843, 1845 and 1849."

http://bit.ly/2w79XVY

Too much of a good thing may lead to too much of a liver as well

When uncontrolled and overabundant, a protein that protects against harmful oxidants appears to fuel liver enlargement and may be linked to host of metabolic conditions

All life is challenged by oxidants -- reactive molecules or compounds that remove electrons from other molecules -- often with adverse effect, commonly referred to as oxidative stress. Consequently, all organisms have evolved specialized antioxidant

defenses. In humans and other multicellular animals, that defense depends upon a protein called NRF2 and its inhibitor, KEAP1.

In a new study, published February 24, 2020 in the *Journal of Hepatology*, a team of scientists, led by postdoctoral fellows Feng He, PhD, and Laura Antonucci, PhD, and senior author Michael Karin, PhD, Distinguished Professor of Pharmacology and Pathology at University of California San Diego School of Medicine, suggest prolonged exposure to NRF2 and KEAP1 may contribute to enlargement of the liver and fatty liver diseases.

NRF2 (Nuclear factor erythroid 2-related factor 2) is the master regulator of the antioxidant response. When cells are healthy and unstressed by oxidants, levels of NRF2 are kept low by KEAP1 (Kelch-like ECH-associated protein 1), which is constantly degrading NRF2.

But in response to oxidative stress, KEAP1 is inactivated, releasing NRF2 from its inhibitory grip. NRF2 levels subsequently build within the cell with the protein entering the nucleus, where it stimulates expression of numerous genes that code for enzymes and other proteins that detoxify harmful oxidants.

"By being able to reduce the devastating impact of oxidative stress, the KEAP1-NRF2 system has long been thought to protect us from cancer and aging," said Karin. "And much effort has been dedicated to the development of NRF2 activators for cancer prevention and age-related diseases. Many such compounds are being sold at health food stores as anti-aging remedies."

But research in recent years has found that several cancers, including liver and lung cancers, harbor mutations that decouple NRF2 from KEAP1, suggesting that persistent NRF2 activation may not be such a good thing after all. Some researchers now believe cancer cells may actually use NRF2 to protect themselves from radiation and chemotherapeutics.

Using a new mouse model whose liver cells express a KEAP1-resistant form of NRF2, Karin and collaborators found that persistent activation of NRF2 in these mice resulted in rapid and dramatic enlargement of the liver, known as hepatomegaly. In humans, hepatomegaly can appear after insulin overdosing, exposure to various toxins, certain viral and bacterial infections or as an indicator of an underlying disease, such as cirrhosis and liver cancer.

Because NRF2-induced hepatomegaly is similar to insulin-induced hepatomegaly, which relies upon activation of a protein kinase called AKT, the research team investigated the involvement of insulin and AKT in NRF2-induced hepatomegaly.

Although no evidence for excessive insulin production was uncovered, the scientists found that AKT (otherwise known as Protein kinase B) was activated in livers expressing the degradation-resistant form of NRF2. The scientists also discovered that inhibiting AKT produced complete reversal of hepatomegaly and rapid restoration of normal liver size and physiology in the mice. And that chronic NRF2 activation causes persistent production of growth factors that activate AKT.

Working with co-corresponding author Beicheng Sun, MD, a liver surgeon at Nanjing University Medical School in China, the team also reported that human hepatomegaly that is caused by either toxin exposure or autoimmune hepatitis also entails NRF2 activation, enhanced growth factor signaling and stimulation of AKT activity.

In addition to liver enlargement, the scientists said persistent NRF2 activation produced excessive fat and glycogen accumulation, suggesting that NRF2 may also be involved in fatty liver disease, such as nonalcoholic fatty liver disease and nonalcoholic steatohepatitis -- common metabolic disorders affecting millions of Americans.

The new findings, said Karin, suggest that AKT inhibitors, some of which have already been evaluated in humans for their anti-cancer activity, may be effective in the treatment and reversal of hepatomegaly, which affects more than 200 million persons worldwide.

Co-authors include: Shinichiro Yamachika, Zechuan Zhang, Koji Taniguchi and Atsushi Umemura, all at UC San Diego; Georgia Hatzivassiliou and Merone Roose-Girma, Genentech; Miguel Reina-Campos, Angeles Duran Molina, Maria T. Diaz-Meco and Jorge Moscat, Sanford-Burnham-Prebys Medical Discovery Institute.

https://wb.md/2T2LGcZ

FDA OKs First Quadrivalent, Adjuvanted Flu Vaccine for Older Adults

The US Food and Drug Administration (FDA) has approved the first quadrivalent, adjuvanted influenza vaccine to protect adults aged 65 years or older against seasonal influenza.

Megan Brooks

The US Food and Drug Administration (FDA) has approved the first quadrivalent, adjuvanted influenza vaccine (*Fluad Quadrivalent*, Seqirus) to protect adults aged 65 years or older against seasonal influenza.

Fluad Quadrivalent uses the same MF59 adjuvant as Seqirus's trivalent Fluad vaccine, "which has an extensive clinical legacy, with 114+ million doses distributed and licensure in 29 countries since it was first approved in 1997," the company said in a news release. The adjuvant is designed to generate a strong, broad, durable immune response.

The approval of the quadrivalent version of Fluad is supported by data from multiple clinical studies that demonstrated safety and efficacy in adults aged 65 years or older against influenza strains included in the vaccine, the company said.

Fluad and Fluad Quadrivalent are inactivated vaccines indicated for immunization against influenza caused by A and B virus subtypes contained in the vaccine.

During the 2018–2019 influenza season, up to 647,000 people in the United States were hospitalized because of influenza-related complications, according to preliminary estimates from the Centers for Disease Control and Prevention (CDC).

Rates of hospitalization and deaths from seasonal flu are higher in older adults compared to young, healthy adults. During the 2017–2018 influenza season, 70% of influenza-related hospitalizations and 90% of influenza-related deaths occurred in this age group, according to the CDC.

The effectiveness of influenza vaccine tends to be lower in older people, owing to age-related decline in immunity.

"Adults 65 years and older are at high risk for influenza-related complications each season and it is important to have influenza vaccines to help protect this vulnerable population," Anjana Narain, Seqirus's executive vice president and general manager, said in the release.

Fluad Quadrivalent offers "another seasonal vaccine option for healthcare providers and their patients in the fight against influenza," Narain said.

The CDC recommends that everyone aged 6 months or older receive an annual flu shot, but it is particularly important for those 65 years and older who are at risk of developing serious complications from influenza.

http://bit.ly/37Wgtfz

Bushfires burned a fifth of Australia's forest: study

"Globally unprecedented" wildfires have destroyed more than a fifth of the country's forests

Australia's wildfires have destroyed more than a fifth of the country's forests, making the blazes "globally unprecedented" following a years-long drought linked to climate change, researchers said Monday.

Climate scientists are currently examining data from the disaster, which destroyed swathes of southeastern Australia, to determine to what extent they can be attributed to rising temperatures.

In a special edition of the journal *Nature Climate Change*, Australian researchers examined several other aspects of the blazes, including investigations into their extent and possible causes.

One study showed that between September 2019 and January 2020 around 5.8 million hectares of broadleaf forest were burned in New South Wales and Victoria.

This accounts for roughly 21 percent of the nation's forested area, making this fire season proportionately the most devastating on record.

"Halfway through Spring 2019 we realised that a very large part of the eastern Australian forest could be burned in this single season," Matthias Boer, from the Hawkesbury Institute for the Environment at Western Sydney University, Penrith, told AFP.

"The shock came from realising that this season was off the charts globally in terms of the percentage of the continental section of a forest biome that burned."

Boer said his study almost certainly underestimates the extent of forest loss as the island state of Tasmania was not covered in the data.

Australia's annual average forest loss to wild fires is typically well below 2 percent.

Droughts linked to sea temperature

Another study published Monday looked at the conditions that made the fires so damaging—a years-long dry spell in Australia's Murray-Darling Basin.

Droughts create more fuel for wildfires and make it harder for forests to recover after each blaze.

Andrew King, from the University of Melbourne, and colleagues looked at a phenomenon known as the Indian Ocean Dipole (IOD), which has a direct effect on rainfall levels in Australia and elsewhere.

Since 2017 much of Australia has experienced widespread drought, something the study attributed to a relative lack of negative IOD events—when there are warmer than normal sea surface temperatures in the east Indian Ocean with cooler waters in the west.

These events tend to shift weather patterns and typically bring greater rainfall to southeast Australia, and are made less frequent as global sea temperatures warm.

King and the team examined rainfall statistics and found that the winter of 2016 saw extremely heavy precipitation and a corresponding negative IOD event.

Since then, the Murray-Darling Basin has experienced 12 consecutive seasons with below-average rainfall, the longest period on record since 1900.

"With climate change there have been projections that there will be more positive IOD events and fewer negative IOD events," King told AFP.

"This would mean that we'd expect more dry seasons in Australia and possibly worse droughts."

Boer said that climate change was all but certain to make Australia more prone to wildfires and urged the government to strengthen fire readiness measures and "take urgent and effective action on climate change."

More information: *In the line of fire, DOI: 10.1038/s41558-020-0720-5, https://nature.com/articles/s41558-020-0720-5*

The role of climate variability in Australian drought, DOI: 10.1038/s41558-020-0718-z , https://nature.com/articles/s41558-020-0718-z

Research is not immune to climate change, DOI: 10.1038/s41558-020-0718-z , https://nature.com/articles/s41558-020-0715-2

Transformative change requires resisting a new normal, DOI: 10.1038/s41558-020-0718-z , https://nature.com/articles/s41558-020-0712-5

A fiery wake-up call for climate science, DOI: 10.1038/s41558-020-0718-z , https://nature.com/articles/s41558-020-0707-2

http://bit.ly/394qTLD

Why Some COVID-19 Cases Are Worse than Others

Emerging data as well as knowledge from the SARS and MERS coronavirus outbreaks yield some clues as to why SARS-CoV-2 affects some people worse than others.

Katarina Zimmer

Like many other respiratory conditions, COVID-19—the disease caused by SARS-CoV-2—can vary widely among patients. The vast majority of confirmed cases are considered mild, involving mostly cold-like symptoms to mild pneumonia, according to the latest and largest set of data on the new coronavirus outbreak released February 17 by the Chinese Center for Disease Control and Prevention.

Fourteen percent of confirmed cases have been "severe," involving serious pneumonia and shortness of breath. Another 5 percent of patients confirmed to have the disease developed respiratory failure, septic shock, and/or multi-organ failure—what the agency calls "critical cases" potentially resulting in death. Roughly 2.3 percent of confirmed cases did result in death.

Scientists are working to understand why some people suffer more from the virus than others. It is also unclear why the new coronavirus—like its cousins SARS and MERS—appears to be more deadly than other coronaviruses that regularly circulate among people each winter and typically cause cold symptoms. "I think it's going to take a really, really long time to understand the mechanistic, biological basis of why some people get sicker than others," says Angela Rasmussen, a virologist at Columbia University's Mailman School of Public Health.

In the meantime, the latest data from China and research on other coronaviruses provide some hints.

Elderly and sick people are most susceptible to severe forms of COVID-19

The latest data from China stem from an analysis of nearly 45,000 confirmed cases, and on the whole suggest that the people most likely to develop severe forms of COVID-19 are those with pre-existing illnesses and the elderly.

While less than 1 percent of people who were otherwise healthy died from the disease, the fatality rate for people with cardiovascular disease was 10.5 percent. That figure was 7.3 percent for diabetes patients and around 6 percent for those with chronic respiratory disease, hypertension, or cancer.

While overall, 2.3 percent of known cases proved fatal—which many experts say is likely an overestimate of the mortality rate, given that many mild cases might go undiagnosed—patients 80 years or older were most at risk, with 14.8 percent of them dying. Deaths occurred in every age group except in children under the age of nine, and, generally speaking, "we see relatively few cases among children," World Health Organization Director General Tedros Adhanom Ghebreyesus said last week.

This pattern of increasing severity with age differs from that of some other viral outbreaks, notably the 1918 flu pandemic, for which mortality was high in young children and in people between 20 and 40 years of age. However, it's broadly consistent with records of the SARS and MERS coronavirus outbreaks, notes Lisa Gralinski, a virologist at the University of North Carolina at Chapel Hill. "If you're over fifty or sixty and you have some other health issues and if you're unlucky enough to be exposed to this virus, it could be very bad," she says.

I think it's going to take a really, really long time to understand the mechanistic, biological basis of why some people get sicker than others.

—Angela Rasmussen, Columbia University

Scientists don't know what exactly happens in older age groups. But based on research on other respiratory viruses, experts theorize

that whether a coronavirus infection takes a turn for the worse depends on a person's immune response. "The virus matters, but the host response matters at least as much, and probably more," says Stanley Perlman, a virologist and pediatric infectious disease specialist at the University of Iowa.

Once SARS-CoV-2 gets inside the human respiratory tract, it's thought to infect and multiply in cells lining the airway, causing damage that kicks the immune system into action. In most people, it should trigger a wave of local inflammation, recruiting immune cells in the vicinity to eradicate the pathogen. The immune response then recedes, and patients recover.

For reasons that aren't entirely clear, some people—especially the elderly and sick—may have dysfunctional immune systems that fail to keep the response to particular pathogens in check. This could cause an uncontrolled immune response, triggering an overproduction of immune cells and their signaling molecules and leading to a cytokine storm often associated with a flood of immune cells into the lung. "That's when you end up with a lot of these really severe inflammatory disease conditions like pneumonia, shortness of breath, inflammation of the airway, and so forth," says Rasmussen.

Local inflammation can turn into widespread inflammation of the lungs, which then has ripple effects across all organs of the body. This could also happen if the virus replicates faster than the immune system can respond, so that it then has to play catch-up to contain the pathogen—a situation that could also cause the immune defense to spiral out of control. "With mice, we know that in some cases, particularly for SARS and MERS coronaviruses, virus replication is very rapid and in some cases overwhelming" to the immune system, says Perlman.

It's harder to explain why young, healthy people also sometimes die from the disease—for instance, Li Wenliang, a 34-year-old doctor who first sounded the alarm about the virus. He died a few weeks after contracting the pathogen.

Genetic and environmental risk factors might help explain the severity of infections. Though it's clear that genetic factors can strongly determine the outcome of viral infections in mice—as some of Rasmussen's work has shown for Ebola, for instance—researchers haven't yet been able to tease out specific genes or variants in mice, let alone in people, that are responsible for varying degrees of illness. Environmental factors, such as smoking or air quality, may also play a role in disease severity, Rasmussen adds.

A lot of research has gone into understanding what causes respiratory failure that results from systemic inflammation of the lungs—also called acute respiratory distress syndrome (ARDS)—that can occur from coronaviruses and other infections. Yet researchers still don't know how it occurs exactly, let alone how to treat it, Gralinksi notes. "It's still a really poorly understood issue."

Men might be more affected by COVID-19 than women

An intriguing finding in the new data released last week is that although similar numbers of men and women have contracted SARS-CoV-2, more men are dying from the disease. The death rate for males was 2.8 percent and 1.7 percent for women. Rasmussen is quick to caution that although the data encompass nearly 45,000 patients, "that's still not that many people to determine if there's really a gender bias—you'd have to look at this in a much larger population of patients in a number of different countries," she says.

That said, if there is a bias, it would be consistent with what epidemiologists have observed during the SARS and MERS outbreaks. In the 2003 SARS outbreak in Hong Kong, for instance, nearly 22 percent of infected men died, compared to around 13 percent of women. In an analysis of MERS infections between 2017 and 2018, around 32 percent of men died, and nearly 26 percent of women. The difference could have something to do with

the fact that the gene for the ACE-2 receptor, which is used by both SARS-CoV-2 and the SARS virus to enter host cells, is found on the X chromosome, she speculates. If it's a particular variant of the protein that makes people more susceptible to the virus, then females could compensate for that one bad variant because they'd have two copies of the X chromosome, whereas men would be stuck with only one copy. Or, "it could be that men are more likely to be smokers and so their lungs are already a bit compromised. There's definitely more to be teased out there," Gralinski says.

Some of Perlman's research, which demonstrated that the sex disparity also holds true in SARS-infected mice, points to the hormone estrogen as possibly having protective effects: Removing the ovaries of infected female mice or blocking the estrogen receptor made the animals more likely to die compared to infected control mice. The effects are probably more pronounced in mice than in people, Perlman tells *The New York Times*.

Does an infection make people immune to the virus?

Whether patients develop antibodies after SARS-CoV-2 infection that will protect them against future infections is still a mystery. Surveys of SARS patients around five or 10 years after their recovery suggest that the coronavirus antibodies don't persist for very long, Gralinski says. "They found either very low levels or no antibodies that were able to recognize SARS proteins."

However, for the new coronavirus, "we would expect some immunity, at least in the short term," she says.

Why different coronaviruses vary in severity

There are seven coronaviruses known to infect people. Four of them—229E, NL63, OC43, and HKU1—typically cause a cold and only rarely result in death. The other three—MERS-CoV, SARS-CoV, and the new SARS-CoV-2—have varying degrees of lethality. In the 2003 SARS outbreak, 10 percent of infected people died. Between 2012 and 2019, MERS killed 23 percent of infected people. Although the case fatality rate of COVID-19 is lower, the virus has already killed more people than the other two outbreaks combined, which some have attributed to the pathogen's fast transmission.

The cold-causing coronaviruses, as well as many other viruses that cause common colds, are typically restricted to the upper respiratory tract, that is, the nose and sinuses. Both SARS-CoV and SARS-CoV-2, however, are capable of invading deep into the lungs, something that is associated with more severe disease.

One possible reason for this is that the virus binds to the ACE-2 receptor on human cells in order to gain entry. This receptor is present in ciliated epithelial cells in the upper and lower airway, as well as in type II pneumocytes, which reside in the alveoli in the lower airway and produce lung-lubricating proteins. "The type II pneumocytes are . . . important for lung function, so this is part of why the lower respiratory disease can be so severe," notes Gralinksi.

The new coronavirus also appears to use the ACE-2 receptor, which may help partially explain why, like SARS, it is more deadly than the other four coronaviruses. Those pathogens use different receptors, except for NL63, which also uses the ACE-2 receptor but binds to it with less affinity, says Gralinski. (MERS is thought to use an entirely different receptor, which is also present in the lower airways.)

Sustained interest required

To understand these questions fully will take time, research, and consistent funding for long-term studies. Coronavirus funding has been criticized for following a boom-and-bust cycle; viral spillovers from animals to people cause an initial surge of interest that tends to wane until the next outbreak occurs, Rasmussen warns.

"I'm hopeful that in this case it will be really apparent to everybody in the world that we need to be funding this type of basic science, fundamental science, to understand these mechanisms of disease,"

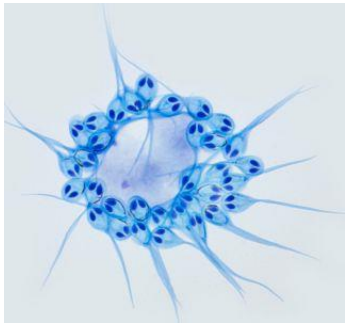
she says. “Otherwise, we’re going to be in the same situation when the next outbreak happens—whether it’s a coronavirus or something else.”

http://bit.ly/2PrUxCC

Scientists discover first known animal that doesn't breathe

This is the first animal on Earth proven to have no mitochondrial genome and no way to breathe.

By Brandon Specktor - Senior Writer



When the parasitic blob known as *Henneguya salminicola* sinks its spores into the flesh of a tasty fish, it does not hold its breath. That's because *H. salminicola* is the only known animal on Earth that does not breathe.

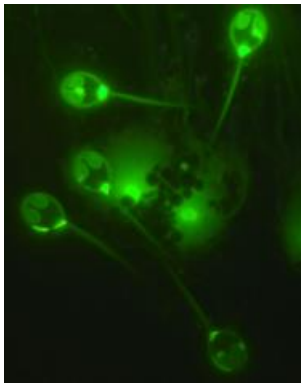
***Spores of the parasite H. salminicola swim under a microscope. Those alien "eyes" are actually stinger cells, one of the few features this organism hasn't evolved away.* (Image: © Stephen Douglas Atkinson)**

If you spent your entire life infecting the dense muscle tissues of fish and underwater worms, like H. salminicola does, you probably wouldn't have much opportunity to turn oxygen into energy, either. However, all other multicellular animals on Earth whose DNA scientists have had a chance to sequence have some respiratory genes. According to a new study published today (Feb. 24) in the journal Proceedings of the National Academy of Sciences, *H. salminicola*'s genome does not.

A microscopic and genomic analysis of the creature revealed that, unlike all other known animals, *H. salminicola* has no mitochondrial genome — the small but crucial portion of DNA stored in an animal's mitochondria that includes genes responsible for respiration.

While that absence is a biological first, it's weirdly in character for the quirky parasite. Like many parasites from the myxozoa class - a group of simple, microscopic swimmers distantly related to jellyfish - H. salminicola may have once looked a lot more like its jelly ancestors but has gradually evolved to have just about none of its multicellular traits.

"They have lost their tissue, their nerve cells, their muscles, everything," study co-author Dorothée Huchon, an evolutionary biologist at Tel Aviv University in Israel, told Live Science. "And now we find they have lost their ability to breathe."



That genetic downsizing likely poses an advantage for parasites like *H. salminicola*, which thrive by reproducing as quickly and as often as possible, Huchon said. Myxozoans have some of the smallest genomes in the animal kingdom, making them highly effective. While *H. salminicola* is relatively benign, other parasites in the family have infected and wiped out entire fishery stocks, Huchon said, making them a threat to both fish and commercial fishers.

***The nucleus of each H. salminicola spore glows green under a fluorescent microscope. Through microscopy and genetic sequencing, the study authors learned that H. salminicola is the only known animal with no mitochondrial DNA.* (Image credit: Stephen Douglas Atkinson)**

When seen popping out of the flesh of a fish in white, oozing bubbles, *H. salminicola* looks like a series of unicellular blobs. (Fish infected with *H. salminicola* are said to have "tapioca disease.") Only the parasite's spores show any complexity. When seen under a microscope, these spores look like bluish sperm cells with two tails and a pair of oval, alien-like eyes.

Those "eyes" are actually stinging cells, Huchon said, which contain no venom but help the parasite latch onto a host when

needed. These stinging cells are some of the only features that *H. salminicola* has not ditched on its journey of evolutionary downsizing.

"Animals are always thought to be multicellular organisms with lots of genes that evolve to be more and more complex," Huchon said. "Here, we see an organism that goes completely the opposite way. They have evolved to be almost unicellular."

So, how does *H. salminicola* acquire energy if it does not breathe? The researchers aren't totally sure. According to Huchon, other similar parasites have proteins that can import ATP (basically, molecular energy) directly from their infected hosts. *H. salminicola* could be doing something similar, but further study of the oddball organism's genome — what's left of it, anyway — is required to find out.

http://bit.ly/3a7YLHy

Weight gain associated with accelerated lung function decline in adulthood

A new study is the first to analyze weight changes in adults and their effects on lung function over a 20-year period

Barcelona - Lung function declines naturally over the course of the human lifespan. However, this decline is steeper in individuals who experience moderate or high weight gain. This was the conclusion of a new study led by the Barcelona Institute for Global Health (ISGlobal), a centre supported by "la Caixa", which analysed the effect of weight changes on respiratory health over a 20-year period. The study, published in the journal Thorax, was based on data collected from 3,700 participants living in different countries in Europe and in Australia and recruited between the ages of 20 and 44 years. Participants repeatedly underwent measurements of weight and lung function--by means of spirometry--between 1991 and 2014. "Although previous research has shown that weight gain is linked to lung function decline, ours is the first study to analyse such a varied population sample over a longer period of time," commented Judith Garcia Aymerich, leader of the study and head of the Non-communicable Diseases and Environment programme at ISGlobal. Most earlier studies have had relatively short follow-up periods--ten years at the most--and focused on adults up to 50 years of age.

The study found that people with a body mass index within the recommended rates, overweight people and obese people all experienced accelerated lung function decline when they gained weight. Conversely, weight loss helped to attenuate lung function decline in obese people. Moreover, people who kept their weight low throughout adulthood exhibited a much less pronounced decline in respiratory health.

Two mechanisms could explain the association between weight gain and pulmonary health. First, weight gain can affect lung function through mechanical effects. "Abdominal and thoracic fat mass is likely to limit the room for lung expansion during inspiration," commented ISGlobal researcher Gabriela Prado Peralta, lead author of the study. Second, weight gain can impair lung function through inflammatory processes, since adipose tissue--the area where fat accumulates--is a source of inflammatory substances that can damage lung tissue and reduce airway diameter.

Maintaining good lung function during adulthood is crucial to prevent chronic respiratory diseases, which nowadays represent a serious public health problem around the world. "Given the epidemic levels of overweight and obesity that we are currently seeing, it is fundamental to understand the effects of weight changes on lung function, which is a powerful predictor of morbidity and mortality in the general population," commented Garcia Aymerich. "The good news is that the negative pulmonary health effects of excess weight and obesity can be reversed through

weight loss. Therefore, public health policies that promote healthy lifestyles can be the key to achieving good pulmonary health."

The study formed part of the Ageing Lungs in European Cohorts (ALEC) Study, coordinated by Imperial College London. It was financed by the European Union's Horizon 2020 research and innovation programme.

Reference

Gabriela P. Peralta, Alessandro Marcon, Anne-Elie Carsin, Michael J Abramson, Simone Accordini, André FS Amaral, Josep M. Antó, Gayan Bowatte, Peter Burney, Angelo Corsico, Pascal Demoly, Shyamali Dharmage, Bertil Forsberg, Elaine Fuertes, Vanessa Garcia-Larsen, Thorarinn Gíslason, José-Antonio Gullón, Joachim Heinrich, Mathias Holm, Deborah L. Jarvis, Christer Janson, Rain Jogi, Ane Johannessen, Bénédicte Leynaert, Jesús Martínez-Moratalla Rovira, Dennis Nowak, Nicole Probst-Hensch, Chantal Raherison, José-Luis Sánchez-Ramos, Torben Sigsgaard, Valérie Siroux, Giulia Squillacioti, Isabel Urrutia, Joost Weyler, Jan-Paul Zock, Judith Garcia-Aymerich.. Body mass index and weight change are associated with adult lung function trajectories: the prospective ECRHS study. Thorax. *February 2020.*

http://bit.ly/2TnGMGn

The Lancet Respiratory Medicine: New therapy could help relieve persistent cough

4-10% of adults worldwide have a chronic cough -- a cough lasting more than 8 weeks

- ***4-10% of adults worldwide have a chronic cough - a cough lasting more than eight weeks.***
- ***Phase 2b clinical trial of drug to treat unexplained chronic cough, a condition that has a significant impact on quality of life, shows promising results.***
- ***Currently, no effective licensed therapies exist for this problem.***

A new treatment - called gefapixant - may reduce the frequency of coughing, including in patients who have suffered from a chronic cough for more than 15 years, according to results from a phase 2b clinical trial which lasted 12 weeks and included 253 people, published in The Lancet Respiratory Medicine journal.

Between four and 10% of adults worldwide suffer from an unexplained chronic cough. Non-smokers with a chronic cough are likely to have an underlying condition such as asthma, or to have been exposed to dust or fumes in the workplace. However, not all people with conditions such as asthma report a chronic cough. This suggests that it's caused by a separate process, which may explain why it often does not respond to treatment for underlying conditions.

When a cough is unexplained and unresponsive to treatment, a patient may be described as having cough hypersensitivity syndrome. Until now, there has been no safe, long-term treatment for this. A target for treatment could be reducing hyperexcitability of the neuronal pathways involved in coughing. Gefapixant blocks a receptor involved in the cough reflex.

Previous studies found that gefapixant could reduce the frequency of coughing when given in a high dose (600mg) over two weeks, and that doses as low as 50mg could reduce coughing over a four-day trial when given twice daily. The new trial, which lasted 12 weeks, was randomised, double-blind and placebo-controlled to study how effective three different doses of gefapixant were and their associated side effects.

"Many patients with a chronic cough are driven to seek treatment because of the significant negative impact it can have on their quality of life, but at the moment physicians are unable to help," says Professor Jacky Smith from the University of Manchester, who led the study. "Ours' is the first study to report a treatment that is safe and effective over the longer term, and phase 3 trials are already underway with an even larger group of people and over a longer timeframe." [1]

In the current study, the researchers recruited 253 patients with an unexplained or untreatable cough that had persisted for an average of 14.5 years.

The patients were recruited from 44 sites across the UK and US. Most (70%, or 177/253) had never smoked. The average age of

patients was 60 and over three-quarters (76%, or 193/253) were women, which resembles the profile of patients who attend cough clinics.

Patients were randomly assigned to receive either a placebo (63 patients) or gefapixant twice daily, every day for 84 days. They were administered one of three doses: 7.5mg (64 patients), 20mg (63 patients) or 50mg (63 patients).

Throughout the study, patients kept a cough severity diary, including reporting how many times they coughed per hour. Cough frequency was also captured objectively, by fitting patients with a sound recording device over four 24-hour periods.

During three treatment visits, participants completed a Leicester Cough Questionnaire, and during six visits they rated the severity of their cough on a scale from "no cough" to "worst possible cough". Clinicians recorded any adverse events that could be associated with treatment.

Before treatment started, patients coughed around 24-29 times per hour. After 12 weeks of treatment, the placebo group coughed 18 times per hour, but this reduced by an additional 37% to 11 coughs per hour in the 50mg group.

There were also some reductions in the 7.5mg and 20mg groups, but these were not statistically significant.

The most common side effect seen in the trial was a change in patients' sense of taste (occurring in three (5%) patients given placebo, six (10%) given 7.5 mg gefapixant, 21 (33%) given 20 mg gefapixant, and 30 (48%) given 50 mg gefapixant).

Dysgeusia and other taste-related adverse experiences led to 10 patients in the 50mg group discontinuing with the study, but most patients who continued to receive treatment said they would be happy to continue for at least a year. It is not yet available on prescription, while clinical testing continues.

During the trial, there was one serious adverse event (frostbite) but this was thought to be unrelated to the drug.

The authors note that a limitation of their study is that it recorded a strong placebo effect. For example, the waking frequency of coughs in the placebo group went down from an average of 28 per hour before treatment to 18 per hour after 12 weeks.

Previous, smaller studies with gefapixant recorded little change in patients given placebo. The authors suggest that patients' expectations in this trial may have been affected by positive results from previous studies, as well as by the high likelihood (75%) of being assigned to a treatment group.

Writing in a linked Comment, lead author Dr Richard Irwin (who was not involved in the study) from the University of Massachusetts Medical School, USA, says: "Based on the unadjusted data shown in table 2, there was an incrementally larger decrease in cough frequency with each successively larger dose, with the cough frequency at 50 mg being the lowest, but the absolute frequency of cough is not reported as being statistically different from placebo.

Because large placebo effects have been seen in other randomized, placebo-controlled cough treatment studies, the authors took this into account by analyzing cough frequency relative to placebo. When this was done, the improvement with the 50mg dose, but not other doses, did reach statistical significance compared with placebo."]

NOTES TO EDITORS

This study was funded by Afferent Pharmaceuticals and supported by the Northern Ireland Clinical Research Network and the UK National Institute of Health Research. It was conducted by researchers from the University of Manchester, Manchester University NHS Foundation Trust, Hull York Medical School, King's College London, Queen's University Belfast, the Center for Cough (Florida, USA) and GetStat Solutions, USA. A full declaration of interests for all authors is provided in the paper.

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

http://bit.ly/3cboOiQ

Billion-year-old green algae is an ancestor of all plants on Earth

Green seaweeds were important players in the ocean, long before their descendants took control on land.

By Laura Geggel - Associate Editor

The oldest green seaweed on record, the ancestor of all land plants, lived about 1 billion years ago, a new study finds.

Scientists have discovered the fossils of what may be the oldest green algae ever known. The newfound seaweed — called *Proterocladus antiquus* — lived about a billion years ago. And even though it was tiny, about 0.07 inches (2 millimeters) in length, the algae had a big role: It could produce oxygen through photosynthesis.

An illustration of how Proterocladus antiquus likely appeared 1 billion years ago. **(Image: © Dinghua Yang; Tang et al., Nature Ecology and Evolution)**

"Its discovery indicates that green plants we see today can be traced back to at least 1 billion years ago, and they started in the ocean before they expanded their territory to the land," study lead researcher Qing Tang, a postdoctoral fellow in the Department of Geosciences at Virginia Tech, told Live Science in an email.

Until now, researchers didn't have hard proof that green algae lived that long ago. Rather, computer models, including those based on molecular clocks, indicated that photosynthesizing plants arose between the Paleoproterozoic era (2.5 billion to 1.6 billion years ago) and the Cryogenian period (720 million to 635 million years ago).

Now that researchers have a fossil, they can confidently say that photosynthesizing plants, a group known as Viridiplantae, lived at least 1 billion years ago, and that they were multicellular, Tang said. "Previously, the oldest widely accepted fossilized green algae was about 800 million years old," said Timothy Gibson, a postdoctoral fellow in the Department of Earth Sciences at Dartmouth College in New Hampshire and the Department of Geology and Geophysics at Yale University, who was not involved with the study. "This work confirms what many have expected based on the existing, though sparse fossil record, which is that green algae likely existed about a billion years ago."

Tang and his colleagues discovered the fossils near Dalian City in Liaoning province of northern China. They had heard there was "a thick pile of well-exposed sedimentary rocks" from the Nanfen Formation dating to about a billion years ago. So, Tang took some of these ancient rocks, mostly mudstone and shale, back to the lab at Virginia Tech.

A detailed fossil of the oldest known green algae on Earth. **(Image credit: Tang et al., Nature Ecology and Evolution)**

Tang was "really excited" when he saw the algae fossil under the microscope. In all, he identified 1,028 specimens. "I showed it to my supervisor [Shuhai Xiao, a professor in the Department of Geosciences at Virginia Tech], and we immediately agreed that this was going to be a very interesting discovery," he said.

Just like modern-day algae, *P. antiquus* has differentiated, branched cells and root-like structures, Tang said. It likely played an important role in the ancient ecosystem by producing oxygen, he said. In addition, it likely provided food and shelter to other organisms.

"Most of the organisms (particularly cyanobacteria) in this period were either planktonic or lying on the seafloor," Tang said. *P. antiquus* also grew on the seafloor, indicating that it could have served as an ideal place for living, hiding, resting for other organisms, he said.

Life on Earth is dependent on photosynthesizing plants and algae for food, yet land plants did not evolve until about 450 million years ago, Tang said. "The new fossil suggests that green seaweeds were important players in the ocean long before their descendants, land plants, took control," he said.

These fossils came from an ancient ocean, but there is still a debate about where green algae originated. "Not everyone agrees with us; some scientists think that green plants started in rivers and lakes, and then conquered the ocean and land later," Xiao said in a statement.

Moreover, green algae isn't the oldest algae on record. "There is strong fossil evidence that red algae existed over a billion years ago, and we know the red and green algae diverged from a common ancestor," Gibson told Live Science in an email. "So, although this doesn't fundamentally change the way I'll think about the evolution of life, the discovery of this green algal fossil helps fill an important gap and strengthens an emerging timeline for the evolution of early, complex life." The study was published online yesterday (Feb. 24) in the journal Nature Ecology and Evolution.

http://bit.ly/2T7b8hf

New Experiment With Human Stem Cells Ends Up Rapidly Curing Diabetes in Mice

Within two weeks their blood glucose levels had returned to normal and stayed that way for many months

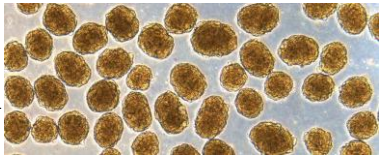
Peter Dockrill

A new technique to convert human stem cells into insulin-producing cells could hold huge promise for future diabetic treatments, if results seen in an experiment with mice can be successfully replicated in humans.

In a study, researchers figured out a new way to coax human pluripotent stem cells (hPSCs) into pancreatic beta cells that make insulin. When these insulin-producing cells were transplanted into mice induced to have an acute form of diabetes, their condition was rapidly cured.

"These mice had very severe diabetes with blood sugar readings of more than 500 milligrams per decilitre of blood – levels that could be fatal for a person," explains biomedical engineer Jeffrey R. Millman from Washington University.

"When we gave the mice the insulin-secreting cells, within two weeks their blood glucose levels had returned to normal and stayed that way for many months."



Human insulin-secreting beta cells under the microscope. **(Millman Laboratory)**

Pluripotent stem cells are essentially blank, undifferentiated cells with the ability to grow into other kinds of cells that exist all throughout the body. Harnessing that potential, in the diabetic context, means researchers could devise ways of tweaking stem cells to become the insulin-producing cells that diabetics lack, helping them to control high blood sugar and stay healthy.

Scientists have been investigating how to do this for years, reporting a number of incremental successes in animal models as our understanding of the processes behind stem cell manipulation increases.

Millman's lab has been busy too. In 2016, they devised a way to produce insulin-secreting cells – derived from patients with type 1 diabetes – that functioned in response to glucose. A few years later, they learned how to augment the level of insulin secretion in stem-cell-derived pancreatic beta cells.

In the new work, they've tackled another challenge: reducing the amount of 'off target' cells produced in these processes, when blank cells differentiate into other kinds of unintended cells.

"A common problem when you're trying to transform a human stem cell into an insulin-producing beta cell – or a neuron or a heart cell – is that you also produce other cells that you don't want," Millman says. "In the case of beta cells, we might get other types of pancreas cells or liver cells."

These 'off target' cells are not harmful, but they're also not functional for purposes like glucose control, which limits the remedial impact of stem cell treatments, given you're working with less therapeutically relevant cells, the researchers explain.

However, a new technique now looks like it can keep cell differentiation on target. In the new study, the team found that transcription factors that drive stem cells towards becoming pancreatic cells are linked to the state of the cell's cytoskeleton, a support structure inside cells that acts as a kind of skeleton, made up of microfilaments of various protein fibres.

One of these proteins is called actin, which plays an important role in cellular function, and, it turns out, cell differentiation as well.

"We found that manipulating cell–biomaterial interactions and the state of the actin cytoskeleton altered the timing of endocrine transcription factor expression and the ability of pancreatic progenitors to differentiate into stem-cell-derived beta cells," the authors explain in their paper.

In other words, we can more efficiently ensure the production of insulin-producing cells by controlling the actin cytoskeleton, and the ability to do that bodes well for the future of stem cell treatments, if the team's mouse model is anything to go by.

"We were able to make more beta cells, and those cells functioned better in the mice, some of which remained cured for more than a year," Millman explains; control animals, who were not given the cell transplants, ended up dying, such was the severity of their induced diabetes.

That's not all. The same cytoskeletal manipulations also showed potential to better control the differentiation of other kinds of cells, including liver, oesophagus, stomach, and intestine cells, the researchers say. If so, the technique might enhance stem cell treatments for other kinds of pathologies, not just diabetes.

Of course, we can't get ahead of ourselves just yet, as the new method has so far only been tested in animals; as the researchers emphasise, we're a long way off being able to heal people with this kind of experimental treatment.

That said, the results are certainly promising, and could point the way to a future where we can do exactly that.

"Our study as a whole emphasises that cytoskeletal dynamics work synergistically with soluble biochemical factors to regulate endodermal cell fate, opening new opportunities to improve differentiation outcomes," the authors conclude.

The findings are reported in *Nature Biotechnology*.

http://bit.ly/2uCZstn

Sex-specific traits of the immune system explain men's susceptibility to obesity

Adipose tissue produces a range of different hormones.

Melbourne researchers have uncovered important differences between the male and female immune system which may explain why men are more susceptible to obesity and metabolism-related associated diseases, such as heart disease, stroke and diabetes

University of Melbourne

Melbourne researchers have uncovered important differences between the male and female immune system which may explain why men are more susceptible to obesity and metabolism-related associated diseases, such as heart disease, stroke and diabetes.

It has long been known that men are more likely than women to develop unhealthy obesity and related metabolic diseases, while women are more prone to certain autoimmune diseases such as arthritis. These findings suggested the male and female immune systems differ, but until now scientists weren't sure how.

Researching male and female adipose tissue - commonly referred to as body fat - a team at the Doherty Institute and the Walter and Eliza Hall Institute discovered striking differences in the numbers and function of an immune cell population called regulatory T cells, or Treg cells, between male and female mice.

Treg cells play a central role in the body by dampening inflammation, autoimmunity and maintaining the health of many tissues, including the adipose tissue.

Importantly, the adipose tissue is not only a storage for energy, but also an endocrine organ that plays a crucial part in regulating metabolism, appetite and inflammation. It also produces a range of different hormones.

Published today in Nature, the team systematically examined every cell type in the adipose tissue and discovered a novel type of stromal - or connecting - cell that communicates with Treg cells and is found only in males. These stromal cells determine how many Treg cells can be recruited to the adipose tissue and how they are being activated.

University of Melbourne Dr Ajithkumar Vasanthakumar, Doherty Institute postdoctoral researcher and first author of the study, said finding these differences between male and female Treg cells was a remarkable breakthrough, as scientists have previously been unable to understand the differences between male and female immune systems.

"Not only did we discover dramatic differences in Treg cells, we also discovered a stromal cell type that responds directly to the male sex hormone, testosterone, and is therefore specific to males," Dr Vasanthakumar said. "This stromal cell makes a signalling molecule, IL-33, which is what Treg cells depend on. So, you have a completely novel chain of events that is regulated in a sex-specific manner."

With the unprecedented worldwide rise of obesity and metabolic disease, University of Melbourne Professor Axel Kallies, senior author and laboratory head at the Doherty Institute, said the findings are important when considering new therapeutic approaches to this global challenge.

"We are now exploring whether similar mechanisms are at play in autoimmune diseases and in cancers," Professor Kallies said.

"For too long the male physiology and the male immune system was considered the 'norm' in research and in clinical studies. Our work shows that important differences exists between the sexes. This means that the strategies to treat a range of diseases may have to be different between men and women."

This work was done in collaboration with researchers at Monash University and the Peter MacCallum Cancer Centre.

http://bit.ly/2TlQJnI

Turbulent times revealed on Asteroid 4 Vesta

Planetary scientists at Curtin University have shed some light on the tumultuous early days of the largely preserved protoplanet Asteroid 4 Vesta, the second largest asteroid in our Solar System.

Research lead Professor Fred Jourdan, from Curtin University's school of Earth and Planetary Sciences, said Vesta is of tremendous interest to scientists trying to understand more about what planets are made of, and how they evolved.

"Vesta is the only largely intact asteroid which shows complete differentiation with a metallic core, a silicate mantle and a thin basaltic crust, and it's also very small, with a diameter of only about 525 kilometres," Professor Jourdan said.

"In a sense it's like a baby planet, and therefore it is easier for scientists to understand it than say, a fully developed, large, rocky planet." To give you an idea of its size, you could squeeze at least three Vesta-size asteroids side by side in the state of New South Wales, Australia.

Vesta was visited by the NASA Dawn spacecraft in 2011, when it was observed that the asteroid had a more complex geological history than previously thought. With the aim of hoping to understand more about the asteroid, the Curtin research team analysed well-preserved samples of volcanic meteorites found in Antarctica that were identified as having fallen to Earth from Vesta.

"Using an argon-argon dating technique, we obtained a series of very precise ages for the meteorites, which gave us four very important pieces of new information about timelines on Vesta," Professor Jourdan said.

"Firstly, the data showed that Vesta was volcanically active for at least 30 million years after its original formation, which happened 4,565 million years ago. While this may seem short, it is in fact significantly longer than what most other numerical models predicted, and was unexpected for such a small asteroid.

"Considering that all the heat-providing radioactive elements such as aluminium 26 would have completely decayed by that time, our research suggests pockets of magmas must have survived on Vesta, and were potentially related to a slow-cooling partial magma ocean located inside the asteroid's crust."

Co-researcher Dr Trudi Kennedy, also from Curtin's School of Earth and Planetary Sciences, said the research also showed the timeframes when very large impacts from asteroids striking Vesta were carving out craters of ten or more kilometres deep from the asteroid's volcanically active crust.

"To put this into perspective, imagine a large asteroid smashing into the main volcanic island of Hawaii and excavating a crater 15 kilometres deep - that gives you an idea of what tumultuous activity was happening on Vesta in the early days of our Solar System," Dr Kennedy said.

Scientists further explored the data to understand what was happening deeper in the asteroid by calculating how long it took for Vesta's deep crustal layer to cool down. Some of these rocks were located too deep in the crust to be affected by asteroid impacts, and yet, being relatively close to the mantle, they were strongly affected by the natural heat gradient of the protoplanet and were metamorphosed as a result.

"What makes this interesting is that our data further confirms the suggestion that the first flows of erupted lava on Vesta were buried deep into its crust by more recent lava flows, essentially layering them on top of each other. They were then 'cooked' by the heat of the protoplanet's mantle, modifying the rocks," Dr Kennedy said.

The team also concluded that the meteorites they analysed were excavated from Vesta during a large impact, possibly 3.5 billion years ago, and were agglomerated deep into a rubble pile asteroid, where they were protected from any subsequent impacts.

A rubble pile asteroid is formed when a group of ejected rocks assemble under their own gravity, creating an asteroid that is essentially a pile of rocks clumped together.

"This is very exciting for us because our new data brings lots of new information about the first 50 million years or so of Vesta's early history, which any future models will now have to take in to account," Dr Kennedy said. "It also raises the point that if volcanism could last longer than previously thought on the protoplanet, then maybe volcanism on the early Earth itself might have been more energetic than we currently think."

The research paper, Timing of the magmatic activity and upper crustal cooking of differentiated asteroid 4 Vesta was published in Geochimica et Cosmochimica Acta *and can be found online here:*

https://www.sciencedirect.com/science/article/pii/S0016703720300594

http://bit.ly/2T5f3eE

Mystery surrounding dinosaur footprints on a cave ceiling in Central Queensland solved

The dinosaur in the cupboard under the stairs

The mystery surrounding dinosaur footprints on a cave ceiling in Central Queensland has been solved, in article published in *Historical Biology*, after more than a half a century.

University of Queensland palaeontologist Dr Anthony Romilio discovered pieces to a decades-old puzzle in an unusual place - a cupboard under the stairs of a suburban Sydney home.

"The town of Mount Morgan near Rockhampton has hundreds of fossil footprints and has the highest dinosaur track diversity for the entire eastern half of Australia," Dr Romilio said.

"Earlier examinations of the ceiling footprints suggested some very curious dinosaur behaviour; that a carnivorous theropod walked on all four legs. "You don't assume *T. rex* used its arms to walk, and we didn't expect one of its earlier predatory relatives of 200 million years ago did either."

Ross Staines measuring the footprints 4.5 metres above the cave floor (c. 1954). **Copyright Staines**

Researchers wanted to determine if this dinosaur did move using its feet and arms, but found accessing research material was difficult.

"For a decade the Mount Morgan track site has been closed, and the published 1950s photographs don't show all the five tracks," Dr Romilio said.

However Dr Romilio had a chance meeting with local dentist Dr Roslyn Dick, whose father found many dinosaur fossils over the years. "I'm sure Anthony didn't believe me until I mentioned my father's name - Ross Staines," Ms Dick said.

"Our father was a geologist and reported on the Mount Morgan caves containing the dinosaur tracks in 1954. "Besides his published account, he had high-resolution photographs and detailed notebooks, and my sisters and I had kept it all. "We even have his dinosaur footprint plaster cast stored under my sister's Harry Potter cupboard in Sydney."

Dr Romilio said the wealth and condition of 'dinosaur information' archived by Ms Dick and her sisters Heather Skinner and Janice Millar was amazing. "I've digitised the analogue photos and made a virtual 3D model of the dinosaur footprint, and left the material back to the family's care," he said. "In combination with our current understanding of dinosaurs, it told a pretty clear-cut story."

The team firstly concluded that all five tracks were foot impressions - that none were dinosaur handprints.

Also the splayed toes and moderately long middle digit of the footprints resembled two-legged herbivorous dinosaur tracks, differing from prints made by theropods. "Rather than one dinosaur walking on four legs, it seems as though we got two dinosaurs for the price of one - both plant-eaters that walked bipedally along the shore of an ancient lake," Dr Romilio said.

"The tracks lining the cave-ceiling were not made by dinosaurs hanging up-side-down, instead the dinosaurs walked on the lake sediment and these imprints were covered in sand. "In the Mount Morgan caves, the softer lake sediment eroded away and left the harder sandstone in-fills."

http://bit.ly/3886hRk

Cannabis compound acts as an antibiotic

CBG helped control methicillin-resistant Staphylococcus aureus infections in mice

Public health agencies worldwide have identified antibiotic resistance of disease-causing bacteria as one of humanity's most critical challenges. However, scientists haven't discovered a new

class of antibiotics in more than 30 years. Now, researchers reporting in *ACS Infectious Diseases* have uncovered the hidden antibiotic potential of a non-psychoactive cannabis compound called cannabigerol (CBG), which helped control methicillin-resistant *Staphylococcus aureus* (MRSA) infections in mice.

For centuries, cannabis plants have been used in folk medicine. Today, scientists are only beginning to investigate whether different cannabis compounds could be used to treat a variety of diseases. Early studies have shown that some cannabinoids can slow the growth of gram-positive bacteria, such as *S. aureus*, but not gram-negative bacteria, such as *E. coli*. Eric Brown and colleagues wanted to test the antibacterial properties of several cannabinoids against both MRSA and gram-negative bacteria.

The researchers tested the antibacterial activity of 18 cannabis-derived molecules, including cannabidiol (CBD), tetrahydrocannabinol (THC) and CBG, against MRSA. They also tested the ability of these substances to prevent the formation of biofilms on surfaces and to kill dormant "persistor" MRSA that are highly resistant to antibiotics. CBG performed the best in these tests, so the researchers chose to study it further. When they treated MRSA-infected mice with CBG, the compound worked as well as vancomycin, a powerful antibiotic. The researchers discovered that CBG targets the cell membrane of gram-positive bacteria, and by itself, it is not effective against gram-negative bacteria, which have an additional outer membrane. However, they found that if they gave CBG with another drug that pokes holes in this outer membrane, CBG could reach the inner membrane and kill gram-negative bacteria.

The authors acknowledge funding from the Canada Research Chairs program, the Canadian Institutes of Health Research Foundation Grant Program and the Michael G. DeGroote Centre for Medicinal Cannabis Research.

The abstract that accompanies this study is available here.

http://bit.ly/3ady1oY

No benefit found in using broad-spectrum antibiotics as initial pneumonia treatment

Doctors who use drugs that target antibiotic-resistant bacteria as a first-line defense against pneumonia should probably reconsider this approach

Doctors who use drugs that target antibiotic-resistant bacteria as a first-line defense against pneumonia should probably reconsider this approach, according to a new study of more than 88,000 veterans hospitalized with the disease. The study, conducted by University of Utah Health and VA Salt Lake City Health Care System researchers, found that pneumonia patients given these medications in the first few days after hospitalization fared no better than those receiving standard medical care for the condition.

"Sometimes in our eagerness to improve outcomes, particularly among critically ill patients, we, as doctors, may be overly broad in our initial treatments. This appears to be true with pneumonia, where we found no benefit associated with use of the so-called 'big gun' antibiotics as an initial treatment to cover resistant organisms, even among those patients who are at high risk for these types of infections." says Matthew Samore, M.D., the study's senior author, a U of U Health professor of medicine, and Director of the Informatics Decision Enhancement and Analytic Sciences Center at the VA Salt Lake City Health Care System.

The study, one of the largest ever to examine trends of antibiotic use in the treatment of pneumonia, appears in the *JAMA Internal Medicine*.

Pneumonia is the eighth leading cause of death in the United States, accounting for more than 1 million hospitalizations and about 50,000 deaths each year. It can be caused by viruses, fungi, and bacteria, including Methicillin-resistant *Staphylococcus aureus*

(MRSA), which can cause a rare but hard-to-treat form of pneumonia.

Unfortunately, determining whether MRSA or other pathogens are responsible for any particular case of pneumonia is difficult. That's because testing sputum (mucus) samples for the cause of pneumonia is often inaccurate, and collecting lung tissue samples can be invasive and risky, especially in patients who are extremely ill.

So, doctors often have to rely on their best judgment to deduce what treatment might work until if and when definitive test results are available, says Barbara Jones, M.D., the study's lead author, a U of U Health assistant professor of internal medicine, and career development awardee of VA Health Research & Development Service.

To determine how this decision-making process affects patient care, Samore, Jones, and colleagues retrospectively examined the medical records of 88,605 pneumonia patients, ages 62 to 81, who were admitted to VA Medical Centers nationwide between 2008 and 2013. The researchers tracked whether these patients were initially treated with standard antibiotic therapy for pneumonia--such as cerftriaxone and azithromycin--or two types of anti-MRSA care:

- ***standard therapy plus vancomycin (an antibiotic,)***
- ***vancomycin without standard therapy.***

The researchers observed that as doctors became more aware of and concerned about MRSA infection in the lungs, they became more likely to use anti-MRSA therapies¬ as an initial treatment, despite the fact that MRSA only accounts for about 2% of pneumonia cases. In fact, use rose from about 20% of patients in 2008 to nearly half of them in 2013. As a result, many of the patients who were treated with anti-MRSA antibiotics probably didn't need them.

The researchers found no discernable benefit of anti-MRSA treatment in addition to standard treatment. In fact, anti-MRSA treatment was associated with a 40 % higher risk of dying within 30 days of discharge, perhaps due to the potentially severe side effects of vancomycin including increased incidence of kidney failure and secondary infections. However, further study is needed to fully determine the underlying causes of this increased risk, according to the researchers.

"Our study calls into question the strategy of broad empiric antibiotic coverage that has previously been promoted by pneumonia practice guidelines," Jones says. "We're not saying that it's never appropriate to use anti-MRSA therapy for treating pneumonia. But in the absence of better tests to identify MRSA as a potential pathogen causing the disease, using anti-MRSA therapies does not seem to offer any advantage over standard treatment therapy.

"Under these circumstances," she adds, "it may be safer for patients if physicians to stick to standard antibiotic treatments for a couple of days to see how patients are doing rather than leaping into anti-MRSA therapy right off the bat."

In addition to Drs. Jones and Samore, Jian Ying, Vanessa Stevens, Candace Haroldson, Tao He, McKenna Nevers, Matthew Christensen, Richard Nelson, Gregory Stoddard, Brian Sauer, Peter Yarbough, Makoto Jones, Matthew Bidwell Goetz, and Tom Greene contributed to this study. The researchers received funding from Veterans Health Research & Development Service and the Centers for Disease Control and Prevention.

http://bit.ly/3cfFlSX

CT provides best diagnosis for COVID-19

Chest CT outperformed lab testing in the diagnosis of 2019 novel coronavirus disease

OAK BROOK, Ill. - In a study of more than 1,000 patients published in the journal Radiology, chest CT outperformed lab testing in the diagnosis of 2019 novel coronavirus disease (COVID-19). The

researchers concluded that CT should be used as the primary screening tool for COVID-19.

In the absence of specific therapeutic drugs or vaccines for COVID-19, it is essential to detect the disease at an early stage and immediately isolate an infected patient from the healthy population.

According to the latest guidelines published by the Chinese government, the diagnosis of COVID-19 must be confirmed by reverse-transcription polymerase chain reaction (RT-PCR) or gene sequencing for respiratory or blood specimens, as the key indicator for hospitalization.

However, with limitations of sample collection and transportation, as well as kit performance, the total positive rate of RT-PCR for throat swab samples has been reported to be about 30% to 60% at initial presentation.

In the current public health emergency, the low sensitivity of RT-PCR implies that a large number of COVID-19 patients won't be identified quickly and may not receive appropriate treatment. In addition, given the highly contagious nature of the virus, they carry a risk of infecting a larger population.

"Early diagnosis of COVID-19 is crucial for disease treatment and control. Compared to RT-PCR, chest CT imaging may be a more reliable, practical and rapid method to diagnose and assess COVID-19, especially in the epidemic area," the authors wrote.

Chest CT, a routine imaging tool for pneumonia diagnosis, is fast and relatively easy to perform. Recent research found that the sensitivity of CT for COVID-19 infection was 98% compared to RT-PCR sensitivity of 71%.

For the current study, researchers at Tongji Hospital in Wuhan, China, set out to investigate the diagnostic value and consistency of chest CT imaging in comparison to RT-PCR assay in COVID-19.

Included in the study were 1,014 patients who underwent both chest CT and RT-PCR tests between January 6 and February 6, 2020. With RT-PCR as reference standard, the performance of chest CT in diagnosing COVID-19 was assessed. For patients with multiple RT-PCR assays, the dynamic conversion of RT-PCR test results (negative to positive, and positive to negative, respectively) was also analyzed as compared with serial chest CT scans.

The results showed that 601 patients (59%) had positive RT-PCR results, and 888 (88%) had positive chest CT scans. The sensitivity of chest CT in suggesting COVID-19 was 97%, based on positive RT-PCR results. In patients with negative RT-PCR results, 75% (308 of 413 patients) had positive chest CT findings. Of these, 48% were considered as highly likely cases, with 33% as probable cases.

By analysis of serial RT-PCR assays and CT scans, the interval between the initial negative to positive RT-PCR results was 4 to 8 days.

"About 81% of the patients with negative RT-PCR results but positive chest CT scans were re-classified as highly likely or probable cases with COVID-19, by the comprehensive analysis of clinical symptoms, typical CT manifestations and dynamic CT follow-ups," the authors wrote.

Find all the latest Radiology and Radiology: Cardiothoracic Imaging COVID-19 research at Special Focus: COVID-19.

"Correlation of Chest CT and RT-PCR Testing in Coronavirus Disease 2019 (COVID-19) in China: A Report of 1014 Cases," Tao Ai, M.D., Ph.D., Zhenlu Yang, M.D., Ph.D., Hongyan Hou, M.D., Chenao Zhan, M.D., Chong Chen, M.D., Wenzhi Lv, Qian Tao, Ph.D., Ziyong Sun, M.D., Liming Xia, M.D., Ph.D.

http://bit.ly/2wf3kku

Drivers of expensive cars less likely to yield for pedestrians: UNLV study

Researchers also found that motorists overall yielded less frequently for men and non-whites

Flashing crosswalk lights are no match for flashy cars, according to a new UNLV study which found that drivers of expensive cars are least likely to stop for crossing pedestrians.

Drivers on a whole aren't all that great at stopping for pedestrians waiting at crosswalks: Of 461 cars that researchers examined, only 28 percent yielded.

But the cost of the car was a significant predictor of driver yielding, with the odds that they'll stop decreasing by 3 percent per $1,000 increase in the car's value. Researchers estimated the cost of each car using pricing categories from Kelley Blue Book.

"It says that pedestrians are facing some challenges when it comes to safety, and it's really concerning," said lead author and UNLV public health professor Courtney Coughenour.

"Drivers need to be made aware that they legally have to yield. It's hard to say whether they're not yielding because they don't know the laws or because they don't want to yield," Coughenour said. "Further study is needed to examine that. Until then, the bigger thing is driver education."

The study, which analyzed video data from an earlier UNLV study, also found that motorists overall yielded less frequently for men and people of color waiting at mid-block crosswalks than for women and whites.

It is also consistent with findings from similar studies on the topics of driver yielding behaviors associated with social class, race, and gender.

The research team said their findings are important to public health, given that pedestrian injury and survivability are low even when struck at low speeds.

According to the AAA Foundation for Traffic Safety, the average risk of severe injury for a pedestrian struck by a vehicle reaches 10 percent at an impact speed of 16 mph, 25 percent at 23 mph, 50 percent at 31 mph, 75 percent at 39 mph, and 90 percent at 46 mph.

Publication Details

"Estimated car cost as a predictor of driver yielding behaviors for pedestrians" appeared in the March 2020 issue of Journal of Transport & Health.

http://bit.ly/32xZSxu

This rainy exoplanet could be ripe for life

Nearby exoplanet with rainclouds in its atmosphere may have habitable conditions at its surface

By Daniel Clery

A nearby exoplanet with rainclouds in its atmosphere may have habitable conditions at its surface, researchers report today. The planet, dubbed K2-18b, is 124 light-years away and 2.6 times the radius of Earth. Last year, astronomers detected clouds of liquid water in the planet's hydrogen-rich atmosphere, a first for such a small planet.

K2-18b, which is midway in size between Earth and Neptune, is in the habitable zone of its star, so liquid water on its surface is possible; but no one knows what its surface is like. Researchers can't say for sure whether it has a rocky exterior and thin atmosphere, like Earth, or a dense hydrogen atmosphere above a high-pressure water-ammonia ocean and metallic core, like Neptune—conditions not at all friendly to life.

Now, a team of researchers in the United Kingdom describe in *The Astrophysical Journal Letters* how they calculated a range of possible atmospheres for the planet, based on its mass, size, and previously measured spectra of light that passed from K2-18b's star through its atmosphere. (Molecules in the planet's atmosphere absorb certain frequencies of light, so if the starlight passes through it on its way to Earth, the light's spectrum can reveal those molecules.) They then used those possibilities to limit what conditions could exist in the planet's interior. Their conclusion: The heart of K2-18b could be anything from a ball of almost pure iron with a hefty hydrogen atmosphere, to something more Neptune-like, to a water world with a lighter atmosphere and ocean conditions similar to Earth (artist's conception above).

The researchers conclude that if such a massive planet could still be habitable, seekers of life beyond our solar system might want to look beyond their usual Earth-size suspects—at worlds far larger than our small rock.

https://nyti.ms/2I7qfRq

Down on the Farm That Harvests Metal From Plants

Hyper-accumulating plants thrive in metallic soil that kills other vegetation, and botanists are testing the potential of phytomining.

By Ian Morse

Nickel-rich sap being taken from a tree in Malaysia. **Antony van der Ent**

Some of Earth's plants have fallen in love with metal. With roots that act practically like magnets, these organisms — about 700 are known — flourish in metal-rich soils that make hundreds of thousands of other plant species flee or die.

Slicing open one of these trees or running the leaves of its bush cousin through a peanut press produces a sap that oozes a neon blue-green. This "juice" is actually one-quarter nickel, far more concentrated than the ore feeding the world's nickel smelters.

The plants not only collect the soil's minerals into their bodies but seem to hoard them to "ridiculous" levels, said Alan Baker, a visiting botany professor at the University of Melbourne who has researched the relationship between plants and their soils since the 1970s. This vegetation could be the world's most efficient, solar-powered mineral smelters. What if, as a partial substitute to traditional, energy-intensive and environmentally costly mining and smelting, the world harvested nickel plants?

Dr. Baker and an international team of colleagues has set its sights on convincing the world the idea is more than just a fun thought experiment. On a plot of land rented from a rural village on the Malaysian side of the island of Borneo, the group has proved it at small scale. Every six to 12 months, a farmer shaves off one foot of growth from these nickel-hyper-accumulating plants and either burns or squeezes the metal out. After a short purification, farmers could hold in their hands roughly 500 pounds of nickel citrate, potentially worth thousands of dollars on international markets.

Now, as the team scales up to the world's largest trial at nearly 50 acres, their target audience is industry. In a decade, the researchers hope that a sizable portion of insatiable consumer demand for base metals and rare minerals could be filled by the same kind of farming that produces the world's coconuts and coffee.

Phytomining, or extracting minerals from hyper-accumulating plants, cannot fully replace traditional mining techniques, Dr. Baker says. But the technology has the additional value of enabling areas with toxic soils to be made productive. Smallholding farmers could grow on metal-rich soils, and mining companies might use these plants to clean up their former mines and waste and even collect some revenue.

"It's icing on the cake," Dr. Baker said.

The father of modern mineral smelting, Georgius Agricola, saw this potential 500 years ago. He smelted plants in his free time. If you knew what to look for in a leaf, he wrote in the 16th century, you could deduce which metals lay in the ground below.

Rufus Chaney, an agronomist at the U.S. Department of Agriculture for 47 years, invented the word "phytomining" in 1983 and with Dr. Baker helped begin the first trial in Oregon in 1996. His name is immortalized in one of the nickel-sucking plants used in the Malaysian plot.

Now, after decades behind the lock and key of patents, Dr. Baker said, "the brakes are off the system."

With patents no longer an issue, the scientists hope the technology can benefit small farmers in Malaysia and Indonesia.

“The hope is that we can show it off and have proof of concept and show people how it works, and that it works,” added Antony van der Ent, a plant scientist at the Sustainable Minerals Institute at the University of Queensland in Australia. His dissertation began the Malaysian project.

Nickel is a crucial element in stainless steel. Its chemical compounds are increasingly used in batteries for electric vehicles and renewable energies. It is toxic to plants, just as it is to humans in high doses. Where nickel is mined and refined, it destroys land and leaves waste.

In areas where soils are naturally rich in nickel, typically in the tropics and Mediterranean basin, plants have either adapted or died off. In New Caledonia, a New Jersey-size French territory in the South Pacific that has been a major source of nickel, botanists know of at least 65 nickel-loving plants.

Such plants are the most common metal-craving vegetation; others suck up cobalt, zinc and similarly crucial metals. With new electronics spurring surging demand for rare minerals, companies are exploring as far as outer space and the bottom of the ocean. Far less explored is one of humanity’s oldest technologies, the farm.

The language of literature on phytomining, or agromining, hints of a future when plant and machine live together: bio-ore, metal farm, metal crops. “Smelting plants” sounds about as incongruous as carving oxygen.

Proponents of phytomining see the greatest potential in Indonesia and the Philippines, two of the world’s biggest nickel ore producers, where hundreds of mines shovel topsoil into smelters. The two countries likely harbor many nickel-hyper-accumulating plants, but research has been scant.

Hyper-accumulators don’t just tolerate metals; their roots crave them. To what benefit? The nickel may help the plant fight off pests, or perhaps it enables the plant to more readily take up potassium, a scarce resource, from the soil. Regardless, there has been no need to genetically modify or selectively breed to increase the plants’ nickel-philia. Nature’s smelters are already as efficient as the extractive industry would want.

They have the potential to remedy the mining industry’s biggest problem: abandoned mines, which pollute waterways. A leftover mine, planted with hyper-accumulators, could salvage the remaining metals for additional revenue. That incentive could persuade companies to invest in rehabilitation or mine-waste cleanup.

Currently, the most common way to extract nickel for electronics requires intense energy — often derived from coal and diesel — and creates heaps of acidic waste. A typical smelter costs hundreds of millions of dollars and requires increasingly scarce ore that is at least 1.2 percent rich with nickel.

In contrast, plants on a small nickel farm could be harvested every six months on land where the nickel concentration is only 0.1 percent. After two decades, the roots would struggle to find enough nickel, but the land would have been sucked dry of its toxic metals, and fertile enough to support more common crops.

That the nickel crop might be so productive and lucrative has led to fears that farmers might push for opening tropical forests for cultivation, foreshadowing another case such as palm oil, a cash crop that has devastated Borneo’s native forests. But that isn’t a likely outcome, the researchers said. Areas with the most phytomining potential tend to be grassy, and few other plants are likely to grow on land selected for mineral farming.

“We can grow these plants on soils where it’s already been deforested,” Dr. Baker said. “It’s a way of putting back, rather than taking away.”

http://bit.ly/3aqwTkK

Judge Rules Unreported Clinical Trial Data Must Be Made Public

The sponsors of upwards of 1,000 clinical trials may be forced to publish data that have gone unpublished over a 10-year period.

Amy Schleunes

Afederal judge in the Southern District of New York has ruled that sponsors of clinical trials conducted between 2007 and 2017 are failing to comply with federal law if they do not post their studies' results to ClinicalTrials.gov, according to *STAT*. The decision stipulates that reporting requirements outlined in a 2017 final rule to the Food and Drug Administration Amendments Act are applicable to trials completed as far back as 2007, and not just those finished after 2017 as government agencies had mistakenly interpreted the law, reports *Endpoints News*.

"This decision brings us one step closer to what federal law requires—providing the American public with complete access to clinical trial results on drugs and medical devices approved by the FDA," the plaintiff's supervising attorney Christopher Morten tells *STAT*, adding that the ruling "makes it harder for drug companies, device manufacturers, and other trial sponsors to keep unfavorable trial results secret."

STAT notes that it had previously investigated the reporting of clinical trial data in 2015, finding that "most research institutions—including leading universities and hospitals in addition to drug companies—routinely break a law that requires them to report the results of human studies of new treatments to the federal government's ClinicalTrials.gov database." *Science* reported earlier this year that the FDA has not imposed fines for violations, nor has the National Institutes of Health withheld grant funding, despite 2017 statements by both agencies promising to enforce the law with penalties for noncompliance.

Peter Lurie, a former associate FDA commissioner, and Charles Seife, a journalism professor at New York University, brought the lawsuit before the court, arguing that the misinterpretation of the rule had negatively affected their work. "The FDA is in charge of making sure that drugs on the market are safe and effective, but without access to data about those drugs, it's nearly impossible to understand whether the agency is doing its job properly," Seife said in a statement on Tuesday, according to *STAT*.

"The court has set aside that erroneous interpretation of the law and has said that the statute means what it has always said," Morten tells *Endpoints News*. "So our hope here is that trial sponsors are going to start, finally, after years of noncompliance, reporting some of that missing data to the patients."

A spokeswoman for the FDA declined to comment to *STAT*, while a spokeswoman for the Department of Health and Human Services tells the outlet that the agency was "evaluating the Court's decision with the Department of Justice to determine our next steps."

http://bit.ly/39qGQOE

Riken institute develops test to detect coronavirus within 30 minutes

Riken have developed a technology that can detect COVID-19 in only 10 to 30 minutes.

YOKOHAMA – The Kanagawa Prefectural Institute of Public Health and the government-affiliated research institute Riken said Thursday that they have developed a technology that can detect the COVID-19 coronavirus in only 10 to 30 minutes.

Kanagawa Gov. Yuji Kuroiwa told a news conference the same day that he will seek special state support so that the new technology, which is still in the research phase, can be used widely.

The polymerase chain reaction (PCR) test method, which is widely used at present, takes one to two hours for results to become available.

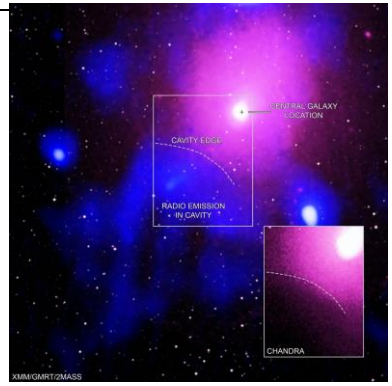
The newly developed technology is at least on par with PCR in terms of accuracy, according to the prefectural institute and Riken.
The institutes confirmed the validity of the new method using COVID-19 samples collected from people who were on the Diamond Princess cruise ship, which has been quarantined off Yokohama. Hundreds of people aboard the ship have been found infected with the virus, which originated in China.
The institutes will conduct further research on the technology as regulatory approval will be required before the testing method can be put it into practical use.
“We’ve taken a step toward practical use” although the work is still in an early stage, said Kengo Usui, who leads Riken’s unit developing the new technology.

http://bit.ly/2vsz31B

Astronomers detect biggest explosion in the history of the universe

Scientists studying a distant galaxy cluster have discovered the biggest explosion seen in the Universe since the Big Bang.

The blast came from a supermassive black hole at the centre of a galaxy hundreds of millions of light-years away.
It released five times more energy than the previous record holder.
Professor Melanie Johnston-Hollitt, from the Curtin University node of the International Centre for Radio Astronomy Research, said the event was extraordinarily energetic.
"We've seen outbursts in the centres of galaxies before but this one is really, really massive," she said. "And we don't know why it's so big. "But it happened very slowly--like an explosion in slow motion that took place over hundreds of millions of years."
The explosion occurred in the Ophiuchus galaxy cluster, about 390 million light-years from Earth. It was so powerful it punched a cavity in the cluster plasma--the super-hot gas surrounding the black hole.



Lead author of the study Dr Simona Giacintucci, from the Naval Research Laboratory in the United States, said the blast was similar to the 1980 eruption of Mount St. Helens, which ripped the top off the mountain. "The difference is that you could fit 15 Milky Way galaxies in a row into the crater this eruption punched into the cluster's hot gas," she said.

This extremely powerful eruption occurred in the Ophiuchus galaxy cluster, which is located about 390 million light-years from Earth. Galaxy clusters are the largest structures in the Universe held together by gravity, containing thousands of individual galaxies, dark matter, and hot gas. **Credit: X-ray: NASA/CXC/Naval Research Lab/Giacintucci, S.; XMM:ESA/XMM; Radio: NCRA/TIFR/GMRTN; Infrared: 2MASS/UMass/IPAC-Caltech/NASA/NSF**

Professor Johnston-Hollitt said the cavity in the cluster plasma had been seen previously with X-ray telescopes.
But scientists initially dismissed the idea that it could have been caused by an energetic outburst, because it would have been too big.
"People were sceptical because the size of outburst," she said. "But it really is that. The Universe is a weird place."
The researchers only realised what they had discovered when they looked at the Ophiuchus galaxy cluster with radio telescopes.
"The radio data fit inside the X-rays like a hand in a glove," said co-author Dr Maxim Markevitch, from NASA's Goddard Space Flight Center. "This is the clincher that tells us an eruption of unprecedented size occurred here."
The discovery was made using four telescopes; NASA's Chandra X-ray Observatory, ESA's XMM-Newton, the Murchison Widefield Array (MWA) in Western Australia and the Giant Metrewave Radio Telescope (GMRT) in India.
Professor Johnston-Hollitt, who is the director of the MWA and an expert in galaxy clusters, likened the finding to discovering the first

dinosaur bones. "It's a bit like archaeology," she said. "We've been given the tools to dig deeper with low frequency radio telescopes so we should be able to find more outbursts like this now."

The finding underscores the importance of studying the Universe at different wavelengths, Professor Johnston-Hollitt said.

"Going back and doing a multi-wavelength study has really made the difference here," she said.

Professor Johnston-Hollitt said the finding is likely to be the first of many. "We made this discovery with Phase 1 of the MWA, when the telescope had 2048 antennas pointed towards the sky," she said. "We're soon going to be gathering observations with 4096 antennas, which should be ten times more sensitive." "I think that's pretty exciting."

ICRAR

The International Centre for Radio Astronomy Research (ICRAR) is a joint venture between Curtin University and The University of Western Australia with support and funding from the State Government of Western Australia.

THE MURCHISON WIDEFIELD ARRAY

The Murchison Widefield Array (MWA) is a low-frequency radio telescope and is the first of four Square Kilometre Array (SKA) precursors to be completed. A consortium of partner institutions from seven countries (Australia, USA, India, New Zealand, Canada, Japan, and China) financed the development, construction, commissioning, and operations of the facility. The MWA consortium is led by Curtin University.

Publication:

'Discovery of a giant radio fossil in the Ophiuchus Galaxy Cluster', published in The Astrophysical Journal *on February 27th, 2020.*

http://bit.ly/3ad6S5F

Drug used for breast, kidney cancers may also extend survival for head and neck cancers

May present a new treatment option for a group of patients whose survival rates have not improved in more than 30 years.

Scottsdale, AZ - A targeted therapy drug used for breast and kidney cancers may also extend progression-free survival for patients with advanced head and neck cancer who are at high risk for recurrence after standard treatment. Patients enrolled in a randomized phase II trial who received the mTOR inhibitor everolimus were more likely to be cancer-free a year after therapy than those who took a placebo drug, and the benefit persisted for those with mutations in their TP53 gene. The findings may present a new treatment option for a group of patients whose survival rates have not improved in more than 30 years.

The study will be presented at the 2020 Multidisciplinary Head and Neck Cancers Symposium, taking place February 27-29 in Scottsdale, Arizona.

"While cure rates tend to be upwards of 85% for patients with head and neck cancers associated with HPV, they tend to be less than 40% for patients with disease related to smoking," said lead author Cherie-Ann O. Nathan, MD, professor and chair of otolaryngology/head and neck surgery at Louisiana State University (LSU) Health Shreveport and director of head and neck surgery at Feist-Weiller Cancer Center. "These patients are recurring most often, and their survival rates have not changed in decades, despite advances in surgery, radiation therapy and chemotherapy."

To address this disparity, the researchers focused on patients with advanced, HPV-negative head and neck squamous cell carcinoma (HNSCC), or HPV-positive disease and smoking history of more than 10 pack-years, and enrolled 52 patients to receive up to one year of either everolimus or a placebo drug. Eligible patients had to be free of disease after either definitive treatment with chemoradiation therapy or surgery followed by chemoradiation. Researchers then tracked how long they remained cancer-free with additional therapy.

After a year, 81% of patients on everolimus remained progression-free, compared to 57% of those in the placebo group (p=0.039). Dr. Nathan clarified that this timepoint was not stipulated a priori and is a post-hoc analysis. Two-year progression-free survival, which was the primary endpoint, continued to favor everolimus but was no

longer significant. Subset analysis determined that for patients with TP53 mutations, the survival difference remained significant for an additional year after they stopped immunotherapy (two-year PFS of 70% vs 22.5%, p=0.036). The difference was not significant at two years for patients without the mutation.

While TP53 mutations occur in almost 80% of HPV-negative, smoking related cases of HNSCC, the potential link between TP53, the mTOR pathway and survival was a surprise to the researchers. "There's really no drug that targets TP53, and so we've never had a targeted therapy for it or considered it an actionable mutation," she said.

Sixteen of the 28 patients on everolimus and seven of the 24 patients on the placebo drug experienced Grade 3 or higher toxicities, including three and five serious adverse events, respectively. Dr. Nathan said the drug's tolerability indicates that it may have potential as longer-term maintenance therapy to delay recurrence for high-risk patients.

"Although the sample size is small, as it closed due to lack of accrual, these finding indicate that patients at high risk for tumor relapse could be given mTOR inhibitors to stall progression and keep any residual cancer cells from growing. Our hope is that head and neck cancer can be treated as chronic disease, similar to some breast cancers," she explained. "Everolimus is used for patients with breast cancer or renal cell cancer for extended periods without major side effects, and there is potential for patients with TP53-mutated head and neck disease to see a survival benefit, as well."

Additional trials are needed to confirm the link between TP53 and survival, as well as to determine the safety of keeping patients with HNSCC on the drug for multiple years.

Dr. Nathan, who is also the current President of the American Head and Neck Society, will present "Multi-Institutional Randomized Double-Blind Phase II Trial of Everolimus vs. Placebo as Adjuvant Therapy in Patients with Locally Advanced Squamous Cell Cancer of the Head and Neck" (Abstract 5) today during the symposium's Plenary Session. The investigator-initiated trial was sponsored by the University of Chicago and funded by Novartis. Email press@astro.org for a copy of the abstract or presentation slides from the meeting.

Attribution to the 2020 Multidisciplinary Head and Neck Cancers Symposium requested in all coverage. This release includes updated information not available in the abstract.

http://bit.ly/38bypmH

Gene loss more important in animal kingdom evolution than previously thought

Study reveals evolution does not always mean more complexity

Scientists have shown that some key points of animal evolution -- like the ones leading to humans or insects -- were associated with a large loss of genes in the genome.

The study, published in *Nature Ecology & Evolution*, compared over 100 genomes to investigate what happened at the gene level during the evolution of animals after their origin.

During evolution, organisms can gain new genes to perform new functions, lose other genes that are not used anymore, and recycle old ones into new functions.

Previous studies have shown that the acquisition of new genes played a major role in the origin of the animal kingdom, and it is assumed that most organisms become more complex by acquiring new genes.

Dr Jordi Paps from the University of Bristol together with PhD student, Cristina Guijarro-Clarke at the University of Essex, and Professor Peter Holland from the University of Oxford, discovered that gene loss has actually been more important during the evolution of the animal kingdom than previously thought.

Animals can be split into major evolutionary lineages. One is deuterostomes: comprising humans and other vertebrates as well as sea stars or sea urchins. Another is ecdysozoans: encompassing the largest group of animals, the arthropods (insects, lobsters, spiders, millipedes), as well as other moulting animals like roundworms.

These two lineages include some of the animals considered to be more complex.

However, the research team's analyses has shown that the respective last common ancestors of deuterostomes and ecdysozoans suffered unprecedented levels of gene losses, and that the increase in complexity or diversity of species is not always coupled with a rise in the number of new genes.

Dr Jordi Paps, lead author and Lecturer from Bristol's School of Biological Sciences, explained: "A larger implication is that the evolution of the animal kingdom is not driven by an increase in the number of genes, and in evolution does not invariably mean becoming more complex.

"We are planning to use the same type of approach to study how the genomes of parasitic animals, such as taenia or roundworms, lose and gain genes to see if we can find therapeutic targets to fight the diseases caused by these parasites."

The next step for the research would be to see if this pattern is also seen in other major lineages in the tree of life, other than animals.

Paper

'Widespread patterns of gene loss in the evolution of the animal kingdom' by Cristina Guijarro-Clarke, Peter W. H. Holland and Jordi Paps in Nature Ecology & Evolution

http://bit.ly/2vfV0Bb

First-ever pathology of the early phase of lung infection with the 2019 novel coronavirus (COVID-19)

First study to describe the pathology of disease caused by SARS-CoV-2, or COVID-19 pneumonia

Denver--An international team of clinicians and researchers for the first time have described the pathology of the SARS-CoV-2, or coronavirus, and published their findings in the *Journal of Thoracic Oncology*, the journal of the International Association for the Study of Lung Cancer.

The article's senior author, Shu-Yuan Xiao, M.D., from the University of Chicago Medicine in Chicago, teamed up with a small group of clinicians from the Zhongnan Hospital of Wuhan University, in Wuhan, China.

"This is the first study to describe the pathology of disease caused by SARS-CoV-2, or COVID-19 pneumonia, since no autopsy or biopsies had been performed thus far," Dr. Xiao said. "This would be the only descriptions of early phase pathology of the disease due to this rare coincidence. There would be no other circumstance that this will happen. Autopsies will only show late or end stage changes of the disease."

The article describes two patients who recently underwent lung lobectomies for adenocarcinoma and were retrospectively found to have had COVID-19 at the time of surgery.

Pathologic examinations revealed that, apart from the tumors, the lungs of both patients exhibited edema, proteinaceous exudate, focal reactive hyperplasia of pneumocytes with patchy inflammatory cellular infiltration, and multinucleated giant cells. Fibroblastic plugs were noted in airspaces.

"Since both patients did not exhibit symptoms of pneumonia at the time of surgery, these changes likely represent an early phase of the lung pathology of COVID-19 pneumonia," Dr. Xiao said.

CASE 1 was a female patient of 84 years of age who was admitted for treatment evaluation of a tumor measuring 1.5 centimeters in the right middle lobe of the lung. The tumor was discovered on chest CT scan at an outside hospital. She had a past medical history of hypertension for 30 years, as well as type 2 diabetes.

Despite comprehensive treatment, assisted oxygenation, and other supportive care, the patient's condition deteriorated, and she died. Subsequent clinical information confirmed that she was exposed to another patient in the same room who was subsequently found to be infected with the 2019 novel coronavirus.

CASE 2 was a male patient of 73 years of age, who presented for elective surgery for lung cancer, in the form of a small in the right lower lobe of the lung. He had a past medical history of hypertension for 20 years, which had been adequately managed. Nine days after lung surgery, he developed a fever with dry cough, chest tightness, and muscle pain. A nucleic acid test for SARS-CoV-2 came back as positive.

He gradually recovered and was discharged after twenty days of treatment in the infectious disease unit.

According to the study, these two incidences also typify a common scenario during the earlier phase of the SARS-CoV-2 outbreak, during which a significant number of healthcare providers became infected in hospitals in Wuhan, and patients in the same hospital room were cross-infected, as they were exposed to unknown infectious sources.

The presence of early lung lesions days before the patients developed symptoms, corresponds to the long incubation period (usually 3-14 days) of COVID-19.

Making it difficult to prevent transmission during the early days of this outbreak, as many healthcare workers in Wuhan became infected, when they were seeing patients without sufficient protection, according to Dr. Xiao. As of today, more than 15 doctors in Wuhan died of COVID-19, from infections while they were taking care of patients. Some of them were previously healthy and as young as 29 years old.

"We believe it is imperative to report the findings of routine histopathology for better understanding of the mechanism by which the SARS-CoV-2 causes lung injury in the unfortunate tens and thousands of patients in Wuhan and worldwide," Dr. Xiao said. Further studies by Dr. Xiao's team and collaborators on COVID-19 pathology through postmortem biopsies are ongoing, which should provide data on the late changes of this disease.

https://wb.md/2TaDl7a

Medical Mystery: Beer-Linked Kidney Failure and Paralysis

A middle-aged man with abdominal pain, vomiting, constipation, and unexplained acute kidney injury

Donavyn Coffey

Eduardo Valle, MD, a second-year medical resident in Brazil, was sitting in the hospital cafeteria with his fellow residents in late December when they heard news of the emergency department's newest patient. A middle-aged man with abdominal pain, vomiting, constipation, and unexplained acute kidney injury had just arrived from a smaller hospital 80 miles away.

160 miles to the north, the man's son-in-law was in the intensive care unit of another hospital in the city of Belo Horizonte with symptoms that were identical but progressing faster than the older man's, a fellow resident told Valle. The son-in-law was showing signs of quadriplegia and required mechanical ventilation.

The residents scattered from the cafeteria to relay the news to their attendings. In what seemed like minutes, their hospital in the city of Juiz de Fora was abuzz with talk of the unexplained illness. "We thought it could be contagious," Valle told Medscape. "Fear was in the air."

Valle volunteered to help the nephrology team research the case. Testing showed the older man had normal blood cell counts, elevated lactic acid, and hepatitis without liver dysfunction. His cranial CT scans appeared normal. After a few days, none of the team's leads had panned out and the father's limbs started to lose function. Meanwhile, three other people from the son-in-law's neighborhood were also admitted to the ICU in Belo Horizonte with similar symptoms.

The strange, linked cases were the start of a medical mystery that took the doctors' intense collaboration to solve as they tried to save

their patients. Seeking help, Valle posted the case on Medscape Consult, a global crowdsourced social media platform on which clinicians share and discuss real cases. "Is this an unknown infection or intoxication?" he wrote. "Any thoughts?"

Doctors from around the world responded to his case suggesting botulism, rhabdomyolysis, and lead poisoning, but none of the suggestions could fully explain the patients' symptoms. Then the patients' family mentioned that the men had shared some beer over the Christmas holiday. A WhatsApp discussion between the doctors in Juiz de Fora and Belo Horizonte confirmed that all five patients drank the same brand of beer before their symptoms started. The doctors began rapidly sharing contamination case studies via the WhatsApp channel until one case of nausea, acute kidney injury, and cranial nerve palsy following a "mystery drink" seemed to match what they were seeing.

A toxicology investigation by police confirmed their suspicion: Diethylene glycol, a poisonous industrial solvent used in antifreeze, was found in beer bottles from the patients' homes and blood samples from four of the patients. But the resolution came too late for Valle's patient. The man died; his kidney biopsy showed acute tubular necrosis and his blood contained diethylene glycol.

Police traced the source of diethylene glycol exposure to a local craft brewer in Belo Horizonte.

The man Valle treated was one of more than 30 reported cases and 6 deaths from the diethylene glycol poisoning outbreak in Brazil's state of Minas Gerais, where Juiz de Fora and Belo Horizonte are located. Police identified the source as a craft brewer, Belorizontina Backer. Brazil's Ministry of Agriculture called the contamination "systemic" in a statement and stopped all production at the brewery until it could be remedied.

A Rare and Tricky Diagnosis

The most well-known diethylene glycol poisoning in the US occurred in 1937, when a pharmaceutical company, S.E. Massengill Co, used it as a solvent in a liquid formulation of the antibiotic sulfanilamide. More than 100 people in the US died after ingesting it, and public outcry prompted the 1938 Federal Food, Drug, and Cosmetic Act that authorized the US Food and Drug Administration to require evidence of safety for new drugs, issue standards for food, and conduct factory inspections. The cases in Brazil were the first recorded diethylene glycol poisonings in the country's history, Valle said.

Renal failure and severe neurological symptoms are pretty typical of diethylene glycol poisoning, Andrew Stolbach, MD, MPH, a medical toxicologist at Johns Hopkins University in Baltimore, Maryland, told Medscape. But because there's no direct test for the substance and such poisonings are rare, the diagnosis can be tricky for most doctors, he said.

"I've only been involved in one case, and that's probably more than most people," Stolbach said. In 2006, he treated a patient who ingested the toxic alcohol via an expectorant that she brought back from Panama.

Early detection is essential to treating diethylene glycol poisoning and preventing its devastating neurologic symptoms. But to do that, "you have to have a high degree of suspicion," Stolbach said.

In the early stages, patients will appear drunk, though perhaps more quickly than usual, according to Eric Judd, MD, a nephrologist at the University of Alabama in Birmingham. The first evidence of diethylene glycol poisoning is a gap in blood osmolarity — one significantly greater than in ethanol intoxication. Running a metabolic panel and doing some calculations to find an osmolarity

gap is one way to detect diethylene glycol poisoning before dangerous symptoms set in, Judd said. Essentially, you'd only find it if you were looking, he said.

After a reported outbreak, doctors nearby need to be acutely mindful of anyone in the ER who appears intoxicated and may have gastrointestinal issues, Judd said.

If spotted early, it's possible that a dose of the alcohol dehydrogenase inhibitor fomepizole could be enough to treat diethylene glycol poisoning, Stolbach said. Preventing the breakdown of diethylene glycol shields the body from its metabolites, which are far more dangerous than the toxic alcohol itself. The severity of symptoms increases as the body metabolizes diethylene glycol, Stolbach told Medscape.

"Once you've made the acid metabolites, we are concerned that you're now on your way to renal failure and stopping new production of metabolites [with fomepizole] won't change that," Stolbach said. At that point, the patient will require hemodialysis, which will only protect against further symptoms if diethylene glycol and its metabolites are filtered out before they damage the nervous system, he said.

Because of the delay between ingestion and symptoms, it can take a while for doctors and public health workers to figure out why and how an outbreak is happening. But "even if we can't offer much to those with advanced neurological symptoms," these poisonings rarely occur as single cases, Stolbach said. There are likely others that physicians will be able to help.

The son-in-law of Valle's patient was diagnosed late. He remains in critical condition in the ICU relying on hemodialysis, mechanical ventilation, and a vasopressor. For more than 2 weeks he showed only discreet eye movement, his nephrologist Fabricio Marques, MD, told Medscape. "So, his ability to nod and communicate is a great victory. If he manages to survive he will most likely have neurological sequelae."

Soon after diethylene glycol was identified as the culprit in Valle's patient, the Minas Gerais State Society of Nephrology issued a warning to all doctors about the risk of contamination and potential symptoms. No other people with diethylene glycol poisoning came to the hospital in Juiz de Fora. Marques saw three other patients with the poisoning and was involved indirectly with at least seven other patients at different hospitals in the city.

For Valle, the takeaway of the case was more than clinical. He observed his advisors modeling collaboration on the cusp of a crisis. The WhatsApp group between the doctors treating the father and those who treated the son-in-law was critical to the case, helping identify the beer as a common exposure and allowing the doctors to discuss a myriad of possible diagnoses before pinpointing the toxin. "I learned when we don't know what's happening with our patient, we have to ask for help," Valle said.

http://bit.ly/2wUK1NO

A Bold and Controversial Idea for Making Breast Milk

The obsession with breastfeeding has inspired a start-up to make human milk outside the human body.

Sarah Zhang

The inconvenient truth about breastfeeding is that breasts are, invariably, attached to a person. A person who could get too sick to breastfeed. A person who might have to go back to work within two weeks of giving birth, because U.S. law does not mandate paid leave. A person who might have no place to pump at work, despite a law that does actually mandate such a room.

stilllifephotographer / Claudia Totir / Getty / Katie Martin / The Atlantic

For understandable and frustrating reasons, many mothers who want to breastfeed—who have internalized years of hearing "Breast is best"—simply cannot.

Enter: a bioreactor of lactating human breast cells.

A small start-up called Biomilq recently announced it has managed to grow human mammary cells that make at least two of the most common components of breast milk: a protein called casein and a sugar called lactose. This is the first step, the company hopes, to making human milk outside the human body.

Breast milk is of course far, far more complex than just casein and lactose. It is made up of at least hundreds of different components: a multitude of proteins, fats, and sugars, but also antibodies, hormones, and beneficial bacteria. Biomilq's founders, Leila Strickland and Michelle Egger, say that they seek to eventually make milk that is "nutritionally" but not necessarily "immunologically" close to breast milk. Experts I spoke with said that mammary cells in a bioreactor simply could not replicate the full complexity and benefits of breast milk. One researcher laughed at the idea.

Biomilq does seem to be onto something though, at least culturally. Since the postwar days of doctors pushing formula as the superior "scientific" option, the conventional and medical wisdom has swung in the opposite direction—to the point where women often feel guilty for being unable to breastfeed. "There's just a feeling of failure: *I can't do this for my child. This is really important*," said Maryanne Perrin, a breast-milk researcher at the University of North Carolina at Greensboro, who has studied women trying to buy breast milk online for their children. "I heard a lot of anxiety in the voices and comments," she added. In other words, there is definitely a demand for human breast milk.

The idea for Biomilq, in fact, came out of Strickland's own struggles to breastfeed as a new mom. Her son had trouble latching after he was born, and she wasn't making enough milk. "During those months of life, my whole world revolved around whether or not my body would produce enough of this food," she says. She wished for an option that was not formula. Strickland has a background in cell biology, so she naturally wondered: *What about breast cells?*

In 2013, she began growing mammary cells in a tiny lab space in North Carolina, and in 2019, she met Egger, a student at Duke's business school and a former food scientist at General Mills, who had worked on products such as Go-Gurt. They officially launched Biomilq late last year to make lab-grown human milk—or as they prefer to call it, "cultured breastmilk." Another start-up based in Singapore, TurtleTree Labs, recently announced it is trying to re-create cow and human milk with cells as well.

Human milk is currently available for sale, but it is not easy to buy. Officially, parents can go to a milk bank to buy donated breast milk that has been screened and pasteurized—but this requires a doctor's prescription and can go for a hefty $4 or $5 an ounce to cover processing costs. (Milk banks also prioritize donor milk for sick or preterm infants in the hospital, for whom cow-based formula is particularly prone to causing a serious gut disease called necrotizing enterocolitis.) Unofficially, parents can go on Facebook or Craigslist or another online marketplace where women share or sell extra breast milk. These markets are cheaper and more convenient, but they're also unregulated. Donors largely follow the honor system for disclosing medications and other health information. Meanwhile, formula is cheap, safe, and widely available in grocery stores. Biomilq promises to combine the "nutrition of breastmilk" with the "practicality of formula."

It's hard to say, at this nascent stage, exactly how still-hypothetical breast milk made by cells in a bioreactor would compare with formula. The cultured human-milk proteins could be more suitable

in a baby's gut than dairy proteins, and sugars specific to human milk could help feed a baby's new gut microbes.

But milk from cells in a bioreactor would still be missing some key components of true breast milk—for the simple reason that the components of breast milk don't come from the breast alone. Natalie Shenker, a breast-milk researcher at Imperial College London, enumerated some examples: Antibodies, which transfer immunity against pathogens from mother to baby, come from the mother's own immune cells in her blood. Hormones, which may shape the baby's brain and behavior, from her endocrine system. Fats, which make up a substantial portion of the calories in milk, from her diet and own stored fatty tissue. (Biomilq suggests that these fats could be supplemented in cultured cells.) Beneficial bacteria that help populate the baby's gut come from the mother's own microbiome. The whole body is responsible for the production of what we call breast milk.

The exact cocktail of protein, sugar, fats, antibodies, hormones, and bacteria in breast milk can change from day to day and even hour to hour. It can change in response to the baby's needs. One hypothesis suggests that a sick baby can communicate via "retrograde milk flow"—more memorably termed "baby spit backwash"—to change the composition of breast milk to help the baby fight off disease. Breast milk is complex and dynamic. Perrin said she applauds any efforts to improve infant nutrition, but "to re-create breast milk in a test tube, I think we're just so far away from that."

Growing enough mammary cells to make any milk at scale is also a huge technical challenge. These cells require expensive nutrients and are incredibly prone to contamination from bacteria. The recent interest in lab-grown meat has prompted a number of companies to work on these problems, but breast milk is likely to face higher scrutiny, deservedly so, because it is for babies. Shenker, who is familiar with the challenges of growing mammary cells from her own research, wondered whether re-creating milk was the best use of resources. Why go through the expensive, unproven process of growing cells to make milk in a bioreactor, she asked, when we already know how to get actual milk—nutritionally complete—from a donor? The problem is not a lack of breast milk on Earth, but a lack of access and distribution.

When I contacted breast-milk researchers to ask about lab-grown breast milk, they ended up changing the topic to barriers faced by women who want to breastfeed. "A lot of moms aren't getting the support they need," said Meghan Azad, a breast-milk researcher at the University of Manitoba. Breastfeeding takes skill, which was lost for a generation when formula was dominant. It takes workplaces that give women the time and flexibility to breastfeed or pump. And it takes a culture that doesn't shame women for breastfeeding in public. And although society makes it hard for women to breastfeed, it also tells them that "Breast is best." The result is a nearly impossible set of expectations.

The appeal of Biomilq is that it's supposed to close the gap—that frustrating space between what mothers are expected to do and what most can realistically do. "We're done making trade-offs between our baby's health, our wellbeing, and the environment," the company's website proclaims. But it also puts the company in the position of both touting the benefits of breastfeeding … and telling women it's okay not to breastfeed. Egger says Biomilq is not about replacing breastfeeding, but supplementing it. "If women can breastfeed even part of the time, they should be wholeheartedly supported in doing that," she says. "We just see this as an opportunity for them to actually continue to enable that process and not having to feel guilt or shame or frustration." She draws a particular contrast with formula companies, which have used aggressive tactics to get into hospitals and influence breastfeeding recommendations. Over the course of the 20th century, these

standardized cans of formula often came to replace the highly personalized breast milk of mothers.

The irony is that if human milk from cells, as a concept, really does take off one day, the more successful it is, the more likely it is to become formula 2.0: another practical, standardized, and commercial product. In fact, formula companies are already adding sugars called "human milk oligosaccharides" to their products, to sell formula that they can say is closer to breast milk.

http://bit.ly/2I71y83

Newts and frogs light up like glow sticks under the right light

Shine the right type of light and they will light up like glow sticks

By Rodrigo Pérez Ortega Feb. 27, 2020 , 11:00 AM

At first glance, most salamanders don't stand out: Their mottled, earth-toned skin helps them blend into the background of forests and streams around the world. But shine the right type of light at them, and they will light up like glow sticks.

Jennifer Y. Lamb and Matthew P. Davis.

That's the finding of a new study, which reveals for the first time that most amphibians, from salamanders to frogs, have biofluorescence, a trait in which fluorescent compounds in the body absorb surrounding light and re-emit it at specific wavelengths, including red, green, and blue. Previously, swell sharks, corals, and some fish were shown to glow when the right light hit, but only a few land-dwelling animals were known to biofluoresce.

In the new study, scientists placed specimens from 32 species—including salamanders; frogs; and limbless, wormlike amphibians known as caecilians—onto a dark background and shone a blue or ultraviolet light on them. Then, they took pictures using a digital camera with a filter that captures green to yellow wavelengths. The researchers found that all of the animals were biofluorescent, they report today in *Scientific Reports*.

Although there were some differences, such as the intensity of the color or the body parts that glowed, they all emitted a greenish to yellow light from their skin (like the alpine newt, above). Some had glittering bones (one salamander's finger bones flashed neon green, for example), and others had sparkling skin mucus and even urine.

This widespread occurrence suggests biofluorescence appeared early in the evolutionary history of amphibians, the researchers say. But why it appeared is another matter entirely. Although some animals use biofluorescence to find mates or communicate, scientists still aren't exactly sure how or why amphibians glow. But, they say, it could help them locate each other under the low light of their natural environments.

http://bit.ly/2PAmEzN

The co-evolution of plants and humans

Botanical historian puts new twist on plant domestication.

By Natalie Parletta

We think we're so clever, but perhaps we underestimate plants.

Edible flora have long evolved ways to move seeds away from their parents to survive and thrive – and humans are just another part of their grand plan, argues Robert Spengler from the Max Planck Institute in Germany.

"Note that if the apple does not fall far from the tree, then the apple seedlings will be overshadowed by the parent tree and not survive," he says.

"Therefore, the apple tree put extensive amounts of energy into producing high-sugar fruits in order to entice animals to spread the seeds."

This included the earliest hominids, long before humans started consciously domesticating plants through breeding, Spengler writes in the journal *Trends in Plant Science*.

A largely theoretical paper, it was inspired by early scholars of evolution such as Darwin and Humboldt – and many of his ideas came to fruition while sitting across from the Schiller Garden House in Jena, where Humboldt famously spend his summers debating similar concepts before conceiving of the cosmos.

"I think the domestication of plants and animals is one of the most important factors in the demographic shifts and cultural changes that have led humanity into the modern world," he says. "Therefore, a solid understanding of how this process occurred is essential when studying humanity."

The manuscript draws from paleontological data to highlight parallels between the evolution of seed-dispersal traits in the wild and domestication traits in the fields of early farmers who started intentionally breeding them.

The phenomenon of parallel evolution also appears in the traits of early domestication across different crop species as humans cultivated and harvested them, producing similar selective pressures – known as "domestication syndrome". For example, grass crops such as wheat, barley, rice and oats developed a tough rachis (the plant's stem that holds the cereal grain to the ear) while legumes, such as peas, lentils and kidney beans, evolved a tough pod.

Winding back to the last Ice Age, Spengler extends his vision beyond these popular crops, noting that megafauna – including humans – were pivotal for spreading wild fruits and enabling them to proliferate.

Bright red cherries, for instance, evolved to attract birds with red-green colour vision who then eat the fruit and drop the seed elsewhere. Larger fruits, unrelated to each other, evolved in parallel to recruit larger animals to disperse their seeds.

Megafaunal mammals may also have facilitated the dispersal of small-seeded grains like quinoa, millet and buckwheat, Spengler posits; the small wild seeds adapted to allow animals to graze on them and pass easily through their digestive systems before evolving larger, thinner coats to enable humans to disperse them more efficiently. "Humans are powerful seed dispersers," he says, "and plants will readily evolve new traits to spread their seeds and colonise new areas more successfully."

Spengler suggests therefore that scholars studying plant domestication need to let go of preconceptions around human intentionality and agency to better understand plant evolution.

"Domestication is not a great human innovation; it is an extension of a natural process.

"By modelling domestication as an equivalent process to evolution in the wild and setting aside the idea of conscious human innovation, we can more effectively study the questions of why and how this process occurred."

http://bit.ly/32KyA7h

New sense discovered in dog noses: the ability to detect heat

Dogs' noses just got a bit more amazing.

By Virginia Morell

Not only are they up to 100 million times more sensitive than ours, they can sense weak thermal radiation—the body heat of mammalian prey, a new study reveals. The find helps explain how canines with impaired sight, hearing, or smell can still hunt successfully.

"It's a fascinating discovery," says Marc Bekoff, an ethologist, expert on canine sniffing, and professor emeritus at the University of Colorado, Boulder, who was not involved in the study. "[It] provides yet another window into the sensory worlds of dogs' highly evolved cold noses."

The ability to sense weak, radiating heat is known in only a handful of animals: black fire beetles, certain snakes, and one species of mammal, the common vampire bat, all of which use it to hunt prey.

Most mammals have naked, smooth skin on the tips of their noses around the nostrils, an area called the rhinarium. But dogs' rhinaria are moist, colder than the ambient temperature, and richly endowed with nerves—all of which suggests an ability to detect not just smell, but heat.

To test the idea, researchers at Lund University and Eötvös Loránd University trained three pet dogs to choose between a warm (31°C) and an ambient-temperature object, each placed 1.6 meters away. The dogs weren't able to see or smell the difference between these objects. (Scientists could only detect the difference by touching the surfaces.) After training, the dogs were tested on their skill in double-blind experiments; all three successfully detected the objects emitting weak thermal radiation, the scientists reveal today in *Scientific Reports*.

Next, the researchers scanned the brains of 13 pet dogs of various breeds in a functional magnetic resonance imaging scanner while presenting the pooches with objects emitting neutral or weak thermal radiation. The left somatosensory cortex in dogs' brains, which delivers inputs from the nose, was more responsive to the warm thermal stimulus than to the neutral one. The scientists identified a cluster of 14 voxels (3D pixels) in this region of the dogs' left hemispheres, but didn't find any such clusters in the right, and none in any part of the dogs' brains in response to the neutral stimulus.

Together, the two experiments show that dogs, like vampire bats, can sense weak hot spots and that a specific region of their brains is activated by this infrared radiation, the scientists say. They suspect dogs inherited the ability from their ancestor, the gray wolf, who may use it to sniff out warm bodies during a hunt.

"The study is consistent with other research that describes the combined dog nose and brain as a sophisticated platform for processing a broad range of signals," says Gary Settles, an emeritus professor of mechanical engineering at Pennsylvania State University, University Park, who has studied dogs' sniffing abilities. He doubts, however, "that the dog rhinarium can distinguish patterns of hot and cold objects at a distance," suggesting dogs' thermal detection skills may not be useful for long distance hunting. "[T]hat needs further study."

If nothing else, the work suggests the extraordinary skills of the sled dog Buck, who tracked prey "not by sight or sound or smell, but by some other and subtler sense" in Jack London's *Call of the Wild*, aren't completely fictional after all.

http://bit.ly/2PBx41M

Cartilage cells, chromosomes and DNA preserved in 75-million-year-old baby duck-billed dinosaur

Microscopic analyses of skull fragments from nestling dinosaurs

Microscopic analyses of skull fragments from these nestling dinosaurs were conducted by Alida Bailleul at the Museum of the Rockies.

In one fragment she noticed some exquisitely preserved cells within preserved calcified cartilage tissues on the edges of a bone. Two cartilage cells were still linked together by an intercellular bridge, morphologically consistent with the end of cell division (see left image below). Internally, dark material resembling a cell nucleus was also visible. One cartilage cell preserved dark elongated structures morphologically consistent with chromosomes (center image below). "I couldn't believe it, my heart almost stopped beating," Bailleul says.

Bailleul and Schweitzer, together with lab director Wenxia Zheng, sought to determine whether original molecules were also preserved in this dinosaur cartilage. The team performed immunological and histochemical analyses on the skull of another nestling Hypacrosaurus from that same nesting ground in Schweitzer's North Carolina laboratory.

The team found that the organic matrix surrounding the fossilized cartilage cells reacted to antibodies of Collagen II, the dominant protein in cartilage in all vertebrates. "This immunological test supports the presence of remnants of original cartilaginous proteins in this dinosaur," Schweitzer says.

The researchers also isolated individual Hypacrosaurus cartilage cells and applied two DNA-stains, DAPI (4?,6-diamidino-2-phenylindole) and PI (propidium iodide). These bind specifically to DNA fragments in extant material, and some of the isolated dinosaur cells showed internal, positive binding in the same pattern as seen in modern cells, suggesting some original dinosaur DNA is preserved (see below, right image).

"These new exciting results add to growing evidence that cells and some of their biomolecules can persist in deep-time. They suggest DNA can preserve for tens of millions of years, and we hope that this study will encourage scientists working on ancient DNA to push current limits and to use new methodology in order to reveal all the unknown molecular secrets that ancient tissues have" Bailleul says.

The possibility that DNA can survive for tens of millions of years is not currently recognized by the scientific community. Rather, based upon kinetic experiments and modelling, it is generally accepted that DNA persists less than 1 million years. These new data support other results that suggest DNA in some form can persist in Mesozoic tissues, and lay the foundation for future efforts to recover and sequence DNA from other very ancient fossils in laboratories worldwide.

This study is lead by Dr. Alida Bailleul (Institute of Vertebrate Paleontology and Paleoanthropology, the Chinese Academy of Sciences) and Dr. Mary Schweitzer (North Carolina State University, NC Museum of Natural Sciences, Lund University and Museum of the Rockies).

link: https://doi.org/10.1093/nsr/nwz206

http://bit.ly/2VzjiAB

Study reveals link between income inequality and French kissing

Income inequality may be linked to how often people French kiss, according to a worldwide study by Abertay University.

The cross-cultural research involved 2,300 participants from 13 different countries across six continents.

Respondents answered a range of questions including how often they French kissed their partner, and how important they thought kissing was.

Their study revealed that people who lived in less equal nations said they kissed their partners more often.

This correlation did not extend to other forms of intimacy such as hugging and sexual intercourse.

Lead researcher Dr. Christopher Watkins, from Abertay's Division of Psychology, said: "The results of this research suggest that the environment we live in is related to differences in this particular form of romantic intimacy.

"French kissing has been shown by others to be related to the quality of a romantic relationship, and our data suggests that we do this more in environments where we have less to fall back on, where a gesture which shows commitment to a relationship would be of greater value.

"Another interesting factor is that, across the nations surveyed, kissing was considered more important at the established phase of a relationship compared to the initial stages of romantic attraction."

The study also found differences in opinions between men and women on the importance of kissing, and about what makes a good kiss.

They found that a good kiss consisted of two components—sensory factors (such as pleasantness of body odor and breath) and "technique, contact and arousal."

Women, on average, placed greater importance than men on sensory factors.

Dr. Watkins added: "What's particularly captivating about the data is that it compliments large-scale research in very remote cultures looking at the existence of romantic mouth-to-mouth kissing.

"Kissing isn't always present in these cultures, and whether it is or is not is connected to the way in which resources are shared in that society.

"Further work could examine regional differences in kissing and romantic intimacy or the importance of the senses in close interactions among couples

More information: *Christopher D. Watkins et al. National income inequality predicts cultural variation in mouth to mouth kissing, Scientific Reports (2019). DOI: 10.1038/s41598-019-43267-7*

http://bit.ly/32GPm7b

Learning difficulties linked to poor brain connectivity

New research suggests it's about 'hubs', not specific brain regions.

By Nick Carne

Different learning difficulties do not, as previously thought, correspond to specific regions of the brain, new British research suggests. Instead, says a team from the University of Cambridge, poor connectivity between "hubs" within the brain is much more strongly related to children's difficulties.

Scientists have struggled to identify areas of the brain that might give rise to learning difficulties such as dyslexia, dyscalculia and developmental language disorder, or to developmental disorders such as attention deficit and hyperactivity disorder (ADHD).

Perhaps, the Cambridge team suggests somewhat provocatively, that's because there are none.

To test this hypothesis, Duncan Astle and colleagues used machine learning to map the brain differences across 479 children: 337 referred with learning-related cognitive problems and 142 from a comparison sample. The algorithm interpreted data taken from a range of cognitive, learning and behavioural measures, as well as from brain scans taken using magnetic resonance imaging (MRI). The results are published in the journal *Current Biology*.

They show that the brain differences did not map onto any labels the children had been given; in other words, there were no brain regions that predicted having ADHD, for example.

More surprisingly, the researchers say, they found that the different brain regions did not even predict specific cognitive difficulties. There was no specific brain deficit for language problems or memory difficulties, for example.

Instead, they found the children's brains were organised around hubs, like an efficient traffic system or social network. Those who had well-connected brain hubs had either very specific cognitive difficulties, such as poor listening skills, or had no cognitive difficulties at all. By contrast, those with poorly connected hubs had widespread and severe cognitive problems.

"The severity of learning difficulties was strongly associated with the connectedness of these hubs, we think because these hubs play a key role in sharing information between brain areas," Astle says.

This work suggests, he adds, that interventions should be less reliant on diagnostic labels.

"It's better to look at their areas of cognitive difficulties and how these can be supported, for example using specific interventions to improve listening skills or language competencies, or at interventions that would be good for the whole class, like how to how to reduce working memory demands during learning."

The findings also may explain why drugs treatments have not been effective for developmental disorders, the researchers say. Drugs tend to target specific types of nerve cells but would have little impact on a hub-based organisation.

http://bit.ly/32HySfl

New Coronavirus May Circulate Forever as a Seasonal, Endemic Pathogen, Experts Fear

The new coronavirus is likely here to stay. Experts think will probably become a permanent part of the human respiratory-virus repertoire.

Aylin Woodward, Business Insider

"This is going to be with us for some time – it's endemic in human populations and not going to go away without a vaccine," Amesh Adalja, an infectious-disease expert at the Johns Hopkins Centre for Health Security, told Business Insider.

The virus causes a disease called COVID-19 that's marked by fevers, coughing, and occasionally severe lung infections. At least 2,800 people have died and more than 82,500 have gotten sick, mostly in China. (For the latest numbers, see Business Insider's live updates here.)

Chinese president Xi Jinping and President Donald Trump have both expressed optimism about impending springtime weather, since the warmth could stymie the virus' spread in a similar way to the seasonal flu. That may be the case, Adalja said: "It may decrease in transmission frequency so that you'll be able to have time to get a vaccine scaled up by the next appearance of it."

But it doesn't mean the coronavirus would go away for good.

Even if the coronavirus becomes seasonal, it's not going anywhere

If the coronavirus winds up fluctuating with the seasons like the flu, it could retreat in summer and return in the fall and winter each year.

"We know respiratory viruses are very seasonal, but not exclusively," William Schaffner, an infectious-disease specialist at Vanderbilt University, told CNN. "One would hope that the gradual spring will help this virus recede. We can't be sure of that."

Respiratory viruses are seasonal because cooler temperatures help harden a protective gel-like coating that surrounds the virus particles while they're in the air. A stronger shell allows them to survive long enough in the air to travel from one person to the next.

The flu virus "survives better in cool, dry temperatures," Amanda Simanek, an epidemiologist at the University of Wisconsin at Milwaukee, told Insider.

But of course, the northern and southern hemispheres don't experience the same seasons at the same time. So once China and the US see warmer weather, countries in South America and Oceania will be entering winter. Plus, some countries don't experience dramatic seasonal changes at all, so "the flu circulates there year round," Adalja said.

Another virus that circulates in the community

Four other human coronaviruses are already endemic in the global population. They're all seasonal, and they typically cause mild common colds, though each can cause pneumonia.

According to Adalja, the new coronavirus may very well be endemic now, too – a member of the club of "community-acquired" constantly circulating coronaviruses.

On Wednesday, the Centres for Disease Control and Prevention (CDC) reported the first possible case of coronavirus "community spread" in the US. The patient is at a hospital in Sacramento, California. That means the new coronavirus is spreading from person to person in the US, Adalja said, rather than just among people who were recently in China. "It's something established in the community," he said.

Adalja added that some public-health experts already suspected that some US coronavirus cases were being missed because of their similarity to other seasonal illnesses. "Likely community spread of mild cases was happening in many countries around the world, mixed in with cold and flu season cases," he said.