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Scientists Claim to Have Found The First Known Extraterrestrial Protein in a Meteorite

A new discovery could be a clue for us to see if life could emerge elsewhere in the Solar System.

Michelle Starr

Using a new analysis technique, scientists think they have found an extraterrestrial protein, tucked inside a meteorite that fell to Earth 30 years ago.

If their results can be replicated, it will be the first protein ever identified that didn't originate here on Earth.

"This paper characterises the first protein to be discovered in a meteorite," the researchers wrote in a paper uploaded to preprint server arXiv. Their work is yet to be peer reviewed, but the implications of this finding are noteworthy.

Over the last few years, meteorites from the wider Solar System have been yielding some building blocks for life as we know it. Cyanide, which could play a role in building molecules necessary for life; ribose, a type of sugar that is found in RNA; and amino acids, organic compounds that combine to form proteins.

Researchers have now revisited the meteorites that yielded the latter. Led by physicist Malcolm McGeoch of superconductor X-ray source supplier PLEX Corporation, the team focussed their search for something more. Using "state-of-the-art" mass spectrometry, they found what they believe to be protein in a meteorite called Acfer 086, found in Algeria in 1990.

While not proof of extraterrestrial living creatures, this protein discovery makes for yet another of life's building blocks to be found in a space rock. There are many processes that can produce protein, but life, as far as we know, can't exist without it.

"In general, they're taking a meteor that has been preserved by a museum and has been analysed previously. And they are modifying the techniques that they're using in order to be able to detect amino acid inside of this meteor, but in a higher signal ratio," astrochemist Chenoa Tremblay of Curtin University in Australia, who was not involved in the research, told ScienceAlert.

Not only did the team find the glycine amino acid with a stronger signal than previous analysis, they found that it was bound with other elements, such as iron and lithium. When they performed modelling to see what was occurring, they found that the glycine wasn't isolated; it was part of a protein.

The researchers are calling this newly discovered protein hemolithin. While hemolithin is structurally similar to terrestrial proteins, its isotopes of deuterium are not isotopes that occur naturally here on Earth. They are, however, isotopes that are not uncommon in meteorites. In addition, the ratio of deuterium to hydrogen is consistent with long-period comets.

This suggests, the researchers argue, that the structure they have identified as protein is of extraterrestrial origin, and possibly formed in the proto-solar disc, over 4.6 billion years ago.

But, they also note that there's a possibility what they found might not be protein. Although the team thinks it's the most likely explanation, it's also possible that their finding is actually a polymer - a broad class of molecules, of which proteins are only one.

So it's a little too early to get too carried away. But, overall, Tremblay is impressed with the work.

"I think this is really exciting," she said. "I think that it's got a lot of really interesting implications and a lot of compelling arguments. And I think it's a really great step forward."

There are several next steps that the research could take. Other scientists can take the spectra, and use modelling software to try to replicate structures that produce the same or similar spectra. That could help determine whether we're looking at protein or polymer. Similar techniques could now be used on other meteorites in which

amino acids have been found, to see if similar structures can be found.

As Tremblay explains, recent studies on the International Space Station have indicated that "protein should be easier to make in space because of the reduced gravity", and astronaut scientists have actually managed to produce quite large protein molecules, stable enough to bring down to Earth.

"So we're pretty sure that proteins are likely to exist in space," she says. "But if we can actually start finding evidence of their existence, and what some of the structures and the common structures might be, I think that's really interesting and exciting."

The research is currently available on arXiv.

http://bit.ly/2TwhBkU

Swamp wallabies conceive new embryo before birth -- a unique reproductive strategy

Swamp wallabies ovulate, mate and form a new embryo before the birth of the previous offspring

Marsupials such as kangaroos or wallabies are known for their very different reproductive strategy compared to other mammals. They give birth to their young at a very early stage and significant development occurs during a lengthy lactation period in which the offspring spends most of its time in a pouch. Although in some marsupials new ovulation happens only a few hours after giving birth, the regular consecutive stages of ovulation, fertilization, pregnancy and lactation are respected - with one exception: Reproduction specialists from the Leibniz Institute for Zoo and Wildlife Research (Leibniz-IZW), Germany, and the University of Melbourne, Australia, recently demonstrated that swamp wallabies ovulate, mate and form a new embryo before the birth of the previous offspring. They thereby continuously support embryos and young at different development stages before and after birth. These findings are published in the *Proceedings of the National Academy of Sciences* of the United States of America.

Using high-resolution ultrasound to monitor reproduction in swamp wallabies during pregnancy, Prof Thomas Hildebrandt (Leibniz-IZW and University of Melbourne), Dr Brandon Menzies and Prof Marilyn Renfree (both from University of Melbourne) were able to confirm what has been suspected for a long time: swamp wallaby females ovulate, mate and form a new embryo whilst already carrying a full-term fetus that they will soon give birth to.

The new embryo enters embryonic diapause until the new-born offspring leaves the pouch nine months later. Thus, when the embryonic diapause is included, females are continuously pregnant throughout their reproductive life, a unique reproductive strategy that completely blurs the normal staged system of reproduction in mammals.

Swamp wallaby. **Credit: Geoff Shaw, University of Melbourne**

This phenomenon is made possible by two anatomically completely separated uteri and cervices connected to ovaries by their oviducts. "This is true for all marsupials, but the unique overlapping reproductive cycles seem to be a special feature of the swamp wallabies", says Renfree. Normally, ovulation alternates between the two ovaries. "All female macropodid marsupials - essentially kangaroos, wallabies and a few other groups of species - except the swamp wallaby have an oestrous cycle longer than the duration of their pregnancy, so females come into oestrus, ovulate and mate within hours after birth." It has been suspected for some time that swamp wallabies might conceive during an active pregnancy, because the oestrous cycle of the swamp wallaby is shorter than the duration of their pregnancy and there have been reports about mating before the birth of the previous offspring. Such a

"superfetation" has previously been only described (by Leibniz-IZW scientists) for the European brown hare where females copulate again three to four days before the birth of the incumbent young, forming new conceptuses during an active pregnancy.

In order to confirm superfetation in swamp wallabies, the scientists removed the pouch young of ten females to reactivate the dormant blastocysts (early stage embryo). They then monitored the development of the blastocyst in four of these ten females using high-resolution ultrasound. All females gave birth at around 30 days after the young had been removed. Parallel to the embryo development in one uterus, the scientists closely examined the opposite ovary. There, follicles started to appear and grow. At day 26 of the pregnancy the ultrasound examination showed that the conceptus had developed into a fetus with the head, limbs and heartbeat clearly visible - and at day 28 and 29 the largest follicle in the opposite (contralateral) ovary had ovulated and a new corpus luteum was evident. The other six females that were not scanned with ultrasound were regularly examined for sperm. Sperm was identified in the urogenital tract one to two days before birth but at no other time. "These results clearly demonstrate that swamp wallabies ovulate and mate one to two days before birth, during an existing pregnancy", says Hildebrandt.

Pregnancies of eutherian mammals (most mammals, i.e. the most taxonomically diverse of the three branches of mammals) greatly exceed the length of the oestrous cycle, so during mammalian evolution, there has been selection pressure to extend the duration of pregnancy. Among marsupials (who form a second taxonomic branch of mammals), gestation in most macropodids encompasses almost the entire duration of the oestrous cycle. The swamp wallaby takes this one step further with its pre-partum oestrus, allowing this marsupial's gestation length to exceed the oestrous cycle length.

Sadly, many of these unique animals have been lost in the current disastrous bushfires in Australia this summer.

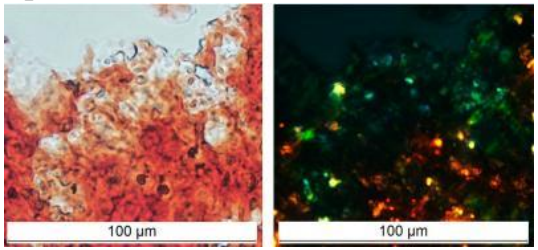
http://bit.ly/2TyCcVF

Scientists find functioning amyloid in healthy brain

Researchers at the Department of Genetics and Biotechnology of St Petersburg University have discovered a functioning amyloid in a healthy brain.

Scientists from St Petersburg University worked with their colleagues from the St Petersburg branch of the Vavilov Institute of General Genetics. They conducted experiments on laboratory rats and showed that the FRX1 protein in the brains of young and healthy animals functions in an amyloid form.

The previously published reports indicate that this protein controls long term memory and emotions: mice that have the FRX1 gene "off" quickly remember even complex mazes, and animals that have too much of this protein do not suffer from depression even after severe stress. In addition, in humans, a failure in the gene encoding FRX1 is linked to autism and schizophrenia.



Protein FXR1, extracted from the brain of healthy rats, is colourised with an amyloid specific dye 'Congo Red' and shows an apple-green glow in polarised light, which is recognised as the 'gold standard' for amyloid identification. **Credit: SPbU**

'Our findings clearly show that developing a universal remedy that will destroy all amyloids in the brain is totally futile. Instead, we need to look for a cure for each specific pathology. The healthy brain was previously known to store only a few protein hormones in amyloid form. They are stored in secretory granules in the hypophysis, but when the time comes, the secretory granules burst and the proteins function in a normal, monomeric form,' said

Alexey Galkin, Professor of the Department of Genetics, Doctor of Biology. 'We have initially proved that the protein can actually function in the brain in amyloid form, both as oligomers and as insoluble aggregates. Also, the amyloid form FRX1 can bind RNA molecules and protect them from degradation.'

The research was conducted by the Research Park of St Petersburg University with equipment provided by the resource centres "Chromas Core Facility" and "The Centre for Molecular and Cell Technologies". The amyloid form of FXR1 protein was discovered by scientists using the amyloid proteome screening method developed by a research team in 2016. Amyloids generally play an important role in many organisms: for example, one of these proteins is found in human pigment cells and affects skin tanning. However, today, scientists are interested in amyloids primarily due to the need to find a cure for neurodegenerative diseases, where these proteins play a key role.

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Wake Forest scientists create world's most sophisticated lab model of the human body

Creating a system of miniaturized organs that can be used to detect harmful and adverse effects of drugs before they are prescribed to patients

Winston-Salem, Nc - Scientists at the Wake Forest Institute for Regenerative Medicine (WFIRM) have developed the world's most sophisticated laboratory model of the human body, creating a system of miniaturized organs that can be used to detect harmful and adverse effects of drugs before they are prescribed to patients. Using such a system in screening potential pharmaceuticals could have a significant impact on speeding new drugs to market, lowering the cost of clinical trials, and reducing or eliminating animal testing.

The system, developed from funding provided by the Defense Threat Reduction Agency (DTRA), is built from many human cell types that are combined into human tissues representing a majority of the organs in the human body such as the heart, liver and lungs. Each of these miniature organs are tiny 3D tissue-like structures about one millionth the size of an adult human organ. The system can be used to mimic tissues/organs and can be used as a testing and predicting platform.

"The most important capability of the human organ tissue system is the ability to determine whether or not a drug is toxic to humans very early in development, and its potential use in personalized medicine," said Anthony Atala, MD, of the Wake Forest Institute for Regenerative Medicine and the study's senior author. "Weeding out problematic drugs early in the development or therapy process can literally save billions of dollars and potentially save lives."

In fact, WFIRM's miniature organ model has already been able to measure toxicity in many drugs approved for human use that were later pulled from the market when it was discovered that these drugs could actually be quite harmful to people. Although toxicity from the recalled drugs was not found initially using standard 2D cell culture systems and animal testing models, and adverse effects were not detected throughout three levels of human clinical trials, the system developed at WFIRM was able to readily detect toxicity, replicating the damage seen in humans.

In a paper published by the journal Biofabrication, the researchers detail how the miniature organs were created and how the human organ tissue system works. Because of the specified individual requirements of each type of tissue, a toolbox of biofabrication techniques was employed to create each miniaturized organ.

Tiny samples of human tissue cells are isolated and engineered into miniature versions of the human organ. They can contain blood vessel cells, immune system cells, and even fibroblasts, the cells in

the connective tissue. Each of these organs, also known as organ tissue equivalents, performs the same functions that they do in the human body. For example, the heart beats about 60 times each minute, the lung breaths the air from the surrounding environment, and the liver breaks down toxic compounds into harmless waste products.

"We knew very early on that we needed to include all of the major cell types that were present in the original organ," said co-author Aleks Skardal, PhD, formerly of WFIRM and now at Ohio State University. "In order to model the body's different responses to toxic compounds, we needed to include all of the cell types that produce these responses."

Another hallmark feature of WFIRM's human organ tissue system is the blood circulatory system. Each system contains media, a substance containing nutrients and oxygen, that is circulated among all the organ types, delivering oxygen and removing waste. The blood system in these devices is very small, employing a technology known as microfluidics to recirculate test compounds through the organ system and remove the drug breakdown products that each organ is producing.

The WFIRM team recognized very early on that drugs and toxic molecules don't move neatly from one organ to the next. Rather than transfer samples from one organ type to the next, the researchers built a microfluidic circuit that recirculates samples, over and over, through each organ in exactly the same way that the heart recirculates molecules through the human body in the blood.

WFIRM's human organ tissue system was not easy to develop. The institute scientists have been working for close to three decades to build large-scale human organs for transplantation into patients. To date, more than 15 tissue and organ products/technologies developed by WFIRM scientists, including muscle, bladder and vaginal organs, have already been tested in humans in clinical trials.

"Creating microscopic human organs for drug testing was a logical extension of the work we have accomplished in building human-scale organs," said co-author Thomas Shupe, PhD, of WFIRM. "Many of the same technologies we have developed at the human-scale level, like including a very natural environment for the cells to live in, also produced excellent results when brought down to the microscopic level."

Because the WFIRM system contains the right cells, in the right numbers from the right species, the data is much more predictive of biological responses expected in normal human beings.

Additional co-authors include: Julio Aleman, Steven Forsythe, Shiny Rajan, Sean Murphy, Mahesh Devarasetty, Nima Pourhabibi Zarandi, Goodwell Nzou, Robert Wicks, Hooman Sadri-Ardekani, Colin Bishop, Shay Soker, and Adam Hall, all of WFIRM.

Authors Skardal, Shupe, Soker, Murphy, Bishop and Atala are inventors on patent rights related to this work owned by Wake Forest University Health Sciences. The patents, whose value may be affected by publication, have the potential to generate royalty income in which the inventors would share.

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Egg stem cells do not exist, new study shows

Researchers have analysed all cell types in the human ovary and found that egg stem cells do not exist

Researchers at Karolinska Institutet in Sweden have analysed all cell types in the human ovary and found that the hotly debated so-called egg stem cells do not exist. The results, published in Nature Communications, open the way for research on improved methods of treating involuntary childlessness.

The researchers used single-cell analysis to study more than 24,000 cells collected from ovarian cortex samples of 21 patients. They also analysed cells collected from the ovarian medulla, allowing them to present a complete cell map of the human ovary.

One of the aims of the study was to establish the existence or non-existence of egg stem cells.

"The question is controversial since some research has reported that such cells do exist, while other studies indicate the opposite," says Fredrik Lanner, researcher in obstetrics and gynaecology at the Department of Clinical Science, Intervention and Technology at Karolinska Institutet, and one of the study's authors.

The question of whether egg stem cells exist affects issues related to fertility treatment, since stem cells have properties that differ from other cells. "Involuntary childlessness and female fertility are huge fields of research," says co-author Pauliina Damdimopoulou, researcher in obstetrics and gynaecology at the same department. "This has been a controversial issue involving the testing of experimental fertility treatments."

The new study substantiates previously reported findings from animal studies - that egg stem cells do not exist. Instead, these are so-called perivascular cells. The new comprehensive map of ovarian cells can contribute to the development of improved methods of treating female infertility, says Damdimopoulou.

"The lack of knowledge about what a normal ovary looks like has held back developments," she says. "This study now lays the ground on which to produce new methods that focus on the egg cells that already exist in the ovary. This could involve letting egg cells mature in test tubes or perhaps developing artificial ovaries in a lab." The results of the new study show that the main cell types in the ovary are egg cells, granulosa cells, immune cells, endothelial cells, perivascular cells and stromal cells.

The study was financed with the support of several bodies, including the Swedish Research Council, the Swedish Childhood Cancer Foundation, Horizon2020 (FREIA project), the Ragnar Söderberg Foundation, the Ming Wai Lau Centre for Reparative Medicine, the Centre for Innovative Medicine and Wallenberg Academy Fellows.

Publication: "Single-cell analysis of human ovarian cortex identifies distinct cell populations but no oogonial stem cells", Magdalena Wagner, Masahito Yoshihara, Iyadh Douagi, Anastasios Damdimopoulos, Haojiang Lu, Karin Pettersson, Kerstin Palm, Shintaro Katayama, Outi Hovatta, Juha Kere, Fredrik Lanner, Pauliina Damdimopoulou, Nature Communications, online March 2, 2020, doi: 10.1038/s41467-020-14936-3.

http://bit.ly/3cxdfmv

Was this life's first meal?

High temperatures and pressures around vents themselves may have jump-started life on Earth, the team argues.

By Robert F. Service

Studies of the origin of life are replete with paradoxes. Take this doozy: Every known organism on Earth uses a suite of proteins—and the DNA that helps build it—to construct the building blocks of our cells. But those very building blocks are also needed to make DNA and proteins.

The solution to this chicken-and-egg conundrum may lie at the site of hydrothermal vents, fissures in the sea floor that spew hot water and a wealth of other chemicals, researchers report today. Scientists say they have found that a trio of metal compounds abundant around the vents can cause hydrogen gas and carbon dioxide (CO_2) to react to form a collection of energy-rich organic compounds critical to cell growth. And the high temperatures and pressures around the vents themselves may have jump-started life on Earth, the team argues.

The new work is "thrilling," says Thomas Carell, an origin of life chemist at Ludwig Maximilian University of Munich who was not affiliated with the new project. The organic molecules the study generated include formate, acetate, and pyruvate, which Carell calls "the most fundamental molecules of energy metabolism," the process of converting nutrients into cell growth. The new results support a long-held idea about the origin of life known as "metabolism first hypothesis." It posits that geochemical processes on early Earth created a stew of simple energy-rich compounds that drove the synthesis of complex molecules, which eventually provided the materials for Darwinian evolution and life.

A clue to this primordial metabolism came in 2016. Researchers led by William Martin, an evolutionary biologist at Heinrich Heine

University of Dusseldorf, scanned the genomes of thousands of bacteria and archaea, identifying 355 proteins encoded by shared genes that likely belonged to a microbial Eve, the last universal common ancestor of all life. Those proteins suggest this primordial microbe thrived in scalding temperatures and ate hydrogen gas, using its electrons to convert inorganic CO_2 dissolved in the ocean into energy-rich organic compounds. That supports the notion that the microbes lived near hydrothermal vents, where those conditions would have been present.

That idea is bolstered by the fact that modern organisms still combine hydrogen and CO_2 to make organic molecules in a process known as the acetyl–coenzyme A (acetyl-CoA) pathway. This process feeds essential organic molecules into biochemical processes that drive the production of proteins, carbohydrates, and lipids, which is at the heart of energy metabolism in cells. The problem, however, is that modern organisms run the acetyl-CoA pathway using 11 enzymes made up of a combined 15,000 amino acids, all finely positioned to carry out their work. And without the right protein machinery or catalyst, if you put hydrogen and CO_2 together, Martin says, "Nothing will happen."

So how could organisms have spontaneously developed their prowess to run the acetyl-CoA pathway? Two years ago, researchers led by Joseph Moran, a chemist at the University of Strasbourg, suggested at least a partial answer. They reported that pure metals, including iron, nickel, and cobalt, could catalyze the reaction of water (water molecules contain hydrogen) and CO_2 to form acetate and pyruvate, key members of the acetyl-CoA pathway. That finding suggests the earliest life could have simply fed on these organic compounds to get a toehold, and over time evolved a suite of proteins to make the reactions even more efficient.

Still, Martin notes, converting water and CO_2 into needed organics isn't how microbial Eve's most closely related modern brethren do it. Rather, these organisms start with hydrogen gas and CO_2. "We wanted to see if we could get this pathway to work without enzymes," Martin says.

He and his colleagues knew hydrothermal vents continually spew out hydrogen gas, driven by reactions between water and metals deep below Earth's crust. And researchers previously determined that CO_2 in early Earth's oceans was about 1000 times more abundant than it is today. So, Martin wondered whether metal-rich minerals common around hydrothermal vents could cause hydrogen to react with CO_2.

To find out, Martin's and Moran's teams joined forces to investigate three iron-rich minerals found near vents: greigite, magnetite, and awaruite. They added these to a water solution and bubbled in hydrogen and CO_2 at 100°C and 25 bars of pressure, conditions common around deep-sea vents. All three minerals catalyzed a reaction of hydrogen and CO_2 to form a mix of organics including formate, acetate, and pyruvate, the group reports today in *Nature Ecology & Evolution*. "What we have here is a sustained source of chemical energy, and it generates these energy-rich molecules used in metabolism," Martin says.

So, was this mix of organics life's first meal? It's a fair bet, says Steven Benner, a chemist at the Foundation for Applied Molecular Evolution. For evolution to begin, life would have needed both a food source and some form of protogenetic molecule to transmit information from one organism to its progeny. How they came together is still unclear. However, any early Darwinian system would need to feed. And, Benner says: "The process described by [Martin's and Moran's team] could certainly have been the source of some of their food."

http://bit.ly/3asrabh

Visceral fat delivers signal to the brain that hurts cognition

Visceral adiposity is considered particularly bad for our bodies and brains

Excessive weight around our middle gives our brain's resident immune cells heavy exposure to a signal that turns them against us, setting in motion a crescendo of inflammation that damages cognition, scientists say.

It's known this visceral adiposity, characterized by an apple-shaped physique, is considered particularly bad for our bodies and brains.

But Medical College of Georgia scientists have shown for the first time one way visceral fat is bad for brains is by enabling easy, excessive access for the proinflammatory protein signal interleukin-1 beta, they report in *The Journal of Clinical Investigation*.

"We have moved beyond correlations saying there is a lot of visceral fat here, and there is cognitive decline here so they may be interacting with each other," says Dr. Alexis M. Stranahan, neuroscientist in the MCG Department of Neuroscience and Regenerative Medicine at Augusta University.

"We have identified a specific signal that is generated in visceral fat, released into the blood that gets through the blood brain barrier and into the brain where it activates microglia and impairs cognition."

The brain typically does not see much of this interleukin-1 beta, but Stranahan and her colleagues have found that visceral adiposity generates high, chronic levels of the signal that in turn over-activate the usually protective microglia, the resident immune cells in our brain.

A bit like a smoldering pot, this chronic inflammation from visceral fat prompts formation of inflammasome complexes that further amplify the immune response and inflammation. The protein NLRP3 is a core component of the inflammasome complex in the fat, and it's what promotes the production and release of interleukin-1 beta by fat cells, and stokes the inflammation fire.

It was known these reactions were causing problems in the body, and now the MCG scientists have evidence they are causing problems in the brain.

To explore brain effects, the scientists knocked NLRP3 out of mice and found the mice were protected against obesity-induced inflammation of the brain and the cognitive problems that can result.

They also transplanted visceral adipose tissue from obese mice and obese mice missing NLRP3 into lean mice recipients and found the transplant from the NLRP3 knockout mouse had essentially no effect.

But the transplant from the obese but genetically intact mice increased levels of interleukin-1 beta in the hippocampus, a center of learning and memory in the brain, and impaired cognition.

They looked further and found that just transplanting the visceral fat caused essentially the same impact as obesity resulting from a high-fat diet, including significantly increasing brain levels of interleukin-1 beta and activating microglia. Mice missing interleukin-1 beta's receptor on the microglia also were protected from these brain ravages.

Their findings enabled the scientists to start putting together the pieces that NLRP3 was working through interleukin-1 beta, which led them to also knock out the receptor for interleukin-1 beta on microglia and confirm that action in the brain.

Microglia typically function as watchdogs, constantly surveilling and roaming the brain, eliminating dead cells and other debris as well as a myriad of other tasks like forming and pruning connections between neurons. Microglia also have receptors for interleukin-1 beta, and the protein, whose many actions include promoting inflammation, easily passes through the protective blood brain barrier.

Microglia's helpful -- or harmful -- actions likely result from signals they are exposed to, and another thing interleukin-1 beta appears to do is prompt microglia to wrap around synapses, possibly exerting damaging pressure and/or releasing substances that actually interfere with conversations between neurons, Stranahan says. In the absence of disease, microglia also are known to embrace synapses but to release good things like brain-derived neurotrophic factor, which is like fertilizer for these invaluable connections.

Happy microglia also have long processes that enable them to reach out and do their many tasks; and inflammation retracts those processes. The scientists found much shorter processes and less complex microglia in mice on a high-fat diet, more changes that didn't happen when NLRP3 was knocked out.

To measure cognitive ability, the scientists looked at mice's ability to navigate a water maze after 12 weeks on a high- or low-fat diet. They found it took the normal, or wild type, mice consuming the higher fat diet as well as the visceral transplant recipients with NLRP3 intact longer to negotiate the water maze. In fact, while they could reach a platform they could see, they had trouble finding one beneath the water's surface that they had been taught to find. Mice with the interleukin-1 receptor knocked out, could find it just fine, Stranahan says.

The high-fat diet, transplant mice also had weaker connections, or synapses, between neurons involved in learning and memory. Mice on a high-fat diet but missing NLRP3 were spared these changes, like mice on a low-fat diet.

Also, like many of us, mice tend to prefer new toys and those on a low-fat diet or with NLRP3 removed were better at recognizing novel objects to play with and their synapses were stronger. The high-fat diet transplant mice seemed not to remember so well which toy they'd already played with.

There is already potential protection out there from brain effects, Stranahan says, noting biologics in use in humans for problems like rheumatoid arthritis and Crohn's disease, that target interleukin-1 beta. "Obesity-induced inflammation occurs over years and so does inflammation in some of these chronic inflammatory diseases," Stranahan says. There is also emerging evidence that bariatric surgery, which sometimes includes removing visceral fat, can improve attention, mood and executive function.

There are many hypotheses about why visceral fat is so inflamed, including its proximity to the gut microbiota, a centerpiece of our immune response, which is programmed to attack invaders.

Increased rates of cognitive decline have been linked to obesity in humans, including shrinkage of key brain areas like the hippocampus, although there also have been contradicting reports about the overall health impact of obesity, the scientists report.

The contradiction in impact may relate to where the fat is found, says Stranahan, whose next goals include studying the apparent protective effects of fat deposited under the skin, called subcutaneous fat, whose benefits may include allowing you to store energy away from the highly inflammatory abdominal area.

Waist to hip ratio is a better indicator of visceral adiposity than the standard body mass index, or BMI, that divides weight by height.

The research was funded by the National Institutes of Health.

Read the full study.

http://bit.ly/2VH7mNq

Molecule found in oranges could reduce obesity and prevent heart disease and diabetes

The equivalent of just two and a half glasses of orange juice a day could reverse obesity and reduce the risk of heart disease and diabetes.

Researchers at Western University are studying a molecule found in sweet oranges and tangerines called nobiletin, which they have

shown to drastically reduce obesity and reverse its negative side-effects.

But why it works remains a mystery.

New research published in the Journal of Lipid Research demonstrates that mice fed a high-fat, high-cholesterol diet that were also given nobiletin were noticeably leaner and had reduced levels of insulin resistance and blood fats compared to mice that were fed a high-fat, high-cholesterol diet alone.

"We went on to show that we can also intervene with nobiletin," said Murray Huff, PhD, a Professor at Western's Schulich School of Medicine & Dentistry who has been studying nobiletin's effects for over a decade. "We've shown that in mice that already have all the negative symptoms of obesity, we can use nobelitin to reverse those symptoms, and even start to regress plaque build-up in the arteries, known as atherosclerosis."

But Huff says he and his team at Robarts Research Institute at Western still haven't been able to pinpoint exactly how nobiletin works. The researchers hypothesized that the molecule was likely acting on the pathway that regulates how fat is handled in the body. Called AMP Kinase, this regulator turns on the machinery in the body that burns fats to create energy, and it also blocks the manufacture of fats.

However, when the researchers studied nobiletin's effects on mice that had been genetically modified to remove AMP Kinase, the effects were the same.

"This result told us that nobiletin is not acting on AMP Kinase, and is bypassing this major regulator of how fat is used in the body," said Huff. "What it still leaves us with is the question - how is nobiletin doing this?"

Huff says while the mystery remains, this result is still clinically important because it shows that nobiletin won't interfere with other drugs that act on the AMP Kinase system. He says current therapeutics for diabetes like metformin for example, work through this pathway.

The next step is to move these studies into humans to determine if nobiletin has the same positive metabolic effects in human trials.

"Obesity and its resulting metabolic syndromes are a huge burden to our health care system, and we have very few interventions that have been shown to work effectively," said Huff. "We need to continue this emphasis on the discovery of new therapeutics."

http://bit.ly/3cvrxnu

The secret to a long life? Matching sex chromosomes

Animals with identical sex chromosomes - live nearly 18% longer than their counterparts with mismatched chromosomes

By Erin Malsbury

When 109-year-old Jessie Gallan was asked about the secret to her long life, she replied “staying away from men.” Other people older than 100 have extolled the virtues of everything from crossword puzzles to tap dancing. One thing they don’t usually mention: chromosomes. Yet, across the animal kingdom, individuals with identical sex chromosomes—including women with double Xs—live nearly 18% longer than their counterparts with mismatched chromosomes, a new study reveals.

In most animals, sex chromosomes help determine whether an individual develops as a male or female. In mammals, females typically have two identical X chromosomes, whereas males have one X and one much smaller, or “reduced,” Y chromosome. Sexes of some animals, such as most male arachnids, lack a second sex chromosome entirely. These chromosomes contribute to the physical differences between males and females. Birds with ZZ sex chromosomes, for example, are male and tend to be more colorful, whereas ZWs are females with typically blander plumage.

Physical traits aren’t the only differences between the sexes. Researchers hypothesize that animals with mismatched sex

chromosomes, such as XY male mammals, could be more vulnerable to genetic mutations, which could result in a shorter life span. But until now, scientists haven't studied this effect across the animal kingdom.

So researchers at the University of New South Wales, Sydney, scoured scientific papers, books, and online databases for sex chromosome and longevity data. They compared the life spans of males and females of 229 animal species across 99 families, 38 orders, and eight classes. On average, the sex with identical chromosomes lives 17.6% longer, they report today in *Biology Letters*. The longevity pattern holds for humans, wild animals, and captive animals across the evolutionary family tree.

"I thought it was really cool how, across insects and fish, we're all showing the same sort of response," says the study's lead author, ecologist Zoe Xirocostas.

Still, the researchers found that the life span disparity varies markedly between species. At one extreme, female German cockroaches (*Blattella germanica*), with XX sex chromosomes, live 77% longer than single-X males. The disparity also varies depending on whether the animal with matching sex chromosomes is female or male. Females with identical sex chromosomes—such as mammals and some reptiles, insects, and fish—live an average of 20.9% longer than males, but in males with matching sex chromosomes, such as birds and butterflies, the life span gain over females is just 7.1%.

This unevenness hints that factors other than the presence of certain sex chromosomes might also strongly influence longevity, the team says. One of these factors could be sexual selection. Exaggerated physical traits and elaborate behaviors make males of some species more attractive to females but require large amounts of energy and take a toll on overall health.

"We know that sexual selection is stronger in males," says evolutionary biologist Gabriel Marais from Claude Bernard University Lyon, who was not involved in the research. Males "pay the cost of this sexual selection by faster aging, and they will die younger," Marais says.

If those males also have reduced or absent sex chromosomes that leave them vulnerable to mutations, the deleterious effects on life span add up, Marais says. In comparison, female birds and butterflies with mismatched sex chromosomes might be more vulnerable to mutations, but they don't face the life span reduction of intense sexual selection.

Further work could help researchers understand how sex chromosomes impact life span. For example, researchers don't yet know whether the size of the reduced sex chromosome corresponds to the difference in life span between males and females. "There are so few papers about this question," Marais says. He praises the new study as an important step in the right direction.

https://nyti.ms/2vFODqK

When a Drug Study Abruptly Ends, Volunteers Are Left to Cope

A participant might commit months or years to a drug trial, only to see it vanish overnight.

By Paula Span

On March 21, 2019, the staff at the Penn Memory Center in Philadelphia was scrambling to learn more about an early-morning announcement: Two pharmaceutical companies, Biogen and Eisai, would discontinue their clinical trial of a drug intended to slow the progression of early Alzheimer's disease.

A "futility analysis" had shown that aducanumab, being studied in more than 3,200 people worldwide, would not prove effective. It was yet another disheartening result; after decades of drug research,

one medication after another — hundreds of them — had failed to prevent, arrest or cure Alzheimer's.

The Penn researchers wanted to be the ones to break the bad news to the 18 participants they had recruited.

"When this effort you contributed months and years to is ending, that's something you want to hear from people you trust," said Emily Largent, a bioethicist and researcher there.

But the Penn staff was too late to inform John Poritsky, a participant with early-onset Alzheimer's, and his wife, Debra Morris. The news had already begun circulating online.

"My friend had sent me a text, 'Did you hear that this study is ending?'" said Dr. Morris, an English professor at the Pennsylvania College of Technology. "I was horrified. Floored. I couldn't believe it."

For nearly a year, they had regularly traveled three hours from their home in Williamsport, Pa., to Philadelphia, where Dr. Poritsky had undergone extensive testing and received monthly infusions without knowing whether he was receiving the drug or a placebo.

"I'd built up a lot of hope," said Dr. Poritsky, 61, a retired English professor. He wasn't surprised to have developed Alzheimer's; his father, grandfather and great-uncle all had the disease. But he had hardly expected a diagnosis before he turned 60.

This drug study, a Phase 3 trial, had allowed him to think not only that he might benefit personally, but that he could help advance science. "I thought, I can be part of something that can cure or arrest this illness," he said. When the plug was suddenly pulled, "I was just devastated."

This scenario occurs with distressing frequency. Most Alzheimer's drug trials are sponsored by publicly held pharmaceutical companies, which must follow federal Securities and Exchange Commission regulations when they disclose information that affects stock prices.

Alerting patients or investigators before notifying shareholders would violate the companies' legal obligations. So they often issue early-morning news releases.

Years ago, most patients probably learned about discontinued trials from researchers and staff whom they had come to know. (The last Alzheimer's medication to receive F.D.A. approval was Namenda, in 2003.)

But with social media and 24-hour digital reporting, plus keen public interest in Alzheimer's drugs, "this has become fast-moving news in a way it wasn't before," Dr. Largent said.

So by the time researchers are able to make phone calls, their patients often have already seen the announcements on Facebook or fielded calls from worried friends.

"It's akin to a trauma, the news that's devastating and the surprising, out-of-the-blue way you learn it," said Dr. Jason Karlawish, a geriatrician who co-directs the Penn Memory Center.

For Phil Gutis, 58, a former New York Times reporter diagnosed with early onset Alzheimer's, "it was a kick in the stomach." Like Dr. Poritsky, he was enrolled in the aducanumab trial, and had learned of its termination from a friend's text. "There should be a better way," he said.

Internationally, the Alzheimer's Association calculates that clinical trials now underway for dementia treatments — drugs, dietary programs, devices and other interventions — aim to enroll more than 56,000 people.

Drug trials for Alzheimer's disease are often a particularly arduous commitment.

"These are not simple protocols," said Dr. Sharon Cohen, a neurologist and principal investigator at the Toronto Memory Program, which had enrolled 29 participants in the aducanumab trial. "The visits are long. They are frequent. There is in-depth testing. Blood draws. M.R.I. scans that may recur. PET scans.

There may be spinal taps. And the study partner" — a family member or friend — "has to attend many of these as well."

Why agree to all that, especially when researchers pointedly explain that the experimental drug may not help and could actually harm patients? Moreover, in a typical double-blind study, half the participants won't even get the drug but will instead receive a placebo.

Researchers and patients describe a mix of motives: desperation, altruism, trust in the investigators and sponsors.

"I thought I was doing this for future generations," Mr. Gutis said. But as he learned more about aducanumab, "there was definitely optimism that this possibly could help me."

Participants also come to value their deepening relationships with the study staff, who know so much about the disease and take such an interest in their condition. "It was almost familial," Dr. Poritsky said.

"We were part of a community and a structure, and it was gone," Dr. Morris said.

The aducanumab study also took an unexpected and uncommon turn. Seven months after ending the trial, Biogen and Esai announced (in another early-morning news release) that a reanalysis, using additional data, indicated that at high doses the drug appeared to reduce cognitive decline after all. They plan to resume an open-label trial (without a placebo) in March and to seek F.D.A. approval.

The development was encouraging, but left study participants feeling especially whipsawed.

In a recent editorial in JAMA Neurology, Drs. Karlawish and Largent argued for a more communicative approach. "We're trying to change the culture of the way we run clinical trials in Alzheimer's research," Dr. Karlawish said in an interview.

Lobbying the S.E.C. to change its regulations would be "infeasible," he acknowledged. But the informed consent process, the researchers wrote, should prepare participants for the possibility of an abrupt end to the trial.

Participants could opt to receive the pharmaceutical company's news release, or a letter, as soon as it is issued, "so you don't feel like you're the last one to know," Dr. Largent said.

The researchers urged companies to share details of what a given study revealed; even failed experiments provide useful information. "It's an important way of demonstrating respect for their contributions," Dr. Largent said.

Finally, study sites should provide support after trials end, by checking on the well-being of participants and referring them to counseling or support groups as needed.

Some of those suggestions may take hold. The Alzheimer's Association and the National Institute on Aging say they plan to meet with drug manufacturers to discuss improving communication with research participants.

The Toronto Memory Center has gone a step further. In 2018 it hosted a lunch for participants and partners after a discontinued trial; the event included a presentation of the results, "to show them what their efforts had led to," Dr. Cohen said. She described the participants as "medical heroes, taking risks to benefit themselves and others."

Last year, at another lunch, the center presented several participants with citizen-scientist awards.

Despite the disappointments, participants often remain eager to join other trials. When aducanumab testing resumes, both Mr. Gutis (who learned that he had been receiving the drug rather than a placebo, and thought it had helped him) and Dr. Poritsky (who thought so too, but had received a placebo) plan to re-enroll.

They will moderate their expectations this time, however.

"You volunteer to be a lab rat," Mr. Gutis said. "But the rat doesn't have high hopes."

http://bit.ly/2x24MHo

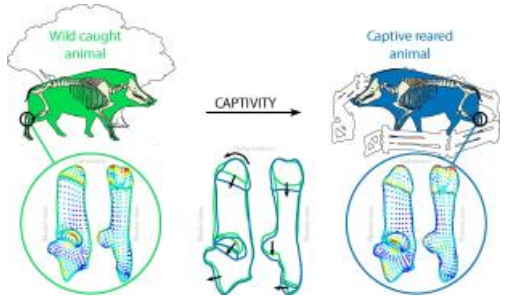
Wild boars provide archaeologists with clues to early domestication

Life spent in captivity has an identifiable effect on the shape of the calcaneus

Until now, archaeozoologists have been unable to reconstruct the earliest stages of domestication: the process of placing wild animals in captivity remained beyond their methodological reach.

Using the wild boar as an experimental model, a multidisciplinary team made up of scientists from the CNRS and the French National Museum of Natural History have shown that a life spent in captivity has an identifiable effect on the shape of the calcaneus, a tarsal bone that plays a propulsive role in locomotion.

Being relatively compact, this bone is well preserved in archaeological contexts, which makes it possible to obtain information about the earliest placing of wild animals in captivity.



Deformation of the calcaneus (tarsal bone) in wild boars reared in captivity compared to wild boars in their natural environment. The coloured dots indicate the degree of deformation (minimum in dark blue, maximum in red). The deformations are mainly related to an elongation of the muscle insertion area in the highest part of the bone. **Credit: Hugo Harbers / AAPSE / CNRS-MNHN**

This modification is caused by changes in the animal's lifestyle, since the bone is reshaped as a result of its movement, the terrain, and muscle stress.

The scientists observed that the shape of the calcaneus was mainly modified in the area of muscle insertions: contrary to what might be expected, captive wild boars displayed greater muscle force than wild boars in their natural environment. It appears that a captive lifestyle turned them from "long-distance runners" into "bodybuilders'".

As well as providing archaeologists with a new methodology, these findings show the speed with which morphological changes can occur when an animal is taken out of its natural environment by humans, and could prove useful in programs reintroducing captive-bred animals into the wild.

These results are published in the journal *Royal Society Open Science* dated March 4, 2020.

More information: *The mark of captivity: plastic responses in the ankle bone of a wild ungulate (Sus scrofa) Royal Society Open Science (2020). royalsocietypublishing.org/doi/10.1098/rsos.192039*

Journal information: Royal Society Open Science *Provided by CNRS*

http://bit.ly/38iJjHn

Archean Earth Was Covered by Global Ocean, New Study Suggests

***The surface of Earth was likely covered by a global ocean 3.24 billion years ago (Archean Eon), according to a new study published in the journal* Nature Geoscience.**

"Our findings could help scientists to better understand how and where single-cell organisms first emerged on Earth," said Dr. Boswell Wing, a researcher in the Department of Geological Sciences at the University of Colorado Boulder.

"The history of life on Earth tracks available niches. If you've got a waterworld, a world covered by ocean, then dry niches are just not going to be available."

In the study, Dr. Wing and colleagues examined 3.24-billion-year-old hydrothermally altered oceanic crust from the Panorama district in the Pilbara Craton of Western Australia.

"There are no samples of really ancient ocean water lying around, but we do have rocks that interacted with that seawater and remembered that interaction," said Dr. Benjamin Johnson, a

scientist at Iowa State University. “The process is like analyzing coffee grounds to gather information about the water that poured through it.”

To do that, the researchers analyzed data from more than 100 rock samples from across the dry terrain. They were looking, in particular, for two different isotopes of oxygen trapped in stone: a slightly heavier atom called oxygen-18 and a lighter one called oxygen-16. They discovered that the ratio of those two isotopes of oxygen may have been a bit off in seawater 3.24 billion years ago — with just a smidge more oxygen-18 atoms than you’d see today.

“Though these mass differences seem small, they are super sensitive,” Dr. Wing said. Sensitive, it turns out, to the presence of continents. “Today’s land masses are covered by clay-rich soils that disproportionately take up heavier oxygen isotopes from the water — like mineral vacuums for oxygen-18,” Dr. Wing said.

The study authors theorized that the most likely explanation for that excess oxygen-18 in the ancient oceans was that there simply weren’t any soil-rich continents around to suck the isotopes up. That doesn’t mean, however, that there weren’t any spots of dry land around. “There’s nothing in what we’ve done that says you can’t have teeny, micro-continents sticking out of the oceans,” Dr. Wing said. “We just don’t think that there were global-scale formation of continental soils like we have today.”

Which leaves a big question: when did plate tectonics push up the chunks of rock that would eventually become the continents we know and love?

The scientists aren’t sure. But they’re planning to scour other, younger rock formations at sites from Arizona to South Africa to see if they can spot when land masses first roared onto the scene.

“Trying to fill that gap is really important,” Dr. Johnson said.

B.W. Johnson & B.A. Wing. 2020. Limited Archaean continental emergence reflected in an early Archaean ^{18}O-enriched ocean. Nat. Geosci *13, 243-248; doi: 10.1038/s41561-020-0538-9*

http://bit.ly/32Pm7PA

What Is The Deal With This Weird Hole on Mars?

Image shows what appears to be a mountain... but completely hollowed out.

Michelle Starr

Mars is a pretty wild and wonderful place, and an image posted to the NASA science blog and Astronomy Photo of the Day this week is a brilliant example. It shows what appears to be a mountain... but completely hollowed out.

While it's not actually the product of some strange mining experiment, the formation is indeed hollow. What you're looking at is a lava tube 'skylight', the product of ancient volcanic activity below the surface of Mars.

The feature is on the western slopes of a shield volcano called Pavonis Mons, the surrounding regions of which show some pretty breathtaking geological features. There are long, snaking lava tubes, fault features called grabens, and, of course, the large volcanic crater itself.

The image above was taken by the Mars HiRise orbiter in 2011, and captured the attention of Mars scientists just because it was so unusual.

Pavonis Mons. **(NASA/JPL/University of Arizona)**

A closer look revealed it to be a skylight - that is, a surface opening to a lava tube below. It's hollow because sometimes lava flows can solidify on the surface while the flow continues below. Then, the flowing lava can drain away, leaving behind lava tube caves. As time goes by, sections of the roof can collapse, creating the skylight.

Analysis of this skylight revealed the opening to be about 35 metres (115 feet) across. The top of the collapsed rubble pile that you can see through the opening is at a depth of about 28 metres (92 feet).

A digital terrain map allowed scientists to calculate the volume of the material that drained out of the conical feature; this, in turn, placed constraints on how deep the pit could be. Based on these calculations, the rubble pile has to be at least 62 metres (203 feet) tall, which means the pit itself had to be at least 90 metres (295 feet) deep prior to the collapse.

That's much bigger than any lava tube found on Earth.

Lava tube caves like this are exciting because they offer some protection from the harsh radiation that bombards Mars. This means that they could be good sites to establish underground bases (if they are accessible; this particular one doesn't look like it's easy to get in and out of). But there's another implication, too. If we're going to look for signs of life on Mars, caves might be the best option.

"Holes such as this are of particular interest because their interior caves are relatively protected from the harsh surface of Mars, making them relatively good candidates to contain Martian life," the APOD post explained. "These pits are therefore prime targets for possible future spacecraft, robots, and even human interplanetary explorers."

Also, while the hole is pretty easy to explain, there is another mystery about this particular skylight. Here on Earth, lava tube skylights tend to look more like the image above (it's about 6 metres or 20 feet across). Exactly how and why this Martian skylight has a conical crater around it is yet to be discovered.

http://bit.ly/2IkMxzi

Bereaved individuals may face higher risk of dying from melanoma

Those who lose a partner are less likely to be diagnosed with melanoma but face a higher risk of dying from the disease

Individuals who experience the loss of a partner are less likely to be diagnosed with melanoma but face an increased risk of dying from the disease, according to research published in the *British Journal of Dermatology*.

The researchers, led by the London School of Hygiene & Tropical Medicine and Aarhus University Hospital, investigated whether bereaved individuals had a higher risk of being diagnosed with, or dying from, melanoma than the non-bereaved. They used data from two large population-based studies between 1997 and 2017 in the UK and Denmark.

They found that melanoma patients who experienced bereavement had a 17% higher risk of dying from their melanoma compared with those who were not bereaved, with similar results seen in both the UK and Denmark.

This study also showed that those who had lost a partner were 12% less likely to be diagnosed with melanoma compared with non-bereaved persons, with 620 and 1667 bereaved diagnosed in the UK and Denmark respectively over the 20 year period, compared with 6430 and 16,166 non-bereaved.

While previous studies have suggested a link between various types of stress and progression of melanoma, which may have played a role in the finding, the researchers suggest that an alternative explanation could be that bereaved people no longer have a close person to help notice skin changes.

This delays detection of a possible melanoma, and therefore diagnosis, until the cancer has progressed to later stages, when it is generally more aggressive and harder to treat.

Each year, 197,000 people are diagnosed with melanoma globally. Melanoma makes up around 5% of all cancer cases in the UK and Denmark. The survival rate of melanoma patients is relatively high, depending on what stage the cancer is at detection. Early detection and treatment are crucial for improving survival.

Angel Wong, lead author and Research Fellow at the London School of Hygiene & Tropical Medicine, said:

"Many factors can influence melanoma survival. Our work suggests that melanoma may take longer to detect in bereaved people, potentially because partners play an important role in spotting early signs of skin cancer. "Support for recently bereaved people, including showing how to properly check their skin, could be vital for early detection of skin cancer, and thus improved survival."

The researchers also encourage family members or caregivers to perform skin examinations for the remaining partner, and call for clinicians to lower their threshold for undertaking skin examinations in bereaved people.

They acknowledge the study's limitations, including the lack of information on some risk factors of melanoma, such as sun exposure or family history, but consider that this had limited impact on the conclusions drawn from this study.

Dr Walayat Hussain of the British Association of Dermatologists said: "Detecting melanoma early can greatly improve survival and partners are key to this. Those without a partner should be vigilant in checking their skin, particularly in hard to reach locations such as the back, scalp, and ears. "Skin cancer is a disease which is most common in older people, who are also most likely to be bereaved, so targeting skin checking advice at this group should be a priority."

Publication

A. Wong, T. Frøslev, L. Dearing, H. Forbes, A, Mulick, K. Mansfield, R. Silverwood, A. Kjærsgaard, H. Sørensen, L. Smeeth, A. Lewin, S. Schmidt, S.M. Langan. The association between partner bereavement and melanoma: cohort studies in the UK and Denmark. British Journal of Dermatology.

http://bit.ly/2wBXfPf

Household chemical use linked to child language delays

Children in low-income homes at risk, study finds

COLUMBUS, Ohio - Young children from low-income homes whose mothers reported frequent use of toxic chemicals such as household cleaners were more likely to show delays in language development by age 2, a new study found.

In addition, the children scored lower on a test of cognitive development. These developmental delays were evident even when the researchers took into account factors such as the education and income of mothers, which are also linked to their children's language and cognitive skills.

The findings provide additional evidence of the need for pediatricians and other health care providers to counsel parents of young children to restrict their use of toxic household chemicals, said Hui Jiang, lead author of the study and senior research associate at The Ohio State University.

"We found that a significant percentage of mothers with young children may commonly expose their children to toxic household chemicals, possibly because they are unaware that such materials may be harmful," said Jiang, who is with Ohio State's Crane Center for Early Childhood Research and Policy.

The study was published online recently in the journal *Clinical Pediatrics*.

The researchers used data on 190 families from the Kids in Columbus Study, a Crane Center research project that followed children born into low-income families in Columbus for five years after birth.

When they first started the study, mothers were asked about their use of household chemicals such as floor and toilet cleaners and solvents during pregnancy. They were asked again when their child was 14 to 23 months old. Mothers also reported whether they had mold in the home, their use of pesticides, and neighborhood pollution sources.

Children's language development was measured when they were between 14 and 23 months old and again when they were 20 to 25 months old. The researchers used a standardized test that examines children's understanding and expression of language - for example,

recognition of objects and people, following directions, and naming objects and pictures.

Findings showed that neighborhood pollution, mold in the house and pesticide use were not significantly linked to child outcomes.

But the more household chemicals mothers reported using regularly after childbirth, the lower the child language and cognitive outcomes at 2 years of age.

There was no link between chemical use during pregnancy and child outcomes, possibly because mothers reported using significantly fewer chemicals during pregnancy.

Exposure to toxic chemicals was reported by about 20 percent of mothers during pregnancy, but that increased to 30 percent when their children were between 1 and 2 years old. Mothers also reported using more household chemicals after childbirth.

"A lot of mothers seem to know to limit exposure to toxic chemicals during pregnancy, but once their child is born, they may think it is no longer a problem," Jiang said.

But research has shown these early years of a child's life are key in many ways, said Laura Justice, co-author of the study and professor of educational psychology at Ohio State. "When kids reach about 2 years old, that is a peak time for brain development," said Justice, who is executive director of The Crane Center.

"If the use of toxic chemicals is interfering with that development, that could lead to problems with language and cognitive growth."

While many mothers may use household cleaners and other toxic chemicals when their children are young, low-income mothers may face particular challenges, Jiang said. For example, they often live in smaller apartments where it may be more difficult to keep children away from chemicals, particularly while they are cleaning.

Jiang noted that this study simply analyzed the relationship between mothers' use of toxic chemicals and later child development and as such can't prove that chemical use caused the developmental delays.

"Future studies are need to more carefully examine the mechanisms through which household toxicants may disrupt early language development," she said.

The findings do show that pediatricians need to emphasize that pregnancy is not the only time for mothers to be concerned about chemical use, Justice said. "Parents need to understand the delicacy of brain development in the first several years of life and their children's susceptibility to chemical exposure," she said.

Other co-authors were Kelly Purtell and Randi Bates, both of Ohio State.

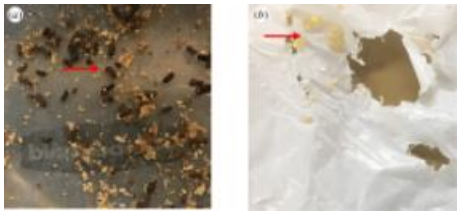
http://bit.ly/2PMnkSH

The caterpillar larvae 'plastivores' that consume and metabolize polyethylene

Greater wax moth caterpillar larvae are "plastivores" that are able to consume and metabolize polyethylene

by Bob Yirka , Phys.org

A team of researchers at Brandon University has found that greater wax moth caterpillar larvae are "plastivores" that are able to consume and metabolize polyethylene. In their paper published in *Proceedings of the Royal Society B*, the group describes their study of the caterpillars and what they learned about them and their gut microbiome.



The consistency of Galleria mellonella excreta was significantly impacted by feeding regime. Honeycomb-fed caterpillars showed a solid form (a), whereas polyethylene-fed caterpillars showed a liquid form within 24 h of feeding (b). **Credit: Proceedings of the Royal Society B: Biological Sciences (2020). DOI: 10.1098/rspb.2020.0112**

Prior research has shown that plastics are becoming a major pollutant. In addition to piling up in landfills, they are also broken down into microplastics, which are polluting the world's oceans.

And while there have been some attempts to curb their use, they are still produced and used in abundance in many parts of the world.

Thus, scientists have been searching for a way to force such materials to degrade faster—natural degradation takes approximately 100 years. In this new effort, the researchers studied wax moths and their larvae, which are known to invade beehives to eat the honeycombs inside.

The researchers with this new effort had learned of anecdotal evidence that the larvae, which exist as caterpillars, eat low-density polyethylene. To find out if this was true, they obtained multiple caterpillars and fed them a diet of plastic grocery bags. They found that 60 of the caterpillars were able to consume approximately 30 square centimeters of the plastic in a week. They also found that the caterpillars could survive for a week eating nothing but the plastic. The researchers also studied the gut microbiomes of several of the caterpillars and identified bacteria that were involved in digesting plastic. They also allowed some of the bacteria to feast on plastic outside of the caterpillar gut and found that some of them were able to survive for up to a year eating nothing but plastic. The researchers also found that there was a symbiotic relationship between the caterpillars and their gut microbiomes—the caterpillars in conjunction with their gut bacteria were able to consume more plastics than the bacteria alone.

The news was not all positive, however—the researchers also found that when the caterpillars fed on plastic, they excreted ethylene glycol, which is toxic.

More information: *Bryan J. Cassone et al. Role of the intestinal microbiome in low-density polyethylene degradation by caterpillar larvae of the greater wax moth, Galleria mellonella, Proceedings of the Royal Society B: Biological Sciences (2020). DOI: 10.1098/rspb.2020.0112*

http://bit.ly/2xgOgUb

Scientists discover new repair mechanism for alcohol-induced DNA damage

New way in which the human body repairs DNA damage caused by acetaldehyde

Researchers of the Hubrecht Institute (KNAW) in Utrecht, The Netherlands, and the MRC Laboratory of Molecular Biology in Cambridge, United Kingdom, have discovered a new way in which the human body repairs DNA damage caused by a degradation product of alcohol. That knowledge underlines the link between alcohol consumption and cancer. The research groups of Puck Knipscheer and Ketan J. Patel worked together on this study and published the results in the scientific journal *Nature* on the 4th of March.

Our DNA is a daily target for a barrage of damage caused by radiation or toxic substances such as alcohol. When alcohol is metabolized, acetaldehyde is formed. Acetaldehyde causes a dangerous kind of DNA damage - the interstrand crosslink (ICL) - that sticks together the two strands of the DNA. As a result, it obstructs cell division and protein production. Ultimately, an accumulation of ICL damage may lead to cell death and cancer.

Defense against DNA damage

Thankfully, every cell in our body possesses a toolkit with which it can repair this type of damage to the DNA. The first line of defense against ICLs caused by acetaldehyde is the ALDH2 enzyme, that largely breaks down acetaldehyde before it causes any harm. However, not everyone profits from this enzyme - about half of the Asian population, more than 2 billion people worldwide, possess a mutation in the gene coding for this enzyme. Because they are not able to break down acetaldehyde, they are more prone to develop alcohol-related cancer.

New line of defense

Scientists from the groups of Puck Knipscheer (Hubrecht Institute) and Ketan J. Patel (MRC Laboratory of Molecular Biology) studied the second line of defense against alcohol-induced ICLs: mechanisms that remove the damage from the DNA. The investigators studied these mechanisms using protein extracts made

from the eggs of the clawed frog (Xenopus laevis), an animal model commonly used in biology research. By using these extracts to repair an ICL formed by acetaldehyde, they discovered the existence of two mechanisms that repair ICL damage: the previously known Fanconi anemia (FA) pathway and a novel, faster route. These two mechanisms differ from each other: in the FA pathway the DNA is cut to remove the ICL, whereas the enzymes in the newly discovered route cut the crosslink itself.

Specific damage

With this research, the scientists provide a mechanistic sneak peek in the process of DNA damage repair. 'We now know that there are multiple ways in which the body can repair ICLs in the DNA', says co-lead author Puck Knipscheer. She thinks that this type of research may lead to a better understanding of treatment for alcohol-related types of cancer. 'But before we can do that, we first have to know exactly how this novel mechanism for ICL repair works.'

Alcohol-derived DNA crosslinks are repaired by two distinct mechanisms. Michael Hodskinson, Alice Bolner, Koichi Sato, Ashley Kamimae-Lanning, Koos Rooijers, Merlijn Witte, Mohan Mahesh, Jan Silhan, Maya Petek, David Williams, Jop Kind, Jason Chin, Ketan Patel, Puck Knipscheer. Nature *2020. DOI: 10.1038/s41586-020-2059-5*

http://bit.ly/2TEiqrY

Travel history should become routine in medical assessments to slow pandemics' spread

Travel history information should be integrated into routine medical assessments to stem the COVID-19 epidemic, as well as future pandemics

DALLAS - Integrating travel history information into routine medical assessments could help stem the rapidly widening COVID-19 epidemic, as well as future pandemics, infectious disease specialists recommend in the Annals of Internal Medicine.

Trish Perl, M.D., M.Sc., Chief of Infectious Diseases and Geographic Medicine at UT Southwestern Medical Center, and Connie Savor Price, M.D., of the University of Colorado School of Medicine, say it's time to add travel history to routine information such as temperature and blood pressure collected in electronic medical records.

"We have the infrastructure to do this easily with the electronic medical record, we just need to implement it in a way to make it useful to the care teams," says Perl, who studies outbreaks and pandemics. "Once the infrastructure is built, we'll also need to communicate what is called 'situational awareness' to ensure that providers know what geographic areas have infections so that they can act accordingly."

A simple, targeted travel history can help put infectious symptoms in context for physicians and caregiver teams, and, if deemed appropriate, trigger more detailed history, further testing, and rapid implementation of protective measures for others in affected households, co-workers or other daily contacts, and health care personnel. Shared electronic health records also can integrate travel history with computerized decision-making support to suggest specific diagnoses in recent travelers, the authors note, in much the same way as trained medical teams routinely ask about tobacco exposure to ascertain levels of cancer and heart disease risk.

The emergence of novel respiratory diseases in the past two decades - including Severe Acute Respiratory Syndrome (SARS) in 2002-2003, Middle East Respiratory Syndrome (MERS) in 2012-2013, Western Africa-based Ebola in 2014, and now COVID-19 from China - demonstrate the need for change. With each wave, "the urgent threat of communicable diseases comes with significant morbidity and mortality, tremendous health care disruptions and resource utilization, and collateral economic and societal costs," Perl and Price write.

"MERS and SARS were associated with very specific travel. MERS was associated with travel to the Arabian Peninsula, and SARS was

associated with travel primarily to Hong Kong, Singapore, and Beijing," Perl says. "Currently COVID is similar in that there are geographic clusters, but those lines may be blurring as the outbreak expands. The challenges and potential stress on the public health infrastructure, including the hospitals which are part of this, will be notable in that we could see large numbers of patients. Our role will not only be to care for these patients but to communicate to them the strategies that they can use to protect themselves."

The Annals commentary suggests that a simple script could be strategically and carefully developed to elicit clues for emerging infectious diseases and information about current emerging pathogen threats. The information could be collected along with the four gold standard vital signs - temperature, heart rate, respiratory rate, and blood pressure - currently used to help U.S.-based medical teams assess patients' health status, triage to appropriate care, determine potential diagnoses, and predict recovery.

"The current outbreak is an opportune time to consider adding travel history to the routine. The COVID outbreak is clearly moving at a tremendous pace, with new clusters appearing daily," says Perl, who holds the Jay P. Sanford Professorship in Infectious Diseases at UTSW. "This pace is a signal to us that it is a matter of time before we will see more of these infections in the U.S. What is different with this outbreak is that this virus is more fit and transmissible and hence there has been much more transmission."

The article appears in the March 3 Annals of Internal Medicine. The authors reported no funding support or conflicts of interest.

http://bit.ly/2TsyaQ1

Our eye movements help us retrieve memories, suggests a new Baycrest study

In a recent study, scientists found that research participants moved their eyes to determine whether they had seen an image before, and that their eye movement patterns could predict mistakes in memory.

In a recent study, scientists at Baycrest's Rotman Research Institute (RRI) found that research participants moved their eyes to determine whether they had seen an image before, and that their eye movement patterns could predict mistakes in memory. They obtained these results using an innovative new eye tracking technique they developed.

"Our findings indicate that eye movements play a functional role in memory retrieval," says Dr. Jennifer Ryan, senior scientist at the RRI and Canada Research Chair in Cognitive Neuroscience of Memory. "They can tell us a lot about someone's memory."

This study builds on previous Baycrest research examining the link between eye movements and memory, including the role of our eye movements in memorization and the weakening connection between our eye movements and our brain activity as we age.

"When we see a picture, a face or something else that we have already seen, our eyes tend to look at the same locations as they did the first time. The brain compares important characteristics of what we are seeing to a mental picture in our memory, and it identifies the two as the same," says Dr. Bradley Buchsbaum, senior scientist at the RRI. "The brain is pretty good at this, even in conditions of lower visibility."

"If we see someone in the distance, or if their face is partially hidden by branches, our brain will compare the features that are visible to a mental picture to determine whether we know that person," says Jordana Wynn, lead researcher on this study, former PhD student at the RRI and current fellow at Harvard University.

This phenomenon is called "pattern completion." When it goes wrong, we may end up mistakenly waving to a stranger if he or she has similar hair or a similar nose to someone we know.

In this study, published in the journal Proceedings of the National Academy of Sciences of the United States of America (PNAS), participants were first asked to memorize a series of 30 new images on a screen. Next, they viewed another series, this time containing both some of the previously seen images and some new-but-similar images. They were then asked to indicate whether they had seen each one before. Their eye movements were tracked during both stages. Each image was shown briefly, ranging from 250 milliseconds to 750 milliseconds, before the participants were instructed to visualize it while looking at a blank screen.

Participants were highly accurate in identifying previously seen images as old, scoring almost 90%. They were more likely to be correct if their eye movements were the same as when they initially saw the image. On the other hand, they performed less well, at 70%, when faced with a new-but-similar image. In the latter case, the more participants repeated their initial viewing pattern instead of focusing on the different aspects of the image, the more likely they were to incorrectly identify the image as old.

To emulate real-world situations where we don't have full information, the researchers also used incomplete, or "degraded," versions of images. This ranged from 0 to 80% degradation, in the form of grey squares covering parts of the image. Remarkably, even when the image was 80% degraded, performance was much better than pure guessing, reflecting the strength of pattern completion.

"Using our eye tracking technique, we were able to map the participants' eye movements and observe that they were mentally picturing an image that they could not see," says Wynn. "They were using pattern completion."

Many studies have examined pattern completion over the past decades, but with one critical weakness. "These studies have all been based on the untested assumption that we can infer pattern completion is happening when participants mistakenly 'recognize' images that they have not seen before," says Wynn. "Our study is the first to use eye movement analysis, rather than behaviour, to show that people are in fact retrieving a memory of an old image when they make this mistake."

This study's findings have important implications in terms of assessing memory. "Some of the traditional tests used to diagnose memory impairments are quite verbal," says Dr. Ryan. "They often require good command of the English language, which can be a problem in a multicultural city like Toronto."

"With eye tracking, you don't have to ask people what they remember. You can just look at their eyes. This gives us a lot more information about their memory than we thought," says Dr. Buchsbaum.

This work was made possible with support from the Canadian Institutes of Health Research (CIHR) and the Natural Sciences and Engineering Research Council of Canada (NSERC).

With additional funding, the researchers could further examine the role of eye movements in memory retrieval. "This could lead to the development of better screening tools for dementia, which is the ultimate hope," says Dr. Ryan.

http://bit.ly/2TLIAcr

First Patient Receives In Vivo CRISPR Editing

Doctors in Oregon delivered the gene editing machinery behind the retina in hopes of treating an inherited form of blindness, according to the companies that developed the therapy.

Jef Akst

Cambridge, Massachusetts–based Editas Medicine and Dublin-based Allergan announced today (March 4) that doctors at the Casey Eye Institute of Oregon Health & Science University in Portland used CRISPR gene editing inside a patient for the first time. They are attempting to treat an inherited form of blindness called Leber congenital amaurosis, the Associated Press reports.

The scientists say they will know within a few weeks if the treatment is working and safe, and plan to test it on additional patients if so.

"We're really excited about this," Harvard Medical School ophthalmology professor Eric Pierce, who is leading a study that the procedure launched, tells NPR. "We're helping open, potentially, an era of gene-editing for therapeutic use that could have impact in many aspects of medicine."

The feat of in vivo gene editing was first achieved in humans in 2017, with the use of zinc finger nucleases to insert the gene for an enzyme that was lacking in a man with Hunter syndrome. But researchers have gravitated toward CRISPR technology thanks to its precision.

In patients with Leber congenital amaurosis, a mutation prevents the expression of a gene called *CEP290* that is critical for sight. Patients typically have poor vision at birth and it can further deteriorate rapidly. Gene therapy is impractical due to the size of the gene—it's too long for standard viral vectors to carry. Instead, the CRISPR-based therapy developed by Editas and Allergan involves delivering, via a hair-sized tube, three drops of fluid reagents behind the retina while the patient is under general anesthesia.

"The gene editing approach is really exciting. We need technology that will be able to deal with problems like these large genes," University of Pennsylvania gene editing expert Jean Bennett, who was not involved in the development of the treatment, tells the AP.

Editas and Allergan plan to recruit a total of 18 patients, aged 3 to 17, to receive the CRISPR-based therapy at one of three different doses, NPR reports. The eye is a good target for these early attempts to do CRISPR in vivo, notes Kiran Musunuru, another gene therapy researcher at the University of Pennsylvania, because the treatment does not have access to the rest of the body. "If something goes wrong, the chance of harm is very small," he tells the AP. "It makes for a good first step for doing gene editing in the body."

Moreover, notes Pierce, the cells of the retina do not turnover, meaning that the edit is permanent. "[T]hat cell will persist hopefully for the life of the patient."

Francis Collins, director of the National Institutes of Health, tells NPR that the achievement marks "a significant moment" in medicine. "All of us dream that a time might be coming where we could apply this approach for thousands of diseases. This is the first time that's being tried in a human being. And it gives us hope that we could extend that to lots of other diseases—if it works and if it's safe."

https://wb.md/2Ioc5vJ

FDA Adds Boxed Warning to Montelukast Over Mental Health Risks

The US Food and Drug Administration (FDA) is strengthening existing warnings about serious behavior and mood-related changes with montelukast (Singulair; Merck and generics), which is used to treat asthma and allergy.

Megan Brooks

日本では商品名シングレア(MSD)、キプレス（杏林製薬）

The agency will add a boxed warning to montelukast advising healthcare providers to avoid prescribing montelukast for patients with mild symptoms, particularly those with allergic rhinitis, according to a drug safety communication. The FDA updated the product labeling in 2008 to include information about neuropsychiatric events reported with use of montelukast.

In response to continued reports of suicide and other adverse events, the FDA reviewed all available data and conducted an observational study. As part of its review, the FDA reevaluated the benefits and risks of montelukast as the treatment landscape has evolved since

the drug was first approved in 1998. Based on their findings, the FDA determined that the risks of montelukast may outweigh the benefits in some patients, particularly when the symptoms of the disease are mild and can be adequately treated with alternative therapies.

For allergic rhinitis in particular, the FDA says montelukast should be reserved for patients who have not responded adequately to other therapies — or who cannot tolerate these therapies.

"We recognize that millions of Americans suffer from asthma or allergies and rely on medication to treat these conditions. The incidence of neuropsychiatric events associated with montelukast is unknown, but some reports are serious, and many patients and health care professionals are not fully aware of these risks," Sally Seymour, MD, director of the Division of Pulmonary, Allergy and Rheumatology Products in the FDA's Center for Drug Evaluation and Research, said in a statement. With the new boxed warning, the FDA aims to make sure patients and medical providers have the information available to make informed treatment decisions, she added. "Importantly, there are many other safe and effective medications to treat allergies with extensive history of use and safety, such that many products are available over the counter without a prescription," Seymour said.

In addition to the boxed warning, the FDA will also require a new medication guide to be given to patients with each montelukast prescription. Healthcare professionals are encouraged to report side effects from montelukast to the FDA's MedWatch program.

http://bit.ly/2vJ6c9y

Study: Organic molecules discovered by Curiosity Rover consistent with early life on Mars

Organic compounds called thiophenes are found on Earth in coal, crude oil and oddly enough, in white truffles, the mushroom beloved by epicureans and wild pigs.

PULLMAN, Wash. - Thiophenes were also recently discovered on Mars, and Washington State University astrobiologist Dirk Schulze-Makuch thinks their presence would be consistent with the presence of early life on Mars.

Schulze-Makuch and Jacob Heinz with the Technische Universität in Berlin explore some of the possible pathways for thiophenes' origins on the red planet in a new paper published in the journal Astrobiology. Their work suggests that a biological process, most likely involving bacteria rather than a truffle though, may have played a role in the organic compound's existence in the Martian soil.

"We identified several biological pathways for thiophenes that seem more likely than chemical ones, but we still need proof," Dirk Schulze-Makuch said. "If you find thiophenes on Earth, then you would think they are biological, but on Mars, of course, the bar to prove that has to be quite a bit higher."

Thiophene molecules have four carbon atoms and a sulfur atom arranged in a ring, and both carbon and sulfur, are bio-essential elements. Yet Schulze-Makuch and Heinz could not exclude non-biological processes leading to the existence of these compounds on Mars.

Meteor impacts provide one possible abiotic explanation. Thiophenes can also be created through thermochemical sulfate reduction, a process that involves a set of compounds being heated to 248 degrees Fahrenheit (120 degrees Celsius) or more.

In the biological scenario, bacteria, which may have existed more than three billion years ago when Mars was warmer and wetter, could have facilitated a sulfate reduction process that results in thiophenes. There are also other pathways where the thiophenes themselves are broken down by bacteria. While the Curiosity Rover has provided many clues, it uses techniques that break larger

molecules up into components, so scientists can only look at the resulting fragments.

Further evidence should come from the next rover, the Rosalind Franklin, which is expected to launch in July 2020. It will be carrying a Mars Organic Molecule Analyzer, or MOMA, which uses a less destructive analyzing method that will allow for the collection of larger molecules.

Schulze-Makuch and Heinz recommend using the data collected by the next rover to look at carbon and sulfur isotopes. Isotopes are variations of the chemical elements that have different numbers of neutrons than the typical form, resulting in differences in mass.

"Organisms are 'lazy'. They would rather use the light isotope variations of the element because it costs them less energy," he said. Organisms alter the ratios of heavy and light isotopes in the compounds they produce that are substantially different from the ratios found in their building blocks, which Schulze-Makuch calls "a telltale signal for life."

Yet even if the next rover returns this isotopic evidence, it may still not be enough to prove definitively that there is, or once was, life on Mars. "As Carl Sagan said 'extraordinary claims require extraordinary evidence,'" Schulze-Makuch said. "I think the proof will really require that we actually send people there, and an astronaut looks through a microscope and sees a moving microbe."

https://nyti.ms/2Ts9IxZ

China's Battle Against Coronavirus: 7 Takeaways

Dr. Bruce Aylward, leader of the team that visited China, details what every country should do to stop the coronavirus.

By Donald G. McNeil Jr.

In an extensive interview with The New York Times, Dr. Bruce Aylward, of the World Health Organization, described what he learned from close observation of China's efforts to contain the coronavirus. Here are seven important lessons.

Aggressive measures work.

New cases have dropped to 200 a day from over 3,000 a day one month ago. After the initial chaos and cover-up in Wuhan, health authorities imposed a lockdown, strict quarantines, mandatory testing and isolation. That prevented what would have been hundreds of thousands of infections.

There aren't many asymptomatic cases.

Testing of 320,000 samples suggests that the known cases are not just the tip of an iceberg. "What we're seeing is a pyramid: Most of it is above ground," Dr. Aylward said.

Be prepared to move medical care online …

To keep the sick and the healthy from mingling in clinics and emergency rooms, online medical consultations and prescriptions became the norm. Two hospitals were erected almost overnight, and open wards in others were rebuilt as isolation units.

… as well as other services.

Students from schools that closed got online lessons. Medications and food parcels were delivered to millions of people who were shut in their homes for a month.

Isolate the infected quickly.

In designated "fever clinics," medical personnel in protective gear took temperatures, did rapid lung CT scans and gave swab tests that produced results in hours. To protect families, the infected were taken to isolation centers; the seriously ill and elderly went to hospitals.

Having to pay may slow containment.

Testing was free in China, as was all care for hospitalized patients. If Americans delay getting tested for fear of the medical bills "that's what could wreak havoc," Dr. Aylward said. "The U.S. has to think this through."

Civic spirit can make a difference.

More than 40,000 doctors and nurses, many of them volunteers, descended on Wuhan. Highway workers became temperature-takers or delivered food. Hospital receptionists took charge of infection control.

Volunteers, Dr. Aylward said, “really saw themselves as on the front lines of protecting the rest of China. And the world.”

https://wb.md/38u0LZs

Concerning Jump in Dementia Diagnoses in Younger Americans

Number of insured Americans aged 30 to 64 years who were diagnosed with early-onset dementia or Alzheimer disease (AD) jumped 200% from 2013 to 2017

Megan Brooks

The number of commercially insured Americans aged 30 to 64 years who were diagnosed with early-onset dementia or Alzheimer disease (AD) jumped 200% from 2013 to 2017, from 4.2 to 12.6 per 10,000, according to a new report from the Blue Cross Blue Shield Association (BCBSA).

Dementia diagnosis rates increased 373% among adults aged 30 to 44 (from 0.9 to 4.4 per 10,000) and 311% among those aged 45 to 54 years (from 2.7 to 10.9 per 10,000). The average age of a person in the commercially insured population who is living with early-onset dementia or AD is 49 years. Women make up 58% of those diagnosed with dementia or AD, the report states.

"The increase in early-onset dementia and Alzheimer's diagnoses among a generation who typically would not expect to encounter these conditions for several decades is concerning, particularly since there is no cure for Alzheimer's disease," Vincent Nelson, MD, president of medical affairs and interim chief medical officer of the BCBSA, told *Medscape Medical News*.

"Additionally, as early-onset dementia and Alzheimer's disease continue to affect younger people, it is important to understand the impact of both forms of dementia on the health of Americans and their caregivers," said Nelson.

The BCBSA report, *Early-Onset Dementia and Alzheimer's Rates Grow for Younger American Adults*, is the latest in the company's Health of America Report series.

Regarding only early-onset AD, the diagnosis rate increased 131% among adults aged 30 to 64 years, from 1.3 per 10,000 in 2013 to 3.0 per 10,000 in 2017. Especially large increases occurred among people aged 30 to 44 (407% increase, from 0.1 to 0.6 per 10,000) and 45 to 54 (242% increase, from 0.6 to 2.0 per 10,000).

Nelson cautioned that the increase in the rate of diagnosis in the 30- to 44-year group is "on a small base size, which means small numerical increases in rate drive substantial percentage changes."

Potential Drivers

He said several factors could be driving an increase in prevalence.

"It could be heightened awareness of symptoms amongst providers, better usage of diagnosis codes, or accumulation of people who are diagnosed with the condition and remain within the commercially insurer population during the study period rather than to an actual increase in the rate of diagnosis year over year," he told *Medscape Medical News*.

The report also notes that for people living with early-onset dementia or AD, the average BCBS Health Index is 62.5, which means these patients have only 63% of optimal health. This amounts to about 11 years of healthy life lost.

The report is based on data from BCBS Axis, a database of medical claims from more than 48 million commercially insured members of BCBS companies, from 2013 to 2017.

Nelson said it's important to keep in mind that the data in this report represent a "point-in-time measurement" of the diagnosis of early-onset dementia and AD among commercially insured American adults aged 30 to 64 years. In addition, the report used medical

claims data, from which causes of diagnosed conditions cannot be determined.

Keith Fargo, PhD, director of scientific programs and outreach at the Alzheimer's Association, urged caution in interpreting the data.

"The numbers in this report only reflect diagnosed cases coded under Blue Cross Blue Shield's insurance network. As we know, Alzheimer's is underdiagnosed, so these numbers are likely not truly representative of the prevalence of younger-onset dementia," Fargo told *Medscape Medical News*.

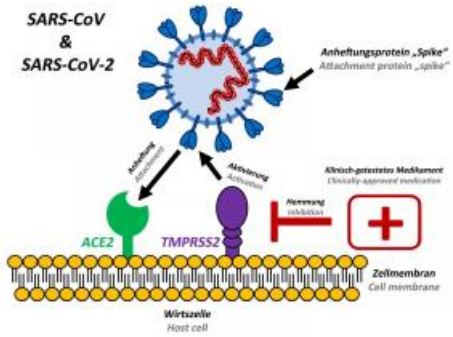
"More epidemiological research is needed to better understand the full scope of individuals affected by younger-onset dementia," said Fargo. The full report is available online.

http://bit.ly/2TONOnU

Preventing spread of SARS coronavirus-2 in humans

Göttingen infection researchers identify potential drug

Several coronaviruses circulate worldwide and constantly infect humans, which normally caused only mild respiratory disease. Currently, however, we are witnessing a worldwide spread of a new coronavirus with more than 90,000 confirmed cases and over 3,000 deaths.



The attachment protein "spike" of the new coronavirus SARS-CoV-2 uses the same cellular attachment factor (ACE2) as SARS-CoV and uses the cellular protease TMPRSS2 for its activation. Existing, clinically approved drugs directed against TMPRSS2 inhibit SARS-CoV-2 infection of lung cells.
Credit: Illustration: Markus Hoffmann

The new virus has been named SARS coronavirus-2 and has been transmitted from animals to humans. It causes a respiratory disease called COVID-19 that may take a severe course. The SARS coronavirus-2 has been spreading since December 2019 and is closely related to the SARS coronavirus that caused the SARS pandemic in 2002/2003. No vaccines or drugs are currently available to combat these viruses.

Stopping virus spread

A team of scientists led by infection biologists from the German Primate Centre and including researchers from Charité, the University of Veterinary Medicine Hannover Foundation, the BG-Unfallklinik Murnau, the LMU Munich, the Robert Koch Institute and the German Center for Infection Research, wanted to find out how the new coronavirus SARS-CoV-2 enters host cells and how this process can be blocked. The researchers identified a cellular protein that is important for the entry of SARS-CoV-2 into lung cells. "Our results show that SARS-CoV-2 requires the protease TMPRSS2, which is present in the human body, to enter cells," says Stefan Pöhlmann, head of the Infection Biology Unit at the German Primate Center. "This protease is a potential target for therapeutic intervention."

Promising drug

Since it is known that the drug camostat mesilate inhibits the protease TMPRSS2, the researchers have investigated whether it can also prevent infection with SARS-CoV-2. "We have tested SARS-CoV-2 isolated from a patient and found that camostat mesilate blocks entry of the virus into lung cells," says Markus Hoffmann, the lead author of the study. Camostat mesilate is a drug approved in Japan for use in pancreatic inflammation. "Our results suggest that camostat mesilate might also protect against COVID-19," says Markus Hoffmann. "This should be investigated in clinical trials."

Original publication

Hoffmann, M et al. (2020). SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically-proven protease inhibitor. Cell, DOI: 10.1016/j.cell.2020.02.052

http://bit.ly/2wKRwGX

This 500 million-year-old 'social network' may have helped sea monsters clone themselves

Rangeomorphs had no mouths, guts, arms, legs or reproductive organs, but an ancient "network" of strings may have helped them dominate the ocean floor anyway.

By Brandon Specktor - Senior Writer

Some of the earliest animals on Earth may have used social networks to chat with each other, review food — and yes — maybe even sext. (See: communicate with each other, share nutrients and possibly reproduce.)

In a study published Thursday (March 5) in the journal Current Biology, researchers looked at hundreds of rangeomorphs — bizarre, fern-like animals that lived in large colonies on the bottom of the ocean from about 571 million to 541 million years ago — fossilized along the coast of Newfoundland, Canada.

Rangeomorphs dominated the seafloor for millions of years, despite having no mouths, guts or way to move around. Part of their success may have been owed to a "social network" of string-like filaments connecting individual members, a new study suggests. **(Image: © Sarah Collins (Cambridge University))**

To the team's surprise, many of the fossil specimens appeared to be connected to each other by long, string-like filaments never seen among animals this old. Individual filaments spanned anywhere from a few inches to 13 feet (4 meters) in length and connected rangeomorphs from seven different species, forming what lead study author Alexander Liu called a primitive "social network" of deep-sea dwellers.

"These organisms seem to have been able to quickly colonize the seafloor, and we often see one dominant species on these fossil beds," Liu, a professor at the University of Cambridge's Department of Earth Sciences, said in a statement. "These filaments may explain how they were able to do that."

Rangeomorphs are thought to be some of the earliest nonmicroscopic animals on Earth, spreading prolifically during the end of the Ediacaran period (roughly 635 million to 541 million years ago) despite having no noticeable mouths, guts, reproductive organs or means of moving around.

An artist's illustration shows a thriving rangeomorph colony on the bottom of the ancient sea. (Filaments not included.) **(Image credit: Charlotte Kenchington)**

Scientists think the creatures dug into the mud on the ocean floor, passively sucking nutrients out of the water using symmetrical, leaf-like branches. Their methods worked well, apparently, as rangeomorph colonies dominated huge plots of the seafloor for 30 million years. Different species ranged from less than 1 inch (0.02 m) to 6.5 feet (2 m) in length, and some may have physically changed shape to better capitalize on the nutrients available around them. You could reasonably call rangeomorphs the "mighty morphin' flower rangers" of the Ediacaran and annoy only a few scientists in the process.

Because rangeomorphs never really moved around, the fossil record includes entire colonies of the creatures preserved as they actually lived. When Liu and his colleagues found fossilized filaments connecting rangeomorphs at 38 different dig sites, it became clear that this sinewy "network" played an important role in connecting individual colony members.

That role, however, remains a mystery. The filaments may have helped stabilize colony members against strong currents, the authors hypothesized, making each colony into a sort of living picket fence. Perhaps the filaments were used to transfer nutrients from animal to animal, sort of how trees connected at the roots can share resources today. Or perhaps the links were a tool for clonal reproduction, a type of asexual reproduction where the parent organism creates multiple identical clones of itself. This would have allowed rangeomorphs to spread across large sections of the seafloor very rapidly, the authors wrote.

Further study of rangeomorph fossils is required to unravel the mystery of these filaments; alas, it seems this social network is password-protected.

http://bit.ly/2vHh73L

Could cancer immunotherapy success depend on gut bacteria?

Gut bacteria can penetrate tumor cells and boost the effectiveness of an experimental immunotherapy that targets the CD47 protein.

DALLAS - Could the response to cancer immunotherapy depend on bacteria that originate in the gut and travel to the tumor?

A study by researchers at UT Southwestern Medical Center and the University of Chicago suggests exactly that, revealing that gut bacteria can penetrate tumor cells and boost the effectiveness of an experimental immunotherapy that targets the CD47 protein.

Using mouse models of malignancy, the scientists found that the intestinal microbe Bifidobacterium accumulates within tumors, transforming anti-CD47 unresponsive tumors into responsive ones.

The team's study, published today in the *Journal of Experimental Medicine*, discovered that the response to treatment depends on the type of bacteria living in the animals' guts. They then identified the mechanism, finding that the combination of antibodies against CD47 and gut bacteria works via the body's STING pathway of innate immunity - the body's first line of defense against infection.

Their experiments used mice from different resource facilities, antibiotic-fed mice, and mice raised in a germ-free environment.

In one experiment, they studied mice raised in two different facilities and that had distinct mixtures of bacteria in their intestines. One group was responsive to anti-CD47 and another was not. The second group became responsive, however, after being housed with the responders, indicating that oral transfer or contact transmission of gut bacteria occurred between groups, the researchers say.

The protein CD47 is expressed in high levels on the surface of many cancer cells, where it acts as a "don't eat me" signal to the immune system's macrophages, commonly known as white blood cells. As a result, anti-CD47, also known as CD47 blockade therapy, is currently under investigation in multiple clinical trials. However, the mouse studies that predated those trials had mixed results, with only some mice responding to the anti-CD47 therapy, explains corresponding author Yang-Xin Fu, M.D., Ph.D., professor of pathology, immunology, and radiation at UT Southwestern.

"We felt we needed to improve anti-CD47 therapy and understand the mechanisms," he says, leading them to wonder about the gut microbiome, the bacteria that grow in the intestines and aid with digestion. That bacterial ecosystem, sometimes called the microbiota, is also known to affect the gut's ability to resist pathogens and the host's response to cancer immunotherapy.

"But how the microbiota does that has been unclear," Fu says. "This study finds that some of the bacteria from the gut travel to the tumor and get into the cells, or microenvironment, where the bacteria facilitate CD47 blockade's ability to attack the tumor. We found it does that via the immune signaling pathway called stimulator of interferon genes (STING)."

The findings suggest that a probiotic might someday be used to improve anti-CD47 therapy, says Fu, a Cancer Prevention and Research Institute (CPRIT) Scholar and holder of the Mary Nell and Ralph B. Rogers Professorship in Immunology at UT Southwestern.

The researchers also found that tumor-bearing mice that normally respond to anti-CD47 treatment failed to respond if their gut bacteria were killed off by antibiotics. In contrast, anti-CD47 treatment became effective in mice that are usually nonresponsive when these animals were supplemented with Bifidobacteria, a type of bacteria that is often found in the gastrointestinal tract of healthy mice and humans.

They further discovered that the bacteria migrate into tumors, activating the STING immune signaling pathway. This sets off production of immune signaling molecules such as type 1 interferons and activating immune cells that appear to attack and destroy the tumor once the anti-CD47 agent nullifies the CD47's "don't eat me" tag, the researchers report. The researchers found that mice genetically unable to activate type 1 interferon failed to respond to the bacteria-immunotherapy approach. Similarly, mice unable to access the STING pathway showed no benefit from the combined bacteria-immunotherapy approach, confirming that STING signaling is essential.

"It is very possible that more than one type of gut microbiota could enhance tumor immunity in a similar way and we would like to investigate that," he adds.

Fu and Ralph R. Weichselbaum, M.D., at the University of Chicago led the study. Co-authors include lead authors Yaoyao Shi and Wenxin Zheng as well as Kaiting Yang, Katharine G. Harris, Kaiyuan Ni, Lai Xue, Wenbin Lin, and Eugene B. Chang, all of the University of Chicago.

The study was supported by the Ludwig Foundation, The Foglia Foundation, National Institutes of Health/National Cancer Institute Provocative Questions grants (R21 CA231273-01, CA141975), and CPRIT grants (RR150072, RP 180725).

http://bit.ly/32ZGj1x

Researchers find evidence of a cosmic impact that caused destruction of one of the world's earliest human settlements

First site to document the direct effects of a fragmented comet on a human settlement.

by Sonia Fernandez, University of California - Santa Barbara

Before the Taqba Dam impounded the Euphrates River in northern Syria in the 1970s, an archaeological site named Abu Hureyra bore witness to the moment ancient nomadic people first settled down and started cultivating crops. A large mound marks the settlement, which now lies under Lake Assad.

But before the lake formed, archaeologists were able to carefully extract and describe much material, including parts of houses, food and tools—an abundance of evidence that allowed them to identify the transition to agriculture nearly 12,800 years ago. It was one of the most significant events in our Earth's cultural and environmental history.

Abu Hureyra, it turns out, has another story to tell. Found among the cereals and grains and splashed on early building material and animal bones was meltglass, some features of which suggest it was formed at extremely high temperatures—far higher than what humans could achieve at the time—or that could be attributed to fire, lighting or volcanism.

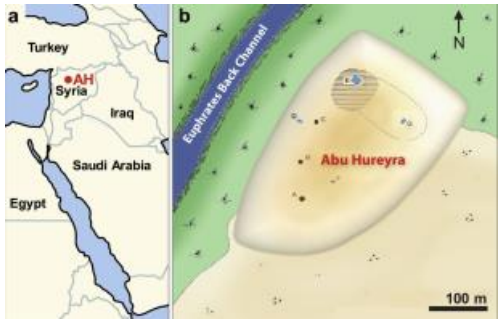
"To help with perspective, such high temperatures would completely melt an automobile in less than a minute," said James Kennett, a UC Santa Barbara emeritus professor of geology. Such intensity, he added, could only have resulted from an extremely violent, high-energy, high-velocity phenomenon, something on the order of a cosmic impact.

Based on materials collected before the site was flooded, Kennett and his colleagues contend Abu Hureyra is the first site to

document the direct effects of a fragmented comet on a human settlement. These fragments are all part of the same comet that likely slammed into Earth and exploded in the atmosphere at the end of the Pleistocene epoch, according to Kennett. This impact contributed to the extinction of most large animals, including mammoths, and American horses and camels; the disappearance of the North American Clovis culture; and to the abrupt onset of the end-glacial Younger Dryas cooling episode.

The team's findings are highlighted in a paper published in the Nature journal *Scientific Reports*.

"Our new discoveries represent much more powerful evidence for very high temperatures that could only be associated with a cosmic impact," said Kennett, who with his colleagues first reported evidence of such an event in the region in 2012.



Location of Abu Hureyra (adapted from Moore et al.. (a) Map of the Middle East, showing Abu Hureyra location (AH) in Syria. (b) Map of the Abu Hureyra tell, showing locations of excavation trenches labeled A-G near a back channel of Euphrates River that is now abandoned. Sediment samples from Trenches D, E, and G (blue rectangles) contain abundance peaks in YDB proxies, including spherules, nanodiamonds, meltglass, and platinum.
Credit: Scientific Reports (2020). DOI: 10.1038/s41598-020-60867-w

Abu Hureyra lies at the easternmost sector of what is known as the Younger Dryas Boundary (YDB) strewnfield, which encompasses about 30 other sites in the Americas, Europe and parts of the Middle East. These sites hold evidence of massive burning, including a widespread carbon-rich "black mat" layer that contains millions of nanodiamonds, high concentrations of platinum and tiny metallic spherules formed at very high temperatures. The YDB impact hypothesis has gained more traction in recent years because of many new discoveries, including a very young impact crater beneath the Hiawatha Glacier of the Greenland ice sheet, and high-temperature meltglass and other similar evidence at an archaeological site in Pilauco, located in southern Chile.

"The Abu Hureyra village would have been abruptly destroyed," Kennett said. Unlike the evidence from Pilauco, which was limited to human butchering of large animals up to but not younger than the YDB impact burn layer, Abu Hureyra shows direct evidence of the disaster on this early human settlement. An impact or an airburst must have occurred sufficiently close to send massive heat and molten glass over the entire early village, Kennett noted.

The glass was analyzed for geochemical composition, shape, structure, formation temperature, magnetic characteristics and water content. Results from the analysis showed that it formed at very high temperatures and included minerals rich in chromium, iron, nickel, sulfides, titanium and even platinum- and iridium-rich melted iron—all of which formed in temperatures higher than 2200 degrees Celsius.

"The critical materials are extremely rare under normal temperatures, but are commonly found during impact events," Kennett said. According to the study, the meltglass was formed "from the nearly instantaneous melting and vaporization of regional biomass, soils and floodplain deposits, followed by instantaneous cooling." Additionally, because the materials found are consistent with those found in the YDB layers at the other sites across the world, it's likely that they resulted from a fragmented comet, as opposed to impacts caused by individual comets or asteroids.

"A single major asteroid impact would not have caused such widely scattered materials like those discovered at Abu Hureyra," Kennett said. "The largest cometary debris clusters are proposed to be capable of causing thousands of airbursts within a span of minutes across one entire hemisphere of Earth. The YDB hypothesis

proposed this mechanism to account for the widely dispersed coeval materials across more than 14,000 kilometers of the Northern and Southern Hemispheres. Our Abu Hureyra discoveries strongly support a major impact event from such a fragmented comet."

More information: *Andrew M. T. Moore et al. Evidence of Cosmic Impact at Abu Hureyra, Syria at the Younger Dryas Onset (~12.8 ka): High-temperature melting at >2200 °C, Scientific Reports (2020). DOI: 10.1038/s41598-020-60867-w*

Research on this study was conducted also by Andrew Moore, from the Rochester Institute of Technology in New York; William M. Napier, from the Armagh Observatory and Planetarium in Norther Ireland; Ted E. Bunch and James H. Wittke, from Northern Arizona University; James C. Weaver, from Harvard University; Malcolm LeCompte and A. Victor Adedji, from Elizabeth State University in North Carolina; Paul Hackley, from the United States Geological Survey; Gunther Kletetschka, from the Czech Academy of the Sciences, Charles University in the Czech Republic and University of Alaska; Robert E. Hermes, from Los Alamos National Laboratory (retired); Joshua J. Razink from the University of Oregon; Michael Willam Gaultois, from the University of Liverpool in the UK; and Allen West, from the Comet Research Group in Arizona.

https://wb.md/2PWWPtC

Infectious Disease Docs in Short Supply Yet 'Critical' for COVID-19 Crisis

As the coronavirus outbreak continues to spread, infectious disease specialists are in short supply and might be overwhelmed by the emergency

Ken Terry

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

As the coronavirus outbreak continues to spread, infectious disease specialists are in short supply and might be overwhelmed by the emergency, Thomas File Jr, MD, president of the Infectious Disease Society of America, told *Medscape Medical News*.

"Depending on the burden on our healthcare systems, we're going to be at the center of caring for these patients," said File, who is a practicing infectious disease specialist at Summa Health in Akron, Ohio. "Also, we have to spend time communicating with the community to dispel some of the myths [related to the novel coronavirus]. So already, we're seeing an increased workload because of this. And if COVID-19 spreads significantly — and I think we have to be prepared that it will — we're going to need a larger workforce to deal with this," he said.

Infectious disease specialists at Summa Health, File added, are overtaxed because of "a very active influenza season," on top of helping the institution prepare for COVID-19 cases. This involves setting up a command center and creating protocols to diagnose and treat patients as they arrive.

In addition, ID specialists are on the front line of coping with "the public health crisis of antimicrobial resistance," he points out. "We have to make sure we're using antibiotics appropriately and promoting the development of new antibiotics so we'll have them available for the future."

File emphasized that COVID-19 is not the only emerging pandemic that ID specialists have had to deal with or will have to deal with in the future. He cited the threats that Zika and SARS posed in past years. "COVID-19 illustrates the need for more trained ID specialists, because we know we're going to be seeing more outbreaks in the future."

"Overworked and Underpaid"

Nevertheless, the number of physicians entering the field has steeply declined in recent years. According to a 2019 Merritt Hawkins report, "Between the 2009-2010 and 2016-2017 fellowship matches, the number of adult ID [infectious disease] programs filling all their positions dropped by 41% and the number of applicants decreased by 31%. In 2015, fewer than half of US ID fellowships filled their incoming classes."

In 2017, there were 9122 infectious-disease specialists in the US, about 1% of the total number of American physicians, according to the American Association of Medical Colleges.

Asked why so few doctors are going into the specialty, File replied, "To put it simply, we're overworked and underpaid."

A 2019 Medscape survey shows ID specialists earned an average of $239,000 a year. That's in the same range as the compensation of primary care physicians. However, File noted, it's about $100,000 less, on average, than what other non–primary-care specialists earn.

The main reason for this, File said, is that ID specialists perform cognitive tasks rather than procedures and are thus compensated under the lower-paying evaluation and management codes. Yet ID specialists manage very complex cases and know how to administer specialized drugs that other physicians may have no experience using.

"We don't do procedures, but we take care of very sick patients in the ICU, which may take hours, and we're not going to be compensated for the value we're providing," File said.

Infectious diseases requiring complex care coordination are commonly observed in settings with high poverty, mental illness, addiction, and incarceration, the Merritt Hawkins report pointed out. File admitted that some young doctors might be hesitant to enter the specialty because of that factor. He noted there has been a steep rise in infectious disease complications stemming from the opioid epidemic, including skin and bloodstream infections.

On the other hand, File said, there are many positive factors that should attract physicians to the infectious-disease specialty. These include the intellectual simulation of research, the opportunity to fight emerging infections in third-world countries, and the ability to cure very sick patients whom other doctors can't help.

"The nice thing about infectious diseases, as compared to some of the other medical subspecialties, is we actually cure patients," he said. "When I see a patient with life-threatening meningitis and we're able to give him the appropriate medicine, he can be cured and leave the hospital perfectly fine. That's very gratifying, and the patients are very appreciative of that as well."

Several studies have shown that ID specialists not only improve outcomes for such patients but also reduce the cost of care, according to File. The Centers for Medicare & Medicaid Services (CMS) should recognize that and increase payments to ID specialists, he said.

As for the US response to the COVID-19 emergency, the ISDA president stated, "It's important for infectious-disease specialists to be able to respond to infectious disease outbreaks and help prepare institutions to respond to them as well. Many of our members are also helping to develop vaccines and therapies. So our specialty is extremely important at this critical time to respond to this outbreak."