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Formation of coal almost turned our planet into a snowball

While burning coal today causes Earth to overheat, about 300 million years ago the formation of that same coal brought our planet close to global glaciation.

For the first time, scientists show the massive effect in a study to be published in the renowned Proceedings of the US Academy of Sciences. When trees in vast forests died during a time called the Carboniferous and the Permian, the carbon dioxide (CO2) they took up from the atmosphere while growing got buried; the plants' debris over time formed most of the coal that today is used as fossil fuel. Consequently, the CO2 concentration in the atmosphere sank drastically and Earth cooled down to a degree it narrowly escaped what scientists call a 'snowball state'.

"It is quite an irony that forming the coal that today is a major factor for dangerous global warming once almost lead to global glaciation," says author Georg Feulner from the Potsdam Institute for Climate Impact Research. "However, this illustrates the enormous dimension of the coal issue. The amount of CO2 stored in Earth's coal reserves was once big enough to push our climate out of balance. When released by burning the coal, the CO2 is again destabilizing the Earth system."

The study examines the sensitivity of the climate in a specific period of Earth's deep past by using a large ensemble of computer simulations. While some of the changes in temperature at that time can clearly be attributed to how our planet's axis was tilted and the way it circled the sun, the study reveals the substantial influence of CO2 concentrations. Estimates based on ancient soils and fossil leaves show that they fluctuated widely and at some point sank to about 100 parts CO2 per million parts of all gases in the atmosphere, and possibly even lower. The model simulations now reveal that global glaciation occurs below 40 parts per million.

Burning that same coal dangerously raises greenhouse gas concentration in our atmosphere

Today, CO2 levels in the atmosphere have reached more than 400 parts per million. Carbon dioxide acts as a greenhouse gas: the Sun warms Earth's surface, but most of the heat radiated by the surface escapes into space; CO2 and other greenhouse gases hinder part of this heat from escaping, hence warming the planet.

"We should definitely keep CO2 levels in the atmosphere below 450 parts per million to keep our climate stable, and ideally much lower than that. Raising the amount of greenhouse gases beyond that limit means pushing ourselves out of the safe operating space of Earth," says Feulner. "Earth's past teaches us that periods of rapid warming were often associated with mass extinction events. This shows that a stable climate is something to appreciate and protect."

Article: Feulner, G. (2017): Formation of most of our coal brought Earth close to global glaciation. Proceedings of the National Academy of Sciences (PNAS)

http://bit.ly/2kN7YjG

Amazon farmers discovered the secret of domesticating wild rice 4,000 years ago

Amazonian farmers discovered how to manipulate wild rice so the plants could provide more food 4,000 years ago, long before Europeans colonised America, archaeologists have discovered.

Experts from the UK and Brazil have found the first evidence that ancient South Americans learned how to grow bigger rice crops with larger grains, but this expertise may have been lost after 1492 when the indigenous population was decimated, research shows.

The evidence of the success of early rice farmers on the vast wetlands near the Guaporé River in Rondônia state, Brazil, could help modern day plant breeders develop rice crops which are less susceptible to disease and more adaptable to the effects of climate change than the Asian varieties. Different species of rice were first grown approximately 11,000 years ago in the Yangtze River, China, and around 2,000 years ago in West Africa.

The University of Exeter study, funded in part by the European Research Council, also shows how important the huge wetlands and tropical forests of lowland South America were in providing food for early human settlers in South America. Ancient inhabitants managed to domesticate cassava, peanuts and chilli peppers crops for food.

The archaeologists analysed 16 samples of microscopic plant remains from ten different time periods found during excavations during 2014 led by the University of São Paulo in South West Amazonia. More phytoliths, hard, microscopic pieces of silica made by plant cells, were found at higher ground level, suggesting rice began to play a larger role in the diet of people who lived in the area - and more was farmed - as time went on.

Changes in the ratio of husk, leaf and stem remains found at different ground levels also suggest the Amazon residents became more efficient harvesters over time, bringing more grain and fewer leaves to the site. The rice grown, Oryza sp, also became bigger over time compared to the wild rice first cultivated by the South Americans. This area has been occupied by humans for at least 10,000 years.

Professor Jose Iriarte, from the University of Exeter, who led the research, said: "This is the first study to identify when wild rice first began to be grown for food in South America. We have found people were growing crops with larger and larger seeds. Even though they were also eating wild and domesticated plants including maize, palm fruits, soursop and squash, wild rice was an important food, and people began to grow it at lake or river edges.

"During a time when the climate was getting wetter and the wetlands expanding, this critical seasonal resource that is ripe at the peak of the flooding season when other resources are dispersed and scarce, residents of Monte Castelo began to grow larger rice"

Evidence for mid-Holocene rice domestication in the Americas by Lautaro Hilbert and Jose Iriarte from the University of Exeter, Elizabeth Veasey, Carlos Augusto Zimpel, Eduardo Goes Neves and Francisco Pugliese from the Universidade de São Paulo, Bronwen S. Whitney from Northumbria University and Myrtle Shock from the Universidade Federal do Oeste de Pará, is published in the journal Nature Ecology and Evolution.

http://bit.ly/2i9P71w

Novel treatment causes cancer to self-destruct without affecting healthy cells

Scientists at Albert Einstein College of Medicine have discovered the first compound that directly makes cancer cells commit suicide while sparing healthy cells.

BRONX, NY-- The new treatment approach, described in today's issue of Cancer Cell, was directed against acute myeloid leukemia (AML) cells but may also have potential for attacking other types of cancers.

"We're hopeful that the targeted compounds we're developing will prove more effective than current anti-cancer therapies by directly causing cancer cells to self-destruct," says Evripidis Gavathiotis, Ph.D., associate professor of biochemistry and of medicine and senior author of the study. "Ideally, our compounds would be combined with other treatments to kill cancer cells faster and more efficiently--and with fewer adverse effects, which are an all-too-common problem with standard chemotherapies."

AML accounts for nearly one-third of all new leukemia cases and kills more than 10,000 Americans each year. The survival rate for patients has remained at about 30 percent for several decades, so better treatments are urgently needed.

The newly discovered compound combats cancer by triggering apoptosis--an important process that rids the body of unwanted or malfunctioning cells. Apoptosis trims excess tissue during embryonic development, for example, and some chemotherapy drugs indirectly induce apoptosis by damaging DNA in cancer cells.

Apoptosis occurs when BAX--the "executioner protein" in cells--is activated by "pro-apoptotic" proteins in the cell. Once activated, BAX molecules home in on and punch lethal holes in mitochondria, the parts of cells that produce energy. But all too often, cancer cells

manage to prevent BAX from killing them. They ensure their survival by producing copious amounts of "anti-apoptotic" proteins that suppress BAX and the proteins that activate it.

"Our novel compound revives suppressed BAX molecules in cancer cells by binding with high affinity to BAX's activation site," says Dr. Gavathiotis. "BAX can then swing into action, killing cancer cells while leaving healthy cells unscathed."

Dr. Gavathiotis was the lead author of a 2008 paper in Nature that first described the structure and shape of BAX's activation site. He has since looked for small molecules that can activate BAX strongly enough to overcome cancer cells' resistance to apoptosis. His team initially used computers to screen more than one million compounds to reveal those with BAX-binding potential. The most promising 500 compounds--many of them newly synthesized by Dr. Gavathiotis' team--were then evaluated in the laboratory.

"A compound dubbed BTSA1 (short for BAX Trigger Site Activator 1) proved to be the most potent BAX activator, causing rapid and extensive apoptosis when added to several different human AML cell lines," says lead author Denis Reyna, M.S., a doctoral student in Dr. Gavathiotis' lab. The researchers next tested BTSA1 in blood samples from patients with high-risk AML. Strikingly, BTSA1 induced apoptosis in the patients' AML cells but did not affect patients' healthy blood-forming stem cells.

Finally, the researchers generated animal models of AML by grafting human AML cells into mice. BTSA1 was given to half the AML mice while the other half served as controls. On average, the BTSA1-treated mice survived significantly longer (55 days) than the control mice (40 days), with 43 percent of BTSA1-treated AML mice alive after 60 days and showing no signs of AML.

Importantly, the mice treated with BTSA1 showed no evidence of toxicity. "BTSA1 activates BAX and causes apoptosis in AML cells while sparing healthy cells and tissues--probably because the cancer cells are primed for apoptosis," says Dr. Gavathiotis. He notes that his study found that AML cells from patients contained significantly higher BAX levels compared with normal blood cells from healthy people. "With more BAX available in AML cells," he explained, "even low BTSA1 doses will trigger enough BAX activation to cause apoptotic death, while sparing healthy cells that contain low levels of BAX or none at all." Plans call for Dr. Gavathiotis and his team to see whether BTSA1 will show similar effectiveness when tested on animal models of other types of cancer.

The paper, "Direct activation of BAX by BTSA1 overcomes apoptosis resistance in acute myeloid leukemia," was published October 9 in Cancer Cell. In addition to Dr. Gavathiotis and Mr. Reyna, other Einstein researchers involved in the study were Thomas P. Garner, Ph.D., Andrea Lopez, M.S., Felix Kopp, Ph.D., Gaurav S. Choudhary, Ph.D., Ashwin Sridharan, M.D., Swathi-Rao Narayanagari, M.S., Kelly Mitchell, M.S., Baoxia Dong, Ph.D., Boris A. Bartholdy, Ph.D., Amit Verma, MB.B.S., and Ulrich Steidl, M.D., Ph.D.

Funding for this research was provided by the National Cancer Institute (NCI), part of the National Institutes of Health (R01CA178394), and awards from the Sidney Kimmel Foundation for Cancer Research, the Gabrielle's Angels Foundation for Cancer Research, and the Pershing Square Sohn Cancer Research Alliance. Partial support was also provided by the Albert Einstein Cancer Center, which is funded by the NCI (P30CA013330).

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UA snakebite treatment makes major advance

Results published showing carbon monoxide-iron-based therapy can inhibit snake venom's effects for up to an hour in animals

TUCSON, Ariz. - A University of Arizona researcher developing a therapy to prevent or delay the dangerous results of rattlesnake and other venomous snakebites in humans has shown that a combination of carbon monoxide and iron inhibits snake venom's effects for up to an hour in animals, a major advance in bringing the treatment to market.

Snake venom is hemotoxic--destructive to the ability of blood to clot--and can cause the destruction of fibrinogen, an essential protein that enables blood to clot and stop excessive bleeding. Snake venom enzymes also can cause abnormally fast clotting, which can lead to heart attack, stroke and damage to the body's organs. Both reactions are inhibited by the therapy.

Vance G. Nielsen, MD, professor and vice chair for research in the UA Department of Anesthesiology at the UA College of Medicine -

Tucson, has confirmed that, if given soon enough after a snake bite, the carbon monoxide-iron-based therapy directly can inhibit snake venom's ability to block blood clotting in laboratory animals for as long as an hour. Dr. Nielsen also demonstrated for the first time in the test tube that the therapy blocks snake venom's ability to cause abrupt clotting. The findings recently were published in the journals Basic & Clinical Pharmacology & Toxicology and the Journal of Thrombosis and Thrombolysis.

Time is of the essence following exposure to rattlesnake venom because without fibrinogen, blood does not clot and the risk of internal bleeding increases, resulting in serious health consequences such as blood entering the brain or intestines. In addition, abnormally fast clotting in the blood vessels can deplete clotting factors and cause excessive bleeding or the clots can block blood vessels, causing lethal loss of blood flow to tissue.

Dr. Nielsen has found that the therapy works against the venom of more than three dozen species of snakes throughout the world.

"The excitement is that we have proven that carbon monoxide has the ability to directly inhibit essentially all hemotoxic venom enzymes in the test tube and that it blocks the effects of the Western Diamondback rattlesnake's venom in animals. The effects on coagulation of some of the deadliest snake venoms in the world--South American, North American and even African, such the cobra's--can be delayed by a treatment that could be delivered with a device much like an EpiPen used for allergic reactions," said Dr. Nielsen, who is working toward developing the treatment to work in humans.

To further advance the research, Dr. Nielsen is seeking commercial backing and is working with Tech Launch Arizona, the UA office that commercializes inventions stemming from university research, to protect the intellectual property of the treatment and strategize ways to get it into the hands of health professionals.

He also is collaborating with toxicologist Leslie Boyer, MD, founding director of the UA VIPER Institute and professor of pathology and pediatrician, who develops antivenom treatments for snakebite and scorpion stings. Dr. Boyer also is a member of the UA BIO5 Institute.

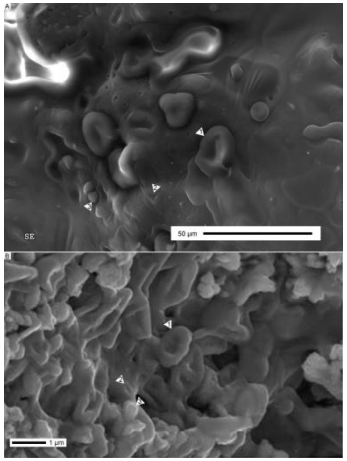
"Our aim is to bring to market a therapy that is safe for humans and animals, has a long shelf life, is readily available and can be stocked in ambulances, or even first-aid kits for campers or hikers, to save lives," said Dr. Nielsen.

This research was supported by grants from the University of Arizona (Tech Launch Arizona Asset Development Award 15-160) and UA Department of Anesthesiology, and the National Institutes of Health's Office of Research Infrastructure Programs, Viper Resource Grant No. 5P40OD010960.

http://bit.ly/2zj575n

Dinosaur blood? New research urges caution regarding fossilized soft tissue

Their findings demonstrate that previous claims showing the preservation of keratin protein in dinosaur fossils are likely to be false.



Similarly, widely publicised claims of dinosaur blood in fossil bones were shown to likely represent an artefact of degraded organic matter rather than actual blood cells.

The researchers undertook experimental treatments that either used microbes to decay tissues or subjected tissues to intense heat and pressure - a process known as maturation - in order to mimic the conditions a fossil experiences deep underground.

Electron microscopy of abiotically-formed structures as an explanation for 'dinosaur blood'. A) Moderately matured turkey skin. B) Proposed blood-like structures in a dinosaur bone (modified from Bertazzo et al. (2015, online Supplementary Fig. 3c) and used under Creative Commons CC-BY license). Presented here with a defined scale bar. Arrowheads indicate several shared structures: (1) concave bulge/fold continuous with the underlying organic material; (2) pit/simple fold; (3) spherical bulge. **University of Bristol**

Evan Saitta from the University of Bristol's School of Earth Science, led the research which has been published in the journal Palaios.

He said: "Decay and mild maturation resulted in some intriguing textural differences in degradation patterns based on the type of keratin such as curling versus crimping of filaments when matured.

"These results may show promise for identifying relatively recent archaeological keratin remains but when maturation conditions are increased to simulate conditions present during burial and fossilisation, the keratin degrades into a foul-smelling, water-soluble fluid that can dissolve or leach away from the fossil."

In another experiment the vacuum conditions of an electron microscope appear to have produced folds, pits and blebs in a sample of degraded turkey skin, similar to those features previously suggested to represent dinosaur blood cells.

The range of sizes and shapes of these experimental and fossil structures is evidence that they form through a non-biological process, as opposed to a biological process like the formation of cells.

Thus, the purported blood cells in these dinosaur bones are likely to be degraded organics, most likely from microbes that invaded the cavities in the bone rather than exceptionally preserved, easily-degradable blood cells. Saitta added: "We've shown that different keratin types show intriguing differences in degradation patterns that might help identify keratinous remains in archaeological material.

"However, when the processes of fossilisation and burial over deep time are simulated, keratin protein fully degrades into a fluid that can be lost from fossils, meaning little utility for studying paleontological remains despite contrary claims."

http://bit.ly/2i9oqT4

Drone designers accidentally explain colour of albatross wings

IT'S not every day that an aerospace engineer raises new questions about bird flight.

But Abdessattar Abdelkefi and his team at New Mexico State University did just that while trying to devise better drones. Many large soaring birds like the albatross have wings that are white underneath and black on top. Previous explanations focused on camouflage, says Graham Martin at the University of Birmingham, UK.

Frans Lanting/National Geographic Creative

But does that colouring really boost endurance in flight? Most soaring needs no flapping of wings; instead, the bird exploits air currents to glide.

Abdelkefi's team discovered that a wing's black upper surface absorbs sunlight very efficiently, causing it to be around 10°C warmer than the lower surface. That effectively lowers air pressure on the upper surface, lowering drag and generating extra lift (Journal of Thermal Biology, doi.org/f96ggw).

Svana Rogalla at the University of Ghent, Belgium, says thermography has proved that the dark upper wing gets hotter in sunlight, but it is too early to pin down its effect on drag. The impact of colour on flight could be a further inducement for birds to make costly melanin pigment to darken feathers, she says.

The team hopes the findings will help them design more efficient and durable drones for use at sea.

http://bit.ly/2ylffwq

Menopause triggers metabolic changes in brain that may promote Alzheimer's

Menopause causes metabolic changes in the brain that may increase the risk of Alzheimer's disease

Menopause causes metabolic changes in the brain that may increase the risk of Alzheimer's disease, a team from Weill Cornell Medicine and the University of Arizona Health Sciences has shown in new research.

The findings, published today in PLoS One, could help solve a longstanding mystery about Alzheimer's, namely, why women get this fatal neurodegenerative disorder more often than men -- even

accounting for the fact that women on average live longer. The investigators say the results also eventually may lead to the development of screening tests and early interventions to reverse or slow the observed metabolic changes.

Alzheimer's afflicts more than 5 million Americans, including one-third of Americans older than 85, and the disease process is known to begin several decades before dementia sets in.

"This study suggests there may be a critical window of opportunity, when women are in their 40s and 50s, to detect metabolic signs of higher Alzheimer's risk and apply strategies to reduce that risk," said lead author Dr. Lisa Mosconi, who was recruited to Weill Cornell Medicine as an associate professor of neuroscience in neurology.

For the study, Dr. Mosconi and her colleagues, including senior author Dr. Roberta Brinton from the University of Arizona Health Sciences in Tucson, used the imaging test positron emission tomography (PET) to measure the use of glucose--a principal fuel source for cellular activity--in the brains of 43 healthy women ages 40 to 60. Of those, 15 were pre-menopausal, 14 were transitioning to menopause (peri-menopause) and 14 were menopausal.

The tests revealed the women who had undergone menopause or were peri-menopausal had markedly lower levels of glucose metabolism in several key brain regions than those who were pre-menopausal. Scientists in prior studies have seen a similar pattern of "hypometabolism" in the brains of patients in the earliest stages of Alzheimer's -- and even in mice that model the disease.

In addition, menopausal and peri-menopausal patients showed lower levels of activity for an important metabolic enzyme called mitochondrial cytochrome oxidase, as well as lower scores on standard memory tests. The strong contrast with pre-menopausal patients remained even when accounting that the menopausal and peri-menopausal women were older.

"Our findings show that the loss of estrogen in menopause doesn't just diminish fertility," said Dr. Mosconi, associate director of the Alzheimer's Prevention Clinic at Weill Cornell Medicine and NewYork-Presbyterian. "It also means the loss of a key neuroprotective element in the female brain and a higher vulnerability to brain aging and Alzheimer's disease. We urgently need to address these problems because, currently, 850 million women worldwide are entering or have entered menopause. Our studies demonstrate that women need medical attention in their 40s, well in advance of any endocrine or neurological symptoms."

The findings add to mounting evidence that there is physiological connection between menopause and Alzheimer's. Dr. Mosconi and colleagues published a study in Neurology in September that linked menopause to increased accumulation of the Alzheimer's-associated protein amyloid beta in the brain. The investigators also observed reduced volumes of gray matter (brain cells) and white matter (nerve fiber bundles) in brain regions that are strongly affected in Alzheimer's.

Menopause long has been known to cause brain-related symptoms, including depression, anxiety, insomnia and cognitive deficits. Scientists widely believe they are caused largely by declines in estrogen levels. Estrogen receptors are found on cells throughout the brain and evidence suggests that reduced signaling through these receptors due to low estrogen levels can leave brain cells generally more vulnerable to disease and dysfunction.

More specifically, the authors suggest that the menopausal fall in estrogen may trigger a shift to a "starvation reaction" in brain cells -- a metabolic state that is beneficial in the short term but can be harmful in the long term.

"Our work indicates that women may need antioxidants to protect their brain activity and mitochondria in combination with strategies to maintain estrogen levels," Dr. Mosconi said, noting that exercise and foods that are rich in antioxidants, such as flaxseeds, also may help boost estrogen production. "We believe that more research is needed to test efficacy and safety of hormonal-replacement therapies at the

very early stages of menopause, and to correlate hormonal changes with risk of Alzheimer's. This is a major priority at our Alzheimer's Prevention Clinic."

Dr. Mosconi and her colleagues now plan to expand their patient group, and also hope to perform longer-term, more comprehensive analyses of neural and metabolic markers during and after menopause. This work may lead to the development of biomarkers that could help investigators identify at-risk patients.

"We really need to follow larger groups of women over long periods to see how this menopausal change in metabolism relates to Alzheimer's," she said.

Said Dr. Brinton, a leading neuroscientist in the field of Alzheimer's, the aging female brain and regenerative therapeutics: "Outcomes of this study will provide critical evidence for early changes in the aging female brain that are relevant to the two-fold greater lifetime risk in Alzheimer's disease. Importantly, these results indicate that we know when to intervene in the aging process to divert the potential for developing this devastating disease."

http://bit.ly/2ylQ24A

Potent Nocebo: The more expensive a harmless cream, the more pain it inflicts

The flip-side of placebo effect is more dangerous side effects—and the pain is real.

Beth Mole - 10/10/2017, 6:17 AM

The mind is a powerful medicine. Given an ineffective treatment, patients can experience real health improvements by simply believing that the treatment works—the placebo effect. But this blissful delusion has a dark side: when a harmless placebo becomes effective, it becomes harmful, too, causing side-effects seen in actual therapies.

In a new study exploring this mysterious “nocebo effect,” researchers pinpoint regions of the brain that seem to be behind phantom injuries. They also assess factors—framing and price—that can increase the potency of the effect. These may be critical to designing and assessing clinical practices and trial results, they argue.

Specifically, researchers gave patients a sham anti-itch cream for eczema (atopic dermatitis) and told them it increases sensitivity to pain as a side effect—which is a side effect of real medicines, but the phony cream shouldn’t have any side effects. Nevertheless, patients not only reported more pain, but the amount of pain they reported depended on the cream’s price and packaging. The cream caused more pain in patients when they were told it had a hefty price tag and came in a brand-name-looking box, compared with when they thought it was a cheap cream that came in a generic-looking box. The researchers, led by neuroscientist Alexandra Tinnermann of University Medical Center Hamburg-Eppendorf, published the results recently in *Science*.

Patients reported no heightened pain when using a control cream, even though the same benign cream was used for all three types: the expensive, cheap, and control. The only differences were the prices, packaging, and the patients’ expectations. The researchers speculate that patients expected the expensive, brand-name-looking drug to simply be more effective than the one that looked like a cheap knock-off. Thus it would be more potent and have stronger side effects.

In an accompanying editorial, pain and placebo expert Luana Colloca says the findings show that nocebo effects may skew clinical trial data and patient’s adherence to drugs.

Given these effects, Dr. Colloca urges:

We should consider how to avoid them in clinical trials and practices—for example, by tailoring patient-clinician communication to balance truthful information about adverse events with expectancies of outcome improvement, exploring patients’ treatment beliefs and negative therapeutic history, and paying attention to framing (i.e., treatment description) and contextual effects (i.e., price).

Pernicious placebo

For the study, Tinnermann and colleagues recruited 49 healthy participants and told them the trial was comparing the pain-sensitizing

side effects of two creams, one cheap and one expensive. Twenty-five participants got the expensive cream and the remaining 24 tested the cheap one. As a reference, the researchers also included a "control cream" that would supposedly have no side effects. In reality, the whole study used only one type of fatty cream, which contained no active ingredient.

Next, the researchers primed the participants for a "nocebo effect" so they could test how the cream's price and packaging altered said effect. To do this, the researchers used a tricky pain test. Each participant rubbed some "control cream" on one patch of their left forearm and some "test cream" (expensive or cheap) on a different patch of the same forearm. After 30 minutes of sinking-in time, the researchers wiped off the creams and applied a small device that would deliver a mildly painful flash of heat. The researchers told the participants that the device would deliver the same painful flash to each patch of treated skin.

Over the skin treated with the control cream, the device delivered a mild blast of heat that would register as a "30" on a pain sensitivity scale calibrated for each participant. But, on the test cream-treated skin patch, the device delivered a more painful blast set to register as a "70." This little lie fed into the participant's expectations that the test creams (cheap or expensive) would boost pain sensitivity, while the control cream would not.

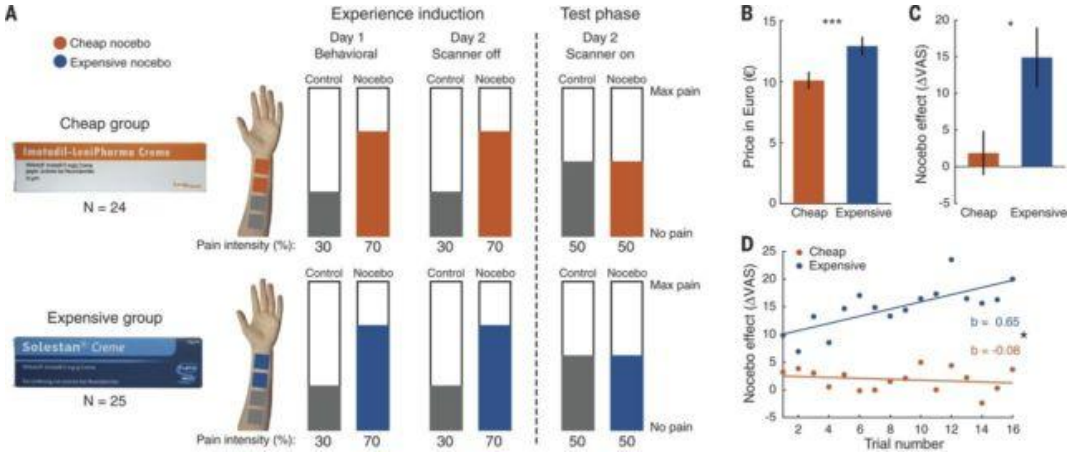
Next, the researchers repeated the pain testing 16 times with each participant over the course of a few days. But, for these tests, the researchers delivered heat blasts that all should have registered as "50" on the calibrated pain scales, regardless of cream treatment. While all of this was going on, the participants were in an MRI machine so researchers could monitor their brain and spinal cord activity.

Mental anguish

As expected, the participants displayed a nocebo effect, collectively reporting pain levels higher than 50 on skin treated with test creams, but around 50 for skin treated with control cream.

Moreover, the participants who tested the supposedly expensive cream reported more pain than those who thought they were testing a cheap cream. And the expensive cream seemed to become more harmful over the 16 trials. In early runs, the cheap-cream testers registered around 55 on the pain scale, while the expensive cream testers landed around 60. By the end of the 16 trials, the cheap testers' pain levels stayed about the same, but the expensive testers' pain jumped to a 70 on the scale.

When the researchers looked at the MRI data, they found that there was more activity in spinal cord regions of the expensive-cream testers. This suggested that the testers weren't just imagining and reporting more pain—they were actually feeling it.



***Enlarge** / (A) Experimental design of the nocebo and value manipulation with photos of the designed medical-cream boxes. (B) The blue cream box was estimated as being significantly more expensive than the orange box. (C) The behavioral nocebo effect was significantly larger in the expensive group than in the cheap group. (D) Time courses of the nocebo effect expressed as slope in a linear regression model (b) differed significantly between groups; VAS, visual analog scale; bars represent means, and error bars represent SEM.*

Tinnermann et al.

The researchers also pinpointed areas of the brain that seemed to be involved in the nocebo effect overall. These are the rostral anterior

cingulate cortex and the periaqueductal gray, which are involved in higher-level functioning and pain, respectively.

Together, the data suggest that the cream's price didn't just alter pain report but activity in the body's pain circuitry. It "modulated coupling between prefrontal areas, brainstem, and spinal cord," Tinnermann and her colleagues concluded. And this might give researchers hints on how to tap into and alter early pain processing.

Science, *2017. DOI: 10.1126/science.aan1221*

http://bit.ly/2q7Bb3A

Whoops: Drug ads gloss over risks with a mind trick—that's backed by the FDA

Drug makers are supposed to be forthcoming with health risks—and the more the better.

Beth Mole - 10/11/2017, 7:20 AM

To protect patients, the Food and Drug Administration requires that direct-to-consumer drug advertisements present a fair balance of information about a drug's potential benefits and its risks.

Otsuka America Pharmaceutical

As such, the ads seen on television or in magazines often contain an almost comically long list of possible side effects—from minor issues, like headaches or dry mouth, to serious problems, like memory loss, liver damage, or compulsive gambling.

On the surface, any such rundown might seem like a deterrent to trying a new drug. But, according to a new study, a laundry list of risks can make drugs appear less risky—the longer, the better, in fact.

In a series of experiments involving more than 3,000 participants, researchers found that when drug ads clumped severe risks alongside trivial ones, consumers viewed the drugs as less risky compared with when they just heard about the severe risks.

"Thus, listing all frequent side effects, both major and minor, does not dampen the drug's attractiveness, but paradoxically increases it," the behavioral researchers, Niro Sivanathan and Hemant Kakkar of London Business School, concluded. They reported their results Monday in *Nature Human Behaviour*.

The effect also fits with the "fuzzy-trace theory," according to behavioral researcher Brian Zikmund-Fisher of the University of Michigan. In an accompanying editorial, Zikmund-Fisher notes that the fuzzy-trace theory suggests that people process information to get a "core gist." A long list of side effects, including both trifling and terrifying ones, may simply translate to an overall, emotionless gist of "this drug has a variety of risks" to consumers, he explains.

Regardless of the psychological explanation, the study's results clearly "underscore the unintended consequences of current advertisements," Sivanathan and Kakkar conclude. And they have a fix for it.

Risky twist

For the study, the researchers first recruited 804 participants who all listened to a real audio commercial for Cymbalta, a drug given to treat depression. Half the participants heard the full 78-second ad. The other half listened to a 75-second clip that omitted some of the minor side effects. Afterward, those who listened to the full commercial rated the drug as having fewer severe side effects than those who heard the shorter clip.

An obvious explanation might be that those listening to the full ad simply didn't pay close attention to the longer list of side effects. But the researchers ruled that out. In fact, in a follow-up survey, the group that listened to the full ad did *better* at remembering the severe side effects than the group that listened to just those side effects. But, of those who heard just the severe side effects, the more of those side effects they remembered, the riskier they deemed the drug.

In all cases, drugs were seen as riskier when the participants only saw information on the most serious side effects, rather than the full list.

In the last experiment, involving around 600 participants, the researchers again replicated this 'dilution effect'—then reversed it. They broke the group into three sections and again provided side effect information for the fictional Xylopinol. The first group got a full list, the second got just the serious side effects, and the last got an emphasized list. Specifically, the text for the serious side effects were in a bolded, 14-point red text while the minor side effects were in a 12-point, regular black text.

They reasoned:

If dilution is the result of averaging all side effects listed, it is plausible that the process is dampened if participants can cognitively isolate major and minor side effects, by assigning greater emphasis/weight to major and less emphasis/weight to minor side effects when evaluating the overall severity of side effects.

The hypothesis held up: participants who saw the weighted side effects considered the drug just as risky as the participants who saw just serious side effects. Those who saw the full list rated the drug as less risky.

Together, Zikmund-Fisher concludes that "this work suggests that the inclusion of more information, especially if it is unfiltered, can actually be counterproductive." But, separating out the categories of risks may "ensure that patients consider the severity of possible negative outcomes, not just be aware that they might occur."

Nature Human Behaviour, 2017. DOI: 10.1038/s41562-017-0223-1 (About DOIs).

http://bit.ly/2xG46lB

Aging slows perception of falls

Seniors need twice as long as young adults to realize they are falling, a delay that puts them at increased risk for serious injury, according to a new study from the University of Waterloo.

The findings will help shape the development of wearable fall prevention technology and allow clinicians to more accurately identify at-risk individuals. Falls are the leading cause of death and hospitalization in Canada.

"Falling threatens one's survival," said Michael Barnett-Cowan, a kinesiology professor at Waterloo and senior author on the study. "When the nervous system's ability to detect a fall and compensate with protective reflexes diminishes, the risk of injury or death increases significantly.

"Age and associated delays will need to be seriously considered when designing any aids to help seniors mitigate this risk."

According to the Public Health Agency of Canada between 20 and 30 per cent of seniors fall each year. Seniors also make up the fastest growing segment of the global population. By 2040, more than one billion people will be over the age of 65.

"Measuring fall perception not only is important in prevention efforts, but also provides information about how the brain processes sensory information and how this changes with age," said Julian Lupo, a graduate student and the study's lead author.

To measure fall perception, researchers presented study participants with a sound at different times relative to a supervised fall. They found that young adults required the fall to happen about 44 milliseconds before the sound in order for both cues to be perceived as occurring simultaneously. But adults over 60 years old required fall onset to occur about 88 milliseconds before the sound.

"This lag means that by the time older adults realize they are falling, it's often too late for for them to consciously do anything about it," said Barnett Cowan. "Given that falls are often the catalyst for a transition to long-term care, these findings highlight both the importance of adequate assessment for older adults and the need to expedite new prevention technology."

Falls are a leading cause of overall injury costs in Canada, with a total economic burden of falls estimated to be $6 billion annually. Seniors who are hospitalized for a fall remain in hospital an average of nine days longer than those hospitalized for any other cause.

The study appears in the journal Gait & Posture.

http://bit.ly/2yLS7YY

Key odorants in world's most expensive beef could help explain its allure

Several key odorants that contribute to the Wagyu beef's alluring aroma detected

Renowned for its soft texture and characteristic flavor, Wagyu beef -- often referred to as Kobe beef in the U.S. -- has become one of the world's most sought-after meats. Now in a study appearing in the Journal of Agricultural and Food Chemistry, scientists report that they have detected several key odorants that contribute to the delicacy's alluring aroma.

Considered by some to be the champagne or caviar of beef, Waygu is one of the rarest and most expensive meats in the world. It comes from Japanese Black cattle --which accounts for 95 percent of Wagyu -- and three other species raised in Japan. The meat's distinctive marbling, juiciness and succulent taste are enhanced by its sweet aroma, known as "wagyuko," that has been compared to coconut or fruit. In recent years, scientists have been trying to nail down what makes Wagyu aroma distinctive from other types of beef. In one study, researchers found that one particular compound appeared to have an important influence on the meat's aroma. But the samples used in that experiment were not cooked at the optimal temperature. To get a better sense of which odorants are responsible for Wagyu's aroma, Satsuki Inagaki and colleagues decided to try a different approach.

The researchers conducted an aroma extraction dilution analysis of Matsusaka-beef (a kind of Wagyu ribeye) and grass-fed Australia beef (loin). The team heated the samples to about 175 degrees Fahrenheit to simulate optimal cooking conditions. Using gas chromatography techniques, the research team detected 10 newly identified compounds in the Wagyu beef aroma, including one previously associated with cooked chicken that had an egg-white odor. Several Wagyu compounds were also found in the Australian beef aroma. However, the researchers say they likely don't smell alike because of the differing amounts of these constituents in the meats. The most potent odorant of Wagyu beef was a compound known to be derived from fatty acids present in the meat. The researchers say that this study not only clarifies which compounds are the main odorants in cooked Wagyu, it also helps confirm that particular types and amounts of unsaturated fatty acids in the beef play a key part in this aromatic process.

The abstract that accompanies this study is available here.

http://bit.ly/2yLb3qE

What do Americans fear most? Chapman University releases 4th annual Survey of American Fears

Chapman University recently completed its fourth annual Chapman University Survey of American Fears (2017)

Chapman University recently completed its fourth annual Chapman University Survey of American Fears (2017). The survey asked respondents about 80 different fears across a broad range of categories including fears about the government, the environment, terrorism, health, natural disasters, and finances, as well as fears of public speaking, spiders, heights, ghosts and many other personal anxieties.

In addition to the set of fears examined in previous waves, the survey team took a closer look at one particular fear-related phenomena: fear of extremism.

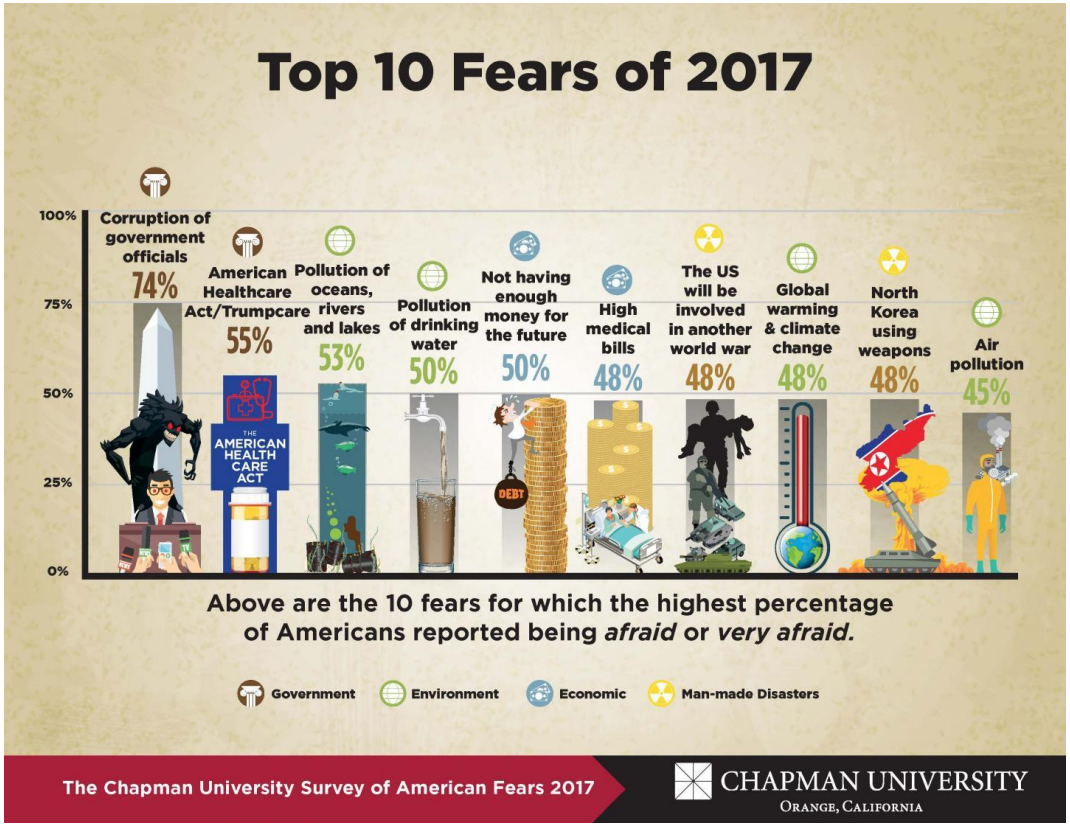
In its fourth year, the annual Chapman University Survey of American Fears included more than 1,207 adult participants from across the nation and all walks of life that is a direct slice of the American population according to census data. The 2017 survey data is organized into four basic categories: personal fears, natural disasters, paranormal fears, and fear of extremism.

The 2017 survey shows that the top 10 things Americans fear the most are:

1) Corruption of government officials (same top fear as 2015 and 2016)
2) American Healthcare Act/Trumpcare (new fear)
3) Pollution of oceans, rivers and lakes (new in top 10)
4) Pollution of drinking water (new in top 10)

5) Not having enough money in the future
6) High medical bills
7) The U.S. will be involved in another world war (new fear)
8) Global warming and climate change
9) North Korea using weapons (new fear)
10) Air pollution

"The 2017 survey data shows us that while some of the top fears have remained, there has also been a pronounced shift to environmental fears," said Christopher Bader, Ph.D., professor of sociology at Chapman University, who led the team effort. "We are beginning to see trends that people tend to fear what they are exposed to in the media. Many of the top 10 fears this year can be directly correlated to the top media stories of the past year."



These are American's Top 10 Fears in 2017. **Chapman University**

Environmental Quality Ranks among Americans' Top Fears

Most striking about American fear in 2017 is that environmental fears figure more prominently than ever before. Environmental issues never cracked the top ten fears in previous surveys. Water pollution ranks third overall, followed closely by drinking water quality.

Water Pollution

- A majority of Americans [53.1 percent] fear pollution of "oceans, rivers and streams."

The fact that water pollution has become such a prominent fear in 2017 may be traced to the reversal of environmental policies of the Obama Administration.

Drinking Water Quality

- 50.4 percent fear for the quality of their drinking water. This could be linked to the prominent news coverage of lead poisoning in the drinking water of Flint, Michigan, during the past year.

Climate Change and Air Pollution

- Americans fear climate change [48 percent] and air pollution [44.9 percent]. These are the eighth and tenth greatest fears, respectively.

The sharp rise in the number of Americans who now say they fear climate change (and air pollution, which contributes to climate change) may be linked to President Trump's controversial decision to withdraw from the Paris Climate Accord.

Fear of Extremism and the Threat to National Security

Americans believe that both Islamic Extremists and White Supremacists represent a threat to national security. Three out of five Americans report they are very afraid or afraid that Islamic Extremists/Jihadists are a threat to national security. After Islamic Extremists/Jihadists, White Supremacists are the only group that a majority of Americans view as a threat to national security (51 percent).

While other types of extremist groups are a concern to large groups of Americans, only those two were identified by a majority of survey respondents. Roughly one-third of Americans identify the following

four as threats: Extreme Anti-Immigration groups, the Militia/Patriot Movement, Left-Wing Revolutionaries, and Extreme Anti-Abortion groups. One in five Americans is afraid Extreme Environmentalists are a threat. "Although the trend isn't perfect, as a general rule, Americans are more afraid of extremist groups that have been discussed in the media," said Ed Day, Ph.D., chair of Chapman's sociology department. "Further, differences between various factions across America on which group represents the greatest threat reflects the political divisions we see in America on other issues."

This fear affects the daily lives of Americans and even leads some to question the value of American freedom?29 percent of Americans report being very afraid or afraid of being a victim of hate crime. One-third agree or strongly agree with the statement, "In order to curb terrorism in this country, it will be necessary to give up some civil liberties." Even more, 35 percent, disagree or strongly disagree with the statement, "We should preserve our freedoms even if it increases the risk of terrorism." As has been seen before, elevated fears over national security can lead to lower support for national values.

America's Knowledge of Disaster Preparedness Outdated, Dangerous

The survey asked Americans about fears of man-made disasters, such as a nuclear melt-down, and nuclear and terror attacks, as well as natural disasters. The survey then asked about their familiarity with safety and preparedness advice/slogans propagated by ready.gov and emergency.cdc.gov

Nuclear Fears

- Nearly half of all Americans [48 percent] fear North Korea using nuclear weapons and 41 percent fear a nuclear attack generally. The prospect of a nuclear meltdown has made 31 percent afraid or very afraid.

"The survey also showed that it's the obsolete, even dangerous, cold war slogan "Duck and Cover" that is familiar to 70 percent of all Americans, said Ann Gordon, Ph.D., director of Chapman University's Henley Lab. "Americans need to unlearn 'Duck and Cover' and replace it with 'Get inside. Stay Inside. Stay Tuned'."

Terrorism and Mass Shooting Fears

- 48 percent fear being the victim of terrorism and 44 percent fear a terror attack in general.

The majority of Americans, 82 percent are familiar with the slogan, "If you see something, say something." However, most Americans are unaware of what constitutes suspicious behavior that should be reported. The fear of being the victim of a mass or random shooting is on the minds of 31 percent, and 35 percent report being familiar with the advice to "Run. Hide. Fight," which is the recommended preparedness slogan for a mass or random shooting.

Natural disasters

- Americans fear many natural disasters and 68 percent believe natural disasters are capable of harming them or their property. Only 38 percent of Americans have heard the advice, "Don't wait. Communicate. Make your emergency plan today." Less than half, 41 percent (up from 32 percent in 2016), actually have an emergency plan in place for their households and 26 percent have such a plan for their pets.

"Whether they're afraid of an attack by North Korea, a pandemic (which 36 percent of Americans fear), or a natural disaster, Americans just aren't prepared," says Dr. Gordon. "Sheltering in place requires some preparation, such as food water, and medicine. Only 34 percent of Americans have such preparations, although 45 percent say they are familiar with the advice to "Prepare. Plan. Stay informed." And in any disaster a battery powered radio is essential to staying informed. This would be a great step towards preparedness for American households."

Paranormal America 2017

The 2017 Chapman University Survey of American Fears includes a battery of items on paranormal beliefs. Currently the most common paranormal belief in the United States is that ancient, advanced

civilizations, such as Atlantis once exited with more than half of respondents (55 percent) agreeing or strongly agreeing with this statement. Slightly more than half (52 percent) believe that places can be haunted by spirits. More than a third (35 percent) believe that that aliens visited Earth in our ancient past and more than a fourth believe aliens have come to Earth in modern times (26 percent). Americans are the most skeptical about Bigfoot, with only 16 percent of Americans expressing belief in its existence. "The survey shows that paranormal beliefs are quite common in the United States by examining how many such beliefs a person holds," said Dr. Bader. "Using the seven paranormal items included on the survey, we find that only a fourth of Americans (25.3 percent) do not hold any of these seven beliefs. However, this means that nearly three-fourths of Americans do believe in something paranormal."

The survey also looked at the personal characteristics that are significantly associated with higher levels of paranormal belief. Simply put, the person with the highest number of paranormal beliefs in the United States as of 2017 will tend to be a lower income, female living in a rural area in the Western states. She tends to be politically conservative and claims to be highly religious, although she actually attends religious services infrequently. She is either currently single or cohabitating with someone and reports her race as "other."

Methodology

The CSAF was conducted online via the SSRS Probability Panel among adults age 18 and older who participated via the web on PC, laptop, tablet or mobile phone. It included 1,207 participants and data collection was conducted from June 28 to July 7, 2017. The SSRS Panel members are recruited randomly from a dual-frame random digit dial (RDD) sample, through the SSRS Omnibus Survey. The SSRS Omnibus survey is a national (50-state), bilingual telephone survey. The sample used for the Chapman University Survey of American Fears mirrors the demographic characteristics of the U.S. Census. For additional methodological details, see the full report.

A comprehensive list of the all the fears from The Chapman Survey on American Fears 2017 can be found http://www.chapman.edu/fearsurvey. In addition to Bader, Day and Gordon, student involvement was key in helping throughout the process.

http://bit.ly/2xFKov7

Advance achieved in dry preservation of mammalian sperm cells

First successful drying and rehydration of domestic cat spermatozoa

In a paper forthcoming in the November issue of the journal Theriogenology, a team of researchers from the University of North Carolina at Charlotte and the Smithsonian Conservation Biology Institute, announced the first successful drying and rehydration of domestic cat spermatozoa using a rapid microwave dehydration method.

The paper's authors, Jennifer Patrick and Gloria Elliott from UNC Charlotte, and Pierre Comizzoli from SCBI, show that the rehydrated spermatozoa have minimal DNA damage and are viable - they are able to produce embryos in vitro. Since the group had previously succeeded in producing viable dehydrated cat eggs, this finding shows the possibility of preserving feline reproductive cells in a dried state.

Far from being an esoteric accomplishment, the successful preservation of cat spermatozoa by dehydration is a potentially important step in addressing key issues involved in the reproductive biology of wild felids.

Many biologists and environmental scientists think that the biosphere is currently in the middle of a "sixth extinction" that may end in a vast reduction of the number of species on the planet and the collapse of vast ecosystems. There is a significant risk that in the near future, species key to the biological diversity of the planet may either go extinct or be so reduced in their genetic diversity that wild populations are not viable.

Science might be able to rapidly and successfully improve the status of small animal populations if more "libraries" of preserved eggs and sperm are available. Scientists could simply use stocks of reproductive

material, preserved in stable, dried form, re-hydrate them and create a population of viable embryos.

Why dried reproductive cells? The idea of preserving sperm, eggs and embryos for later use is not new, but generally the preferred preservation technique is for these materials to be frozen. Cryopreservation is a proven technology for preserving germ cells and embryos but there are problems with this approach, considering future uncertainty. Storage at freezing temperatures requires constant energy supplies, expensive technology and facilities, and complex upkeep operations- all difficult and costly things to continuously maintain over long periods of time, especially under occasionally adverse conditions.

Nature suggests another, perhaps more robust, solution: cellular stasis through dehydration. Plants, fungi and bacteria, do this commonly, putting their genetic material in spores, cysts, pollen and seeds, which keep it preserved for short periods - and also, sometimes, for much longer time scales - and allow it to be transported across distances as well.

Some animals that live in harsh deserts and other extreme environments -- such as brine shrimp and tardigrades ("water bears") -- have also developed the ability to put their biology into a state of dehydrated stasis, sometimes for long periods. They do this by producing and accumulating high concentrations of disaccharide sugars (like trehalose) in their cells, which replaces the water lost during dehydration and solidifies to a glass - really highly viscous liquid that stops chemical activity and immobilizes enzymes - an ambient-temperature freezing of cellular structures and activity, a molecular-level version of insects frozen in amber.

"When you are thinking about long-term preservation of organisms, you aren't concerned with just electrical interruptions. Flooding and other weather events can require the relocation of samples under duress," Elliott notes. "Frozen samples aren't easily transportable whereas if your samples are stored as dry packets - just like dried fruits or any dry goods you have on a shelf - you can toss your collection in a bag and out the door you go. That's the concept - not only to keep the cost of storage low, but to make specimens easily transportable, facilitating the sharing or relocation of specimens."

The preservation method that Elliott's research team is investigating involves suspending cells in a dilute trehalose solution, and then concentrating it by removing the water with a gentle microwave-assisted heating process so that a trehalose glass forms, immobilizing biological molecules at ambient temperatures, similar to freezing.

Reproductive cells have previously been similarly dry-preserved with trehalose, using a freeze-drying technique, but the microwave-assisted method is faster and might allow for more extensive use of the technology.

"This allows us to get these preservation technologies into some low resource settings - third world countries such as developing nations,," Elliott said. "If you consider specimens for biodiversity research - those countries are not set up for that kind of collection and this method of preservation opens up that possibility."

The finding also expands the range of mammalian species whose germ cells can be successfully dry-preserved. Previous experiments have successfully dry-preserved sperm and egg cells in rats and mice, but the biology of rodent germ cells is significantly different from those of other mammals, including cats and humans. In rodents, the sperm cell is relatively simple and contains primarily just the male genetic material, while in cats and humans it also contains the centrosome, a cell structure necessary for cellular division and the successful development of an embryo. Since the centrosome is vital to reproduction and since sperm are small cellular structures, cat sperm are potentially more challenging to preserve than rodent sperm.

"This is the first time this has ever been done with cat sperm, and cat sperm are closer to human sperm than are rodent sperm," Elliott notes. "There has been a lot of work done on rats, but the rat is not necessarily a good model for centrosomal inheritance, which could

affect fertility. This is why we believe the domestic cat model is a better model for humans than rodents, and this finding is significant," she said.

The reproductive success rate of the team's re-hydrated sperm was 6.5%, compared with a rate of 15% with fresh sperm, a reduction of viability, but still acceptable for preservation purposes. Rehydrated sperm were not motile, but that too was not critical for producing viable embryos.

"When we're drying and storing samples for the purpose of creating embryos, we don't have to have fully intact sperm as we will be doing intracytoplasmic sperm injections with the rehydrated samples," Elliott noted. "You don't have to have a tail, you don't have to have completely intact sperm heads - you are essentially injecting critical sperm components. The sperm heads don't have to be in fantastic shape but you do have to ensure that certain critical components are intact, including the centrosome."

Though the finding is a proof-of-concept, work remains to be done in developing and proving the technology. Elliott notes that it remains to be seen whether the dryness level currently achieved is high enough for long-term preservation without any refrigeration, and also whether further drying is possible. Once these conditions have been optimized, then testing needs to be done to ensure that the embryos can mature into healthy kittens.

The paper can be accessed online at http://www.theriojournal.com/article/S0093-691X(17)30369-2/fulltext

http://bit.ly/2ykdIqw

Planet Nine Does Exist, NASA Evidence Suggests

Planet Nine, a world about 10 times more massive than Earth that may lie undiscovered in the far outer solar system.

By Samantha Mathewson, Space.com Contributor

Planet Nine is out there, and astronomers are determined to find it, according to a new statement from NASA. In fact, mounting evidence suggests it's hard to imagine our solar system without the unseen world.

The hypothetical planet is believed to be about 10 times more massive than Earth and located in the dark, outer reaches of the solar system, approximately 20 times farther from the sun than Neptune is. While the mysterious world still has yet to be found, astronomers have discovered a number of strange features of our solar system that are best explained by the presence of a ninth planet, according to the NASA statement.

"There are now five different lines of observational evidence pointing to the existence of Planet Nine," Konstantin Batygin, a planetary astrophysicist at the California Institute of Technology (Caltech) in Pasadena, said in the statement. "If you were to remove this explanation and imagine Planet Nine does not exist, then you generate more problems than you solve. All of a sudden, you have five different puzzles, and you must come up with five different theories to explain them."

In 2016, Batygin and co-author Mike Brown, an astronomer at Caltech, published a study that examined the elliptical orbits of six known objects in the Kuiper Belt, a distant region of icy bodies stretching from Neptune outward toward interstellar space. Their findings revealed that all of those Kuiper Belt objects have elliptical orbits that point in the same direction and are tilted about 30 degrees "downward" compared to the plane in which the eight official planets circle the sun, according to the statement.

Using computer simulations of the solar system with a Planet Nine, Batygin and Brown also showed that there should be even more objects tilted a whopping 90 degrees with respect to the solar plane. Further investigation revealed that five such objects were already known to fit these parameters, the researchers said.

Since then, the astronomers have found new evidence that further supports the existence of Planet Nine. With help from Elizabeth Bailey, an astrophysicist and planetary scientist at Caltech, the team showed that Planet Nine's influence might have tilted the planets of our solar system, which would explain why the zone in which the

eight major planets orbit the sun is tilted by about 6 degrees compared to the sun's equator.

"Over long periods of time, Planet Nine will make the entire solar-system plane precess, or wobble, just like a top on a table," Batygin said in the statement. Finally, the researchers demonstrate how Planet Nine's presence could explain why Kuiper Belt objects orbit in the opposite direction from everything else in the solar system.

"No other model can explain the weirdness of these high-inclination orbits," Batygin said in the statement. "It turns out that Planet Nine provides a natural avenue for their generation. These things have been twisted out of the solar system plane with help from Planet Nine and then scattered inward by Neptune."

Going forward, the researchers plan to use the Subaru Telescope at Mauna Kea Observatory in Hawaii to find Planet Nine, and then deduce where the mysterious world came from.

The most common type of planets discovered around other stars in our galaxy has been what astronomers call "super Earths" — rocky worlds that are larger than Earth but smaller than Neptune. However, no such planet has yet been discovered in our solar system, meaning that Planet Nine could be our missing "super Earth," the researchers said.

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Surprising facts about how we talk to babies

Here's an experiment to try next time you meet a baby, try holding a normal conversation. It is very difficult, isn't it? Yes it is! Oh, yes it is!

Caspar Addyman

When we talk to babies we all naturally switch into a high energy, sing song tone. We use simple words and short sentences. We sound excited. Our pitch rises at the end of the sentence. These particular characteristics of "parentese" or infant-directed speech (IDS) seem to be common across many languages.

A new study, published in Current Biology, has suggested there are universal changes in vocal timbre when talking to babies. Timbre describes the quality of a voice or a musical instrument. The difference between a violin and a trumpet playing the same note is a difference in timbre.

Elise Piazza, a postdoctoral researcher at the Princeton Neuroscience Institute, invited 12 English-speaking mothers to Princeton Baby Lab and recorded them talking to their babies (aged eight to 12 months) and to an adult. The recordings were converted into "vocal fingerprints" using a standard statistical method. This produces a unique frequency profile for a given speaker that can reliably discriminate one speaker from another based on timbre.

Elise and her colleagues, Marius Iordan and Casey Lew-Williams, then used a computer algorithm to compare adult and infant-directed speech. This seemed to show that all mothers consistently alter the timbre of their voice when talking to babies.

The authors ran several controls to show that this is not just a result of mothers speaking in a higher pitch to babies. But the real test came when a further 12 mothers speaking nine different languages, including Spanish, Russian and Cantonese, were also recorded. The algorithm picked up the same difference between their adult- and infant-directed speech.

Elise describes the change as a "cue mothers implicitly use to support babies' language learning". The next hypothesis is that infants might detect this difference to help them know when they are being addressed. The researchers are looking for ways to test this. It would be consistent with what we already know about IDS: we do it to help babies learn.

Patricia Kuhl has shown that IDS exaggerates the differences between vowel sounds, making it easier for babies to discriminate words. This pattern was found in English, Russian and Swedish. Other research found that IDS has the acoustic features of happy, adult-directed speech, and the authors said that "what is special is the widespread expression of emotion to infants in comparison with the more inhibited expression of emotion in typical adult interactions".

Babies learning language perform some amazing feats. From the muffled confines of the womb, they have already learned enough that, at birth, they prefer their mother's voice and her native language to another woman or another language.

A recent study found that premature babies in intensive care make more vocalisations in response to hearing adults' speech. If adults stop responding, infants notice and also cease.

Testing five-month-old infants with this procedure also found that the infants ceased vocalising. Moreover, the more in tune these infants were to their caregiver's behaviour at five months, the better their language comprehension was at 13 months.

In another charming study, researchers recorded proto-speech of three- to four-month-old infants talking to themselves. The babies expressed a full range of emotions in their squeals, growls and gurgles.

Clearing up a mystery

Incidentally, this new research may also clear up a mystery from my own work. Last year when we were helping Imogen Heap create a song that makes babies happy, we advised her to make sure she recorded it in the presence of her 18-month-old daughter. Research from the 1990s showed babies can tell the difference; they prefer singing that is genuinely infant directed. I never quite believed this at the time but now this new measure of timbre will let us test this out.

For babies, just as for adults, language is truly learned in conversation. From the very beginning, babies want to join in and proto-conversations start between mothers and their newborns; nursing mothers wait for pauses in their infants' actions to talk to them. This new research highlights a universal signal that is there to let babies know that we are talking to them.

Yes we are! Oh, yes we are!

Disclosure statement

Caspar Addyman received funding from C&G Baby Club to help create the Happy Song.

Partners

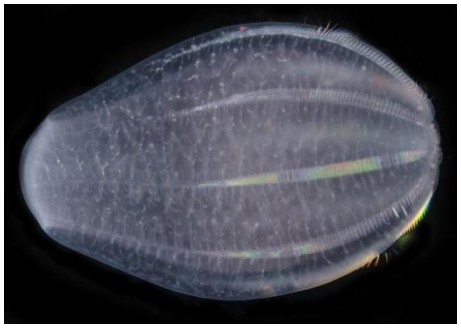
Goldsmiths, University of London provides funding as a founding partner of The Conversation UK.

http://bit.ly/2yqGvtt

Comb jellies possibly first lineage to branch off evolutionary tree

Further evidence that a group of marine animals were the first to break away from all other animals

by Adam Jones



A researcher at The University of Alabama was part of a new study that provides further evidence in support of a controversial hypothesis that a group of marine animals commonly called comb jellies were the first to break away from all other animals, making it the oldest surviving animal lineage.

Beroe abyssicola is a type of comb jelly examined as part of the study. **University of Alabama in Tuscaloosa**

Dr. Kevin M. Kocot, UA assistant professor in biological sciences and curator of invertebrate zoology in the Alabama Museum of Natural History, is a co-author on a paper published in Nature Ecology & Evolution that outlines the findings.

The work was led by Dr. Nathan Whelan as a post-doctoral researcher in the lab of Dr. Ken Halanych, professor of biological sciences at Auburn University and director of Molette Biology Laboratory for Environmental and Climate Change Studies.

Comb jellies, whose scientific name is Ctenophora, are a group of invertebrates who swim with rows of cilia, often referred to as combs. Found worldwide, they are a crucial part of marine food chains.

Ctenophores comprise approximately 200 described species with complicated and unresolved relationships among the various lineages. Additionally, ctenophores are a diverse group with numerous physiological and ecological differences among species.

By sequencing active genes (transcriptomes) from 27 different species of comb jellies spanning the diversity of the group and conducting

genome-scale phylogenetic analyses, the research team reconstructed the evolutionary history of the group and inferred the evolution of key ctenophore characters.

Using a molecular clock analysis, the team found that comb jellies split off from other animals 88 to 350 million years ago, much earlier than previously suspected. The analysis supports the conclusion that comb jellies, not the simpler sponges, are the sister group to all other animals.

"Taken together, these results have important implications for our understanding of early animal evolution and provide insight into a poorly-known but fascinating group of marine invertebrates," Kocot said.

Morphologically simple animals, sponges lack nerves, muscles, and perhaps even true tissues, but, despite evolutionary simplicity, it is possible sponges evolved from a more complex animal, simplifying secondarily. "If sponges are secondarily simplified, it means they are probably kind of weird, and may not tell us as much about ourselves as we previously thought," Kocot said.

It is also possible sponges represent the ancestral morphology of animals and that ctenophores independently derived complex characters such as nerves and muscles. Previous research by this team published in Nature in 2014 showed that comb jellies pattern their nervous system using different genes than other animals, a result some have interpreted as evidence for independent evolution of neurons in this group.

"We were surprised to discover just how different the early evolution of animals is compared to what has been traditionally assumed," said Halanych. "We found interesting and major changes in lifestyle, including feeding habits and habitat preferences, with some animals being benthic and others pelagic.

"Understanding relationships within ctenophores, or comb jellies, is paramount to understanding some of the important features found in early animals, such as the evolution of the nervous system and muscles. Interestingly, the earliest branching ctenophore began developing muscles like those found in bilateral animals."

Whelan earned his doctorate in biological sciences from UA in 2013 and is now the director of U.S. Fish and Wildlife Service's Southeast Conservation Genetics Lab.

"Our work for this project reveals important patterns about early animal evolution and begins to unravel mysteries surrounding the diversity of comb jellies," Whelan said. "By adding new data and continuing to challenge conventional wisdom, we have obtained much stronger results than in the past."

The team also included the lab of Dr. Leonid Moroz, distinguished professor of neuroscience, genetics, biology and chemistry at the University of Florida.

"Comb jellies are extremely fragile marine organisms," said Moroz. "Most of them can only be studied within their natural habitats. Thus, we must find them, perform experiments on a ship, make samples, and even sequence in open oceans, sometimes thousands of miles offshore. "Every collection is an adventure by itself—from cold Antarctica to hot equatorial seas—to understand how Mother Nature made muscles and neurons in these creatures independently from the rest of animals. A fun job for a neuroscientist, and everyone, indeed!"

The paper, "Ctenophore relationships and their placement as the sister group to all other animals," appears online and will be published in an upcoming issue of Nature Ecology & Evolution.

Nathan V. Whelan et al. Ctenophore relationships and their placement as the sister group to all other animals, Nature Ecology & Evolution (2017). [DOI: 10.1038/s41559-017-0331-3](https://doi.org/10.1038/s41559-017-0331-3)

http://bit.ly/2wWTDTy

Ischemic stroke patients not receiving life-saving treatment, study finds

Ischemic stroke patients who do not receive intravelous (IV) alteplase, a clot-dissolving medication, are significantly less likely to survive, according to researchers at Georgia State University.

Ischemic stroke is the most common type of stroke. It occurs when a vessel that supplies oxygen-rich blood to the brain becomes blocked, often by a blood clot. IV alteplase was approved by the Food and Drug Administration as a treatment for acute ischemic stroke in 1996 and is known to reduce disability and improve functionality by restoring blood flow to the brain. Yet two decades later, less than 10 percent of patients receive the treatment.

The study, published in the American Journal of Emergency Medicine, analyzed 2008-13 data from the Georgia Coverdell Acute Stroke Registry, and linked it to 2008-13 hospital discharge and 2008-14 death data in Georgia. The investigators found that one year after discharge, acute ischemic stroke patients who did not receive IV alteplase treatment had a 49 percent higher likelihood of death.

"Clinicians may be hesitant to administer IV alteplase because of concerns about the drug's complications, which can include bleeding," said Dr. Moges Ido, the study's lead author and a part-time instructor at Georgia State's School of Public Health. "But this study indicates that unless major contraindications are present, patients should be offered this treatment as a life-saving measure."

The study authors examined data from 9,620 patients who were treated at 48 hospitals. They excluded patients who weren't eligible to receive the treatment because of contraindications, such as a recent history of brain surgery. Only a quarter of the eligible patients received IV alteplase.

Previous randomized studies have shown some long-term mortality reduction for patients treated with IV alteplase but the results were not statistically significant. This study demonstrates that IV alteplase is associated with reduced risk of death, and that eligible patients should be identified and treated swiftly.

The study's co-authors include Dr. Ike Okosun and Dr. Richard Rothenberg of Georgia State, as well as Dr. Michael Frankel of Emory University.

The authors received no funding for the research. The Georgia Coverdell Acute Stroke Registry is funded by the Centers for Disease Control and Prevention.

To read the study, visit http://www.sciencedirect.com/science/article/pii/S0735675717306411.

http://bit.ly/2hHnQzq

Cholesterol byproduct hijacks immune cells, lets breast cancer spread

High cholesterol levels have been associated with breast cancer spreading to other sites in the body

CHAMPAIGN, Ill. -- High cholesterol levels have been associated with breast cancer spreading to other sites in the body, but doctors and researchers don't know the cause for the link.

A new study by University of Illinois researchers found that the culprit is a byproduct of cholesterol metabolism that acts on specific immune cells so that they facilitate the cancer's spread instead of stopping it.

The study, published in the journal *Nature Communications*, identifies new potential drug targets that could inhibit the creation or actions of the dangerous cholesterol byproduct, a molecule called 27HC.

"Breast cancer impacts roughly 1 in 8 women.

We've developed fairly good strategies for the initial treatment of the disease, but many women will experience metastatic breast cancer, when the breast cancer has spread to other organs, and at that point we really don't have effective therapies.

We want to find what drives that process and whether we can target that with drugs," said Erik Nelson, a professor of molecular and integrative physiology who led the study.

Nelson's group fed mice with breast cancer tumors a diet high in cholesterol.

The researchers confirmed that high levels of cholesterol increased tumor growth and metastasis, and that mice treated with cholesterol-lowering drugs called statins had less metastasis.

Then they went further, specifically inhibiting the enzyme that makes 27HC during cholesterol metabolism.

"By inhibiting the enzyme that makes 27HC, we found a suppressor effect on breast cancer metastasis. This suggests that a drug treatment targeting this enzyme could be an effective therapeutic," said Amy

Baek, a postdoctoral researcher at Illinois and the first author of the paper.

The researchers also saw unusual activity among specific immune cells - certain types of neutrophils and T-cells - at metastatic sites high in 27HC.

"Normally, your body's immune system has the capacity to attack cancer," Nelson said, "but we found that 27HC works on immune cells to fool them into thinking the cancer is fine. It's hijacking the immune system to help the cancer spread."

See a video of Nelson describing the study on YouTube.

Because 27HC acts through the immune system, and not on the breast cancer itself, the researchers believe their findings have broad applicability for solid tumors.

They performed experiments looking at colon cancer, lung cancer, melanoma and pancreatic cancer, and found that 27HC increased metastasis for all the tumor types, suggesting that a treatment targeting 27HC could be effective across multiple cancer types.

The researchers are working to further understand the pathway by which 27HC affects the immune cells.

With clinical partners at Carle Foundation Hospital in Urbana, the team is working to establish whether 27HC has the same pathway in human patients as in mice.

"We hope to develop small-molecule drugs to inhibit 27HC," Nelson said.

"In the meantime, there are good cholesterol-lowering drugs available on the market: statins. Cancer patients at risk for high cholesterol might want to talk to their doctors about it."

Nelson also is affiliated with the Cancer Center, the division of nutritional sciences and the Carl R. Woese Institute for Genomic Biology at Illinois. The National Institutes of Health and the Susan G. Komen Foundation supported this work.

Editor's notes: To reach Erik Nelson, call 217-244-5477; email enels@illinois.edu

The paper "The cholesterol metabolite 27 hydroxycholesterol facilitates breast cancer metastasis through its actions on immune cells" is available online.

http://bit.ly/2qcr11A

Magic mushroom extract changes brains of people with depression

Psilocybin, a hallucinogenic compound found in magic mushrooms, may help re-set the activity of neural circuits in the brain that are involved in depression.

By New Scientist staff and Press Association

Magic mushroom enthusiasts have long believed that the drug's ability to induce profound-feeling experiences could be therapeutically useful. Brain-imaging studies have shown that psilocybin targets areas of the brain overactive in depression.

Last year, Robin Carhart-Harris of Imperial College London and his colleagues conducted the first clinical trial of using psilocybin to treat depression, and got some encouraging results. The trial only involved 12 people and no control group, but the team found that after two sessions of psilocybin-assisted psychotherapy, all of the volunteers had reduced symptoms.

Now Carhart-Harris and his team have shown that psilocybin seems to cause changes in the brains of people with depression. The study involved 19 people who, like in the previous study, had depression that had not been helped by conventional treatments.

Mood reset

Each volunteer was given a 10 mg and 25 mg dose of psilocybin, seven days apart. Brain scans showed that, after taking the drug, activity in some regions of the brain reduced. These areas included the amygdala, which plays a role in processing stress and fear. The participants reported an immediate improvement in mood that lasted for up to five weeks.

"We have shown for the first time clear changes in brain activity in depressed people treated with psilocybin after failing to respond to conventional treatments," says Carhart-Harris. "Several of our patients described feeling 'reset' after the treatment."

"This is further evidence that psilocybin may turn out to be effective for the most stubborn depression," says Paul Morrison, of King's College London. "Developments in this area are a priority in psychiatry. Some people can go through years of suffering, which resist all standard therapies." Carhart-Harris's team warned that people should not attempt to self-medicate with psychedelic drugs.

Journal reference: Scientific Reports, DOI: 10.1038/s41598-017-13282-7

http://bit.ly/2xGn5N7

Learning and staying in shape key to longer lifespan, study finds

People who are overweight cut their life expectancy by two months for every extra kilogramme of weight they carry, research suggests.

A major study of the genes that underpin longevity has also found that education leads to a longer life, with almost a year added for each year spent studying beyond school.

Other key findings are that people who give up smoking, study for longer and are open to new experiences might expect to live longer.

Scientists at the University of Edinburgh analysed genetic information from more than 600,000 people alongside records of their parents' lifespan.

Because people share half of their genetic information with each of their parents, the team were able to calculate the impact of various genes on life expectancy.

Lifestyle choices are influenced to a certain extent by our DNA - genes, for example, have been linked to increased alcohol consumption and addiction. The researchers were therefore able to work out which have the greatest influence on lifespan.

Their method was designed to rule out the chances that any observed associations could be caused by a separate, linked factor. This enabled them to pinpoint exactly which lifestyle factors cause people to live longer, or shorter, lives.

They found that cigarette smoking and traits associated with lung cancer had the greatest impact on shortening lifespan.

For example, smoking a packet of cigarettes per day over a lifetime knocks an average of seven years off life expectancy, they calculated. But smokers who give up can eventually expect to live as long as somebody who has never smoked.

Body fat and other factors linked to diabetes also have a negative influence on life expectancy.

The study also identified two new DNA differences that affect lifespan. The first - in a gene that affects blood cholesterol levels - reduces lifespan by around eight months. The second - in a gene linked to the immune system - adds around half a year to life expectancy.

The research, published in Nature Communications, was funded by the Medical Research Council.

Data was drawn from 25 separate population studies from Europe, Australia and North America, including the UK Biobank - a major study into the role of genetics and lifestyle in health and disease.

Professor Jim Wilson, of the University of Edinburgh's Usher Institute, said: "The power of big data and genetics allow us to compare the effect of different behaviours and diseases in terms of months and years of life lost or gained, and to distinguish between mere association and causal effect."

Dr Peter Joshi, Chancellor's Fellow at the University of Edinburgh's Usher Institute, said: "Our study has estimated the causal effect of lifestyle choices. We found that, on average, smoking a pack a day reduces lifespan by seven years, whilst losing one kilogram of weight will increase your lifespan by two months."

http://bit.ly/2kRHldy

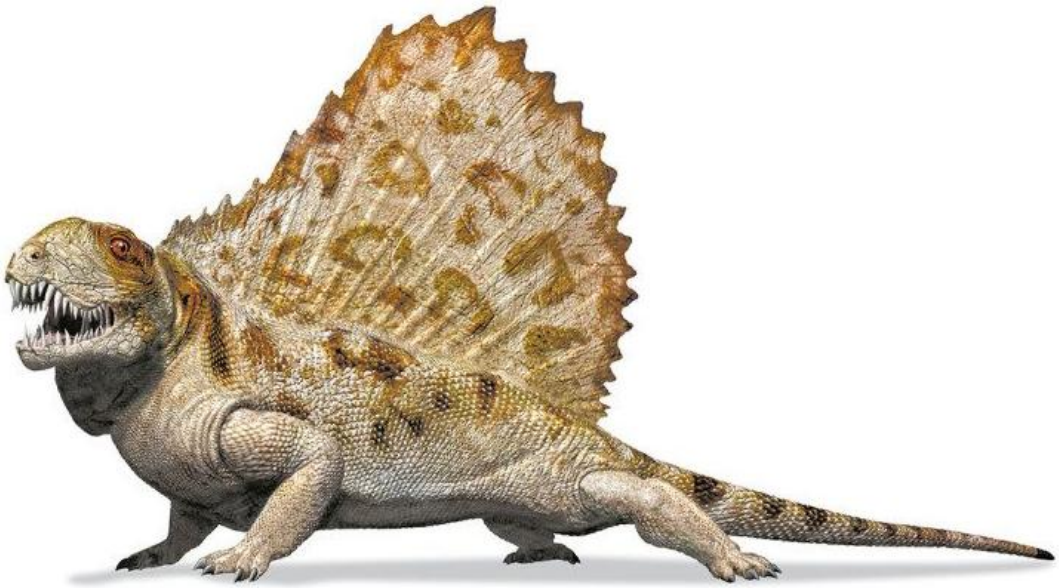
We've drawn iconic sail-wearing Dimetrodon wrong for 100 years

Dimetrodon*, one of the most recognisable of the pre-dinosaur predators, is due a makeover.*

By Colin Barras

For more than a century, it has been depicted as a sluggish, belly-dragging beast with sprawling legs – but it might actually have held its

legs in a more upright position and kept its stomach off the ground as it walked.



Dimetrodon *might have walked a lot taller than this* Dorling Kindersley/Getty

Often mistaken for a dinosaur, *Dimetrodon* actually belonged to a group called the pelycosaurs that were more closely related to mammals. It lived between about 290 and 272 million years ago, with some species measuring more than 3 metres from nose to tail. Its most iconic feature was a gigantic sail on its back, the function of which is still debated.

Nineteenth Century artists drew *Dimetrodon* as a sluggish-looking animal with legs sprawled out to each side of its body, resting its weight on an enormous belly – and even in the 21st century nothing much has changed.

"I was baffled as I was going through the literature how little this had been questioned," says Caroline Abbott at the College of William & Mary in Williamsburg, Virginia. It's particularly surprising given that the fossil trackways left by *Dimetrodon* seem to tell a different story. The relatively narrow distance between left and right sets of footprints suggest *Dimetrodon* did not have sprawling legs.

"That's where the real head-scratcher is," says Abbott. "The trackways are more narrow than you'd expect and in a lot of cases they lack belly dragging marks."

Modern moves

With her colleague Hans-Dieter Sues at the Smithsonian Institution in Washington DC, Abbott measured *Dimetrodon* bones, and looked at the configuration of the skeleton at the shoulder and the hip. She then compared this information with data collected from 11 living mammals – including the short-beaked echidna – and 12 living reptiles, including the Komodo dragon, the savannah monitor and the spectacled caiman.

When Abbott and Sues used software to run their data, they found that *Dimetrodon* seemed to most closely match the caiman, a crocodilian that can hold its legs vertically enough to raise its body off the ground – particularly when it runs. *Dimetrodon* might have held its body in a similar way.

"That's the best I have right now," says Abbott, who will present her findings at a meeting of the Geological Society of America in Seattle later this month. "But I'm hoping that as I broaden the modern analogues I look at, and do more complicated stats, I can pinpoint that a bit better."

Sprawling logic

Spencer Lucas at the New Mexico Museum of Natural History and Science in Albuquerque agrees that *Dimetrodon*'s posture needs a reassessment. He suggested as much in the late 1990s, after he and his colleague Adrian Hunt studied *Dimetrodon* trackways.

"When we wrote that paper we were just throwing the gauntlet down and saying: look, the trackways are showing something really different than anybody has thought from the skeletons," says Lucas. "But we didn't try to resolve it."

He says some palaeontologists did offer an explanation – that *Dimetrodon* thrashed its spine from side to side so much as it walked

that it could leave narrow sets of footprints despite having sprawled legs. Abbott and Sues are suggesting a different solution, he says.

Lucas thinks the debate could be resolved by returning to the *Dimetrodon* trackways and using them to assess how fast the animals were moving. The "thrashing spine" idea assumes they were lumbering along slowly, whereas Abbott and Sues's reconstruction would be more consistent with an animal moving at speed – some crocodiles can run at more than 10 miles per hour.

"If this is a pelycosaur moving quickly in a crocodilian-like fashion that would support [Abbott's] argument," says Lucas.

http://bit.ly/2hGCOFK

GM Mosquitoes Closer to Release in U.S.

The EPA is now in charge of regulating the use of Oxitec's strain of* Aedes aegypti*, genetically engineered to reduce populations of the insects.

By Abby Olena | October 13, 2017

Last week (October 5), the United States Food and Drug Administration (FDA) announced that the US Environmental Protection Agency (EPA) will assume responsibility for overseeing the approval and use of mosquitoes genetically engineered to act as pesticides, specifically, a variety of *Aedes aegypti* generated by UK company Oxitec. This regulatory change could lead to pilot releases of the mosquitoes in the U.S. sometime in the next year.

***An adult* Aedes aegypti *mosquito emerges from its pupal case.* OXITEC**

"We hope within the next three to six months we will get regulatory permission to go ahead [with] releases of our mosquitoes in the U.S," says Derric Nimmo, a scientist at Oxitec.

"*Aedes aegypti* transmit dengue, Zika, and other viral diseases," explains North Carolina State University entomologist Fred Gould. Because vaccine development has thus far been challenging and the available dengue vaccine is only partially effective, the current strategy for combatting these diseases is insect control, which includes spraying millions of dollars worth of insecticides. As an alternative, biotech firms have been working on developing tools like the genetically modified (GM) mosquitoes and mosquitoes infected with *Wolbachia*, a bacterium that can disrupt virus transmission from mosquito to human. "You need to come at it from all directions responsibly," Gould adds.

Nimmo says that Oxitec initially worked with the US Department of Agriculture, and then with the FDA in cooperation with experts from the EPA and the Centers for Disease Control and Prevention (CDC). In August 2016, an FDA assessment—prepared with input from EPA and CDC officials—suggested that deploying Oxitec's genetically modified (GM) mosquitoes would have no significant impact on the environment at a proposed release site in the Florida Keys.

It was a good sign for Oxitec, but residents balked at being a test site. And the FDA had yet to give approval for the insects' release. In the guidance issued last week, the FDA clarified that the Oxitec mosquitoes are not drugs because their use is not intended to cure or treat disease, but to limit mosquito populations, thereby functioning as a pesticide.

The switch from FDA to EPA oversight reflects the EPA's role in approval of pesticides, including traditional chemical pesticides used for mosquito control and others okayed by the agency that include GM microbial components. The EPA has also approved experimental release of *Wolbachia*-infected *A. aegypti* in Fresno County and Orange County, California, as well as in Monroe County, Florida, the location of the Florida Keys.

"EPA will regulate [genetically engineered] mosquitoes in the same way the agency regulates other pesticides," an EPA spokesperson writes in an email to *The Scientist*. "The Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) gives EPA the authority to

regulate the distribution, sale, and use of pesticide products to ensure they do not cause unreasonable adverse effects on people or the environment."

Approval times vary depending on the type of application, according to the EPA spokesperson. "At this point, EPA has not received an application from Oxitec," says the spokesperson, but typically, organizations begin by applying for an experimental use permit, at which point the agency has seven months to reach a decision. After collecting data in field testing, the organization can then apply for registration under FIFRA, and then the EPA has 13 to 25 months to complete its review.

Because experts from the EPA have collaborated with the FDA throughout Oxitec's application process—including on the August 2016 finding that the environmental impacts of releasing the mosquitoes would be minimal—Nimmo is optimistic that the EPA's regulatory process could move quickly.

Oxitec researchers have engineered their mosquitoes with both a fluorescent reporter gene and a self-limiting gene that kills the insects at a young age, before they can reproduce. They breed adults by adding tetracycline to the insects' water, which inactivates the self-limiting gene, allowing larvae to grow to adulthood. Then they sort and release adult male mosquitoes, which mate with wild females.

Oxitec mosquito larvae glow red, while wild-type larvae do not. **OXITEC**

Because there is not enough tetracycline in the environment to shut down the self-limiting gene, the progeny of GM-wildtype matings die young. Oxitec scientists determine how many males have mated with wild females by monitoring the presence of the fluorescent reporter in larvae they collect in simple traps and then adjust how many GM male insects they release.

The Florida Keys Mosquito Control District spends about $1.1 million per year on monitoring populations and deploying conventional insecticides to reduce *A. aegypti* numbers by half. The Florida Department of Health has recorded multiple locally acquired cases of both dengue and Zika virus in recent years, making the state a prime target for mosquito population reduction. Officials from the Florida Keys Mosquito Control District have already partnered with Oxitec to plan a pilot release, but cannot proceed without regulatory approval.

In field trials in the Cayman Islands, Panama, and Brazil, the release of Oxitec male mosquitoes has resulted in a greater than 90 percent reduction in *A. aegypti* populations. The company has also seen positive results beyond their pilot trials. A collaboration with officials in Piracicaba, Brazil, has led to the successful treatment of a neighborhood of 5,000 residents that is in the process of being expanded to cover an area that houses 300,000 people. A new facility near Piracicaba can produce 60 million GM male mosquitoes per week and serve a human population of 3 million.

"This is not a new technology," says Nimmo. "We've been deploying this in the field for seven years."

http://bit.ly/2xGOsXk

An Experiment That Didn't Work

My PhD thesis research was a dead end, but that's why it was important

By Maryam Zaringhalam on October 13, 2017

Knowledge is a big subject. Ignorance is bigger. And it is more interesting.
—Stuart Firestein, *Ignorance: How it Drives Science*

Ever tried. Ever failed. No matter. Try again. Fail again. Fail better.
—Samuel Beckett in *Failure: Why Science Is So Successful*

My first week in the lab, my boss plopped a book with the bold title *Ignorance: How it Drives Science*. And now, as I wrap up writing my dissertation, she has given me its sequel, *Failure: Why Science Is So Successful*. Preternatural optimist that she is, she did not gift these books out of pessimism or wry passive aggression. Rather, she

believed they contained important lessons. Lessons that perfectly bookend my Ph.D. career.

My time in the lab began with ignorance—not the wide-eyed, first-year graduate student variety, but the rigorous brand that embraces an open question. A great conundrum in modern biology is how life's great diversity stems from four letters—A, C, G, and T—arranged in a near-infinite array to compose life's blueprint molecule: DNA. Now, consider that every cell in your body contains the exact same complement of DNA. Yet a heart cell looks and acts completely different from a brain cell which looks and acts completely different from a skin cell. So how did a heart cell, a brain cell, and a skin cell arrive at such different biological fates when given the exact same set of molecular blueprints?

To deploy the blueprint's directions, instructions must first be transcribed to an intermediate molecule—the RNA—which then delivers them to the cellular machinery for execution. So understanding the dynamics of RNA, smack at the front lines of cellular activity, can help us understand how diversity emerges from the same DNA blueprint.

RNA is similarly composed of a four-letter alphabet: A, C, G, and U. That alphabet can be expanded upon with a library of over 100 chemical tweaks to fine-tune RNA function—a small M added to an A or a chemical S to a U. Of these alphabetical adornments, one stands out as the most ubiquitous: a subtle structural change in the genetic letter U to a pseudo-U, or pseudouridine (Ψ). Here, ignorance comes to play.

While Ψ was first discovered in the 1950s, we still don't know much about its precise biological function today, except that without Ψ, cells die. We do, however, have some clues—one that particularly piqued my interest. Introducing Ψs into a set of instructions that dictate how a protein is made changed the way those instructions were interpreted by the cell. Ψ unexpectedly recoded RNA's message beyond the mandates of the genetic code—a code considered fully cracked in the 1960s.

So in Ψ, I found a candidate for how diversity arises from DNA's hard-coded instructions. But that study was undertaken in an artificial system, which left open the question: where does Ψ naturally lie? By understanding *where* Ψs are, we might begin to uncover *what* exactly they do to affect how cells behave. When I wound my way to this question, we still had no methods to map Ψs beyond a few varieties of RNA. So, with the power of next-generation sequencing technologies that first emerged to map the human genome, I went Ψ-hunting.

Meanwhile, the allure of Ψ had entered into the zeitgeist, calling researchers from around the world to endeavor on the same Ψ-charting quest. I was beat to the punch when four methods—three of which were released back-to-back-to-back—were published spotting Ψs in a whole host of RNAs. I decided to make the best of being quadruply beat to the punch and compared each group's Ψ maps, partly out of curiosity, but mostly because I was asked to review the techniques as an objective fifth party. All four methods were based on the same principle, so their results should overlap well with one another. But they did not. And here enters failure.

Of the hundreds to thousands of Ψs catalogued by each method, only a small fraction of sites were found by them all. I was genuinely surprised by the result. So I hunkered down and thought through a host of technical and biological caveats that were not detailed in the original publications. I then tried to apply one of those methods to map Ψs in African trypanosomes, the single-celled parasites that cause African sleeping sickness. But, try as I might, I could not get the method to work. And so, more failure.

Failure is the natural product of risk, and there's nothing riskier than the pursuit of ignorance—asking those big bold questions that probe the unknown. But while the practice of science is riddled with failures—from the banal failures of day-to-day life at the bench to the heroic, paradigm shifting failures that populate the book called

Failure—many scientists are uncomfortable with the idea. We publish our innovations, the stories of how our ignorance led to success. Where the "publish or perish" mantra prevails, these stories are essential to making a name for ourselves and securing grant money. So there is little incentive to replicate the work of others or report experimental failure. In fact, there is barely a medium to publish these sorts of efforts, which are relegated to the bottom of the file drawer.

But the scientific method hinges on self-correction, which requires transparent reporting of positive (or negative) data and corroboration (or contradiction) of previous experiments. And so I wanted to share my work, to open it up to comment, to transform my failure into something productive. If I couldn't get these Ψ mapping methods to work in my hands, that's a problem worth sharing because chances are, I'm not alone. This is how we avoid chasing false leads, how we improve our practices, how we move science forward. These tenets lie at the heart of the "open science" movement, which I have come to embrace as I have ventured to share the failed fruits of my doctoral work.

Of course, open science is easier said than done. The increasing competitiveness of certain scientific fields has disincentivized transparency and collaboration. There is also a value judgment that comes with sharing experimental failure—a vulnerability that your peers will view your efforts as sloppy, rather than earnest and honest. So distributing negative or non-confirmatory data comes with an extra burden of proof.

Still, policy reforms and open science advocates are working to incentivize practices that foster open collaboration. Open-source software like the Open Science Framework now exist for collaborative sharing of data and data-processing workflows. Peer-reviewed publications like *F1000Research* are now accepting negative or non-confirmatory data of the sort I generated during my thesis. Preprint servers—which allow for direct uploading of complete manuscripts without formal peer review (but open for comment) and have long been embraced by the physics community—are now gaining steam in the life sciences thanks to the work of advocacy groups like ASAPbio.

It's now been a year since I defended my dissertation, and I've taken up the open science call as an AAAS Science & Technology Policy Fellow. My day job is to think about how we can move science towards a culture of sharing. While I haven't uncovered any mysteries in the world of RNA biology, I have learned that science needs to fail better. Because in science, things often don't work out the way we think they should, and we are left with our ignorance. But the narratives we form around failure—transparently, openly, and together—can be just as valuable as those we form around success.