http://www.eurekalert.org/pub_releases/2016-06/uosf-urf061216.php

USF researchers find stroke damages blood-spinal cord barrier

Stroke's long-term effects on blood-spinal cord barrier can lead to 'an increasingly toxic environment' in spinal cord and 'significant input on disease pathology'

Tampa, Fla. - A team of researchers at the University of South Florida investigating the short and long-term effects of ischemic stroke in a rodent model has found that stroke can cause long-term damage to the blood-spinal cord barrier (BSCB), creating a "toxic environment" in the spinal cord that might leave stroke survivors susceptible to motor dysfunction and disease pathology.

The paper describing their study was recently published online and will appear in an upcoming issue of Journal of Neuropathology and Experimental Neurology.

"This study, carried out using laboratory rats modeling stroke, demonstrated that ischemic stroke - in both its subacute and chronic stages - damages the BSCB in a variety of ways, creating a toxic environment in the spinal cord that can lead to further disability and exacerbate disease pathology," said study lead author Dr. Svitlana Garbuzova-Davis, associate professor in USF's Center of Excellence for Aging and Brain Repair, Department of Neurosurgery and Brain Repair.

"The aim of our study was to evaluate post-stroke BSCB condition that might lead to the development of more effective therapies for stroke survivors."

The BSCB provides a specialized protective 'microenvironment' for neural cells in the spinal cord. Substantial vascular damage is a major pathologic feature of both subacute and chronic stroke caused by an extended period of microvascular permeability after the BSCB loses integrity. Damage to the BSCB, explained the researchers, plays a fundamental role in the development of several pathological conditions, including abnormal motor function.

The researchers, who evaluated the BSCB in test animals at seven and 30 days after stroke modeling, found that ischemic stroke damaged the gray and white matter in the cervical spinal cord on both sides of the spinal column, based on analysis of electron microscope images.

Among the effects were damage to neural cells called 'astrocytes,' loss of motor neurons, reduced integrity of a tight junction protein between barrier cells, and swollen axons with damaged myelin in ascending and descending tracts connecting to the brain.

They also found stroke-associated 'upregulation' of Beclin-1 in endothelial cells composing the BSCB. Beclin-1, explained the researchers, helps induce autophagy, an activity associated with removal of various intracellular components. They also observed a decrease in LC3B, an essential autophagy protein, at a later stage post-stroke.

These observations of Beclin-1 and LC3B suggest an impaired post-stroke autophagy process in spinal cord capillaries, inducing endothelial cell degeneration.

These stroke-related alterations in the cervical spinal cord indicate pervasive and long-lasting BSCB damage that would severely affect spinal cord function, wrote the researchers, adding that the widespread microvascular impairment in the gray and white matter of the cervical spinal cord aggravated motor neuron deterioration and had the potential to cause motor dysfunction.

"Because our investigations on the post-stroke microvascular alterations, including BSCB damage, have just begun, many questions remain," said senior author Dr. Cesario Borlongan, professor and director of the USF Center of Excellence for Aging and Brain Repair.

"Specifically, the protein expression responsible for endothelial cell degeneration and tight junction damage we identified in this study needs to be confirmed through further tests. Also, behavioral tests of motor function in post-stroke animals in correlation with BSCB damage are needed. These questions and others will be addressed in our future studies."

Dr. Paul R. Sanberg, Distinguished University Professor, a co-author of the paper, concluded that "these novel data showing BSCB damage in subacute and chronic ischemic stroke may lead to development of new therapeutic approaches for patients with ischemic cerebral infarction."

Blood-Spinal Cord Barrier Alterations in Subacute and Chronic Stages of a Rat Model of Focal Cerebral Ischemia. Svitlana Garbuzova-Davis; Edward Haller; Naoki Tajiri; Avery Thomson; Jennifer Barretta; Stephanie N. Williams; Eithan D. Haim; Hua Qin; Aric Frisina-Deyo; Jerry V. Abraham; Paul R. Sanberg; Harry Van Loveren; Cesario V. Borlongan. Journal of Neuropathology & Experimental Neurology 2016; doi: 10.1093/jnen/nlw040.

http://bit.ly/1Y0PHvT

Whistling Sling Bullets Were Roman Troops' Secret 'Terror Weapon'

Some 1,800 years ago, Roman troops used "whistling" sling bullets as a "terror weapon" against their barbarian foes, according to archaeologists who found the cast lead bullets at a site in Scotland.

By Tom Metcalfe, Live Science Contributor | June 13, 2016 06:49am ET

Weighing about 1 ounce (30 grams), each of the bullets had been drilled with a 0.2-inch (5 millimeters) hole that the researchers think was designed to give the soaring bullets a sharp buzzing or whistling noise in flight. The bullets were found recently at Burnswark Hill in southwestern Scotland, where a massive Roman attack against native defenders in a hilltop fort took place in the second century A.D.

These holes converted the bullets into a "terror weapon," said archaeologist John Reid of the Trimontium Trust, a Scottish historical society directing the first major archaeological investigation in 50 years of the Burnswark Hill site.

"You don't just have these silent but deadly bullets flying over; you've got a sound effect coming off them that would keep the defenders' heads down," Reid told Live Science. "Every army likes an edge over its opponents, so this was an ingenious edge on the permutation of sling bullets."

Some of the Roman sling bullets found at the Burnswark Hill battle site in Scotland. The two smallest bullets, shown at the bottom of this image, are drilled with a hole that makes them whistle in flight. **John Reid/Trimontium Trust**

The whistling bullets were also smaller than typical sling bullets, and the researchers think the soldiers may have used several of them in their slings — made from two long cords held in the throwing hand, attached to a pouch that holds the ammunition — so they could hurl multiple bullets at a target with one throw. "You can easily shoot them in groups of three of four, so you get a scattergun effect," Reid said. "We think they're for close-quarter skirmishing, for getting quite close to the enemy."

Sling bullets and stones are a common find at Roman army battle sites in Europe. The largest are typically shaped like lemons and weigh up to 2 ounces (60 grams), Reid said. Smaller bullets shaped like acorns — a symbol the Romans considered lucky — have also been found at Burnswark Hill and other sites in Scotland.

About 20 percent of the lead sling bullets found at Burnswark Hill had been drilled with holes, which represented a significant amount of effort to prepare enough ammunition for an assault, Reid said. "It's a tremendous amount of work to do, to just chuck them away," he said.

Burnswark Hill from the north, with one of the Roman camps visible on the slopes. **John Reid/Trimontium Trust**

Sling weapon secrets

Whistling sling bullets haven't been found at any other Roman sites, but ceramic sling bullets with holes punched out have been discovered at battle sites in Greece from the second and third centuries B.C, Reid said.

Many archaeologists had assumed that the holes in the Greek bullets were reservoirs for poison, he said. But in slinging experiments using about 100 replicas of the whistling bullets, Reid found that they would have been little use as poisoned weapons.

"The holes are too small, and there's no guarantee that these are going to penetrate skin," Reid said. "And they are ballistically inferior: They don't fly as far, don't fly as fast and don't have the same momentum [as larger sling bullets] — so why put poison holes in only the little ones?"

Reid's brother, a keen fisherman, offered some insight into their possible purpose when he suggested the bullets were designed to make noise in flight.

"I said, 'Don't be stupid; you've no idea what you're talking about. You're not an archaeologist,'" Reid joked. "And he said, 'No, but I'm a fisherman, and when I cast my line with lead weights that have got holes in them like that, they whistle.'" "Suddenly, a light bulb came on in my head — that's what they're about. They're for making a noise," Reid said.

Deadly in expert hands

At the time of the Roman attack on Burnswark Hill, slings were used mainly by specialized units of auxiliary troops ("auxilia") recruited to fight alongside the Roman legions. Among the most feared were slingers from the Balearic Islands, an archipelago near Spain in the western Mediterranean, who fought for the Roman general Julius Caesar in his unsuccessful invasions of Britain in 55 B.C. and 54 B.C. "These guys were expert slingers; they'd been doing this the whole of their lives," Reid said. In the hands of an expert, a heavy sling bullet or stone could reach speeds of up to 100 mph (160 km/h): "The biggest sling stones are very powerful — they could literally take off the top of your head," Reid said.

Burnswark Hill lies a few miles north of the line of Roman forts and ramparts known as Hadrian's Wall, built during the reign of the emperor Hadrian between A.D. 117 and 138.

Reid said the Roman attack on the Burnswark Hill fort was probably part of the military campaign ordered by Hadrian's successor, the emperor Antoninus Pius, to conquer Scotland north of the wall. "We think it was an all-out assault on the hilltop, to demonstrate to the natives what would happen to them if they resisted," Reid said.

But the Scottish tribes fought back hard for more than 20 years, and in A.D. 158, the Romans gave up their plans to conquer the north and pulled their legions back to Hadrian's Wall. "Scotland is rather like Afghanistan in many respects," Reid said. "The terrain is pretty inhospitable, certainly the farther north you go, and the isolation and long supply lines would make it difficult for servicing an army that far north."

http://www.eurekalert.org/pub_releases/2016-06/aaos-chl061316.php

Caffeine has little to no benefit after 3 nights of sleep restriction

New study shows caffeine is not sufficient to prevent performance decline long term

DARIEN, IL - A new study found that after restricting sleep to 5 hours per night, caffeine use no longer improved alertness or performance after three nights.

Results show that relative to placebo, caffeine significantly improved Psychomotor Vigilance Task (PVT) performance during the first 2 days, but not the last 3 days of sleep restriction.

"We were particularly surprised that the performance advantage conferred by two daily 200 mg doses of caffeine was lost after three nights of sleep restriction," said lead author Tracy Jill Doty, PhD, research scientist at Walter Reed Army Institute of Research. "These results are important, because caffeine is a stimulant widely used to counteract performance decline following periods of restricted sleep. The data from this study suggests that the same effective daily dose of caffeine is not sufficient to prevent performance decline over multiple days of restricted sleep."

The research abstract was published recently in an online supplement of the journal Sleep and will be presented Monday, June 13 and Tuesday, June 14, in Denver at SLEEP 2016, the 30th Anniversary Meeting of the Associated Professional Sleep Societies LLC (APSS).

The study group consisted of 48 healthy individuals who participated in a double blind, placebo-controlled study. Sleep was restricted to five hours of time in bed for a total of five days. Participants were administered either 200 mg of caffeine or a placebo twice daily. A cognitive task battery was administered hourly during the wake periods and included a 10-minute PVT, Profile of Mood States (POMS), and the Stanford Sleepiness Scale (SSS). A modified Maintenance of Wakefulness Test (mMWT) was administered six times per day.

The study was supported by the Department of Defense Military Operational Medicine Research Program.

Abstract Title: Caffeine Efficacy Across a Simulated 5-day Work Week with Sleep Restriction
Abstract ID: 0254

http://bit.ly/1XvKfQD

A Brief History of Bog Butter

Turf cutters in Ireland regularly find chunks of butter deep in the nation's peat bogs. What is the stuff doing there?

By Jason Daley

Recently, Jack Conway was "cutting turf," the term for digging up blocks of moss in Emlagh peat bog in County Meath, Ireland, when he discovered a 22-pound lump of butter. The find, believed to be 2,000 years old, according to the *Irish Times*, isn't an unusual occurrence in Ireland, where every year, people digging up peat moss to heat their homes encounter chunks of the dairy.

The discoveries, which are called Bog Butter, can be thousands of years old. In 2009, a 77-pound, 3,000-year-old oak barrel of the stuff was found in County Kildare. In 2013, a turf cutter in County Offaly found a 100-pound, 5,000-year-old chunk. Many examples of the butter are found in Irish museums, including the place dedicated to the golden spread, Cork's Butter Museum.

(National Museum of Northern Ireland)

So what is Bog Butter? It's exactly what it sounds like—butter made from cow's milk, buried in a bog. What makes it special is its age. After spending so much time in the cool, damp peat, it starts to take on the appearance and consistency of paraffin wax. According to a study on bog butter by researchers from the University of Bristol, some of the chunks are non-dairy. When analyzing carbon isotopes in nine samples of the butter, they found that six of them were indeed dairy products, while the other three were from animals, perhaps tallow (rendered fat) stored for later use.

In a paper published in the *Journal of Irish Archaeology*, Caroline Earwood explains that bog butter is usually found in earthenware pots, wooden containers, animal skins, or wrapped in bark and takes on a pungent, cheesy odor. Looking at over 274 instances of bog butter from the Iron Age to medieval times, Earwood concluded that early Celtic people probably sunk the butter in the bog simply to preserve it or protect from thieves. The cool, low-oxygen, high acid environment of the bog made a perfect natural refrigerator. Seeing as butter was a valuable commodity and was used to pay taxes, saving it for times of drought, famine, or war would have been a good idea.

There are other theories about the butter as well. It could also have been buried in the bog as an offering to the gods or spirits, the *Irish Times* notes. The Bristol researchers wonder whether burying the butter in the peat was a type of food processing that changed the chemical composition of the butter to make it tastier.

Savina Donohoe, Curator of Cavan County Museum, which accepted Conway's butter lump before sending it to the National Museum of Ireland for analysis, tells UTV Ireland the Conway's big pat is thought to be thousands of years old, but that won't be confirmed until researchers test the twigs and bark stuck to the butterball. Donohoe, who handled the stuff, said it smelled familiar.

"It did smell like butter, after I had held it in my hands, my hands really did smell of butter. There was even a smell of butter in the room it was in," Donohoe says.

Though Irish celebrity chef Kevin Thornton took a bite of bog butter in 2014, Andy Halpin, assistant keeper at the National Museum's Irish Antiquities Division, advises the *Irish Times* that it's probably not wise to sample the Iron Age delicacy.

For those curious, Ben Reade, head of Culinary Research and Development at Nordic Food Lab created his own ancient butter recipe back in 2012. Reade's guinea pigs had mixed things to say about the taste. "The organoleptic [sensory] qualities of this product were to many surprising, causing disgust in some and enjoyment in others," he writes. "The fat absorbs a considerable amount of flavor from its surroundings, gaining flavor notes which were described primarily as 'animal' or 'gamey', 'moss', 'funky', 'pungent', and 'salami'."

http://www.eurekalert.org/pub_releases/2016-06/uosc-agc061316.php

A gene called Prkci helps organize organisms and their organs

A gene called Prkci can point cells in the right direction, according to a new study in Developmental Biology.

In the study, USC Stem Cell researcher In Kyoung Mah from the laboratory of Francesca Mariani and colleagues demonstrated Prkci's role in organizing cells into balls and tubes during early embryo and organ formation.

In their experiments, the researchers used mouse stem cells to form what are known as embryoid bodies, or clusters of cells that mimic the early development of embryos and organs in a Petri dish.

Stem cells self-organize to form a hollow ball of cells. **In Kyoung Mah, Francesca Mariani**

In these embryoid bodies, as in embryos and organs cells organize themselves into layers of tissue, called "epithelia," that separate the inside from the outside. To do so, each cell has an "apical" side designed to line developing cavities and surfaces, and a "basal" end designed to connect to adjoining cells. Without Prkci, the cells can't organize themselves in the correct apical to basal direction--which is known as polarity--and cavities in the embryoid body don't form

Other processes required for forming embryoid body cavities, such as the rate that cells proliferate or die, continued normally in the absence of Prkci--further underscoring that the gene specifically affects polarity.

However, the researchers found that they could restore normal polarity in the cells lacking Prkci by mixing in an equal number of normal cells with functional Prkci. This suggests that the cells with Prkci sent some unknown molecular signal to the cells lacking Prkci, telling them which way to turn.

"Our findings may impact those studying embryonic and organ development, organization and maintenance," said senior author Mariani, principal investigator at the Eli and Edythe Broad Center for Regenerative Medicine and Stem Cell Research at USC. "Identification of this polarizing signal could help develop clinical strategies to realign cells when they become disoriented, as often occurs in cancers that affect organ epithelia such as lung, breast and prostate."

Co-authors include: Rachel Soloff from the University of California, San Diego; Audrey K. Izuhara and Daniel L. Lakeland from USC; and Charles Wang from the City of Hope Comprehensive Cancer Center.

The project was supported by USC, the Robert E. and May R. Wright Foundation, and a California Institute for Regenerative Medicine (CIRM) Bridges to Stem Cell Research Award.

http://www.eurekalert.org/pub_releases/2016-06/aaos-saf061416.php

Sleepiness and fatigue linked to brain atrophy in cognitively normal elderly

Excessive daytime sleepiness and fatigue symptoms may be clinical markers of accelerated brain aging

DARIEN, IL - A new study found that normal older adults who experience excessive sleepiness during the day or significant fatigue may have more brain atrophy than expected for their age, particularly in areas of the brain that are more susceptible to aging and Alzheimer's disease.

Results show that subjects with excessive daytime sleepiness or fatigue not only had more disturbed sleep, but also significantly lower cognitive scores and more medical comorbidities.

"Our results may help to identify individuals at higher susceptibility or risk for dementia prior to symptom onset so that appropriate interventions can be undertaken early to prevent progression to dementia," said lead author, Diego Z. Carvalho, MD, a resident physician of neurology at the Mayo Clinic in Rochester, Minnesota.

The research abstract was published recently in an online supplement of the journal Sleep and will be presented Tuesday, June 14, and Wednesday, June 15, in Denver at SLEEP 2016, the 30th Anniversary Meeting of the Associated Professional Sleep Societies LLC (APSS).

In the Mayo Clinic Study of Aging, the authors identified 1,374 cognitively normal elderly aged 50 years and older who completed sleepiness and fatigue surveys and had a baseline structural magnetic resonance imaging (MRI).

Excessive daytime sleepiness was defined as Epworth Sleepiness Scale of 10 or more. Fatigue severity was assessed with the Beck Depression Inventory-II.

The study was supported by the National Institute on Aging.

Abstract Title: Sleepiness and Fatigue associated with Brain Atrophy in Cognitively Normal Elderly: Mayo Clinic Study of Aging

http://www.eurekalert.org/pub_releases/2016-06/uob-ccb061416.php

Chill coffee beans for a more flavorsome brew, say scientists

University of Bath scientists say brewing more flavorsome coffee could be as simple as chilling the beans before grinding

In the lead up to the World Barista Championships, University of Bath scientists say brewing more flavoursome coffee could be as simple as chilling the beans before grinding.

A team from the University working with renowned Bath coffee shop Colonna & Smalls found that chilling roasted beans before grinding resulted in narrower distribution of small particles, which during the brewing process allows access to more flavour from the same amount of coffee.

Coffee is among the most valuable traded commodities globally, worth $17.9T USD to the US economy in 2015 alone. This discovery could have big implications for the coffee industry and might even allow domestic coffee connoisseurs to brew tastier beverages.

The team studied the effect of grinding beans at different temperatures, from room temperature to -196°C, and discovered that the colder the beans the finer and more uniform the particles were from the grind.

That's important, because small uniform coffee grinds allow for better extraction of the flavour compounds - allowing you to brew more coffee and get more flavour.

Dr Christopher Hendon, a chemistry PhD student at the University of Bath at the time of the study, now working at the Massachusetts Institute of Technology, said: "What you're looking for is a grind that has the smallest difference between the smallest and largest particle. If you have small grinds you can push flavour extraction upwards. We found that chilling the beans tightens up this process and can give higher extractions with less variance in the flavour - so you would have to brew it for less time, or could get more coffee from the same beans.

"It will alter the taste, because subtle changes in particle size distributions make a huge difference in rate of extraction. I wouldn't be surprised if people struggled to achieve balanced extractions.

"It could have a major impact for the industry. People are trying to produce a very high quality drink with really quite powerful tools and are willing to try new things."

The study, highlighted in Nature, is published in Scientific Reports.

Maxwell Colonna-Dashwood, co-owner of Colonna & Smalls, said: "Grinding coffee may seem quite straightforward - break coffee up into a lot of tiny bits so you can dissolve it in water. But like the whole world of coffee the subtleties of the process have a huge impact on the flavour and quality of the cup of coffee. The ability to understand grinding more comprehensively has the dual impact of allowing us to make better tasting coffee and to be more efficient in the way we do that.

"The research suggests that temperature of bean needs to be more constant to help us achieve consistent grinds. It suggests that cooler temperatures will allow us to maximise surface area and utilise more of the coffee. All of this will impact on how we prepare coffee in the industry, I bet we will see the impact of this paper in coffee competitions around the globe, but also in the research and development of new grinding technology for the market place."

The World Barista Championships take place in Dublin between 22-25 June.

The effect of bean origin and temperature on grinding roasted coffee is published at: http://www.nature.com/articles/srep24483 doi:10.1038/srep24483

http://www.eurekalert.org/pub_releases/2016-06/du-ooa061416.php

Origin of a myth: The second trauma cure for amnesia

Why people still believe you need a second 'conk' to remember things

Quick, when Fred Flintstone had a bowling ball fall on his head that made him forget who he was, what was the way to fix him again?

Dropping another bowling ball on him, obviously.

While that worked in "The Flintstones" world and many other fictional realms, the medical community knows that like doesn't cure like when it comes to head trauma.

However, a shockingly high level of the general public endorse the Flintstones solution, with 38-46 percent believing that a second blow to the head could cure amnesia, according to Drexel's Mary Spiers. And, believe it or not, that belief was spurred by members of the medical community dating as far back as the early 19th century.

Spiers, PhD, associate professor in the College of Arts and Sciences' Department of Psychology, traced the origins of the double-trauma amnesia cure belief in a paper for Neurology titled, "The Head Trauma Amnesia Cure: The Making of a Medical Myth."

For a long time, scientists worked to figure out why the brain had two hemispheres.

"Studying the brain in the past was very challenging for several reasons," Spiers explained. "There was no way to look into the living brain, as powerful functional

imaging now allows us to do. Also, many people, including physicians, philosophers and those in the arts, speculated about the function of the brain, the soul and consciousness, so there were many competing ideas."

At one point, scientists landed on the idea that it was a double organ, like a person's eyes or ears, two pieces that were redundant -- doing the same work.

Around the turn of the 19th century, a French scientist named Francois Xavier Bichat decided that the two hemispheres acted in synchrony. One side mirrored the other, and vice versa.

As such, he reasoned that an injury to one side of the head would throw off the other, "untouched" side.

"[Bichat] seriously proposed the notion that a second blow could restore the wits of someone who had a previous concussion," Spiers wrote in her paper. "Bichat justified this idea by reasoning that hemispheres that are in balance with each other functioned better, while those out of balance cause perceptual and intellectual confusion."

Bichat never cited any specific cases to back up his theory and, ironically enough, he died of a probable head injury in 1802.

"From my reading of Bichat's work, it seems that he felt that the second trauma amnesia cure was a common occurrence and didn't need the citation of an individual case," Spiers said. "This was not unusual at the time, to forgo evidence like that."

Despite backup to his claims, Bichat's ideas continued on after his death and became known as Bichat's Law of Symmetry. Books in the following decades cited brain asymmetry as the root of different mental health issues.

Compounding the symmetry idea was also the dominant thought that human memories could never be lost. However, Samuel Taylor Coleridge -- a philosopher, not a physician -- was credited with popularizing that idea.

It wasn't until the mid-1800s that scientists began to realize that taking a hit to the head might just destroy memories completely. A second blow wasn't likely to jump-start the brain, they realized, but create further damage.

By this time, however, enough anecdotes about curing amnesia with a second head trauma were floating around from otherwise respectable scientists that the theory invaded the general public's consciousness. With "no hard and fast lines between scientific and popular writing," myths like the second trauma amnesia cure circulated out of control, according to Spiers.

Even as modern scientists began to fully understand the brain, the theory still stuck with a large amount of the public, resulting in the lumps we continue to see on cartoon characters' heads.

"One of the issues we see in the persistence of this myth is that understanding how the brain forgets, recovers and/or loses information is a complicated matter that is still being studied by brain scientists," Spiers said. "As individuals, we may have had the experience of a 'memory jog' or cue that reminds us of a long-forgotten memory. Because our own experiences serve as powerful evidence to us, this reinforces the myth that all memories are forever stored in the brain and only need some sort of jolt to come back."

But, obviously, that jolt isn't exactly advisable.

"In the case of a traumatic brain injury, learning and memory may be temporarily or permanently impaired due to swelling and injured or destroyed neurons," Spiers concluded. "Some memories may return as the brain recovers, but a second brain injury is never a good treatment for a first brain injury."

http://bit.ly/1WTDnwA

'Mysterious Object' May Be First 'Extinct' Meteorite

A newly uncovered meteorite may be the first-ever "extinct" meteorite — a member of a class of meteorite that no longer falls to Earth.

The ancient rock may yield insights on a cosmic impact that created most of the meteorites that now crash on Earth, and which may have influenced the evolution of life on Earth, researchers said.

The most common meteorites on Earth, which make up about 85 percent of the rocks that fall onto this planet from space, are known as ordinary chondrites. Chondrites are made up of tiny round pellets known as chondrules, which form when molten mineral droplets quickly cool in space. These stony meteorites are thought to come from similarly rocky asteroids.

A newly found fossil meteorite is of a kind different than any ever found, suggesting it may come from a parent asteroid consumed by collisions whose fragments no longer fall to Earth. **Birger Schmitz**

The most common kind of ordinary chondrite is known as the L-type, which makes up about 47 percent of those rocks. Previous research on meteorites embedded in ancient marine limestone revealed that about 470 million years ago, there was an at least hundredfold rise in the number of L-type chondrites that crashed onto Earth. This suggested that the parent asteroid of all the L-type chondrites experienced a major collision with another asteroid at about that time.

This cosmic impact occurred during the Ordovician Period, when major changes in Earth's marine animal diversity occurred, such as the first appearance of coral reefs. A better understanding of this extraterrestrial collision could shed light on astronomical disturbances that might have influenced Earth, said study lead author Birger Schmitz, a geologist at Lund University in Sweden.

"If we see that changes in the asteroid belt correlate with changes in Earth's biosphere or climate, then there is probably a connection and we will be able to better tie Earth's history to the history of the solar system," Schmitz told Space.com. "Earth scientists have for the past 200 years had a tendency to look on Earth as a closed system, but the discovery of the asteroid impact that killed off the dinosaurs 65 million years ago made at least some earth scientists understand that the history of life and Earth is connected to the astronomical realm."

Now researchers say they may have discovered a meteorite that is a remnant of the asteroid that smashed into the parent of the L-type chondrites.

"The single meteorite that we found on the Ordovician seafloor is of a type that we do not know of from today's world," Schmitz told Space.com. "This hints that the types of meteorites that fell on Earth in the ancient past were very different than those falling today."

More than 100 fossil meteorites embedded in marine limestone have been found in Sweden's Thorsberg quarry. The meteorites fell to Earth around 470 million years ago after asteroids smashed into one another.

More than 100 fossil meteorites embedded in marine limestone have been found in Sweden's Thorsberg quarry. The meteorites fell to Earth around 470 million years ago after asteroids smashed into one another. **Birger Schmitz**

The newfound meteorite is a rock about 3.15 inches (8 centimeters) long that is about 470 million years old. It was unearthed in Thorsberg quarry near the Swedish village Österplana alongside more than 100 L-type chondrites of similar age.

The meteorite possesses grains of crystals known as spinels that are very different from those found in all other known meteorites. Further analysis of the strange meteorite found that its ratio of chromium to oxygen isotopes is unlike any seen from known meteorite types. "For a long time we called the meteorite the 'Mysterious Object' because we could not understand what it was," Schmitz said.

Schmitz and his colleagues measured how long the newfound meteorite had been exposed to cosmic rays, a dating technique called cosmic ray exposure, and they found that the impacts that gave birth to the meteorite, now named Österplana, or Öst 65, and to the L-type chondrites found with Öst 65 both occurred about 1 million years before all these meteorites crashed on Earth. This suggests that the impact that formed Öst 65 was the same one that destroyed the parent of the L-type chondrites, the scientists said.

The researchers said the parent asteroid of Öst 65 may have been almost destroyed during its collision with the progenitor of the L-type chondrites, which could explain why this kind of meteorite was previously not discovered on Earth.

"This is the first documented example of an extinct meteorite — that is, a type of meteorite that no longer falls on Earth today," Schmitz said. "We knew of extinct animals, and it has been speculated that there is something like extinct meteorites, but this is the first one found."

The findings suggest that the meteorites largely found on Earth today may not give a full picture of the kinds of bodies in the asteroid belt more than 500 million years ago, or in the nebula cloud of gas and dust that gave birth to the solar system about 4.6 billion years ago.

"We base our view of how the solar system formed and evolved on the meteorites that fall on Earth today," Schmitz said. "If these meteorites are not representative of what has been falling on Earth in the past, we have to take that into consideration when reconstructing how the original nebula condensed into solid planets and asteroids."

Future research may discover other classes of extinct meteorites, the researchers said. The scientists detailed their findings online today (June 14) in the journal Nature Communications.

http://www.bbc.com/news/world-latin-america-36532935

Zika virus: Risk of spread from Olympics 'very low' says WHO

The World Health Organization (WHO) says there is a "very low risk" of Zika virus spreading globally as a result of holding the Olympics in Brazil.

There is no need to move the Olympics from Rio de Janeiro, or to postpone or cancel them, WHO experts said.

The WHO reaffirmed earlier advice against imposing any travel or trade restrictions on areas affected by the virus, which is spread by mosquitoes.

Zika has been linked to birth defects. The Olympics will be held in August.

The WHO has already declared Zika a global public health emergency. It has advised pregnant women to avoid travelling to the Games, and visitors to take precautions to avoid mosquito bites. But despite the concern voiced by some scientists, the WHO said mosquito activity was relatively low in Brazil in August.

Brazilian officials expect about 380,000 foreign visitors to come for the Rio Olympics. Millions of travellers already visit Brazil every year, so not holding the Olympics there would not reduce the numbers significantly, the WHO added.

The outbreak began in Brazil a year ago, but now more than 60 countries and territories have continuing transmission.

More than 1,400 cases of microcephaly in babies have been linked to Zika in Brazil. The babies were born with abnormally small heads, a condition threatening their brain development. The virus has also been linked to a rare nervous system disorder, Guillain-Barre syndrome.

Last month 150 doctors, scientists and bioethicists from more than a dozen countries signed an open letter urging the WHO to consider postponing or moving the Rio Olympics because of the spread of Zika.

http://www.eurekalert.org/pub_releases/2016-06/uomm-ssp061516.php

Sylvester scientists provide proof of concept for potential new class of cancer drugs

Small-molecule inhibitor of the Notch pathway paves the way for a potential new class of personalized cancer medicines

MIAMI - A recent study led by scientists at Sylvester Comprehensive Cancer Center at the University of Miami Miller School of Medicine, in collaboration with the Univerity of Maryland School of Pharmacy and StemSynergy Therapeutics, Inc., has identified a small-molecule inhibitor of the Notch pathway, paving the way for a potential new class of personalized cancer medicines. Aberrant activity in the Notch pathway contributes to the initiation and maintenance of cancer stem cells. The study was published online in the journal Cancer Research.

"The Notch pathway is an exceedingly attractive therapeutic target in cancer, but the full range of potential targets within the pathway has been underexplored," said Anthony J. Capobianco, Ph.D., director of the Molecular Oncology Research Program at Sylvester and corresponding author of the study. "To date, there are no small-molecule inhibitors that directly target the intracellular Notch pathway directly. We've been trying to target this pathway for more than15 years and this is the first example of a targeted therapeutic specific for Notch that has an effect on human-derived malignant tumors."

In this study, the team of scientists attacked the core of Notch activity - a complex of three proteins that directs a specific program of transcription critical for the survival of the tumor. In collaboration with Alex MacKerell, Ph.D., director of the Computer-Aided Drug Design (CADD) Center at the Univerity of Maryland School of Pharmacy, the team used computational drug discovery to identify a small-molecule inhibitor, termed Inhibitor of Mastermind Recruitment 1 (IMR-1), that disrupted the recruitment of Mastermind-like protein 1 (Maml1) to the Notch transcription complex - a function that in turn abrogates Notch target gene transcription. More important, IMR-1 inhibited the growth of Notch-dependent cell lines and significantly supressed the growth of patient-derived tumors in mouse xenograft studies.

"CADD offers the potential to identify therapeutic agents for challenging drug targets, including those involved in cancer," said MacKerell. "In this study, we were able to apply CADD to identify potential drug-binding sites on the previously uncharted Notch transcriptional complex and then screen more than one million drug-like compounds to identify those with a high probability of binding to the complex and blocking its function. The success of this approach in identifying the novel Notch inhibitor emphasizes the utility of CADD in jump-starting research efforts toward the development of novel therapeutic approaches to the treatment of cancer and other diseases."

"Our findings suggest that a novel class of Notch inhibitors targeting Maml1 may represent a new paradigm for Notch-based anticancer therapeutics," said Capobianco, who is also professor of surgery at the Miller School. "As a next step, we plan on moving this laboratory research from human-derived disease models to cancer patients over the next years."

The study was supported by the National Cancer Institute (NCI R01CA083736-12A1, NCI R01CA125044-02), the National Institutes of Health (R01GM081635, R01GM103926, and T32HD007502), the Samuel Waxman Cancer Research Foundation, the University of Maryland School of Pharmacy's CADD Center, the Braman Family Breast Cancer Institute's Women's Cancer League Developmental Grant, Sylvester Comprehensive Cancer Center, and the Dewitt Daughtry Family Department of Surgery.

http://nyti.ms/1UCtqBm

Dr. Philip Majerus, Who Discerned Aspirin's Heart Benefits, Dies at 79

Dr. Philip W. Majerus was one of the first to recommend that all adults take aspirin daily.

By SAM ROBERTS JUNE 14, 2016

Philip W. Majerus, a biochemist who was credited as being the first to theorize that taking small doses of aspirin regularly can prevent heart attacks and strokes in vulnerable patients, died on June 8 at his home in St. Louis. He was 79.

The cause was prostate cancer, his wife, Dr. Elaine Majerus, said. He had taught at the Washington University School of Medicine in St. Louis for almost 50 years.

Even before his findings were confirmed in a study by other researchers a decade later, Dr. Majerus was taking aspirin daily.

"I was already convinced that aspirin prevented heart attacks," he recalled in the journal Advances in Biological Regulation in 2014. "I was unwilling to be randomized into a trial where I might end up with the placebo. I refused to participate."

Dr. Majerus recommended that "all adults should take an aspirin daily unless they are among the few percent of the population that cannot tolerate the drug." The cardiovascular benefit of aspirin was fully achieved by 50 to 75 milligrams daily, he said, and "there is no evidence that branded aspirin, which is much more expensive, is in any way superior to the generic version."

Later studies found that for people in their 50s who are vulnerable to heart disease, taking daily doses of aspirin reduces the risk of heart disease.

In 1998, Dr. Majerus received the Bristol-Myers Squibb Award for Distinguished Achievement in Cardiovascular Metabolic Research for his findings, which were credited with saving countless lives.

When he received the award, Circulation, the journal of the American Heart Association, said it was Dr. Majerus who "first proposed that low-dose aspirin could be used to treat people at risk of heart attack, stroke and other ailments associated with blood clots."

He later theorized that aspirin could also be effective in preventing some forms of cancer, pointing the way to recent studies indicating that daily doses of aspirin also reduces the risk of colon cancer.

Philip Warren Majerus was born in Chicago on July 10, 1936, the son of Clarence Majerus, a manufacturer who owned a five-and-dime store in Quincy, Ill., and the former Helen Mathis.

He received a Bachelor of Science degree from the University of Notre Dame in 1958, graduated from Washington University School of Medicine and did postdoctoral training at the National Institutes of Health. He joined the Washington University faculty in 1966 and retired in 2014 as a professor of medicine and biochemistry and molecular biophysics.

"I got my start in biochemistry because of the Vietnam War," he recalled in The Journal of Biological Chemistry. "As I was finishing my medical residency at Massachusetts General Hospital in 1963, I had two choices going forward: Either I could go to Vietnam as a physician, or I could become a research associate in the United States Public Health Service at the National Institutes of Health. The choice was easy."

As early as the 1950s, studies had demonstrated that aspirin reduced clotting; one California doctor, Lawrence Craven, reported that he had prescribed daily doses to thousands of patients without "a single case of detectable coronary or cerebral thrombosis."

In the 1970s, Dr. Majerus and his postdoctoral research fellow, Gerald Roth, focused on the impact of aspirin on platelets, small cells that precipitate clotting when a blood vessel is injured. They clump together and a clot forms and seals the wound.

"Late one afternoon, I looked in the St. Louis phone directory for aspirin and found a company in town, Rexall, that made aspirin tablets," Dr. Majerus recalled in 1978. "I called after hours, and a man answered the phone. I explained what I wanted: 100 bottles of 100 tablets containing 160 MG aspirin and the same number of bottles of a matched placebo. The man said he could make them without any problem, and he delivered them to my lab the next morning at no charge."

He studied patients who were being treated for kidney failure and, to facilitate dialysis, had shunts, which can cause clotting, inserted in their arms. After six months, 18 of the 25 patients who were taking a placebo developed a blood clot, compared with six of the 19 who were given aspirin.

Investigating how aspirin inhibited clotting, Dr. Majerus concluded that the medicine modified an enzyme that leads to the formation of a platelet-made molecule that constricts blood vessels and aggregates platelets. The pills' effect lasts for the platelets' life span, typically about two weeks.

"Phil Majerus, more than any other individual, has produced the most original body of work on biochemistry of platelets as it relates to thrombosis," Prof. Joseph L. Goldstein, a Nobel laureate at the University of Texas Southwestern Medical Center in Dallas, said when the Bristol-Myers Squibb Award was announced.

Harvey Weiss and John Vane were among the other scientists who pioneered research into the efficacy of aspirin in preventing heart attacks. Dr. David Sackett, who died last year, conducted clinical trials that confirmed their findings as he developed what became known as evidence-based medicine.

Dr. Majerus's first marriage, to the former Janet Brakensiek, ended in divorce. In addition to his wife, the former Elaine Flansburg, he is survived by three daughters and a son from his first marriage — Suzanne Thompson, Mary Juliet Del Valle, Mary Karen Majerus, and David Majerus — four grandchildren and two sisters, Diane Brewer and Kathy Burke.

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Making vinyl records even groovier

Audiophiles have reason to celebrate.

Vinyl records are experiencing a comeback, and scientists are working to make their sound quality even better. An article in Chemical & Engineering News (C&EN), the weekly newsmagazine of the American Chemical Society, takes a

look at how past inventions led to the classic vinyl record, or LP, and what the future might hold.

Matt Davenport, associate editor at C&EN, notes that early iterations of sound recording devices were actually tubular, dating back to Thomas Edison's invention of the phonograph in 1877. His original cylinder wrapped in tin foil gave way to a wax version created in the lab of another great inventor, Alexander Graham Bell. New studies of wax cylinders suggest that the material is very stable over time when handled properly. But more convenient flat records eventually took over. Initially, they were made of celluloid and rubber, and then shellac became the industry standard until the more user-friendly format of vinyl records came along in the mid-20th century. Then came cassettes, CDs and then MP3s.

But rather than going the way of the wax cylinder, LPs have weathered the digital revolution. Sales in the U.S. last year exceeded $400 million. It was vinyl's best year since 1988, even beating out revenue from one of today's most popular forms of music consumption, free online streaming. Now chemists are experimenting with different vinyl formulations to create records with higher quality sound. If they succeed, even more listeners could migrate back to the old-school technology.

http://www.eurekalert.org/pub_releases/2016-06/uosc-phd061516.php

Piping hot drinks may lead to cancer of the esophagus

After examining a larger data set, World Health Organization reverses previous findings that coffee and yerba mate might cause cancer

Drinking piping hot coffee, tea and the caffeine-infused beverage yerba mate probably causes cancer, the World Health Organization announced Wednesday.

Beverages surpassing 149 degrees Fahrenheit (65 degrees Celsius) may increase the risk of tumors in the esophagus, which resides in the chest area below the throat, according to USC's Mariana Stern and 22 other scientists from 10 countries. They met at the WHO's International Agency for Research on Cancer in Lyon, France, in May to determine if drinking coffee, mate or other very hot beverages causes cancer. Their results were published in the journal Lancet on June 15.

"Enjoy your coffee or mate, but make sure it's not very hot," said Stern, an associate professor of preventive medicine and urology at the Keck School of Medicine of USC. "There is physical evidence that very hot beverages can contribute to cell injury in the esophagus and thus contribute to cancer formation."

The group scoured more than 1,000 studies on over 20 different types of cancer. The scientists concluded drinking any beverage hotter than 149 degrees Fahrenheit is "probably carcinogenetic to humans," placing scalding hot drinks in the same category as DDT, frying food at high temperatures, consumption of red meat and the human papillomavirus.

According to the National Coffee Association, coffee waiting to be served should sit at 180-185 degrees Fahrenheit (82-85 degrees Celsius). That's around the temperature McDonald's restaurants served coffee before a well-known lawsuit prompted the fast food chain to sell coffee at a temperature of 10 degrees lower - still far above what the researchers consider safe.

In the United States, the average coffee drinking temperature is around 140 degrees Fahrenheit (60 degrees Celsius). The temperature varies between 99-190 degrees Fahrenheit (37-88 degrees Celsius), Stern said.

"We were now able to evaluate more carefully the effect of mate itself from the effect of temperature, and we concluded that the observed links between mate drinking and cancer of the esophagus seem to be largely driven by drinking mate very hot," Stern said. "Similar associations are seen for other very hot beverages, like tea or coffee."

Stern and her colleagues noted that drinking yerba mate at very high temperatures - between 150 and right below the boiling point of 212 degrees Fahrenheit (66-100 degrees Celsius) - is common practice in certain countries in South America, including Argentina, Uruguay and Paraguay.

A cup of coffee a day may keep liver cancer away

The scientists downgraded a cup of joe from "possibly carcinogenic" and hot mate from "probably carcinogenic" to safe for consumption as long as neither are scalding hot.

In 1991, the WHO gave coffee that classification based on a much smaller database of studies. Now, the scientists highlighted some studies that associated coffee with cancer when the real culprit was probably tobacco smoking, which is highly correlated with heavy coffee drinking, according to the report.

Late last year, Stern participated in a WHO group that concluded consuming processed meat - bacon, salami, sausages, hot dogs and deli meats - causes cancer.

However, the news about coffee was not grim. The researchers estimate that a cup of coffee a day decreases the risk of liver cancer by 15 percent. In other words, the scientists are giving coffee lovers a free pass to drink as much coffee as their bladders can handle.

"For many cancer types, we found clear evidence that coffee is not carcinogenic," Stern said. "In fact, we found that coffee protects against some cancers such as liver and uterine endometrium cancer."

The WHO's International Agency for Research on Cancer (IARC), which celebrated its 50th anniversary last week, produces evidence-based science for global cancer control policies. One of the organization's key philosophies is most cancers are linked to environmental factors and thus are preventable.

The preventive medicine department at Keck Medicine of USC has contributed greatly to IARC initiatives and the intractable problem that is cancer. Other preventive medicine professors who have participated in the IARC's cancer monograph program include Thomas Mack; Anna Wu, co-leader of the Cancer Control Research Program at the USC Norris Comprehensive Cancer Center; and Jonathan Samet, director of the USC Institute for Global Health and distinguished professor and Flora L. Thornton chair of the preventive medicine department. Together these scientists have been involved since the 1980s and have shared their expertise in topics such as solar ultraviolet radiation, smoking, Chinese salted fish, tobacco smoke and involuntary smoking, and cell phone radiation.

http://www.eurekalert.org/pub_releases/2016-06/uomh-fpt061316.php

Four paths to the end of life -- 1 far more expensive than others -- emerge in new study

Results from Medicare analysis conflict with popular ideas about where most dollars are spent in the last year of life -- and where potential cost savings might lie

ANN ARBOR, Mich. -- Last-ditch, high-tech heroic treatments. Days in the hospital intensive care unit. You might think this is what makes dying in America so expensive - and that it's where we should focus efforts to spend the nation's healthcare dollars more wisely.

But a new study finds that for nearly half of older Americans, the pattern of high spending on healthcare was already in motion a full year before they died.

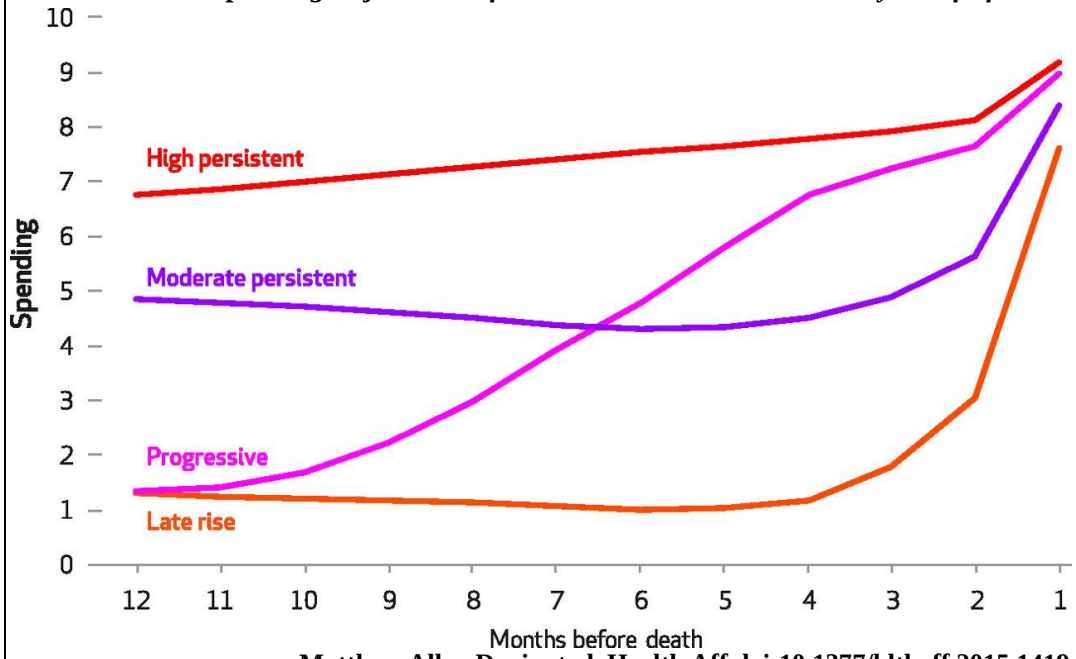
That's thanks to the care they received for their multiple chronic health conditions -- including many doctor visits and regular hospital stays over the year, not just in their final days.

As a result, the study shows, the last year of life for this large group of seniors costs the Medicare system five times as much as the care received by the much smaller group of seniors who have a sudden burst of very expensive care in their last few weeks of life. The findings have clear implications for efforts to improve care, and contain the growth of costs, at the end of life.

The study shows four clear patterns of end-of-life spending, newly identified through an analysis of Medicare data by team led by University of Michigan researchers. They have published their findings in Health Affairs.

Lead author Matthew A. Davis, Ph.D., M.P.H., an assistant professor at the U-M School of Nursing and member of the U-M Institute for Healthcare Policy and Innovation, says the findings surprised him and his colleagues from the U-M Medical School and School of Public Health, and the Dartmouth Institute for Health Policy and Clinical Practice.

Health care spending trajectories of Medicare decedents in the last year of life.



Matthew Allen Davis et al. Health Aff doi:10.1377/hlthaff.2015.1419

"We were expecting to find the most common pattern to be explosive healthcare spending in the final months of life. In fact, only 12 percent of older adults in our study showed this 'late rise' pattern of healthcare spending," he says.

"Our research points to having to do a better job taking care of people who have multiple chronic conditions in a way that maintains or improves the quality of care they receive, but with cost in mind," he continues. "This also suggests that if we focus purely on care for those with a poor prognosis, we won't be able to contain the growth of health costs that you might anticipate."

The team named the four patterns of end-of-life healthcare spending:

High persistent: This group made up nearly half of the Medicare participants studied and had high (and slightly rising) spending throughout the final year of life. In the last year of life, their care cost Medicare around $59,394 (the median value), and they had twice as many outpatient visits to medical specialists as other groups. They also were more likely to spend time in hospitals and skilled nursing facilities, and more likely to get treated using life-prolonging treatments: a respirator, dialysis or a feeding tube.

Moderate Persistent - This group made up 29 percent of the patients studied. Their final year started with moderately high amounts of spending, then it dipped

down for a while, and then went up in the last few months of life. Their care cost about $18,408 in that final year.

Progressive - This group only accounted for 10 percent of the patients, but had the second-highest costs, with a median of $37,036. These individuals had very low spending at the start of their last year of life, but it rose steadily, in a straight line, throughout the last year of life. This group was also the most likely to use hospice care, perhaps because they and their families and physicians had a good sense that they did not have long to live.

Late Rise - With just $11,166 in median health care costs in their final year, this group made up only 12 percent of the total group. They had very low health spending up until a few months before they died, far lower numbers of physician visits and hospital stays, and no or few chronic conditions. They were more likely to die during a hospital stay that included time in an ICU and had the second-highest use of life-prolonging treatments.

There were no clear differences in the healthcare spending patterns when the researchers compared people who had specific major diseases such as cancer, cardiovascular disease and organ failure. Instead, the driving force behind the spending pattern that each person followed appeared to be based on the number of different health conditions he or she had.

Davis and his colleagues used 2011-2012 data from the Centers for Medicare and Medicaid Services. The data were from nearly 100,000 randomly sampled traditional Medicare participants who died in 2012. They drew their sample from data on nearly 1.3 million Americans aged 66 to 99 who died during the period studied.

The study did not account for prescription drug and out-of-pocket spending, nor data on seniors enrolled in Medicare Advantage plans managed by private companies. Another recent U-M study found that Medicare Advantage participants tend to be healthier in their last year of life than those in traditional fee-for-service Medicare.

The study period coincided with the early stages of the "population health" movement, which has increased since that time. Medicare, through programs such as Accountable Care Organizations, is incentivizing doctors' groups and hospitals to improve care and the patient experience while containing cost growth, by offering them extra payment if they achieve goals across a broad swath of patients enrolled in traditional Medicare.

This has led to care management programs and efforts to support patients between doctor visits or when new issues crop up, which may help with the complex patients who had the highest spending rates in the new study.

In addition to Davis, the study's authors include Julie P.W. Bynum at Dartmouth and U-M's Brahmajee Nallamothu, M.D., M.P.H., and Mousumi Banerjee, Ph.D., M.S. The study was funded by the National Institute on Aging at the National Institutes of Health (AG019783) and NIH grant AT006162. Reference: Health Affairs 35, No. 7, DOI:10.1377/hlthaff.2015.1419

http://bit.ly/1YyRiao

Is there life through the looking-glass? The riddle of life's single-handedness

The big questions is: why is life as we know it right-handed rather than left-handed?

Rowena Ball *The Conversation*

Try shaking a colleague's *left* hand with your *right* hand. It just doesn't work, does it? Your right palm and her or his left palm cannot mesh comfortably because hands are *chiral* objects, having non-superimposable mirror images.

All objects have a mirror image (with the exception of vampires), but only objects that are not superimposable on their mirror image are chiral. So when we say that an object and its mirror image *are* superimposable, we mean that if we were to bring the image from behind the mirror, it could be made to coincide exactly with the object.

So a three-dimensional object is either chiral, or it is not.

Life's building blocks are chiral

Molecules are tiny, three-dimensional objects too, and many of them are chiral. Louis Pasteur discovered this in 1848. A chiral molecule and its mirror image are called a pair of enantiomers. In the non-living universe, enantiomers of chiral molecules are expected to occur in equal parts, called racemic mixtures.

Chiral molecules that have been detected in interstellar dust and gas clouds are hydrogen peroxide and, this week, propylene oxide.

Some of the most important molecules of life, such as the nucleotides that make up the polymeric nucleic acids DNA and RNA, exist *in principle* as pairs of enantiomers known as D and L, or "left-handed" and "right-handed" forms.

A fact that has puzzled scientists for generations is that living organisms contain only D nucleotides! In other words, life is *homochiral*.

In itself, the homochirality of life is unremarkable. Scientists have shown in the lab that heterochiral DNA and RNA cannot function, or even form. But the big questions is: why is life as we know it D rather than L?

What was the mechanism, at the origin of life, by which D nucleotide polymers were selected and amplified to homochirality, while the L species became extinct?

Most of the other main building blocks of life – the amino acids – are chiral too, and in this case life uses the L enantiomers exclusively. Last year, it was proposed that a special type of L-glycine (normal glycine is the simplest amino acid, and is

not chiral), may have helped produce the other L amino acids. But this mechanism cannot have directed the D-nucleotides of life, such as DNA and RNA.

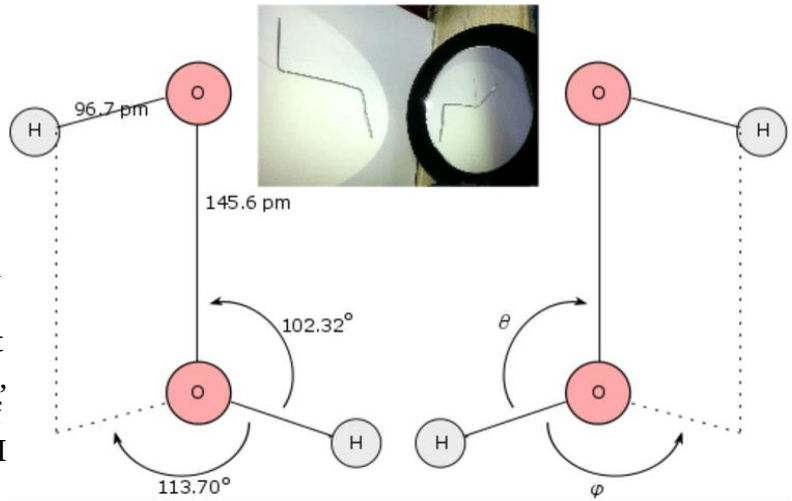
Enter hydrogen peroxide

Late last year, my colleague and I proposed that hydrogen peroxide was the agent that mediated amplification of an initial small excess of D polynucleotides to homochirality.

We know that hydrogen peroxide is present on Mars, Enceladus and Europa, and it was produced on the ancient Earth, more than 3.8 billion years ago, which is around the time that life emerged. As mentioned above, it has also been detected outside the solar system.

In our previous research, we showed that hydrogen peroxide may have provided the essential periodic drive for pre-cellular proto life (the "RNA world").

In our most recent study, we focused on another remarkable property of hydrogen peroxide: it is the smallest and simplest chiral molecule itself, occurring as a pair of enantiomers called M and P.



Projections of 3-dimensional structural representations of the M (left) and P (right) enantiomers of hydrogen peroxide. The inset shows a model for the P enantiomer, which we fabricated in the office from a paper clip; its image reflected in the framed oval mirror is the M enantiomer.

Now, chirality begets chirality. This is a consequence of Curie's principle, which states that "the symmetry of a cause is always preserved in its effects". In other words, to achieve a chirally selective synthesis, separation or amplification, a chiral agent or force is needed.

In fact, chiral organic peroxides have been used in the lab to mediate the production of homochiral molecules. This tells us that, in principle, hydrogen peroxide can act similarly.

It is thought that a small excess of L-amino acids was "rained" onto the ancient Earth by meteorite bombardment, and scientists have found that a small excess of L-amino acids can catalyse formation of small excesses of D-nucleotide precursors. This, we proposed, led to a marginal excess of D-polynucleotides over L-polynucleotides, and a bias to D-chains of longer mean length than L-chains in the RNA world.

In the primordial soup, local excesses of one or other hydrogen peroxide enantiomer would have occurred. Specific interactions with polynucleotides destabilise the shorter L-chains more than the longer, more robust, D-chains.

With a greater fraction of L-chains over D-chains destabilised, hydrogen peroxide can then "go in for the kill", with one enantiomer (let us say M) preferentially oxidising L-chains.

Overall, this process works in favour of increasing the fraction and average length of D-chains at the expense of L-species.

But the hydrogen peroxide itself remains a racemic mixture, on average, meaning that over time and space it has a balance of M and P enantiomers. So we have a subtle reinforcement effect: the fraction D/P increases while the fraction L/M decreases over time.

Thus, the emergence of homochirality *in itself* confers a significant advantage on replicating RNA species.

But could there be mirror-image life made of L-nucleic acids elsewhere in the universe?

Well, all I can say at this stage is that when one reflects on it (or attempts to, so to speak), in a sense we are all vampires, made of molecules that have no natural mirror images on this world, and forever searching the universe for our lost reflections.

http://bit.ly/2654kmf

How a Transgender Woman Could Get Pregnant

The uncharted territory of uterus transplants is sparking patients' interest, but surgeons and endocrinologists remain wary

By Dina Fine Maron on June 15, 2016

When Mats Brännström first dreamed of performing uterus transplants, he envisioned helping women who were born without the organ or had to have hysterectomies. He wanted to give them a chance at birthing their own children, especially in countries like his native Sweden where surrogacy is illegal.

He auditioned the procedure in female rodents. Then he moved on to sheep and baboons. Two years ago, in a medical first, he managed to help a human womb–transplant patient deliver her own baby boy. In other patients, four more babies followed.

But his monumental feats have had an unintended effect: igniting hopes among some transwomen (those whose birth certificates read "male" but who identify as female) that they might one day carry their own children.

Cecile Unger, a specialist in female pelvic medicine at Cleveland Clinic, says several of the roughly 40 male-to-female transgender patients she saw in the past year have asked her about uterine transplants. One patient, she says, asked if she should wait to have her sex reassignment surgery until she could have a uterine transplant at the same time. (Unger's advice was no.) Marci Bowers, a gynecological surgeon in northern California at Mills–Peninsula Medical Center, says that a handful of her male-to-female patients—"fewer than 5 percent"— ask about transplants. Boston Medical Center endocrinologist Joshua Safer says he, too, has fielded such requests among a small number of his transgender patients. With each patient, the subsequent conversations were an exercise in tamping down expectations.

To date there are no hard answers about whether such a fantastical-sounding procedure could enable a transwoman to carry a child. The operation has not been explored in animal trials, let alone in humans. Yet with six planned uterine transplant clinical trials among natal female patients across the U.S. and Europe reproductive researchers are hoping to become more comfortable with the surgery in the coming years. A string of successes could set a precedent that—along with patient interest—may crack open the door for other applications, including helping transwomen. "A lot of this work [in women] is intended to go down that road but no one is talking about that," says Mark Sauer, a professor of obstetrics and gynecology at Columbia University.

Such a future is hard to imagine, at least in the near term. The surgery is still very experimental, even among natal women. Just over a dozen uterus transplants have been performed so far—with mixed results. One day after the first U.S. attempt, for example, the 26-year-old Cleveland Clinic patient had to have the transplanted organ removed due to complications. And only the Brännström group's procedures have led to babies. More efforts are expected in the United States: Cleveland Clinic, Baylor University Medical Center, Brigham and Women's Hospital, and the University of Nebraska Medical Center are all registered to perform small pilot trials with female patients who are hoping to carry their own children.

A Risky Prospect

The trouble is that uterine transplants are extremely complex and resource-intensive, requiring dozens of health personnel and careful coordination. First a uterus and its accompanying veins and arteries must be removed from a donor, either a living volunteer or a cadaver. Then the organ must be quickly implanted and must function correctly—ultimately producing menstruation in its recipient. If the patient does not have further complications, a year later a doctor may then implant an embryo created via in vitro fertilization. The resulting baby would have to be born through cesarean section—as a safety precaution to limit stress on the transplanted organ, and because the patient cannot feel labor contractions (nerves are not transplanted with the uterus). Following the transplant and throughout the pregnancy the patient has to take powerful antirejection drugs that come with the risk of problematic side effects.

The dynamic process of pregnancy also requires much more than simply having a womb to host a fetus, so the hurdles would be even greater for a transwoman. To support a fetus through pregnancy a transgender recipient would also need the right hormonal milieu and the vasculature to feed the uterus, along with a vagina. For individuals who are willing to take these extreme steps, reproductive specialists say such a breakthrough could be theoretically possible—just not easy.

Here is how it could work: First, a patient would likely need castration surgery and high doses of exogenous hormones because high levels of male sex hormones, called androgens, could threaten pregnancy. (Although hormone treatments can be powerful, patients would likely need to be castrated because the therapy might not be enough to maintain the pregnancy among patients with testes.) The patient would also need surgery to create a "neovagina" that would be connected to the transplant uterus, to shed menses and give doctors access to the uterus for follow-up care.

A small number of surgeons already have experience creating artificial vaginas and connecting them to uterine transplants. Most of Brännström's transplant patients have been women with a condition called Rokitansky syndrome, and as a result they lack the upper part of the vagina and had to have a neovagina surgically made—typically by extending the lower vagina. Separately, surgeons that specialize in working with transwomen also often create neovaginas after castration, using skin from the penis and the scrotum.

Biological Connection

Even if the hormonal and anatomical challenges are overcome, for someone who was born producing sperm instead of eggs there would be one more hurdle: Before castration that person's sperm must be collected and combined with a donor's or partner's egg to make an embryo via in vitro fertilization, and that embryo would have to be frozen until the transplant patient is ready. If the embryo is successfully implanted, the transwoman would then naturally produce the placenta required to sustain the pregnancy and begin to lactate in preparation for breast-feeding, Cleveland Clinic's Unger says.

Experts disagree about what would be the biggest barrier to pulling off these theoretical transplants and pregnancies. Giuliano Testa, a transplant surgeon at Baylor University Medical Center who will soon be directing uterine transplant surgeries among natal women, says the hormones would likely prove the biggest

obstacle. “It would really be a feat of unknown proportions,” Testa says. “I would never do this.” But he concedes the transplants are not out of the question. “At the end of the day it is two arteries and two veins that are connected with fine surgical techniques.”

Unger—who is not involved in Cleveland Clinic’s uterine transplant team trial—worries about a consistent and ample blood flow to the fetus. Bowers, who is transgender herself, says she is concerned about dangers to the fetus from a potentially unstable biological environment and unforeseen risks for the mother-to-be. “I respect reproduction and I don’t think we will ever see this in my lifetime in a transgender woman,” she says. “That’s what I tell my patients.”

Costs and ethics also pose significant barriers. Many transgender patients have already been saving for years to pay for male-to-female genital surgery— which can cost around $24,000 without insurance coverage—so a uterine transplant could be out of financial reach, Unger says. And some doctors working on the frontlines with transgender patients have expressed concerns about the ethics involved in the risks. Sauer, the gynecologist from Columbia, says that with options including surrogacy and adoption available in many locations, an experimental surgery to help patients give birth—not save their lives—seems like a huge risk. Safer, medical director for the Center of Transgender Medicine and Surgery at Boston Medical Center, agrees. “If you are going to die without a transplant, of course you take [antirejection] drugs. But this is not the case here,” he says. “This is not life and death.”

The American Society for Reproductive Medicine’s Ethics Committee is already discussing how uterine transplants could be prioritized, says Sauer, who is a member of that panel. Yet there is no discussion yet about how transgender candidates would be included in the mix. Additionally, it is unclear how demand for a uterus would be weighed by a hospital or an organization like the United Network for Organ Sharing.

Yet interest in uterine transplants is growing: Brännström, the Swedish surgeon who led the prior transplant work among women, says his inbox is now inundated with messages from less-traditional patients. “I get e-mails from all over the world on this, sometimes from gay males with one partner that would like to carry a child,” he says. Brännström does not plan to perform such procedures himself—instead he wants to focus on women who were born without a uterus or lost it due to cancer or another illness. The next natural step for those interested in assisting transgender or male patients, however, would likely be tackling this procedure among women with a rare condition called androgen insensitivity syndrome, he says. A person with AIS appears largely female, but has no uterus and is genetically male.

Amid these complex discussions there is one bright spot, the relative ease of finding the organs. Already one group has proved rich in willing donors: people who are transitioning from female to male and have also decided to have their uteruses removed. Unger says among her female-to-male patients, “one in three” have asked if they could donate the organs. Because there is no protocol set up to deal with these offers (Cleveland Clinic’s trial uses cadaver uteruses), they are currently turned down. Such potential donors may seem ideal because they are not pursuing a hysterectomy due to disease. But a major catch is the medical risk they face: A standard hysterectomy takes between a half-hour and an hour, but preparing a uterus and its associated blood vessels for transplant would keep such patients under the knife for as long as 10 or 11 hours. Clearly, the ethics of such donations would have to be studied extensively, Unger says. Like uterine transplants for transgender patients, this is all uncharted territory.

http://www.eurekalert.org/pub_releases/2016-06/osu-wlw061516.php

Women's long work hours linked to alarming increases in cancer, heart disease

Study links overtime to early development of chronic, life-threatening illness

COLUMBUS, Ohio - Women who put in long hours for the bulk of their careers may pay a steep price: life-threatening illnesses, including heart disease and cancer.

Work weeks that averaged 60 hours or more over three decades appear to triple the risk of diabetes, cancer, heart trouble and arthritis for women, according to new research from The Ohio State University.

The risk begins to climb when women put in more than 40 hours and takes a decidedly bad turn above 50 hours, researchers found.

"Women - especially women who have to juggle multiple roles - feel the effects of intensive work experiences and that can set the table for a variety of illnesses and disability," said Allard Dembe, professor of health services management and policy and lead author of the study, published online this week in the Journal of Occupational and Environmental Medicine.

"People don't think that much about how their early work experiences affect them down the road," he said. "Women in their 20s, 30s and 40s are setting themselves up for problems later in life."

Men with tough work schedules appeared to fare much better, found the researchers, who analyzed data from interviews with almost 7,500 people who were part of the National Longitudinal Survey of Youth.

Women tend to take on the lion's share of family responsibility and may face more pressure and stress than men when they work long hours, previous research

shows. On top of that, work for women may be less satisfying because of the need to balance work demands with family obligations, Dembe said.

Employers and government regulators should be aware of the risks, especially to women who are required to regularly toil beyond a 40-hour work week, he said. Companies benefit in terms of quality of work and medical costs when their workers are healthier, Dembe said.

More scheduling flexibility and on-the-job health coaching, screening and support could go a long way toward reducing the chances employees become sick or die as a result of chronic conditions, he said.

The researchers analyzed the relationship between serious disease and hours worked over a 32-year period.

Previous research has shown that workers who put in long hours face more stress, have more sleep and digestive trouble and are more fatigued. Their work performance suffers and they have more injuries on the job.

But prior to this study, efforts to examine a connection between long hours and chronic illness have had mixed results, in large part because it's difficult to obtain long-term data on work patterns and health, Dembe said.

This study used data from the National Longitudinal Survey of Youth 1979, administered by Ohio State's Center for Human Resource Research and sponsored by the U.S. Bureau of Labor Statistics, which includes interviews with more than 12,000 Americans born between 1957 and 1964.

Dembe and his collaborator, Mayo Clinic researcher and former Ohio State doctoral student Xiaoxi Yao, examined data for survey participants who were at least 40 in 1998, when interview questions began to include questions about health status and chronic conditions.

They averaged the self-reported hours worked each week over 32 years and compared the hours worked to the incidence of eight chronic diseases: heart disease, cancer (except skin cancer), arthritis or rheumatism, diabetes or high blood sugar, chronic lung disease including bronchitis or emphysema, asthma, depression and high blood pressure. They also examined the results by gender.

A minority of the full-time workers in the study put in 40 hours or fewer per week. Fifty-six percent worked an average of 41 to 50 hours; 13 percent worked an average of 51-60 hours; and 3 percent averaged more than 60 hours.

The results among female workers were striking, Dembe said. The analysis found a clear and strong relationship between long hours and heart disease, cancer, arthritis and diabetes.

Men who worked long hours had a higher incidence of arthritis, but none of the other chronic diseases. And those men who worked moderately long hours (41 to 50 hours weekly) had lower risk of heart disease, lung disease and depression than those who worked 40 hours or fewer.

Because the data addresses chronic diseases reported by age 40 or 50, this study speaks only to early-onset disease and doesn't shed light on the possible associations between long hours and lifetime risks, which could prove even more profound, Dembe said.

"The early onset and identification of chronic diseases may not only reduce individuals' life expectancy and quality of life, but also increase health care costs in the long term," Dembe and Yao wrote in the paper.

One limitation of the study is that it relies on average hours per week and doesn't provide answers about the differences between those who consistently worked long hours and those whose careers were full of long hours at first but who found themselves with more free time later on, the researchers said.

It also does not address the potential differences between mandatory overtime and discretionary overtime.

"It could make a difference," Dembe said. "You might still be working hard, but the fact that it's your choice might help you stay healthier."

The study was supported by the U.S. Centers for Disease Control and Prevention and the National Institute of Occupational Safety and Health.

http://www.eurekalert.org/pub_releases/2016-06/bifr-pap061516.php

Pre and post testing show reversal of memory loss from Alzheimer's disease in 10 patients

Small trial from the Buck Institute and UCLA succeeds using systems approach to memory disorders

Results from quantitative MRI and neuropsychological testing show unprecedented improvements in ten patients with early Alzheimer's disease (AD) or its precursors following treatment with a programmatic and personalized therapy. Results from an approach dubbed metabolic enhancement for neurodegeneration are now available online in the journal Aging.

The study, which comes jointly from the Buck Institute for Research on Aging and the UCLA Easton Laboratories for Neurodegenerative Disease Research, is the first to objectively show that memory loss in patients can be reversed, and improvement sustained, using a complex, 36-point therapeutic personalized program that involves comprehensive changes in diet, brain stimulation, exercise, optimization of sleep, specific pharmaceuticals and vitamins, and multiple additional steps that affect brain chemistry.

"All of these patients had either well-defined mild cognitive impairment (MCI), subjective cognitive impairment (SCI) or had been diagnosed with AD before beginning the program," said author Dale Bredesen, MD, a professor at the Buck

Institute and professor at the Easton Laboratories for Neurodegenerative Disease Research at UCLA, who noted that patients who had had to discontinue work were able to return to work and those struggling at their jobs were able to improve their performance. "Follow up testing showed some of the patients going from abnormal to normal."

One of the more striking cases involved a 66-year old professional man whose neuropsychological testing was compatible with a diagnoses of MCI and whose PET scan showed reduced glucose utilization indicative of AD. An MRI showed hippocampal volume at only the 17th percentile for his age. After 10 months on the protocol a follow-up MRI showed a dramatic increase of his hippocampal volume to the 75th percentile, with an associated absolute increase in volume of nearly 12 percent.

In another instance, a 69-year old professional man and entrepreneur, who was in the process of shutting down his business, went on the protocol after 11 years of progressive memory loss. After six months, his wife, co-workers and he noted improvement in memory. A life-long ability to add columns of numbers rapidly in his head returned and he reported an ability to remember his schedule and recognize faces at work. After 22 months on the protocol he returned for follow-up quantitative neuropsychological testing; results showed marked improvements in all categories with his long-term recall increasing from the 3rd to 84th percentile. He is expanding his business.

Another patient, a 49-year old woman who noted progressive difficulty with word finding and facial recognition went on the protocol after undergoing quantitative neuropsychological testing at a major university. She had been told she was in the early stages of cognitive decline and was therefore ineligible for an Alzheimer's prevention program. After several months on the protocol she noted a clear improvement in recall, reading, navigating, vocabulary, mental clarity and facial recognition. Her foreign language ability had returned. Nine months after beginning the program she did a repeat of the neuropsychological testing at the same university site. She no longer showed evidence of cognitive decline.

All but one of the ten patients included in the study are at genetic risk for AD, carrying at least one copy of the APOE4 allele. Five of the patients carry two copies of APOE4 which gives them a 10-12 fold increased risk of developing AD. "We're entering a new era," said Bredesen. "The old advice was to avoid testing for APOE because there was nothing that could be done about it. Now we're recommending that people find out their genetic status as early as possible so they can go on prevention." Sixty-five percent of the Alzheimer's cases in this country involve APOE4; with seven million people carrying two copies of the ApoE4 allele.

Bredesen' s systems-based approach to reverse memory loss follows the abject failure of monotherapies designed to treat AD and the success of combination therapies to treat other chronic illnesses such as cardiovascular disease, cancer and HIV.

Bredesen says decades of biomedical research, both in his and other labs, has revealed that an extensive network of molecular interactions is involved in AD pathogenesis, suggesting that a broader-based therapeutic approach may be more effective. "Imagine having a roof with 36 holes in it, and your drug patched one hole very well--the drug may have worked, a single 'hole' may have been fixed, but you still have 35 other leaks, and so the underlying process may not be affected much," Bredesen said.

"We think addressing multiple targets within the molecular network may be additive, or even synergistic, and that such a combinatorial approach may enhance drug candidate performance, as well."

While encouraged by the results of the study, Bredesen admits more needs to be done. "The magnitude of improvement in these ten patients is unprecedented, providing additional objective evidence that this programmatic approach to cognitive decline is highly effective," Bredesen said. "Even though we see the far-reaching implications of this success, we also realize that this is a very small study that needs to be replicated in larger numbers at various sites." Plans for larger studies are underway.

Cognitive decline is often listed as the major concern of older adults. Already, Alzheimer's disease affects approximately 5.4 million Americans and 30 million people globally. Without effective prevention and treatment, the prospects for the future are bleak. By 2050, it's estimated that 160 million people globally will have the disease, including 13 million Americans, leading to potential bankruptcy of the Medicare system. Unlike several other chronic illnesses, Alzheimer's disease is on the rise--recent estimates suggest that AD has become the third leading cause of death in the United States behind cardiovascular disease and cancer.

THE BREDESEN PROTOCOL, Dr. Bredesen's book describing for a lay audience the interventions described in this paper, will be released by Penguin Random House in May 2017. Dr. Bredesen hopes to eventually transform the perception and reality of Alzheimer's disease from a death sentence to a preventable reversible condition.

Citation: Reversal of Cognitive Decline in Alzheimer's Disease

Other collaborators on the study include Edwin C. Amos, Jonathan Canick, Mary Ackerley, Cyrus Raji, Milan Fiala, and Jamila Ahdidan. Multiple entities provided support for the research which supported the study. They include the National Institutes of Health (AG16570, AG034427 and AG036975). Please see paper for the complete list.

http://www.eurekalert.org/pub_releases/2016-06/cp-ntr060916.php

Need to remember something? Exercise 4 hours later!

A new study suggests an intriguing strategy to boost memory for what you've just learned: hit the gym four hours later.

The findings reported in the Cell Press journal Current Biology on June 16 show that physical exercise after learning improves memory and memory traces, but only if the exercise is done in a specific time window and not immediately after learning.

"It shows that we can improve memory consolidation by doing sports after learning," says Guillén Fernández of the Donders Institute at the Radboud University Medical Center in the Netherlands.

In the new study, Fernández, along with Eelco van Dongen and their colleagues, tested the effects of a single session of physical exercise after learning on memory consolidation and long-term memory. Seventy-two study participants learned 90 picture-location associations over a period of approximately 40 minutes before being randomly assigned to one of three groups: one group performed exercise immediately, the second performed exercise four hours later, and the third did not perform any exercise. The exercise consisted of 35 minutes of interval training on an exercise bike at an intensity of up to 80 percent of participants' maximum heart rates. Forty-eight hours later, participants returned for a test to show how much they remembered while their brains were imaged via magnetic resonance imaging (MRI).

The researchers found that those who exercised four hours after their learning session retained the information better two days later than those who exercised either immediately or not at all. The brain images also showed that exercise after a time delay was associated with more precise representations in the hippocampus, an area important to learning and memory, when an individual answered a question correctly.

"Our results suggest that appropriately timed physical exercise can improve long-term memory and highlight the potential of exercise as an intervention in educational and clinical settings," the researchers conclude.

It's not yet clear exactly how or why delayed exercise has this effect on memory. However, earlier studies of laboratory animals suggest that naturally occurring chemical compounds in the body known as catecholamines, including dopamine and norepinephrine, can improve memory consolidation, the researchers say. One way to boost catecholamines is through physical exercise.

Fernández says they will now use a similar experimental setup to study the timing and molecular underpinnings of exercise and its influence on learning and memory in more detail.

The researchers were supported by a grant from the European Research Council.

Current Biology, van Dongen et al.: "Physical Exercise Performed Four Hours after Learning Improves Memory Retention and Increases Hippocampal Pattern Similarity during Retrieval" http://www.cell.com/current-biology/fulltext/S0960-9822(16)30465-1

http://www.eurekalert.org/pub_releases/2016-06/cp-ass061016.php

A single species of gut bacteria can reverse autism-related social behavior in mice

Absence of a species of gut bacteria causes social deficits in mice

The absence of a one specific species of gut bacteria causes social deficits in mice, researchers at Baylor College of Medicine report June 16, 2016 in Cell. By adding this bacteria species back to the guts of affected mice, the researchers were able to reverse some of their behavioral deficits, which are reminiscent of symptoms of autism spectrum disorders (ASDs) in humans. The investigators are now looking to explore the effects of probiotics on neurodevelopmental disorders in future work.

"Other research groups are trying to use drugs or electrical brain stimulation as a way to reverse some of the behavioral symptoms associated with neurodevelopmental disorders -- but here we have, perhaps, a new approach," says senior author Mauro Costa-Mattioli, a neuroscientist at Baylor College of Medicine. "Whether it would be effective in humans, we don't know yet, but it is an extremely exciting way of affecting the brain from the gut."

The inspiration for the paper came from human epidemiological studies that have found that maternal obesity during pregnancy could increase children's risk of developing neurodevelopmental disorders, including ASDs. In addition, some individuals with ASD also report recurring gastrointestinal problems. With emerging research showing how diet can change the gut microbiome and how gut microbes can influence the brain, Costa-Mattioli and his co-authors suspected there could be a connection.

To begin, the researchers fed approximately 60 female mice a high-fat diet that was the rough equivalent of consistently eating fast food multiple times a day. They bred the mice daily and waited for them to bear young. The offspring stayed with their mother for three weeks and then were weaned onto a normal diet. After a month, these offspring showed behavioral deficits, such as spending less time in contact with their peers and not initiating interactions.

"First we wanted to see if there was a difference in the microbiome between the offspring of mouse mothers fed a normal diet versus those of mothers fed a high-fat diet. So, we used 16S ribosomal RNA gene sequencing to determine the bacterial composition of their gut. We found a clear difference in the microbiota of the two maternal diet groups," says first author Shelly Buffington, a

postdoctoral fellow in Costa-Mattioli's lab. "The sequencing data was so consistent that by looking at the microbiome of an individual mouse we could predict whether its behavior would be impaired."

Buffington next tested whether the specific differences in the microbiome were causative factors underlying the social impairments in offspring of mothers fed a high-fat diet. Because mice eat each other's poop, the researchers housed the animals together so that they would acquire microbiota from their cagemates. When socially impaired three-week-old mice born to mothers on a high-fat diet were paired with normal mice, a full restoration of the gut microbiome and a concurrent improvement in behavior was observed within four weeks. The investigators concluded that one or more beneficial bacterial species might be important for normal social behavior. Fecal-transplant experiments in mice without microbiota (germ-free mice) provided causal evidence that an imbalanced microbial ecology in the mice born to mothers on a high-fat diet is responsible for their social deficits.

The investigators next wanted to know the specific bacterial species that could be affecting the social behavior of the mice. Whole-genome shotgun sequencing revealed one type of bacteria, Lactobacillus reuteri, which was reduced more than nine-fold in the microbiome of mice born to mothers on the high-fat diet.

"We cultured a strain of Lactobacillus (L.) reuteri originally isolated from human breast milk and introduced it into the water of the high-fat-diet offspring. We found that treatment with this single bacterial strain was able to rescue their social behavior," Buffington says. Other ASD-related behaviors, such as anxiety, were not restored by the reconstitution of the bacteria. Interestingly, the authors found that L. reuteri also promoted the production of the "bonding hormone" oxytocin, which is known to play a crucial role in social behavior and has been associated with autism in humans.

The authors wondered whether the reward circuitry in the socially impaired mice was dysfunctional. "We found that in response to social interaction there was a lack of synaptic potentiation in a key reward area of the brain that could be seen in the normal control mice," Costa-Mattiol says. "When we put the bacteria back in the maternal-high-fat-diet offspring, we could also restore the changes in synaptic function in the reward circuitry."

The researchers believe that their work, which uses a human bacteria species to promote oxytocin levels and improve social behavioral deficits in deficient mice, could be explored as a probiotic intervention for the treatment of neurodevelopmental disorders in humans. "This is where the science is unexpectedly leading us. We could potentially see this type of approach developing quite quickly not only for the treatment of ASD but also for other neurodevelopmental disorders; anyway, this is my gut feeling," Costa-Mattioli says.

Others who contributed to the research include Gonzalo Viana Di Prisco, Thomas A. Auchtung, Nadim J. Ajami, and Joseph F. Petrosino, all at Baylor College of Medicine.

The research was supported by funding from the National Institutes of Health, the Alkek Foundation, and Baylor College of Medicine.

Cell, Buffington et al.: "Microbial reconstitution reverses maternal diet-induced social and synaptic deficits in offspring" http://www.cell.com/cell/fulltext/S0092-8674(16)30730-9

http://www.eurekalert.org/pub_releases/2016-06/dnl-srd061616.php

Sandia researchers discover mechanism for Rift Valley fever virus infection

Virus uses known cancer pathway

LIVERMORE, Calif. -- Viruses can't live without us -- literally. As obligate parasites, viruses need a host cell to survive and grow. Scientists are exploiting this characteristic by developing therapeutics that close off pathways necessary for viral infection, essentially stopping pathogens in their tracks.

Rift Valley fever virus (RVFV) and other members of the bunyavirus family may soon be added to the list of viruses denied access to a human host. Sandia National Laboratories researchers have discovered a mechanism by which RVFV hijacks the host machinery to cause infection. This mechanism offers a new approach toward developing countermeasures against this deadly virus, which in severe human infections causes fatal hepatitis with hemorrhagic fever, encephalitis and retinal vasculitis.

The results are reported in a paper, "A Genome-Wide RNAi Screen Identifies a Role for Wnt/Beta-Catenin Signaling During Rift Valley Fever Virus Infection," recently published in the Journal of Virology. The work was funded by Sandia's Laboratory Directed Research and Development program.

RVFV uses a cancer pathway

Little is known about the fundamental infection mechanisms and interactions between bunyaviruses and their host cells. Led by Sandia virologist Brooke Harmon, the researchers discovered that Wnt signaling is essential for bunyavirus infection.

The Wnt signaling pathway, which regulates critical cell processes, such as proliferation and differentiation, is already under heavy investigation by medical researchers because of its association with breast, melanoma, prostrate, lung, ovarian and other cancers and with Type II diabetes. Clinical trials are underway for cancer treatments targeting the Wnt pathway. "We can take advantage of the work on cancer therapeutics. Inhibitors of this pathway are already being

developed for several cancers. As those therapies move through clinical trials, we can apply them to infectious diseases," said Harmon.

Rift Valley a priority pathogen

You may not have heard of RVFV, but it's a familiar threat to anyone working in infectious diseases. The National Institute of Allergy and Infectious Diseases lists RVFV as a category A priority pathogen, meaning it poses the highest risk to national security and public health.

"Rift Valley combines some of the most sinister aspects of both Ebola and Zika into one virus," explained Harmon. "Like Ebola, it can cause hemorrhagic fever and be lethal within days of infection. Like Zika, it's transmitted by mosquitoes, can cause neurological disease in humans, and results in frequent miscarriages and fetal deformities in livestock."

Today RVFV predominantly affects animals, livestock in particular. Like most viruses transmitted by mosquitos, RVFV circulates predominantly in wild animals but has the potential to spill over into human populations, similar to avian influenza and West Nile virus.

While endemic to Africa, RVFV has spread to the Arabian Peninsula and has the capacity to emerge into further territories. Since the late 1990s, large-scale RVFV outbreaks in eastern and southern Africa, Mauritania, Saudi Arabia and Yemen have severely affected the health and economy of tens of thousands of humans and infected hundreds of thousands of livestock.

Bunyavirus family uses Wnt

Harmon and Sandia researcher Oscar Negrete began the project about five years ago by using high-throughput RNA interference to screen the entire human genome against RVFV. The researchers looked for genes that were required for virus infection, meaning that the virus cannot infect cells missing that gene.

From that initial screen, conducted at the University of California, Berkeley, and further screening at Sandia, they narrowed the field down to 381 genes of interest. "When we functionally clustered those genes, we found that the Wnt pathway was the most represented," said Negrete.

To test their hypothesis that the Wnt pathway is critical to RVFV infection, the researchers tested a vaccine strain of the virus. When those results supported their theory, they conducted the same experiments on wild type virus in a Biosafety Level-3 laboratory at Lawrence Livermore National Laboratory.

They expanded the testing to other members of the bunyavirus family like La Crosse virus and California encephalitis virus and found the same results. "This was somewhat unexpected because divergent bunyaviruses typically have their own unique features of infection. The fact that they shared this same pathway is exciting because it indicates Wnt signaling may be necessary to the virus family as a whole," said Negrete.

Getting ahead of the next big outbreak

The next step, said Negrete, is to further investigate the mechanisms of infection. The researchers also plan to look for other mechanisms of RVFV infection using CRISPR, or clustered regularly interspaced short palindromic repeats, which is complementary to RNA interference. This understanding can aid in the design of effective host-directed anti-viral therapeutics.

"We keep chasing these viruses. An outbreak like Zika happens and that's when the push begins for a therapeutic. We need to get out in front of the next big one because recent history has taught us that deadly diseases can rapidly spread from animals to humans and beyond endemic zones," said Harmon. "If there is an outbreak of RVFV or another bunyavirus, we hope to already have something in the arsenal."

Sandia National Laboratories is a multi-program laboratory operated by Sandia Corporation, a wholly owned subsidiary of Lockheed Martin Corp., for the U.S. Department of Energy's National Nuclear Security Administration. With main facilities in Albuquerque, N.M., and Livermore, Calif., Sandia has major R&D responsibilities in national security, energy and environmental technologies and economic competitiveness.

http://www.eurekalert.org/pub_releases/2016-06/tju-nmc061616.php

Natural molecule could improve Parkinson's

A natural molecule shows benefit in a preliminary clinical trial for Parkinson's disease

PHILADELPHIA - The natural molecule, n-acetylcysteine (NAC), with strong antioxidant effects, shows potential benefit as part of the management for patients with Parkinson's disease, according to a study published today in the journal PLOS ONE.

Combining clinical evaluations of a patient's mental and physical abilities with brain imaging studies that tracked the levels of dopamine, the lack of which is thought to cause Parkinson's, doctors from the Departments of Integrative Medicine, Neurology, and Radiology, at Thomas Jefferson University showed that patients receiving NAC improved on both measures.

Current treatments for Parkinson's disease are generally limited to temporarily replacing dopamine in the brain as well as some medications designed to slow the progression of the disease process. Recently, researchers have shown that oxidative stress in the brain may play a critical role in the Parkinson's disease process, and that this stress also lowers levels of glutathione, a chemical produced by the brain to counteract oxidative stress. Studies in brain cells showed that NAC

helps reduce oxidative damage to neurons by helping restore the levels of the antioxidant glutathione. NAC is an oral supplement that can be obtained at most nutrition stores, and interestingly also comes in an intravenous form which is used to protect the liver in acetaminophen overdose.

"This study reveals a potentially new avenue for managing Parkinson's patients and shows that n-acetylcysteine may have a unique physiological effect that alters the disease process and enables dopamine neurons to recover some function," said senior author on the paper Daniel Monti, M.D., M.B.A., Director of the Myrna Brind Center of Integrative Medicine, and the Brind-Marcus Center of Integrative Medicine at Thomas Jefferson University.

In this study, Parkinson's patients who continued their current standard of care treatment, were placed into two groups. The first group received a combination of oral and intravenous (IV) NAC for three months. These patients received 50mg/kg NAC intravenously once per week and 600mg NAC orally 2x per day on the non IV days.

The second group, the control patients, received only their standard of care for Parkinson's treatment. Patients were evaluated initially, before starting the NAC and then after three months of receiving the NAC while the control patients were simply evaluated initially and three months later.

The evaluation consisted of standard clinical measures such as the Unified Parkinson's Disease Rating Scale (UPDRS), a survey administered by doctors to help determine the stage of disease, and a brain scan via DaTscan SPECT imaging, which measures the amount of dopamine transporter in the basal ganglia, the area most affected by the Parkinson's disease process.

Compared to controls, the patients receiving NAC had improvements of 4-9 percent in dopamine transporter binding and also had improvements in their UPDRS score of about 13 percent.

"We have not previously seen an intervention for Parkinson's disease have this kind of effect on the brain," said first author and neuro-imaging expert Andrew Newberg, M.D., Professor at the Sidney Kimmel Medical College at Jefferson and Director of Research at the Myrna Brind Center of Integrative Medicine. The investigators hope that this research will open up new avenues of treatment for Parkinson's disease patients.

This study was funded by a gift from the Marcus Foundation. The authors report no conflicts of interest.

Article reference: DA Monti, et al., "N-Acetyl Cysteine May Support Dopamine Neurons in Parkinson's Disease: Preliminary Clinical and Cell Line Data," PLOS ONE, DOI: 10.1371/journal.pone.0157602, 2016.

http://bit.ly/1UqlCkX

Glow-Hard: Luminous Cement Could Light Roads, Structures

Scientists at Michoacan University have modified the internal structure of cement so that with additives, the material becomes phosphorescent in the dark

By Berta Carreño on June 16, 2016

A bicycle lane inspired in Van Gogh's Starry Night can be found in the Netherlands. It was built using phosphorescent tiles, so at night passersby see where they are going without the need of electricity-consuming lighting. But despite the beauty of the scene, only a handful of constructions worldwide have this kind of lighting, because the microscopic structure of common building materials—such as cement, concrete or brick—prohibits adding this property.

A bicycle lane inspired in Van Gogh's Starry Night can be found in the Netherlands. It was built using phosphorescent tiles. **Studio Roosegaarde**

But this could soon change. José Carlos Rubio Ávalos, a researcher at Michoacan University of San Nicolás de Hidalgo in Mexico, and his team have designed a new type of phosphorescent cement that could illuminate highways, bike paths or buildings without using electricity.

Using the same raw materials with which cement is manufactured and by adding certain additives, scientists modified the optical properties of the material, and it became phosphorescent. "Cement is an opaque body, it does not allow the passage of light to the interior, so we must make a change in its microstructure to allow a partial entry of light into the interior for it to have this behavior," Rubio Ávalos says.

By using additives, scientists are able to prevent the formation of crystals that occur normally during the production of cement, creating a material with a noncrystalline structure—similar to glass—that allows passage of light inside. Varying the proportion of additives added while manufacturing the cement regulates both its luminescent intensity and color—so as not to dazzle drivers, if used on roads, for example.

And although it is manufactured like ordinary cement, the change in the microscopic structure needed to make it glow modifies the structural properties of the material—thus it may not have the same applications as the ordinary kind, and is intended to be used on surfaces as a coating material. Because of the inorganic nature of the cement components, the material can have a very long shelf life

when compared with other phosphorescent materials such as plastics or paints—but this will always depend on how it is used.

Phosphorescent materials absorb energy from radiation such as the ultraviolet light emitted by the sun—or by lamps, if indoors—energy they later emit as light, which can be seen after dark. As it loads up energetically with ultraviolet rays, even on cloudy days the cement will be able to absorb enough energy to glow during dark periods for up to 12 hours.

According to Carmen Andrade, researcher at the Spanish National Research Council (CSIC) Institute of Building Sciences in Madrid, "It's an application that can be worth developing in countries and areas with poor access to electricity in communities with poor life levels, as it doesn't consume electricity." But she also adds, "cement is a very alkaline material, so the stability of these compounds should be studied [...] and also how to repair it."

The project, which represents the first patent for Michoacan University is in commercialization phase. Rubio Avalos' plans, however, go beyond cement;, he wants to develop a range of products capable of luminescence, this one is just the first.

http://bit.ly/1V80lK7

If We Want to Send Astronauts to Mars, We Must Go Back to the Moon First

It's not just a way station to Mars—it's a way to build new industries

By Clive R. Neal on July 1, 2016

A few months ago, when European Space Agency director general Johann-Dietrich Woerner laid out a vision for his agency to lead the way in establishing an international Moon Village, I had a feeling of déjà vu. In January 2004 President George W. Bush announced his own Vision for Space Exploration, in which the U.S. would lead the world back to the moon. Once we had gone there, and humans had learned to live and work successfully on another world, we would head on to Mars as the ultimate destination.

Bush's idea was inspiring enough that, in addition to NASA, no fewer than 13 international space agencies signed on to participate in developing a plan for reaching the moon. Unfortunately, the plan's implementation was badly flawed. NASA tried to relive the glory days of Apollo by focusing on one-use vehicles that would transport everything to the moon from Earth. Apollo was a fantastic achievement, but it was not sustainable, which was in part why the program was canceled in the early 1970s. Bush's vision proved too expensive to sustain as well, and in 2010 President Barack Obama declared that the U.S. had no need to go back to the moon, saying, in essence, that we've been there, done that. Instead, he said, we would go to Mars without taking that interim step.

But a return to the moon is crucial to the future of human space exploration—and not just for the experience it would give us in off-world living. Our satellite is also rich in resources, notably water ice, which can be split via electrolysis into oxygen and hydrogen. These elements can then be used in fuel cells and in making liquid rocket fuel. If we are ultimately heading to Mars (or anywhere else), hauling that fuel off the surface of Earth is terribly inefficient. Much better to launch it from the moon, where gravity is one sixth as strong.

A return to the moon could also inspire the next generation and advance technology just as Apollo did—but do so in a sustainable, stepwise manner. The taxpayer needs to see a return on investment for this endeavor and not only in technology development. For example, a spacecraft-refueling depot orbiting the moon—supplied with fuel refined from lunar resources, privately operated and selling its products to various space agencies—is one commercial on-ramp to bring the moon into our economic sphere of influence. Such activities could result in a major reduction in launch mass from Earth's surface, thereby cutting the cost of space missions. This has the potential to create a slew of industries that in turn create high-tech and well-paid jobs.

The immediate next step in lunar exploration should be robotic prospectors on the lunar surface to define the extent, form, distribution, and ease of extractability and refinement of those resources identified from orbit. An international effort could facilitate this critical operation. NASA does have a Resource Prospector mission in development, but it is being done on a shoestring budget that could be cut at any time. Russia also has a Lunar-Resurs program under development, partnering closely with the European Space Agency. And let us not forget China, which became in 2013 the third nation to successfully soft-land on the moon. China plans to return lunar samples to Earth within the next couple of years, again following the U.S. and Russia.

Currently the U.S. vision for human space exploration is to use a robotic spacecraft to capture a small boulder from an asteroid, about one meter in diameter, and redirect it to an orbit around the moon. Humans will then explore that boulder as practice for an eventual voyage to Mars. But this so-called Asteroid Redirect Mission will have no applicability to Mars, largely because working in microgravity is a very different proposition from working on the surface of a planet. Basically, it is a fast track to nowhere.

Which brings us back to Woerner's Moon Village, which spacefaring nations applauded when it was presented at the ESA-led "Moon 2020-2030" meeting last December. Right now the U.S. is standing on the sidelines, watching other nations move on. Yes, Mars is the ultimate destination, but our country has an ill-defined pathway on how to get there. The moon is the enabling asset and the key to our

achieving that goal. We need to redefine the way we look at human space exploration such that any money spent on space travel can be viewed as an investment in the future.

http://www.eurekalert.org/pub_releases/2016-06/uoa-ads061316.php

Ancient DNA shows perfect storm felled Ice Age giants

South American megafauna were finally felled by a perfect storm of a rapidly warming climate and humans

Giant Ice Age species including elephant-sized sloths and powerful sabre-toothed cats that once roamed the windswept plains of Patagonia, southern South America, were finally felled by a perfect storm of a rapidly warming climate and humans, a new study has shown.

Research led by the Australian Centre for Ancient DNA (ACAD) at the University of Adelaide, published today in Science Advances, has revealed that it was only when the climate warmed, long after humans first arrived in Patagonia, did the megafauna suddenly die off around 12,300 years ago. The timing and cause of rapid extinctions of the megafauna has remained a mystery for centuries.

"Patagonia turns out to be the Rosetta Stone - it shows that human colonisation didn't immediately result in extinctions, but only as long as it stayed cold," says study leader Professor Alan Cooper, ACAD Director. "Instead, more than 1000 years of human occupation passed before a rapid warming event occurred, and then the megafauna were extinct within a hundred years."

The researchers, including from the University of Colorado Boulder, University of New South Wales and University of Magallanes in Patagonia, studied ancient DNA extracted from radiocarbon-dated bones and teeth found in caves across Patagonia, and Tierra del Fuego, to trace the genetic history of the populations. Species such as the South American horse, giant jaguar and sabre-toothed cat, and the enormous one-tonne short-faced bear (the largest land-based mammalian carnivore) were found widely across Patagonia, but seemed to disappear shortly after humans arrived.

The pattern of rapid human colonisation through the Americas, coinciding with contrasting temperature trends in each continent, allowed the researchers to disentangle the relative impact of human arrival and climate change.

"The Americas are unique in that humans moved through two continents, from Alaska to Patagonia, in just 1500 years," says Professor Chris Turney, from the University of New South Wales. "As they did so, they passed through distinctly different climate states - warm in the north, and cold in the south. As a result, we can contrast human impacts under the different climatic conditions."

The only large species to survive were the ancestors of today's llama and alpaca - the guanaco and vicuna -- and even these species almost went extinct.

"The ancient genetic data show that only the late arrival in Patagonia of a population of guanacos from the north saved the species, all other populations became extinct," says lead author Dr Jessica Metcalf, from the University of Colorado Boulder.

"In 1936 Fell's cave, a small rock shelter in Patagonia, was the first site in the world to show that humans had hunted Ice Age megafauna. So it seems appropriate that we're now using the bones from the area to reveal the key role of climate warming, and humans, in the megafaunal extinctions," says Dr Fabiana Martin, at the University of Magallanes.

http://bit.ly/28IYVcI

'Daisy-chain' gene drive vanishes after only a few generations

Could gene drives stop malaria?

By Michael Le Page

It's a Catch-22. We have to field-test gene drives to determine if they are safe to use to stop the spread of malaria, for example. But these bits of self-copying DNA could spread to every member of a species, making field tests risky. "A release anywhere is likely a release everywhere," says Kevin Esvelt at the Massachusetts Institute of Technology.

But his team may have the answer. It has come up with a way to make gene drives self-limiting, so they spread rapidly through a population at first but gradually vanish after, say, 50 or a hundred generations.

Not only could this make it possible to safely test gene drives in the wild, it could also allow cities and countries to use them locally without have to worry about the risk of worldwide spread.

Most plants and animals have matching pairs of chromosomes, but pass down only one of each pair to each of their offspring – the other comes from the other parent.

This means that if you add a piece of DNA to one chromosome, normally only half the offspring will inherit it. Gene drives cheat by "copying and pasting" themselves to the other chromosome, meaning all offspring inherit them and they can spread rapidly throughout a population.

Natural gene drives have been around for hundreds of millions of years. In the past two years, biologists have created artificial versions based on the CRISPR gene editing system.

Malaria reduction

These artificial drives are being tested in nematode worms, fruit flies and mosquitoes in several labs around the world. At Imperial College London, for instance, Andrea Crisanti's group is testing prototypes of a gene drive designed to tackle malaria by reducing mosquito populations.

Flaws in these prototypes mean they probably wouldn't spread indefinitely if they escaped into the wild. But even these shouldn't be field-tested because of the risks from spreading to just part of a wild population, Esvelt says. "In terms of risk it doesn't matter. If it spreads to 50 per cent, that's damaging enough," he says.

To create gene drives that don't spread indefinitely, the team split them up into three or more parts – which Esvelt calls elements – to create a "daisy chain".

Each element contains one or more genes that contribute towards the whole gene drive. In Esvelt's design, element A can only copy and paste itself if element B is present. Element B can only copy and paste itself if element C is present. And element C, crucially, cannot copy and paste itself at all – it can only spread by normal breeding, to half of offspring.

The idea is to release thousands of mosquitoes, say, carrying all three elements. When they mate with wild mosquitoes, all the offspring will inherit element A and B, but only half will inherit element C. In the following generations, element B will spread rapidly and A will spread even more rapidly, but C will gradually die out. Once it does, B will start to disappear, and finally A will too.

Daisy-chain drives

Esvelt's team have unveiled their plans ahead of creating and testing these daisy-chain gene drives in nematodes. "I firmly believe we don't have the right to run this kind of experiment without telling people what we are going to do," he says.

The team's modelling suggests that if only a few animals are released, the drive's spread would be limited and it would soon die out. If enough animals are released, though, element A could spread to 100 per cent of a local population. And by adding more elements to the daisy chain, the gene drive could be made to persist longer in the wild.

This could allow local use of gene drives. Suppose the US wanted to release a gene drive that would halt the spread of Lyme disease by making the white-footed mice that carry the disease-causing bacterium immune to it. A conventional gene drive would spread to mice in Canada and Mexico, so approval from their governments would be needed too. With a daisy-chain drive, the spread could be limited. Esvelt is exploring the possibility of combating Lyme disease this way but stresses that it is a long way off.

Another possibility, he says, would be to use a daisy-chain gene drive to help save Hawaii's native birds, which are being wiped out by avian malaria. The gene drive could be used to eliminate the mosquito species that carries the disease.

With a conventional gene drive, a single mosquito stowing away in someone's luggage could spread the drive around the tropics. If the daisy-chain drives work as planned, a single mosquito couldn't spread the drive very far at all.

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http://bit.ly/28IoIzf

Did snakes evolve from ancient sea serpents?

Did snakes evolve on land or underwater?

Mike Lee Alessandro Palci

One of the enduring controversies in evolution is why snakes evolved their long, limbless bodies.

The prevailing theory is that they evolved from lizards and are really just an extreme type of legless lizard. And as many long-bodied lizards are burrowers, there is a widespread view that snakes developed their serpentine bodies underground.

But a study of a primordial four-legged fossil snake published this week suggests it was aquatic. This suggests snakes lost their legs and elongated their bodies underwater, for eel-like swimming, before crawling ashore aeons later.

***Small fossil, big controversy:* Tetrapodophis*, a tiny fossil snake with four-legs (photomontage of part and counterpart).* Michael Caldwell and Alessandro Palci University of Alberta/Flinders University & South Australian Museum, Author provided**

The fossil in question is one of the most exquisite and controversial fossils of modern times. Dubbed *Tetrapodophis* (meaning "four-legged snake"), it lived alongside the dinosaurs in what is now Brazil, about 120 million years ago.

Amazingly, almost every single bone is preserved in this tiny worm-sized fossil, including four small but perfectly-formed legs.

What the fossil says

This little creature was previously thought to be a burrower, and indeed looks a bit like a worm. But the study by our team suggests it has the wrong body shape for digging: the tail is too long and the legs too delicate.

Conversely, *Tetrapodophis* possesses a range of adaptations characteristic of aquatic animals, including seals, sea turtles and ancient sea-lizards such as mosasaurs and dolichosaurs.

Many wrist and ankle elements were made of cartilage rather than bone, and the limb joints were poorly developed. Such weak limbs are often found in aquatic animals where buoyancy helps with support.

The hands and feet were also surprisingly flipper-like, with a thickened first digit strengthening the leading edge – like the front edge of an aeroplane wing or turtle flipper.

A sea serpent

Tetrapodophis therefore has many hallmarks of marine habits. It wasn't a little earthworm, but rather a Lilliputian sea serpent.

Intriguingly, there are other archaic fossil snakes that are unequivocally marine, such as the two-legged *Pachyrhachis* with its paddle-shaped rear end.

And a recent reptile evolutionary tree proposes that the nearest relatives of snakes are not burrowing legless lizards, but the ancient sea lizards discussed above.

This kinship is supported by aquatic adaptations that we found shared by *Tetrapodophis*, *Pachyrhachis* and sea lizards.

Tetrapodophis *reinterpreted as a marine snake – the original sea serpent.* Alessandro Palci and Michael Lee Flinders University & South Australian Museum

All of this is consistent with the view that snakes evolved from aquatic lizards, losing their legs and elongating their bodies for eel-like swimming. This idea was more widely touted in the past but had recently fallen out of favour.

But there remain some important potential difficulties with the aquatic theory.

Today, snakes are tremendously successful on all continents except Antarctica.

If the earliest snakes were marine, how and why did they struggle ashore?

There are also some other primitive snakes that were unquestionably terrestrial, such as *Najash* from Argentina, which also still has two little legs.

The mangrove sea snakes from north-east Australia might solve this mystery. These modern snakes are not closely related to the archaic fossil marine snakes, yet their lifestyles might have been very similar.

Mangrove sea snakes inhabit the intertidal zone and are equally adept crawling on land and swimming in the ocean, so if the first snakes had similar habits, a permanent shift into land (or into the water) would have been relatively easy.

This ecological plasticity would explain why many early snakes appear to be terrestrial and many others aquatic. It might also explain why *Tetrapodophis* has some worm-like traits, and some sea serpent traits, leading to debates about where it lived.

A controversial single specimen

The ongoing interest in *Tetrapodophis* raises other important issues. There is only a single specimen of this potential link between lizards and snakes, making it priceless and utterly unique.

The fossil deposits where it was found have been scoured extensively for decades, so it is unlikely another one will surface anytime soon. It's thus far more important than *Archaeopteryx*, the famous dinosaur-bird intermediate, which is known from 11 specimens.

Yet, the provenance and curation of this most important fossil remains highly problematic. While *Tetrapodophis* was being studied, it resided in the Bürgermeister-Müller-Museum in Germany, but documents to demonstrate that it was legally exported from Brazil have not been forthcoming.

The specimen is also privately owned and only "on loan" to that museum. While there has been a firm promise that it will be available in perpetuity for scientific study, enforcing this might be challenging, and it could easily disappear back into a private collection at any time.

It is widely conceded that science is facing a "reproducibility crisis". For scientific studies to be verifiable (i.e. repeatable by others), there should be open access to the primary data upon which those claims are based.

For palaeontologists, this means fossils – especially pivotal ones – must be available for all scientists to examine in perpetuity, enabling independent confirmation (or refutation) of published observations. This is best achieved by making sure all studied fossils are owned and curated by a recognised museum.

It is worrying that a fossil that is arguably ten times more important than *Archaeopteryx* could someday easily vanish from science without a trace.

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http://bit.ly/28JkIST

New 'Artificial Synapses' Could Let Supercomputers Mimic the Human Brain

New 'Artificial Synapses' Could Let Supercomputers Mimic the Human Brain

By Charles Q. Choi, Live Science Contributor | June 17, 2016 05:19pm ET

Large-scale brain-like machines with human-like abilities to solve problems could become a reality, now that researchers have invented microscopic gadgets that mimic the connections between neurons in the human brain better than any previous devices.

The new research could lead to better robots, self-driving cars, data mining, medical diagnosis, stock-trading analysis and "other smart human-interactive systems and machines in the future," said Tae-Woo Lee, a materials scientistat the

Pohang University of Science and Technology in Korea and senior author of the study.

The human brain's enormous computing power stems from its connections. Previous research suggested that the brain has approximately 100 billion neurons and roughly 1 quadrillion (1 million billion) connections wiring these cells together. At each of these connections, or synapses, a neuron typically fires about 10 times per second.

In principle, the human brain can perform about 10 quadrillion operations per second. In comparison, the world's fastest supercomputer, Tianhe-2 in China, is capable of carrying out up to about 55 quadrillion calculations per second, according to the TOP500 project, which ranks the 500 most powerful computers in the world. However, previous research suggests that the human brain consumes only about 20 watts of power, which is barely enough to run a dim light bulb, whereas Tianhe-2 consumes about 17.8 megawatts of power, which is enough to run about 900,000 such light bulbs, TOP500 notes.

Scientists would like to build computers that mimic the human brain's power and efficiency. "Development of artificial synapses with comparable behaviors of biological ones will be a critical step," Lee told Live Science.

Until now, artificial synapses consumed much more energy than biological synapses do. Previous research suggested that biological synapses consume about 10 femtojoules every time a neuron fires. Now, Lee and his colleagues have created artificial synapses that require only about 1.23 femtojoules per synaptic event, making them the lowest-energy artificial synapses developed yet, they said. (For comparison, a small apple falling about 3.3 feet (1 meter) to Earth would generate about 1 quadrillion femtojoules of kinetic energy.)

This research suggests that the "energy consumption and memory density of artificial brains will ultimately rival, and even exceed, [those of] biological brains in the future," Lee said.

These new artificial synapses are a kind of transistor, or electronic switch. By flicking on and off, they can mimic how a synapse fires.

The researchers fabricated 144 synaptic transistors on a 4-inch (10-centimeter) wafer. At the heart of these devices are wires that are 200 to 300 nanometers (billionths of a meter) wide. (For comparison, the average human hair is about 100,000 nanometers wide.) The small features of the devices help to lower the amount of energy they consume, the researchers said.

The new devices are made out of one kind of organic material wrapped around another. These materials help the artificial synapses trap or release electrically charged ions, mimicking how biological synapses work, and how an electric switch can be flicked on or off, the researchers explained.

The artificial synapses mimic the structure of actual human nerve fibers' long shape and flexibility. In principle, the researchers could also arrange these devices in 3D grids, somewhat imitating the human brain, Lee said. However, advances in 3D printing are needed to create such 3D grids of artificial synapses, he added.

The researchers are now working to develop organic nanowires only a few dozen nanometers wide, Lee said. They also think that they can reduce synaptic transistor energy consumption even further by tinkering with the selection and structure of the materials they use, he added.

The scientists detailed their findings online June 17 in the journal Science Advances.

http://www.eurekalert.org/pub_releases/2016-06/uob-maw061616.php

Mammals almost wiped out with the dinosaurs

Over 90 per cent of mammal species were wiped out by the same asteroid that killed the dinosaurs in the Cretaceous period 66 million years ago, significantly more than previously thought.

A study by researchers at the Milner Centre for Evolution at the University of Bath and published in the Journal of Evolutionary Biology, reviewed all mammal species known from the end of the Cretaceous period in North America. Their results showed that over 93 per cent became extinct across the Cretaceous-Paleogene (K-Pg) boundary, but that they also recovered far more quickly than previously thought.

The scientists analysed the published fossil record from western North America from two million years before the Cretaceous-Paleogene boundary, until 300,000 years after the asteroid hit. They compared species diversity before and after this extinction event to estimate the severity of the event and how quickly the mammals recovered. The extinction rates were much higher than previous estimates based on more limited data sets.

Dr Nick Longrich from the Milner Centre for Evolution, in the University of Bath's Department for Biology & Biochemistry, explained: "The species that are most vulnerable to extinction are the rare ones, and because they are rare, their fossils are less likely to be found. The species that tend to survive are more common, so we tend to find them.

"The fossil record is biased in favour of the species that survived. As bad as things looked before, including more data shows the extinction was more severe than previously believed."

The researchers say this explains why the severity of the extinction event was previously underestimated. With more fossils included, the data includes more rare species that died out.

Following the asteroid hit, most of the plants and animals would have died, so the survivors probably fed on insects eating dead plants and animals. With so little food, only small species survived. The biggest animals to survive on land would have been no larger than a cat. The fact that that most mammals were small helps explain why they were able to survive.

Yet the researchers found that mammals also recovered more rapidly than previously thought, not only gaining back the lost diversity in species quickly but soon doubling the number of species found before the extinction. The recovery took just 300,000 years, a short time in evolutionary terms.

Dr Longrich added: "Because mammals did so well after the extinction, we have tended to assume that it didn't hit them as hard. However our analysis shows that the mammals were hit harder than most groups of animals, such as lizards, turtles, crocodilians, but they proved to be far more adaptable in the aftermath.

"It wasn't low extinction rates, but the ability to recover and adapt in the aftermath that led the mammals to take over."

Surprisingly, the recovery from the extinction took place differently in different parts of the continent. The species found in Montana were distinct from those in nearby Wyoming, for example.

"You might expect to see the same few survivors all across the continent. But that's not what we found," said Longrich. "After this extinction event, there was an explosion of diversity, and it was driven by having different evolutionary experiments going on simultaneously in different locations.

"This may have helped drive the recovery. With so many different species evolving in different directions in different parts of the world, evolution was more likely to stumble across new evolutionary paths."

http://nyti.ms/28JpMoO

As Wind Power Lifts Wyoming's Fortunes, Coal Miners Are Left in the Dust

Wyoming's energy landscape is transforming along with the nation's

By CORAL DAVENPORT JUNE 19, 2016

GILLETTE, Wyo. — After Kullin Orcutt lost his job at the Peabody coal mine this spring, he knew what he needed to do: join the exodus. "Leave Gillette, leave the state," he said.

Mr. Orcutt is a third-generation miner and one of 592 coal workers who have been laid off here since January. Thousands more job cuts are expected this summer.

More people will follow Mr. Orcutt. While many businesses in Gillette are struggling to stay open, a U-Haul dealer has been nearly sold out since the school year ended this month.

But 200 miles to the southwest, in Carbon County, where Wyoming's first coal mine opened a century ago, the mood is different. The last coal mine closed a decade ago, but the county may soon be home to the largest wind farm in North America, if not the world.

"Coal is hurting, but wind power is our bright spot on the horizon," said Cindy Wallace, the director of the Carbon County Economic Development Corporation. "Eventually, we could be the wind capital of Wyoming, the U.S., the world."

In Wyoming, the country's biggest coal-producing state, the energy landscape is transforming along with the nation's, but in a state of 584,000 people, that change is happening at hyperspeed.

That transition has left men like Mr. Orcutt behind. The new positions and financial opportunities offered by wind and other new-energy industries are not replacing all the jobs going up in coal smoke.

Many of the current jobs are out of state, at wind turbine factories in Colorado and Iowa. Millions of dollars' worth of out-of-state investments are flowing into Wyoming's wind projects, but much of the profit will flow out of state, as well. The thousands of coal workers who will probably lose their jobs do not necessarily have the technical skills to operate wind farms. In any case, new wind jobs will number in the hundreds, not the thousands.

So when Mr. Orcutt left Gillette this spring, he did not head for the wind fields of Carbon County. Instead, he moved to Shelby, Mont., for a job at a privately run prison, leaving behind his wife and son in a groaning two-bedroom apartment that they share with Mr. Orcutt's sister, her husband — a welder who was laid off from the coal mines — and that couple's three children.

"It's hard being here without them, but here I have a job," he said. "In Gillette, those jobs are gone forever."

The numbers bear out his decision, said Robert W. Godby, an energy economist and professor at the University of Wyoming.

"Wind energy is certainly lucrative," he said. "That's why so many investors are interested. But it doesn't create nearly the economic impact of the fossil fuel industry."

Today, about 66 percent of the electricity in the United States is produced by coal and natural gas, and just 7 percent is produced by renewable sources such as wind and solar. But market forces and government regulations are rapidly changing that picture.

A glut of inexpensive natural gas has cut into coal's dominance of America's power market. And President Obama's climate change regulations, known as the Clean Power Plan, take direct aim at coal, the No. 1 cause of planet-warming greenhouse gases.

The Department of the Interior has already declared a halt on new coal mining on public lands, a move with an outsize impact on Wyoming, where a majority of mines are on federal property.

And the international Paris agreement on climate change could make the efforts to end the burning of coal a global campaign.

All of these policies are closing the remaining coal-fired plants and freezing the construction of new ones, but they also aim to aggressively increase the production of renewable power. The Clean Power Plan contains a goal for 20 percent of the nation's electricity to come from wind, solar and other clean sources by 2030. Hillary Clinton, the presumptive Democratic presidential nominee, has pledged to raise that amount to 33 percent by 2027.

Companies from around the world are looking to Wyoming's wind to meet that demand.

"There's enough wind in Wyoming to power the entire country," said Michael Goggin, the senior director of research at the American Wind Energy Association.

Wyoming's Republican governor, Matt Mead, is skeptical of human-caused climate change, and has been an outspoken opponent of Mr. Obama's climate change agenda. Still, he also sees economic opportunity in wind power.

"We've been a dig-and-ship state, exporting energy to the rest of the country," Mr. Mead said in an interview in his office. "With the advances in wind turbines, why shouldn't we be leading that at the University of Wyoming? Why don't we do more to bring wind manufacturing to the state?"

Perhaps the biggest winner in Wyoming's wind boom will be one man: Philip F. Anschutz, a Colorado billionaire and major Republican donor. His company, the Anschutz Corporation, is building the Carbon County wind farm on 200 acres owned by Mr. Anschutz and the federal government.

When completed, the site will be the largest wind power producer in North America, generating enough electricity to light a million homes — far more than Wyoming needs.

Mr. Anschutz is also planning to build the TransWest Express, a 730-mile power line that would take Wyoming's wind energy to Las Vegas and California. Construction on both projects is expected to begin late this year or early 2017.

On a recent day, Bill Miller, the president and chief executive of the Anschutz Corporation, drove his truck through the Carbon County site's rocky mesas, which channel near-constant wind across the green plain. The only visible inhabitants were cows, antelopes, prairie dogs and rattlesnakes.

Although wind power has traditionally been more expensive than fossil fuels, Mr. Miller said the Anschutz wind project will be large enough to make wind as cheap, if not cheaper, than coal power.

"We can produce wind power here that's competitive with anything: coal, natural gas," Mr. Miller said.

Mr. Miller estimates that the construction of the wind farm will create about 900 seasonal jobs over the decade it will take to build it, and about 150 full-time jobs to operate and maintain it.

In the nearby town of Rawlins, he said, a branch of Western Wyoming Community College has already started programs to train wind power technicians.

"You'll be able to take a coal miner from Gillette — he can go to the community college here for the skills, and get a job as a wind technician," Mr. Miller said.

But, he conceded, "Am I going to replace 800 lost coal jobs in Gillette with new wind jobs? No."

Another big winner in the Wyoming wind boom may be a Venezuelan company, Viridis Eolia Corporation, which also plans to build a large-scale wind farm near Carbon County, one second in size in North America only to the Anschutz project.

"It's the wave of the future," Juan Carlos Carpio Delfino, Viridis Eolia's chief executive, said at an energy conference at Little America, a golf resort outside Cheyenne.

"With Obama's clean power regulations, and the signing of the Paris agreement, it creates a stable market for wind — and this is the best wind in North America."

That remains cold comfort to Wyoming's coal community. Mr. Godby estimates that in the coming years, Wyoming could lose up to 10,000 jobs related to the coal industry.

Last month, officials from the Interior Department held a public hearing in Casper to gather input on the current halt on new coal mining on the state's public lands.

During the meeting, Jillian Balow, the Wyoming superintendent of public instruction, spoke before a crowd of hundreds, her voice cracking.

"We have reached the point where the restrictions and regulations for the industry are past our ability to adapt," she said. "It has put thousands of hard-working people out of work and is devastating families."

"Give us a chance," she pleaded.