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Research suggests common blood cancer could be prevented before it develops

Reveals how a common symptomless condition can develop into the blood cancer myeloma

Researchers from the University of Birmingham and hospitals across the West Midlands have revealed how a common symptomless condition can develop into the blood cancer myeloma.

They discovered that changes in the bone marrow needed for the cancer to grow have already taken hold in the preceding condition, raising the possibility that early medical intervention could prevent this incurable type of cancer from taking root. The research, which was funded by the blood cancer charity Bloodwise, is published today in the journal Leukemia.

Myeloma affects the plasma cells, a type of white blood cell that originates in the bone marrow. Diagnosed in over 4,000 people a year in the UK, fewer than half of patients survive for longer than five years after diagnosis. Symptoms often include debilitating and painful bone damage, anaemia and nausea.

Myeloma almost always progresses from an apparently benign condition known as 'MGUS', which is especially common in the older population - as many as 7% of people over the age of 85 have MGUS. Only around one in 100 MGUS patients will develop myeloma each year and there is currently no way of accurately predicting which patients will do so, or when.

Myeloma never spreads to other organs, suggesting that myeloma cells rely on support from other cells in the bone marrow environment to survive. The Birmingham researchers showed that early on in MGUS development, cells that make up the bone marrow connective tissue change their behaviour, and become more supportive of cancer growth. They found that a key gene, called 'PADI2' becomes particularly overactive in these connective tissue cells, which leads to the overproduction of a signalling molecule called interleukin-6 (IL-6).

Connective tissue cells release IL-6 into the bone marrow, where it binds with receptors on the surface of cancerous plasma cells, instructing them to multiply rapidly and resist cell death signals. It is already known that the presence of high levels of IL6 in a patient's bone marrow significantly reduces the effectiveness of a key chemotherapy drug called bortezomib.

The researchers believe that drugs designed to target the PADI2 gene in MGUS and myeloma patients could significantly reduce the supportive signalling that myeloma cells depend on, and may increase the effectiveness of current treatments.

Significantly, the PADI2 gene has also been linked with the development of other types of cancer, rheumatoid arthritis, Alzheimer's disease and autoimmune disease, so any drug developed could have wider applications beyond myeloma treatment.

Dr Daniel Tennant, who led the research at the University of Birmingham, said: "It is now clear that the bone marrow of patients with MGUS, traditionally thought of as a benign condition, is significantly different to that of healthy individuals. The bone marrow environment in these patients appears capable of supporting cancer growth, even though the majority of patients will not progress to myeloma. While this research is in the early stages, it offers the exciting possibility that early intervention could potentially delay or even prevent cancer development."

Dr Alasdair Rankin, Director of Research at the blood cancer charity Bloodwise, said: "There is an urgent need for new treatments for myeloma, which, as well as being largely incurable, can have a devastating impact on quality of life. With an increasing elderly population, MGUS and myeloma are only going to become more common. Drugs designed to remove the support system myeloma uses to grow could be an effective way of treating the disease, or even preventing it altogether."

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Is the agile wallaby man's new best friend?

Scientists name top 5 animals that are suitable to be kept as new pets

Looking for a new pet? If so, consider the Agile Wallaby or the Asian Palm Civet. Responding to the growing trend in keeping exotic animals as pets a team, led by Dr. Paul Koene, has developed a methodology to assess the suitability of mammals to be kept domestically in a new study published in Frontiers in Veterinary Science.

The top five animals were: the Sika Deer, Agile Wallaby, Tamar Wallaby, Llama, and Asian Palm Civet, which were all judged to be suitable pets by the scientists from the Wageningen University and Research Centre, in the Netherlands. So, will the Sika Deer challenge the common canine for the title of man's best friend?

"The main influence of this work is methodological. In the Netherlands many mammal species are kept and for a long time the government wanted to guarantee the welfare of animals," said Dr. Koene; "Therefore the Dutch Animal Act was made stating that mammals should not be kept unless they are production animals, or are species that are suitable to be kept by anyone without special knowledge or skills."

In order to determine if this is the case for a given animal species a list of suitable candidates had to be created. Then a method was devised to place each mammal species in a rank order, ranging from suitable to unsuitable.

The team began by conducting a web-based survey to discover which animals were most frequently kept as pets in the Netherlands. Other mammals were then added to the list based on data from veterinarians and rescue centers.

In the first instance the 90 most common species were selected. Animals classed as 'production animals' such as rabbits, guinea pigs and hamsters are allowed to be kept by anyone and so were not analyzed.

A wide range of bibliographic data was sourced in order to create the one-line criteria statements that the mammals chosen for analysis were graded against. These one-liners were then assigned a score related to behavioral needs or welfare risks.

The risks were assessed on the reported one-liners of the species in both captivity and the wild. Animals with high scores had high behavioral needs and high health, welfare and human relationship risks.

Three teams worked together to produce the final pet suitability rank order. The first team selected one-line statements for each animal. The second team assessed the strength of one-line statements about behavior, health, welfare and human-animal relationship in both captivity and the wild. A third team assessed the suitability based on all assessed strengths for that animal to be a pet.

Dr. Koene explained: "A team is now completing the full list, analyzing the other 270 mammals. They are also looking at how to determine the suitability of birds and reptiles in future. "So, the impact of the study is that there is a framework and shared database that could be further developed in a more widely used context, for instance across the EU, the US or even worldwide."

However, Dr. Koene does not envisage that Agile Wallabies will replace dogs and cats in man's affections anytime soon. "Dogs and cats are a special kind of pets, because of their way of housing (free roaming), of variation in breeds, the vast amount of literature and of the delicacy of the subject and so were not analyzed, and wallabies will certainly not replace them."

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Is traumatic brain injury associated with late-life neurodegenerative conditions?

TBI not associated with late-life mild cognitive impairment, or dementia but appears with risk for other neurodegenerative and neuropathologic findings

Traumatic brain injury (TBI) with loss of consciousness was not associated with late-life mild cognitive impairment, Alzheimer disease or dementia but it appeared to be associated with increased risk for other neurodegenerative and neuropathologic findings, according to a new article published online by JAMA Neurology.

Most TBIs are mild and most people return to their prior level of functioning. Still, concern over late-life effects of TBIs has grown with increased awareness of repetitive head trauma in athletes and head injuries suffered by service members in military conflicts. But most TBIs are not sports related or caused by combat injuries so understanding late-life effects in nonathlete civilians is important.

Paul K. Crane, M.D., M.P.H., of the University of Washington, Seattle, and coauthors analyzed data from 7,130 participants in three other studies, including older religious clergy, older residents from Chicago-area retirement homes and subsidized housing, and older Seattle-area Group Health members. The average age of participants was nearly 80 and 865 reported a history of TBI with loss of consciousness (LOC).

Although 1,537 cases of dementia and 117 cases of Parkinson disease (PD) were identified in follow-up, the authors reported no association was found between TBI with LOC and dementia or Alzheimer disease (AD). Authors did, however, report associations between TBI with LOC and increased risk for PD, progression of parkinsonism, Lewy body accumulation and microinfarcts, which are small strokes.

Study limitations include that data from participants may not be broadly representative of the ethnically diverse U.S. population and other mitigating factors may have affected the findings. "Traumatic brain injury with LOC sustained early in life is not innocuous and appears to be associated with neurodegenerative conditions, although not AD," the article concludes.

(JAMA Neurol. Published online July 11, 2016. doi:10.1001/jamaneurol.2016.1948.

http://www.eurekalert.org/pub_releases/2016-07/sumc-fr071116.php

First-ever restoration of vision achieved in mice, Stanford researcher says

Experiments conducted under the leadership of a Stanford University School of Medicine investigator have succeeded, for the first time, in restoring multiple key aspects of vision in mammals.

In experiments in mice described in a study to be published online July 11 in Nature Neuroscience, the scientists coaxed optic-nerve cables, responsible for conveying visual information from the eye to the brain, into regenerating after they had been completely severed, and found that they could retrace their former routes and re-establish connections with the appropriate parts of the brain.

That unprecedented, if partial, restoration could pave the way to future work that enables blind people to see.

The animals' condition prior to the scientists' efforts to regrow the eye-to brain-connections resembled glaucoma, the second-leading cause of blindness after cataracts. Cataracts can often be surgically removed, but there's no cure for

glaucoma, said the study's senior author, Andrew Huberman, PhD, an associate professor of neurobiology. Jung-Hwan Albert Lim, a graduate student at the University of California-San Diego, is the lead author.

Glaucoma, caused by excessive pressure on the optic nerve, affects nearly 70 million people worldwide. Vision loss due to optic-nerve damage can also accrue from injuries, retinal detachment, pituitary tumors, various brain cancers and other sources.

Thin sheet of cells

The retina, a thin sheet of cells no more than half as thick as a credit card, is the light-sensing part of the eye. If nerve cells were offices, this tiny patch of tissue would be Manhattan. Photoreceptor cells in the back of the retina react to different wavelengths of light by sending electrically coded information to other cells in the retina called retinal ganglion cells, of which there are as many as 30 types, each specializing in processing a particular aspect of vision, such as upward motion, motion in general or the color red. The ganglion cells project long, electric-wire-like processes called axons, which extend down the optic nerve in a bundle and then fan out to numerous regions of the brain, where they connect with other nerve cells to inform them about the visual world.

"Somehow the brain can interpret these electrical signals to say, 'Wow, that's a fast-moving car coming my way -- I'd better get back on the sidewalk,'" said Huberman.

"More than a third of the human brain is dedicated to the processing of visual information," he said. "Over two dozen brain areas get direct signals from retinal ganglion cells. These areas are involved in not only what we typically think of as vision, but also circadian rhythms and mood."

Retinal ganglion cells are the only nerve cells connecting the eye to the brain, said Huberman. "When those cells' axons are severed, it's like pulling the vision plug right out of the outlet," he added.

Axons in eye don't regenerate

When axons in the brain and spinal cord of a mammal such as a mouse or a human have been damaged, they don't regenerate on their own. (The only known exception is olfactory sensory nerve cells.) The retina, too, is actually part of the brain, said Huberman. Damage to mammalian retinal ganglion cells' axons spells permanent vision loss.

Mammalian axons located outside the central nervous system do regenerate, though. And during early development, brain and spinal-cord nerve cells abundantly sprout and send forth axons that somehow find their way through a thicket of intervening brain tissue to their distant targets. In a full-grown adult human, the axons snaking from retinal ganglion cells to one distant brain structure called the superior colliculus can reach 6 to 8 inches in length.

While many factors are responsible for adult brain cells' lack of regenerative capacity, one well-studied cause is the winding down, over time, of a growth-enhancing cascade of molecular interactions, known as the mTOR pathway, within these cells.

In the study, adult mice in which the optic nerve in one eye had been crushed were treated with either a regimen of intensive daily exposure to high-contrast visual stimulation, in the form of constant images of a moving black-and-white grid, or biochemical manipulations that kicked the mTOR pathway within their retinal ganglion cells back into high gear, or both. The mice were tested three weeks later for their ability to respond to certain visual stimuli, and their brains were examined to see if any axonal regrowth had occurred.

Importantly, while retinal ganglion cells' axons in the crushed optic nerve had been obliterated, the front-line photoreceptor cells and those cells' connections to the retinal ganglion cells in the damaged eye remained intact.

Success of combined approach

While either visual stimulation or mTOR-pathway reactivation produced some modest axonal regrowth from retinal ganglion cells in mice's damaged eye, the regrowth extended only to the optic chiasm, where healthy axons exit the optic nerve and make their way to diverse brain structures. But when the two approaches were combined -- and if the mouse's undamaged eye was temporarily obstructed in order to encourage active use of the damaged eye -- substantial numbers of axons grew beyond the optic chiasm and migrated to their appropriate destinations in the brain.

"Somehow these retinal ganglion cells' axons retained their own GPS systems," Huberman said. "They went to the right places, and they did not go to the wrong places."

Tests of the mice's vision indicated that visual input from the photoreceptor cells in their damaged eye was reaching retinal ganglion cells in the same eye and, crucially, being conveyed to appropriate downstream brain structures essential to processing that visual input. One test, for example, involved the projection of an expanding dark circle -- analogous to a bird of prey's approach -- onto the visual field of the damaged eye. In response, most of the mice subjected to both mTOR-pathway upregulation and visual stimulation, as well as obstruction of their remaining good eye, did what they would be expected to do in the wild: They headed for the shelter of a "safety zone" in the experimental set-up.

In other words, the regenerating axons, having grown back to diverse brain structures, had established functional links with these targets. The mice's once-blind eye could now see.

Restored vision incomplete

However, even mice whose behavior showed restored vision on some tests, including the one described above, failed other tests that probably required finer visual discrimination, said Huberman. He noted that the investigators could prove that axons from two specific retinal ganglion cell types had reached their targets, but lacked molecular labels that would have let them determine whether axons emanating from the rest of the other subtypes had done so. Further progress, he suggested, will depend on boosting total numbers of retinal ganglion cell axons that successfully extend back to and establish former contact with their target structures, as well as finding ways to engage and assess most or all of the roughly 30 subtypes of retinal ganglion cells.

"We're working on that now," Huberman said.

The study was conducted in collaboration with researchers at UCSD, Harvard University and Utah State University.

Funding for the study was provided by the National Eye Institute (grant R01 EY026100) and the Glaucoma Research Foundation.

Stanford's Department of Neurobiology also supported the work.

http://www.eurekalert.org/pub_releases/2016-07/bm-mso070716.php

Milestone study on pomegranate anti-aging mechanism reported by Amazentis SA and EPFL

Breakthrough findings on urolithin A, a pomegranate metabolite, on muscle aging, published in Nature Medicine; Amazentis announces first human clinical trial

Lausanne, Switzerland - Amazentis SA, an innovative life sciences company applying scientific breakthroughs in nutrition to manage health conditions linked to aging, announced today a collaborative publication in Nature Medicine with the École Polytechnique Fédérale de Lausanne (EPFL), demonstrating that the Company's lead product candidate, urolithin A, improves mitochondrial and muscle function, resulting in enhanced muscle strength and endurance during aging. Amazentis is presently evaluating urolithin A in a first human clinical trial with results expected in 2017.

Urolithin A is generated by gut microflora as a natural metabolite of ellagitannins, a class of compounds found in the pomegranate and other fruits and nuts. "We are excited to publish the first data that demonstrate the effects of this gut metabolite on mitochondrial and muscle function," commented Johan Auwerx, Professor at the École Polytechnique Fédérale de Lausanne (EPFL), Switzerland, and lead author. "We believe this research is a milestone in current anti-aging efforts, which have previously focused on traditional pharmaceutical modalities, and illustrates the opportunity of rigorously tested nutritional bioactive agents that we consider to have outstanding potential for human health."

Urolithin A: a potent gut metabolite to rejuvenate mitochondria and reverse muscle aging

Oral administration of urolithin A leads to an improved mitochondrial function by stimulating mitophagy, a process by which damaged mitochondria are recycled to permit a renewal with healthy mitochondria.

"Mitophagy declines in cells as we age, and the reduction in mitochondrial function in the muscles of the elderly is thought to be one of the main causes of age-related muscle impairment. We believe our research, uncovering the health benefits of urolithin A, holds promise in reversing muscle aging," stated Patrick Aebischer, co-author on the article, EPFL President and Chairman and co-founder of Amazentis.

The results are being reported in the current issue of Nature Medicine in an article titled, "*Urolithin A induces mitophagy and prolongs lifespan in C. elegans and increases muscle function in rodents*" (doi:10.1038/nm.4132, http://www.nature.com/nm/journal/vaop/ncurrent/full/nm.4132.html).

Age-related muscle decline: a compelling market opportunity for urolithin A

Declining skeletal muscle mass and the resulting loss of strength are hallmarks of aging. These changes can become debilitating and lead to a condition termed sarcopenia, which is thought to affect 30% of those over 60 years old and greater than 50% of individuals over 80 years. Current estimates in the United States project there will be greater than 75 million adults over 60 years by the year 2020. The resulting reductions in quality of life and independence as a result of muscle decline constitute a growing healthcare issue in the aging population. There are currently no pharmaceutical therapies to treat age-related decline in muscle function and sarcopenia. Nutritional strategies have had limited impact to date, and new scientifically validated solutions are urgently needed.

Upon consumption of pomegranate juice, compounds known as ellagitannins are broken down in the stomach and then transformed by intestinal bacteria into urolithin A. This biotransformation has been shown to vary widely across individuals, with some showing high or low conversion rates, while others have different compositions of microflora and are unable to perform the conversion. Consequently, supplementing individuals with products designed to deliver carefully calibrated doses of urolithin A can overcome this natural diversity in gut microflora found in the general population.

Amazentis has established a technology portfolio and proprietary knowhow around urolithin A, enabling the manufacture and development of advanced nutrition products for oral delivery.

Chris Rinsch, Ph.D., a co-author and CEO and co-founder of Amazentis, commented, "Based on the rigorous science being published in Nature Medicine, we have advanced our lead product delivering urolithin A into clinical trials. We believe that this discovery will open the door to a new approach for managing muscle decline by rejuvenating mitochondria. Our vision is to translate breakthrough scientific discoveries in nutrition into clinically validated consumer health products that address today's unmet needs in an aging population."

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If life can make it here, it can make it anywhere

WSU scientist explores the likelihood of complex life existing elsewhere in the universe

If the origin of life is common on other worlds, the universe should be a cosmic zoo full of complex multicellular organisms.

Dirk Schulze-Makuch, a Washington State University astrobiologist, uses the evolution of Earth life as a model to predict what humans might find living on distant planets and moons in a new paper published in the journal Life.

The results of his work, conducted in collaboration with William Bains, a biochemist working for the Massachusetts Institute of Technology, show that once life originates, the evolution of organisms functionally similar to plants or animals on Earth will naturally follow given enough time and a suitable environment.

"If the origin of life can occur rather easily, a percentage of organisms on other worlds will reach higher levels of animal- or plant-like complexity," Schulze-Makuch said. "On the other hand, if the origin of life is a rare event, then chances are we live in a rather empty universe."

Evolutionary answers

There are physical and chemical limits to how life can evolve, and scientists have determined that many of those requirements have been met on Earth. Therefore, the route Earthly lifeforms took from simple, single-celled organisms to successively more complex entities can give hints of how life might play out elsewhere in the cosmos.

In their study, Schulze-Makuch and Bains first identified the key evolutionary innovations that drove the development of Earth life from microbes to space-faring humans. These include the transition from single cell life to multicellular life, the rise of photosynthesis, the evolution of macroscopic life and the rise of intelligent life.

Then they analyzed whether or not these important evolutionary occurrences happened many times in different organisms or were due to random, isolated events.

They found that most of the critical innovations were "invented" several times. For example, photosynthesis originated independently at four different points in life's history, and multicellularity arose several times in different classes of organisms.

"Given that we have multiple examples of these key evolutionary adaptions occurring along the path from the simplest organism to humans, we must accept that they are not extremely improbable, but that it 'only' takes a long time and the proper conditions for them to arise," Schulze-Makuch said. "Therefore, in any world where life has arisen and sufficient energy flux exists, we are confident that we will find complex, animal-like life."

The one caveat is that the research doesn't address the likelihood of the origin of life occurring elsewhere or of there being aliens with human like intelligence. Earth is the only planet where life is known to exist, and humans are the only known species to have developed technology. So it is impossible to say whether this should be a common occurrence on other worlds, a very rare event or something in between, Schulze-Makuch said.

Future implications

The work has major implications for the search for life on other worlds. Schulze-Makuch and Bains write that not only should scientists expect to find microbial biosignatures on a planet with life, but also signatures resulting from large and complex, multicellular organisms such as vegetation's red edge, which is the wavelength of light suggesting the existence of plant life.

"In particular, our research is relevant to the selection of tools scientists use in searching for life on planets in other solar systems," Schulze-Makuch said. "On future missions, researchers at NASA, the SETI (search for extraterrestrial intelligence) Institute and other organizations should consider using instruments that are capable of finding signatures of a global and diverse biosphere on other worlds."

http://www.eurekalert.org/pub_releases/2016-07/afri-ad071116.php

Alzheimer's detected before symptoms via new eye technology

Human clinical trials scheduled

Rockville, Md. - Scientists may have overcome a major roadblock in the development of Alzheimer's therapies by creating a new technology to observe -- in the back of the eye -- progression of the disease before the onset of symptoms. Clinical trials are to start in July to test the technology in humans according to a

paper recently published in Investigative Ophthalmology & Visual Science (IOVS).

The paper, titled "Early detection of amyloidopathy in Alzheimer's mice by hyperspectral endoscopy" builds upon previous work in cells by detecting changes in the retina of mice predisposed to develop Alzheimer's.

Early detection of Alzheimer's is critical for two reasons. "First, effective treatments need to be administered well before patients show actual neurological signs," said author Robert Vince, PhD, of the Center for Drug Design at the University of Minnesota (UMN). "Second, since there are no available early detection techniques, drugs currently cannot be tested to determine if they are effective against early Alzheimer's disease. An early diagnostic tool like ours could help the development of drugs as well."

Looking through the eye to see the brain is a key advantage of the new technology. "The retina of the eye is not just 'connected' to the brain -- it is part of the central nervous system," said author Swati More, PhD, also of the Center for Drug Design at UMN. While the brain and retina undergo similar changes due to Alzheimer's disease, "unlike the brain, the retina is easily accessible to us, making changes in the retina easier to observe."

"We saw changes in the retinas of Alzheimer's mice before the typical age at which neurological signs are observed," said More. "The results are close to our best-case scenario for outcomes of this project."

For more information on participating in the clinical trial, please visit the trial website.

http://nyti.ms/29AMr3c

A Cavity-Fighting Liquid Lets Kids Avoid Dentists' Drills

An alternative: an antimicrobial liquid that can be brushed on cavities to stop tooth decay

By CATHERINE SAINT LOUIS JULY 11, 2016

Nobody looks forward to having a cavity drilled and filled by a dentist. Now there's an alternative: an antimicrobial liquid that can be brushed on cavities to stop tooth decay — painlessly.

The liquid is called silver diamine fluoride, or S.D.F. It's been used for decades in Japan, but it's been available in the United States, under the brand name Advantage Arrest, for just about a year.

The Food and Drug Administration cleared silver diamine fluoride for use as a tooth desensitizer for adults 21 and older. But studies show it can halt the progression of cavities and prevent them, and dentists are increasingly using it off-label for those purposes.

"The upside, the great one, is you don't need to drill and you don't need an injection," said Dr. Margherita Fontana, a professor of cariology at the University of Michigan.

Silver diamine fluoride is already used in hundreds of dental offices. Medicaid patients in Oregon are receiving the treatment, and at least 18 dental schools have started teaching the next generation of pediatric dentists how to use it.

Dr. Richard Niederman, the chairman of the epidemiology and health promotion department at the New York University College of Dentistry, said, "Being able to paint it on in 30 seconds with no noise, no drilling, is better, faster, cheaper."

"I would encourage parents to ask for it," he added. "It's less trauma for the kid."

The main downside is aesthetic: Silver diamine fluoride blackens the brownish decay on a tooth. That may not matter on a back molar or a baby tooth that will fall out, but some patients are likely to be deterred by the prospect of a dark spot on a visible tooth.

Until more insurers cover it, patients also have to cover the cost. Still, it's relatively inexpensive. Dr. Michelle Urschel, an anesthesiologist, was happy to pay $25 to have Dr. Jeanette MacLean, a pediatric dentist in Glendale, Ariz., paint over a cavity that her son Knox, 4, had recently developed. A cavity that had to be drilled cost $151. The liquid "was very affordable," Dr. Urschel said.

The noninvasive treatment may be ideal for the indigent, nursing home residents and others who have trouble finding care. And many anxious dental patients want to dodge the drill. But the liquid may be especially useful for children. Nearly a quarter of 2- to 5-year-olds have cavities, according to the Centers for Disease Control and Prevention.

Some preschoolers with severe cavities must be treated in a hospital under general anesthesia, even though it may pose risks to the developing brain.

"S.D.F. gives us an opportunity to decrease the number of toddlers with cavities going to the O.R.," said Dr. Arwa Owais, an associate professor of pediatric dentistry at the University of Iowa.

Dr. Laurence Hyacinthe, a pediatric dentist in Harlem, used silver diamine fluoride on eight uncooperative children whose parents wanted to delay a trip to the operating room.

Dr. MacLean said, "People assume that parents will reject it because of poor aesthetics." But "if it means preventing a child from having to be sedated or having their tooth drilled and filled, there are many parents who choose S.D.F.," she added.

Alejandra Bujeiro, 32, was delighted that her 3-year-old daughter, Natalia, didn't have to have two cavities filled in the back of her mouth. Instead Dr. Eyal Simchi,

a pediatric dentist in Elmwood Park, N.J., brushed silver diamine fluoride on the decay.

Two front teeth, however, were drilled. Next time, Ms. Bujeiro said, she'd opt for silver diamine fluoride. "I would use it in baby teeth even if it's in front," she said. As for the discoloration? "You can't see it too much."

Silver diamine fluoride has another advantage over traditional treatment: It kills the bacteria that cause decay. A second treatment applied six to 18 months after the first markedly arrests cavities, studies have shown. "S.D.F. reduces the incidence of new caries and progression of current caries by about 80 percent," said Dr. Niederman, who is updating an evidence review of silver diamine fluoride published in 2009. Fillings, by contrast, do not cure an oral infection.

"There's nothing that goes on in an operating room that treats the underlying problem," said Dr. Peter Milgrom, a professor of pediatric dentistry at the University of Washington who was instrumental in receiving F.D.A. clearance for silver diamine fluoride and has a financial stake in Advantage Arrest.

That's why some children must have dental treatment under anesthesia twice.

Bacterial infections also cause acne, but a "dermatologist doesn't take a scalpel and cut off your pimples," said Dr. Jason Hirsch, a pediatric dentist in Royal Palm Beach, Fla. Yet "that's how dentistry has approached cavities." Dr. Hirsch has a Facebook page called SDF Action, where dentists can discuss individual cases.

In January, Oregon became the first state to reimburse Medicaid providers for treating cavities with silver diamine fluoride. "It's a completely new paradigm" that offers "significant savings," said Dr. Bruce W. Austin, the dental director of the Oregon Health Authority.

"You need only a drop to treat five teeth, and it comes out to pennies per tooth," said Dr. Scott L. Tomar, a University of Florida dentistry professor who treats some Medicaid patients.

Toddlers in low-income families sometimes have to wait a year for fillings in an operating room. The new alternative is "a huge deal," said Dr. Tomar, the chairman of the oral health section of the American Public Health Association.

Silver diamine fluoride also may help nursing-home residents, who often experience severe cavities if their teeth aren't routinely brushed. Transporting and treating frail patients, assuming they can afford to see a dentist, can be difficult. But now some patients can be quickly treated where they live.

Still, silver diamine fluoride is no silver bullet. Patients with mouth sores or a silver allergy can't use it. Severe cavities — huge holes that trap food and plaque — still require fillings.

At dental conferences, Dr. Tomar and Dr. Fontana lecture about the treatment. They ask audiences if they are using it; so far, just a few hands go up.

http://www.eurekalert.org/pub_releases/2016-07/nhla-ndf071216.php

Newly discovered features of collagen may help shed light on disease processes

NIH study shows abundant structural protein is dynamic, not just an inert scaffold for cells

WHAT: Scientists at the National Institutes of Health are reporting new, unexpected details about the fundamental structure of collagen, the most abundant protein in the human body. In lab experiments, they demonstrated that collagen, once viewed as inert, forms structures that regulate how certain enzymes break down and remodel body tissue. The finding of this regulatory system provides a molecular view of the potential role of physical forces at work in heart disease, cancer, arthritis, and other disease-related processes, they say. The study appears in the current online issue of the Proceedings of the National Academy of Sciences.

Scientists have known for years that collagen remodeling plays an important role in a wide variety of biological processes ranging from wound healing to cancer growth. In particular, researchers know that collagen is broken down by a certain class of enzymes called matrix metalloproteinases (MMPs), but exactly how they did this remained somewhat of a mystery, until now.

In the NIH study, the scientists isolated individual, nano-sized collagen fibrils from rat-tail tendons. They then exposed the collagen fibrils to fluorescently-labeled human MMP enzymes. Using video microscopy, the scientists tracked thousands of enzymes moving along a fibril. Unexpectedly, the scientists observed that the enzymes preferred to attach at certain sites along the fibril, and over time these attachment sites slowly moved, or disappeared and reappeared in other positions. These observations revealed collagen fibrils have defects that spontaneously form and heal. In the presence of tension, such as when tendons stretch, defects are likely eliminated, preventing enzymes from breaking down collagen that is loaded by physical force, the researchers suggest. In short, they identified a possible strain-sensitive mechanism for regulating tissue remodeling.

In addition to primary support by the National Heart, Lung, and Blood Institute (NHLBI), the current study is also supported by the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) and the National Cancer Institute (NCI). All are part of the National Institutes of Health.

WHO: Keir C. Neuman, Ph.D., senior investigator in the Laboratory of Single Molecule Biophysics at the NHLBI and corresponding author of the study, is available to comment on the findings and implications of this research.

http://www.eurekalert.org/pub_releases/2016-07/wtsi-rhq071116.php

Red hair gene variation drives up skin cancer mutations

Burden of mutations comparable to 2 extra decades of sun exposure

For the first time, researchers at the Wellcome Trust Sanger Institute and University of Leeds have proved that gene variants associated with red hair, pale skin and freckles are linked to a higher number of genetic mutations in skin cancers. The burden of mutations associated with these variants is comparable to an extra 21 years of sun exposure in people without this variant.

The research, published today in Nature Communications, showed that even a single copy of a red hair-associated MC1R gene variant increased the number of mutations in melanoma skin cancer; the most serious form of skin cancer. Many non-red haired people carry these common variants and the study shows that everyone needs to be careful about sun exposure.

Red-headed people make up between one and two percent of the world's population but about 6 per cent of the UK population. They have two copies of a variant of the MC1R gene which affects the type of melanin pigment they produce, leading to red hair, freckles, pale skin and a strong tendency to burn in the sun.

Dr David Adams, joint lead researcher at the Wellcome Trust Sanger Institute, said: "It has been known for a while that a person with red hair has an increased likelihood of developing skin cancer, but this is the first time that the gene has been proven to be associated with skin cancers with more mutations.

"Unexpectedly, we also showed that people with only a single copy of the gene variant still have a much higher number of tumour mutations than the rest of the population. This is one of the first examples of a common genetic profile having a large impact on a cancer genome and could help better identify people at higher risk of developing skin cancer."

The researchers analysed publically available data-sets of tumour DNA sequences collected from more than 400 people. They found an average of 42 per cent more sun-associated mutations in tumours from people carrying the gene variant.

Professor Tim Bishop, joint lead author and Director of the Leeds Institute of Cancer and Pathology at the University of Leeds, said: "This is the first study to look at how the inherited MC1R gene affects the number of spontaneous mutations in skin cancers and has significant implications for understanding how skin cancers form. It has only been possible due to the large-scale data available. The tumours were sequenced in the USA, from patients all over the world and the data was made freely accessible to all researchers. This study illustrates how important international collaboration and free public access to data-sets is to research."

Exposure to ultraviolet light from either sunlight or sunbeds causes damage to DNA and it has been thought that the type of skin pigment associated with red-heads could allow more UV to reach the DNA. While this may be one mechanism of damage, the study also revealed that the MC1R gene variation not only increased the number of spontaneous mutations caused by ultraviolet light, but also raised the level of other mutations in the tumours. This suggests that biological processes exist in cancer development in people with MC1R variation that are not solely related to ultraviolet light.

Dr Julie Sharp, head of health and patient information at Cancer Research UK, said: "This important research explains why red-haired people have to be so careful about covering up in strong sun. It also underlines that it isn't just people with red hair who need to protect themselves from too much sun. People who tend to burn rather than tan, or who have fair skin, hair or eyes, or who have freckles or moles are also at higher risk.

"For all of us the best way to protect skin when the sun is strong is to spend time in the shade between 11am and 3pm, and to cover up with a t-shirt, hat and sunglasses. And sunscreen helps protect the parts you can't cover; use one with at least SPF15 and 4 or more stars, put on plenty and reapply regularly."

Publication: Carla D. Robles-Espinoza, Nicola D. Roberts, Shuyang Chen et al. (2016) Germline MC1R status influences somatic mutation burden in melanoma. Nature Communications. DOI: 10.1038/NCOMMS12064

http://bit.ly/29FK3xY

Lifting Weights? No Need to Go Heavy

You don't need to feel wimpy for lifting little weight at the gym: A new study finds that lifting light weights is just as effective as lifting heavy ones for building muscle.

By Rachael Rettner, Senior Writer | July 12, 2016 06:12pm ET

The key is to lift the weights more times (meaning a greater number of repetitions) so that your muscles get just as tired as they would with heavier weights, the researchers said.

"Fatigue is the great equalizer here," study researcher Stuart Phillips, a professor of kinesiology at McMaster University in Ontario, Canada, said in a statement. "Lift to the point of exhaustion, and it doesn't matter whether the weights are heavy or light."

The study involved 49 experienced weight lifters who were divided into two groups. One group lifted lighter weights (between 30 and 50 percent of the maximum weight the individuals could lift), for 20 to 25 repetitions per set (each set was repeated three times). The other group lifted heavier weights (between 75 and 90 percent of the maximum weight the people could lift) for eight to 12

repetitions per set. This strength-training workout was performed four days a week, for 12 weeks.

At the end of the study, participants gave samples of muscle tissue and had their bodies scanned so researchers could look for changes in muscle fiber size and muscle mass, which are important measures of strength.

The two groups showed similar improvements in the amount of lean muscle mass in their bodies and the size of their muscle fibers, the study found. The groups also showed similar improvements on tests of muscle strength.

Although elite athletes may be unlikely to change their workout regimens based on the new findings, the study may have implications for average Joes who want to increase strength, the researchers said.

"For the 'mere mortal' who wants to get stronger, we've shown that you can take a break from lifting heavy weights and not compromise any gains," Phillips said. "It's also a new choice, which could appeal to the masses and get people to take up something they should be doing for their health."

The findings add to those of a previous study by the same group of researchers, which found that lifting lighter weights was just as effective as lifting heavier weights for building muscle in men who were not experienced weight lifters.

The new study was published online May 12 in the Journal of Applied Physiology.

http://bit.ly/29Su3W8

Mystery of what sleep does to our brains may finally be solved

It is one of life's great enigmas: why do we sleep?

By Clare Wilson

Now we have the best evidence yet of what sleep is for – allowing housekeeping processes to take place that stop our brains becoming overloaded with new memories.

All animals studied so far have been found to sleep, but the reason for their slumber has eluded us. When lab rats are deprived of sleep, they die within a month, and when people go for a few days without sleeping, they start to hallucinate and may have epileptic seizures.

One idea is that sleep helps us consolidate new memories, as people do better in tests if they get a chance to sleep after learning. We know that, while awake, fresh memories are recorded by reinforcing connections between brain cells, but the memory processes that take place while we sleep have remained unclear.

Support is growing for a theory that sleep evolved so that connections in the brain can be pruned down during slumber, making room for fresh memories to form the next day. "Sleep is the price we pay for learning," says Giulio Tononi of the University of Wisconsin-Madison, who developed the idea.

Now we have the most direct evidence yet that he's right. Tononi's team measured the size of these connections or synapses in brain slices taken from mice. The synapses in samples taken at the end of a period of sleep were 18 per cent smaller than those in samples taken from before sleep, showing that the synapses between neurons are weakened during slumber.

A good night's sleep

Tononi announced these findings at the Federation of European Neuroscience Societies meeting in Copenhagen, Denmark, last week. "The data was very solid and well documented," says Maiken Nedergaard of the University of Rochester, who attended the conference.

"It's an extremely elegant idea," says Vladyslav Vyazovskiy of the University of Oxford

If the housekeeping theory is right, it would explain why, when we miss a night's sleep, the next day we find it harder to concentrate and learn new information – we may have less capacity to encode new experiences. The finding suggests that, as well as it being important to get a good night's sleep after learning something, we should also try to sleep well the night before.

It could also explain why, if our sleep is interrupted, we feel less refreshed the next day. There is some indirect evidence that deep, slow-wave sleep is best for pruning back synapses, and it takes time for our brains to reach this level of unconsciousness.

Waking refreshed

Previous evidence has also supported the housekeeping theory. For instance, EEG recordings show that the human brain is less electrically responsive at the start of the day – after a good night's sleep – than at the end, suggesting that the connections may be weaker. And in rats, the levels of a molecule called the AMPA receptor – which is involved in the functioning of synapses – are lower at the start of their wake periods.

The latest brain-slice findings that synapses get smaller is the most direct evidence yet that the housekeeping theory is right, says Vyazovskiy. "Structural evidence is very important," he says. "That's much less affected by other confounding factors."

Protecting what matters

Getting this data was a Herculean task, says Tononi. They collected tiny chunks of brain tissue, sliced it into ultrathin sections and used these to create 3D models of the brain tissue to identify the synapses. As there were nearly 7000 synapses, it took seven researchers four years.

The team did not know which mouse was which until last month, says Tononi, when they broke the identification code, and found their theory stood up.

“People had been working for years to count these things. You start having stress about whether it’s really possible for all these synapses to start getting fatter and then thin again,” says Tononi. The team also discovered that some synapses seem to be protected – the biggest fifth stayed the same size. It’s as if the brain is preserving its most important memories, says Tononi. “You keep what matters.”

http://www.bbc.com/news/health-36774751

Treat sepsis 'the same as heart attacks'

Suspected sepsis in patients must be treated as an emergency in the same way as heart attacks are, England's health watchdog says.

By Smitha Mundasad Health reporter

National Institute of Health and Care Excellence guidance urges medics to consider sepsis early on when treating any patients unwell with infections. The problem, caused when the body's immune system overreacts to infection, leads to 44,000 UK deaths a year. But experts estimate between 5,000 and 13,000 could be avoided.

Sepsis can lead to severe organ failure, shock and death if not treated early enough. But initial symptoms - such as a rapid breathing or feeling generally unwell - can be vague, making it difficult to set apart from other conditions.

'Complicated medicine'

In its first guidance on the issue, NICE acknowledges it is a complex medical problem. But the health watchdog says GPs, paramedics and hospital staff must make "Could this be sepsis?" the first consideration for anyone unwell with an infection - in much the same way that medics consider the possibility of a heart attack for patients with chest pain.

Prof Mark Baker, from NICE, told the BBC: "The problem with those patients who died unnecessarily of sepsis is that staff did not think about it soon enough."

He added: "This is complicated medicine. "It requires a depth of thought and experience and a way of examining patients which isn't always there - particularly because of time pressures and partly because we have got used to implementing guidelines without thinking."

Cornwall mother Melissa Mead, whose one-year-old son William died from sepsis in 2014 after potential signs of the condition were missed by NHS 111 staff and GPs, welcomed the move. She added: "This could not come any sooner. Sadly we have been touched in very real terms by sepsis and could not agree more that clinicians need to start asking: 'Could this be sepsis?'"

What is sepsis?

Sepsis happens when the body's immune system - the way the body responds to bugs and germs - goes into overdrive. The initial problem can be quite mild and start anywhere - from a cut on the finger to a chest or urine infection, for example.

But when the immune system overreacts, this can lead to an unintended but catastrophic attack on the body. If left untreated, this sets off a cascade of reactions - from shock to organ failure and even death. There is a lot of research going on to attempt to find out what exactly triggers this sometimes fatal reaction.

Meanwhile, Dr Maureen Baker, of the Royal College of General Practitioners, said: "The diagnosis of sepsis is a huge worry for GPs, as initial symptoms can be similar to common viral illnesses, so we welcome any guidance or support to help us identify it as early as possible."

The guidelines say patients with possible sepsis should be sent to hospital in an ambulance and treated urgently by senior staff. Separately, NHS Improvement has launched an initiative to tackle children's health.

'Sad and frustrating'

It encourages parents to speak up if their child's health is deteriorating and urges staff to work more closely with parents.

Dr Mike Durkin, NHS national director of patient safety, said: "Time and time again, and is some cases tragically too late, we see that some children could have received better care if healthcare providers worked with parents to understand and treat deterioration in health.

"There have been far too many cases covered in the media on the failure to treat sepsis that have highlighted the sad and frustrating instances of parents repeatedly flagging concerns about their children."

http://www.bbc.com/news/health-36782323

Over 40s 'have more babies' than under 20s

Women over 40 are having more babies than the under 20s for the first time in nearly 70 years, official figures for England and Wales show.

By James Gallagher Health and science reporter, BBC News website

The Office for National Statistics data showed there were 697,852 live births in 2015. There were 15.2 births per 1,000 women aged over 40, compared with just 14.5 per 1,000 women in their teens. The last time the over 40s had the higher fertility rate was in 1947, in the wake of WWII.

The figures show two key trends in who is having children and when in England and Wales. The teenage pregnancy rate has been in long-term decline and has more than halved from the 33 births per 1,000 teenagers in 1990. Meanwhile, pregnancies have soared in older age groups from 5.3 per 1,000 in 1990.

The average age of having a child is now 30.3 - a figure that has been increasing since 1975. Advances in fertility treatment as well as more women in higher education and attitudes around the importance of a career and the rising costs of childbearing are behind the rise, the ONS says.

Liz McLaren, head of vital statistics outputs at the ONS, said: "The trend for women to have babies at older ages continued in 2015. "Over the last 40 years, the percentage of live births to women aged 35 and over has increased considerably.

"Women aged 40 and over now have a higher fertility rate than women aged under 20 - this was last recorded in the 1940s."

The data also shows that fertility rates have dropped in all age groups under 25 while increasing for all age groups 30 and over. Women aged between 30 and 34 have the highest fertility of any age group - with 111 births per 1,000 women.

The number of births to women born outside the UK has also continued its rise, reaching 27.5% of all births.

Prof Adam Balen, the chairman of the British Fertility Society, said: "We know that female fertility starts to decline gradually from the late 20s and more rapidly from the mid-30s onwards. "While the risks should never be overplayed, men and women should be aware that reproductive outcomes are poorer in older women.

"As well as it potentially taking longer to get pregnant, later maternity can involve a greater risk of miscarriage, a more complicated labour, and medical intervention at the birth."

The British Pregnancy Advisory Service said: "The trend towards older motherhood is here to stay, and there are many understandable reasons why women today are waiting longer to start or expand their families than those in previous decades. "Rather than bemoaning this development, we should seek to understand and support the decisions women make.

"More affordable childcare and improved maternity rights may make it easier for some women to start their families earlier if they wish, but we also need to ensure we have high quality reproductive healthcare services configured to meet women's needs, whatever the age at which they conceive."

http://www.eurekalert.org/pub_releases/2016-07/gsoa-vrt071116.php

Viruses revealed to be a major driver of human evolution

Study tracking protein adaptation over millions of years yields insights relevant to fighting today's viruses

BETHESDA, MD - The constant battle between pathogens and their hosts has long been recognized as a key driver of evolution, but until now scientists have not had the tools to look at these patterns globally across species and genomes. In a new study, researchers apply big-data analysis to reveal the full extent of viruses' impact on the evolution of humans and other mammals.

Their findings suggest an astonishing 30 percent of all protein adaptations since humans' divergence with chimpanzees have been driven by viruses.

"When you have a pandemic or an epidemic at some point in evolution, the population that is targeted by the virus either adapts, or goes extinct. We knew that, but what really surprised us is the strength and clarity of the pattern we found," said David Enard, Ph.D., a postdoctoral fellow at Stanford University and the study's first author. "This is the first time that viruses have been shown to have such a strong impact on adaptation."

The study was recently published in the journal eLife and will be presented at The Allied Genetics Conference, a meeting hosted by the Genetics Society of America, on July 14.

Proteins perform a vast array of functions that keep our cells ticking. By revealing how small tweaks in protein shape and composition have helped humans and other mammals respond to viruses, the study could help researchers find new therapeutic leads against today's viral threats.

"We're learning which parts of the cell have been used to fight viruses in the past, presumably without detrimental effects on the organism," said the study's senior author, Dmitri Petrov, Ph.D., Michelle and Kevin Douglas Professor of Biology and Associate Chair of the Biology Department at Stanford. "That should give us an insight on the pressure points and help us find proteins to investigate for new therapies."

Previous research on the interactions between viruses and proteins has focused almost exclusively on individual proteins that are directly involved in the immune response--the most logical place you would expect to find adaptations driven by viruses. This is the first study to take a global look at all types of proteins.

"The big advancement here is that it's not only very specialized immune proteins that adapt against viruses," said Enard. "Pretty much any type of protein that comes into contact with viruses can participate in the adaptation against viruses. It turns out that there is at least as much adaptation outside of the immune response as within it."

The team's first step was to identify all the proteins that are known to physically interact with viruses. After painstakingly reviewing tens of thousands of scientific abstracts, Enard culled the list to about 1,300 proteins of interest. His next step was to build big-data algorithms to scour genomic databases and compare the evolution of virus-interacting proteins to that of other proteins.

The results revealed that adaptations have occurred three times as frequently in virus-interacting proteins compared with other proteins.

"We're all interested in how it is that we and other organisms have evolved, and in the pressures that made us what we are," said Petrov. "The discovery that this constant battle with viruses has shaped us in every aspect--not just the few proteins that fight infections, but everything--is profound. All organisms have been living with viruses for billions of years; this work shows that those interactions have affected every part of the cell."

Viruses hijack nearly every function of a host organism's cells in order to replicate and spread, so it makes sense that they would drive the evolution of the cellular machinery to a greater extent than other evolutionary pressures such as predation or environmental conditions. The study sheds light on some longstanding biological mysteries, such as why closely-related species have evolved different machinery to perform identical cellular functions, like DNA replication or the production of membranes. Researchers previously did not know what evolutionary force could have caused such changes. "This paper is the first with data that is large enough and clean enough to explain a lot of these puzzles in one fell swoop," said Petrov.

The team is now using the findings to dig deeper into past viral epidemics, hoping for insights to help fight disease today. For example, HIV-like viruses have swept through the populations of our ancestors as well as other animal species at multiple points throughout evolutionary history. Looking at the effects of such viruses on specific populations could yield a new understanding of our constant war with viruses--and how we might win the next big battle.

Viruses are a dominant driver of protein adaptation in mammals: David Enard, Le Cai, Carina Gwennap, Dmitri A Petrov eLife May 2016 5:e12469 doi: http://dx.doi.org/10.7554/eLife.12469 https://elifesciences.org/content/5/e12469
This work is funded by NIH grants R01GM089926 and R01GM097415.

http://bit.ly/2afkMGD

Founders of Western civilisation were prehistoric dope dealers

It must have been something in the air. During a short time window at the end of the last ice age, Stone Age humans in Europe and Asia independently began using a new plant: cannabis.

By Colin Barras

That's the conclusion of a review of cannabis archaeology, which also links an intensification of cannabis use in East Asia with the rise of transcontinental trade at the dawn of the Bronze Age, some 5000 years ago.

Central Eurasia's Yamnaya people – thought to be one of the three key tribes that founded European civilisation – dispersed eastwards at this time and are thought to have spread cannabis, and possibly its psychoactive use, throughout Eurasia.

The pollen, fruit and fibres of cannabis have been turning up in Eurasian archaeological digs for decades.

Tengwen Long and Pavel Tarasov at the Free University of Berlin, Germany, and their colleagues have now compiled a database of this archaeological literature to identify trends and patterns in prehistoric cannabis use.

It is often assumed that cannabis was first used, and possibly domesticated, somewhere in China or Central Asia, the researchers say – but their database points to an alternative.

Some of the most recent studies included in the database suggest that the herb entered the archaeological record of Japan and Eastern Europe at almost exactly the same time, between about 11,500 and 10,200 years ago.

"The cannabis plant seems to have been distributed widely from as early as 10,000 years ago, or even earlier," says Long.

Weed as a cash crop

The researchers suggest that different groups of people across the Eurasian landmass independently began using the plant at this time – perhaps for its psychoactive properties or as a source of food or medicine, or even to make textiles from its fibres.

However, Tarasov and Long's database suggests it was only in western Eurasia that cannabis was then used regularly by humans down the millennia. Early records of its use in East Asia are fairly scattered, says Long.

This pattern seems to have changed about 5000 years ago, at the start of the Bronze Age, when cannabis use in East Asia apparently intensified.

Tarasov and Long think this timing is significant. By then, nomadic pastoralists on the Eurasian steppe had mastered horse riding, allowing them to cover vast distances and begin forging transcontinental trade networks following the same routes that would become the famous Silk Road several millennia later.

This earlier "Bronze Road" allowed all sorts of commodities to spread between west and east, potentially including cannabis.

"It's a hypothesis that requires more evidence to test," says Long, but he points out that the high value of cannabis would have made it an ideal exchangeable good at the time – a "cash crop before cash".

And independent lines of evidence suggest that commodities and people were on the move in the early Bronze Age. For instance, Long says that wheat, which was cultivated about 10,000 years ago in the Near East, first appeared in China 5000 years ago.

Ancient DNA studies published in the last few years also confirm that one nomadic pastoral population of the steppe – the Yamnaya – began spreading both east and west at this time too.

Stoned age?

Rob Clarke at the International Hemp Association in Amsterdam, the Netherlands, who has written extensively on the prehistory of cannabis, welcomes the up-to-date work – and says it backs his conclusions that cannabis was domesticated in

more than one place. The proposed link between the spread of cannabis and changes at the dawn of the Bronze Age does not surprise him.

Because people can use cannabis in so many ways, we can't be sure that its Bronze Age spread was linked specifically to its psychoactive properties, says Ernest Small at Agriculture and Agri-Food Canada in Ottawa.

However, there are reasons to believe that its mind-bending properties were a factor. Some researchers have suggested that burned cannabis seeds found at archaeological sites hint that the Yamnaya carried the idea of smoking cannabis with them as they spread across Eurasia.

David Anthony at Hartwick College in Oneonta, New York, who studies the Yamnaya, says the population may have used cannabis for its psychoactive properties on certain special occasions. "The expansion of cannabis use as a drug does seem to be linked to movements out of the steppe," he says. "Cannabis might have been reserved for special feasts or rituals."

What's more, Barney Warf at the University of Kansas in Lawrence says that we know from early Greek historians that post-Bronze Age nomadic pastoralists of the steppe who came after the Yamnaya – the Scythians – regularly used cannabis as a drug. "People talk about Herodotus's accounts of hanging out in the Crimean peninsula smoking weed with the Scythians," he says.

Warf says the new work is fascinating, and should encourage more researchers to explore the history and prehistory of cannabis. "I think there's a largely untold story of cannabis in Europe from the Bronze Age up until the Renaissance," he says.

Reference: Vegetation History and Archaeobotany, *DOI: 10.1007/s00334-016-0579-6*

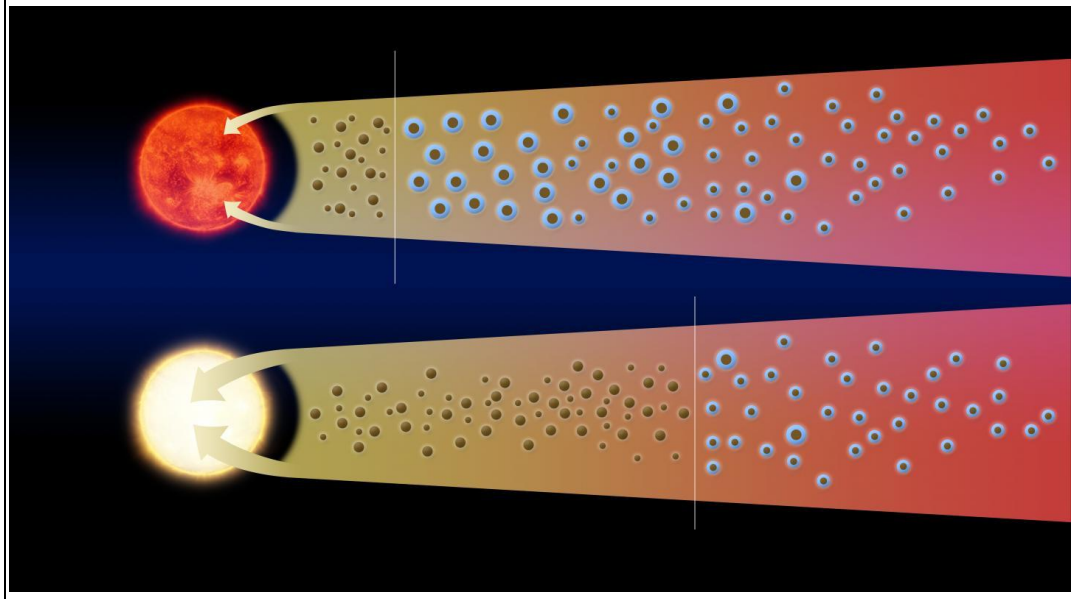
http://www.eurekalert.org/pub_releases/2016-07/nrao-sob071216.php

Stellar outburst brings water snowline into view

A violent outburst by the young star V883 Orionis has given astronomers their first view of a water "snowline" in a protoplanetary disk - the transition point around the star where the temperature and pressure are low enough for water ice to form.

An abrupt increase in the brightness of the star "flash heated" the inner portion of the disk, pushing the water snowline out much farther than normal, enabling astronomers to image it with the Atacama Large Millimeter/submillimeter Array (ALMA). Under normal conditions, the water snowline would be much too close to the protostar to observe directly, even with ALMA's remarkable resolution.

Typically, heat from a young Sun-like star prevents water molecules from freezing within a radius of about three astronomical units, around 450 million kilometers, from the star. (An astronomical unit - AU - is the average distance from the Earth to the Sun). Beyond that point, known as the snowline, water condenses to form a layer of ice on dust grains and other particles.



This illustration shows how the outburst of the young star V883 Orionis has displaced the water snowline much further out from the star, and rendered it detectable with ALMA. **ALMA (ESO/NAOJ/NRAO)/L. Cieza**

An abrupt and powerful increase in the brightness of V883 Orionis, however, has pushed the water snowline out to approximately 40 AU (about 6 billion kilometers), a distance that corresponds roughly to the orbit of Pluto in our solar system.

Even though V883 Orionis is only 30 percent more massive than our Sun, it is currently 400 times more luminous and much hotter, thanks to its recent outburst triggered by material from the disk falling onto the surface of the star.

"The ALMA observations came as a surprise to us," said Lucas Cieza, an astronomer at Diego Portales University, Santiago, Chile, and lead author of a paper describing these results published in the journal *Nature*.

"Our observations were designed to image disk fragmentation, which is one of the proposed mechanisms for the formation of giant planets. We saw none of that, as the disk is probably too warm to fragment despite its very large mass. Instead, we found what looks like a ring at 40 AU. This illustrates well the transformational power of ALMA, which delivers exciting results even if they are not the ones we were looking for."

"The distribution of water ice around a young star is fundamental to planet formation and even the development of life on Earth. ALMA's observation sheds important light on how and where this happens in protoplanetary disks when young planets are still forming," said Zhaohuan Zhu, an astronomer at Princeton University, New Jersey, and co-author on the paper. "We now have direct evidence that a frosty region conducive to planet formation exists around other stars."

Water ice helps regulate the agglomeration of dust grains into larger and larger particles. Astronomers believe that within the snowline, where water is vaporized, conditions favor the formation of smaller, rocky planets like Mars and Earth. Outside the water snowline, the presence of ice allows for the rapid formation of snowballs and cometary bodies, which facilitate the formation of massive gaseous planets such as Jupiter. "Since water ice is more abundant than dust itself beyond the snowline, planets can aggregate more solid material and form bigger and faster there. In this way, giant planets like Jupiter and Saturn can form before the protoplanetary disk is gone," noted Zhu.

The discovery that these outbursts may blast the water snow line to about 10 times its typical radius is very significant to the development of reliable planetary formation models. Such outbursts are believed to be a stage in the evolution of most planetary systems, so this may be the first observation of a common occurrence. In that case, this direct observation from ALMA could contribute substantially to an improved understanding of how planets throughout the Universe form and evolve. It also sheds light on how water ice may have been distributed in our own protoplanetary disk.

The star V883 Orionis is located approximately 1,350 light-years from Earth in the Orion Nebula Cluster. At this distance, ALMA was able to achieve a resolution of about 12 AU -- enough to resolve the water snowline in this system but insufficient to do so around a typical young star.

The National Radio Astronomy Observatory is a facility of the National Science Foundation, operated under cooperative agreement by Associated Universities, Inc.

More information:

The team is composed of Lucas A. Cieza (Universidad Diego Portales, Santiago, Chile), Simon Casassus (Universidad de Chile, Santiago, Chile), John Tobin (Leiden Observatory, Leiden University, The Netherlands), Steven Bos (Leiden Observatory, Leiden University, The Netherlands), Jonathan P. Williams (University of Hawaii at Manoa, Honolulu, Hawai`i, USA), Sebastian Perez (Universidad de Chile, Santiago, Chile), Zhaohuan Zhu (Princeton University, Princeton, New Jersey, USA), Claudio Cáceres (Universidad Valparaiso, Valparaiso, Chile), Hector Canovas (Universidad Valparaiso, Valparaiso, Chile), Michael M. Dunham (Harvard-Smithsonian Center for Astrophysics, Cambridge, Massachusetts, USA), Antonio Hales (Joint ALMA Observatory, Santiago, Chile), Jose L. Prieto (Universidad Diego Portales, Santiago, Chile), David A. Principe (Universidad Diego Portales, Santiago, Chile), Matthias R. Schreiber (Universidad Valparaiso, Valparaiso, Chile), Dary Ruiz-Rodriguez (Australian National University, Mount Stromlo Observatory, Canberra, Australia) and Alice Zurlo (Universidad Diego Portales & Universidad de Chile, Santiago, Chile). Cieza and several other authors on this paper are part of the Protoplanetary Disks Millennium Scientific Initiative (ICM) Nucleus (MAD Nucleus), which is a joint collaboration hosted by the Universidad de Chile (UCH), Universidad Diego Portales (UDP), Universidad Católica (PUC) and the Universidad de Valparaíso (UV).

http://www.eurekalert.org/pub_releases/2016-07/uovh-snr071316.php

Shocking new role found for the immune system: Controlling social interaction

It's of 'profound' importance to proper social functioning, UVA determines

CHARLOTTESVILLE, Va. - In a startling discovery that raises fundamental questions about human behavior, researchers at the University of Virginia School of Medicine have determined that the immune system directly affects - and even controls - creatures' social behavior, such as their desire to interact with others. So could immune system problems contribute to an inability to have normal social interactions? The answer appears to be yes, and that finding could have great implications for neurological conditions such as autism-spectrum disorders and schizophrenia.

"The brain and the adaptive immune system were thought to be isolated from each other, and any immune activity in the brain was perceived as sign of a pathology. And now, not only are we showing that they are closely interacting, but some of our behavior traits might have evolved because of our immune response to pathogens," explained Jonathan Kipnis, PhD, chairman of UVA's Department of Neuroscience. "It's crazy, but maybe we are just multicellular battlefields for two ancient forces: pathogens and the immune system. Part of our personality may actually be dictated by the immune system."

Evolutionary Forces at Work

It was only last year that Kipnis, the director of UVA's Center for Brain Immunology and Glia, and his team discovered that meningeal vessels directly link the brain with the lymphatic system. That overturned decades of textbook teaching that the brain was "immune privileged," lacking a direct connection to the immune system. The discovery opened the door for entirely new ways of thinking about how the brain and the immune system interact.

The follow-up finding is equally illuminating, shedding light on both the workings of the brain and on evolution itself. The relationship between people and pathogens, the researchers suggest, could have directly affected the development of our social behavior, allowing us to engage in the social interactions necessary for the survival of the species while developing ways for our immune systems to protect us from the diseases that accompany those interactions. Social behavior is, of course, in the interest of pathogens, as it allows them to spread.

The UVA researchers have shown that a specific immune molecule, interferon gamma, seems to be critical for social behavior and that a variety of creatures, such as flies, zebrafish, mice and rats, activate interferon gamma responses when they are social. Normally, this molecule is produced by the immune system in

response to bacteria, viruses or parasites. Blocking the molecule in mice using genetic modification made regions of the brain hyperactive, causing the mice to become less social. Restoring the molecule restored the brain connectivity and behavior to normal. In a paper outlining their findings, the researchers note the immune molecule plays a "profound role in maintaining proper social function."

"It's extremely critical for an organism to be social for the survival of the species. It's important for foraging, sexual reproduction, gathering, hunting," said Anthony J. Filiano, PhD, Hartwell postdoctoral fellow in the Kipnis lab and lead author of the study. "So the hypothesis is that when organisms come together, you have a higher propensity to spread infection. So you need to be social, but [in doing so] you have a higher chance of spreading pathogens. The idea is that interferon gamma, in evolution, has been used as a more efficient way to both boost social behavior while boosting an anti-pathogen response."

Understanding the Implications

The researchers note that a malfunctioning immune system may be responsible for "social deficits in numerous neurological and psychiatric disorders." But exactly what this might mean for autism and other specific conditions requires further investigation. It is unlikely that any one molecule will be responsible for disease or the key to a cure, the researchers believe; instead, the causes are likely to be much more complex. But the discovery that the immune system - and possibly germs, by extension - can control our interactions raises many exciting avenues for scientists to explore, both in terms of battling neurological disorders and understanding human behavior.

"Immune molecules are actually defining how the brain is functioning. So, what is the overall impact of the immune system on our brain development and function?" Kipnis said. "I think the philosophical aspects of this work are very interesting, but it also has potentially very important clinical implications."

Findings Published

Kipnis and his team worked closely with UVA's Department of Pharmacology and the group of Vladimir Litvak, PhD, at the University of Massachusetts Medical School. Litvak's team developed a computational approach to investigate the complex dialogue between immune signaling and brain function in health and disease. "Using this approach we predicted a role for interferon gamma, an important cytokine secreted by T lymphocytes, in promoting social brain functions," Litvak said. "Our findings contribute to a deeper understanding of social dysfunction in neurological disorders, such as autism and schizophrenia, and may open new avenues for therapeutic approaches."

The findings have been published online by the prestigious journal Nature. The article was written by Filiano, Yang Xu, Nicholas J. Tustison, Rachel L. Marsh, Wendy Baker, Igor Smirnov, Christopher C. Overall, Sachin P. Gadani, Stephen D. Turner, Zhiping Weng, Sayeda Najamussahar Peerzade, Hao Chen, Kevin S. Lee, Michael M. Scott, Mark P. Beenhakker, Litvak and Kipnis.

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http://www.eurekalert.org/pub_releases/2016-07/tl-tlo071216.php

The Lancet: Obesity linked to premature death, with greatest effect in men

A study of 3.9 million adults published today in The Lancet finds that being overweight or obese is associated with an increased risk of premature death.

The risks of coronary heart disease, stroke, respiratory disease and cancer are all increased. Overall, the excess risk of premature death (before age 70) among those who are overweight or obese is about three times as great in men as in women.

WHO estimates that 1.3 billion adults worldwide are overweight, and that a further 600 million are obese. The prevalence of adult obesity is 20% in Europe and 31% in North America. WHO uses body-mass index (BMI, in kg/m2), which relates weight to height, and defines BMI 18.5-25 as normal, 25-30 as overweight, 30-35 as moderately obese, and over 40 as severely obese.

For example, for height 1.6m (5'3") overweight is about 60-80 kg (140-170 lb; 10-12 stone), and for height 1.8m (5'11") overweight is about 80-100 kg (180-210 pounds; 13-15 stone). Normal BMI spans a range of similar length below this; moderate obesity spans a range of similar length above.

"On average, overweight people lose about one year of life expectancy, and moderately obese people lose about three years of life expectancy" says Dr. Emanuele Di Angelantonio from the University of Cambridge, Cambridge, UK, the lead author. "We also found that men who were obese were at much higher risk of premature death than obese women. This is consistent with previous observations that obese men have greater insulin resistance, liver fat levels, and diabetes risk than women." [1]

The study found an increased risk of premature death for people who were underweight, as well as for people classed as overweight. The risk increased steadily and steeply as BMI increased. A similar trend was seen in many parts of the world (figure 1) and for all four main causes of death (figure 4).

Where the risk of death before age 70 would be 19% and 11% for men and women with a normal BMI [2], the study found that it would be 29.5% and 14.6% for moderately obese men and women (BMI 30-35). This corresponds to an absolute increase of 10.5% for men, and 3.6% for women - three times as big

(Appendix p. 45). The authors defined premature deaths as those at ages 35-69 years.

The new study brings together information on the causes of any deaths in 3.9 million adults from 189 previous studies in Europe, North America and elsewhere. At entry to the study all were aged between 20 and 90 years old, and were non-smokers who were not known to have any chronic disease when their BMI was recorded. The analysis is of those who then survived at least another five years. Of 3951455 participants (69% women, Appendix p. 22), 385879 died.

The study also estimated the population-attributable fraction for mortality due to overweight and obesity (PAF) - ie, the reduction in deaths in a population that would occur if a risk factor were eliminated. The authors say that assuming that the associations between high BMI and mortality are largely causal, if those who were overweight or obese had WHO-defined normal levels of BMI, then the proportion of premature deaths that would be avoided would be about one in 7 in Europe and one in 5 in North America.

"Obesity is second only to smoking as a cause of premature death in Europe and North America," says co-author Professor Sir Richard Peto, University of Oxford, Oxford, UK. "Smoking causes about a quarter of all premature deaths in Europe and in North America, and smokers can halve their risk of premature death by stopping. But, overweight and obesity now cause about 1 in 7 of all premature deaths in Europe and 1 in 5 of all premature deaths in North America." [1]

The researchers also broke down the normal BMI range and found a slightly increased risk at the lower end of it (at 18.5-20 kg/m2).

The authors note that one important limitation is that their only measure of obesity was BMI, which does not assess fat distribution in different parts of the body, muscle mass, or obesity-related metabolic factors such as blood sugar or cholesterol.

Writing in a linked Comment, Dr David Berrigan, Dr Richard Troiano and Dr Barry Graubard from the National Cancer Institute, National Institutes of Health, Bethesda, MD, USA, discuss the methodological limitations of global studies measuring BMI and mortality and the need for improved study designs, as well as the challenges that remain in the effort to translate epidemiological evidence of excess body weight and mortality into effective guidelines and public health interventions. They say: "Challenges in deriving global public health recommendations are unlikely to be resolved by ever larger datasets without further developments in study data and design."

The study funders included the UK Medical Research Council, British Heart Foundation, Cancer Research UK, National Institute of Health Research, US National Institutes of Health.

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

[2] *These risks of 19% and 11% for men and women with normal BMI are intermediate between the risks now seen for men and women in Europe and North America.*
http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(16)30175-1/abstract

http://bit.ly/29ISyCY

Why the Olympics Actually Won't Cause Zika to Spread Everywhere

CDC predicts that Olympics will put only 4 countries at risk for importing Zika

By Sara G. Miller, Staff Writer | July 13, 2016 02:36pm ET

With the 2016 Olympic Games in Brazil less than a month away, concerns are mounting that the international event may spread the Zika virus to more countries around the world. Indeed, global travel has been contributing to the spread of virus in the Western Hemisphere since at least 2015, according to a new report from the Centers for Disease Control and Prevention (CDC).

However, the new report, released today (July 13), should help quell fears for many countries that do not currently have the Zika virus: The CDC predicted that the Olympics will put only four countries at risk for importing Zika.

However, the agency also recommended that pregnant women in the U.S. avoid traveling to the Olympics. The virus has been linked with severe brain problems, including a condition called microcephaly, in babies born to women infected during pregnancy.

August and September are winter months in the Southern Hemisphere, and so the weather in Rio de Janeiro, Brazil, during the Olympics will be cooler and drier than at other times of the year. This type of weather typically reduces mosquito populations and therefore lowers the risk of infection, the CDC said. [Zika Virus News: Complete Coverage of the 2016 Outbreak]

Between 350,000 and 500,000 people from more than 200 countries are expected to ravel to Rio de Janeiro in August and September for the Olympic and Paralympic Games, according to the Brazilian Tourist Board. However, these estimates represent less than 0.25 percent of the number of travelers who visited Zika-affected countries in 2015, according to the report. More travelers would mean a greater likelihood of spreading Zika.

In the new report, researchers at the CDC looked at the 167 countries where no cases of the Zika virus have been reported. (The United States, where Zika has been documented, was therefore not included in the 167 countries.) The researchers said that 148 of these countries should not be considered at risk for importing Zika from the Olympics, because they do not have populations of the Aedes aegypti mosquito, which carries Zika, in August and September.

Of the 19 remaining countries, the CDC researchers predicted that only four — Chad, Djibouti, Eritrea and Yemen — are at risk for importing the Zika virus because of people traveling to the Olympics and returning home with the virus. The other 15 countries will have too few travelers attending the Olympics for it to be likely they'd bring home the virus, the researchers said.

The researchers noted that these estimates were based on five "worst-case scenarios." These scenarios assumed that Zika transmission would not decrease during the winter months, that preventive measures to protect against mosquito bites would not be taken, that anyone who was infected with Zika would have symptoms when they returned to their home countries, that people who were infected would return home immediately and that the home countries would not use precautions to prevent mosquito bites in their home countries.

Though the risk of Zika is low, the CDC still encouraged people traveling to Rio de Janeiro to take certain precautions:

Pregnant women should not travel to the Olympics.

Travelers should take protective measures to prevent mosquito bites (such as using insect repellent and wearing long-sleeved shirts and long pants) while at the Olympics, and for three weeks after returning to their home countries.

To prevent sexual transmission of Zika, travelers should use condoms or abstain from sex. Males in particular should use condoms for eight weeks after travel, or, if they do get Zika, for six months from the start of symptoms.

Males who travel to the Olympics and who have pregnant partners should use condoms or abstain from sex for the duration of their partners' pregnancies.

Couples who travel to the Olympics and want to get pregnant afterward should wait at least eight weeks, or six months if the male partner has a symptomatic Zika infection.

http://www.livescience.com/55393-obama-paper-jama.html

Paper in a Top Medical Journal Has Unexpected Author: Barack Obama

In an unusual move for a sitting president, Barack Obama has published a scholarly paper in a scientific journal.

By Rachael Rettner, Senior Writer | July 13, 2016 02:59pm ET

The paper, which discusses the success and future of the Affordable Care Act (ACA), was published Monday (July 11) in the prestigious medical journal JAMA.

It may be the first time a sitting president has authored a complete academic article — with an abstract, findings and conclusions — that's been published in a scientific journal, at least in recent history.

However, several other presidents have written commentaries or opinion pieces that have been published in scientific journals during their presidency, including George W. Bush, who wrote about access to health care in a paper published in JAMA in 2004, and Bill Clinton, who wrote a commentary published in the journal Science in 1997.

Obama's journal article analyzes data gathered from other reports and studies, and highlights some of the successes of the ACA, including a drop in the percentage of Americans who do not have health insurance. After the act became law, the uninsured rate dropped by 43 percent, from 16 percent of Americans in 2010 to 9.1 percent in 2015, the paper says.

Still, Obama said, the country continues to face challenges on the way to improving its health care system. "Despite this progress, too many Americans still strain to pay for their physician visits and prescriptions, cover their deductibles, or pay their monthly insurance bills; struggle to navigate a complex, sometimes bewildering system; and remain uninsured," Obama wrote.

To make sure Americans have enough insurance options and to keep insurance costs low, Obama encouraged Congress to revisit the "public option" plan, meaning a government-run insurance plan that would compete in the insurance marketplace alongside private plans. This public option could be available in parts of the country where insurance options are limited, he said.

Obama also recommended policies that could help reduce the cost of prescription drugs, including those that "give the federal government the authority to negotiate prices for certain high-priced drugs."

Obama's article was not peer-reviewed, but it went through several rounds of editing and fact-checking, according to Bloomberg.

http://www.eurekalert.org/pub_releases/2016-07/uorm-way071216.php

What are your chances of living 2 years? Doctors, cancer patients, differ

Vast majority of patients don't know their doctors held different opinions about the prognosis

Misunderstandings about prognosis between patients with advanced cancer and their doctors was common, in a study reported in JAMA Oncology, and the vast majority of patients didn't know that their doctors held different opinions about how long they might live.

"We've discovered two important things happening between oncologists and patients with advanced cancer," said co-author Ronald M. Epstein, M.D., professor of Family Medicine, Psychiatry, and Oncology at the University of Rochester Medical Center, and one of the nation's leading authorities on doctor-patient communications.

"First, some patients might know the doctor's prognosis estimate but the patient chooses to disagree, often because they believe other sources," Epstein said. "And second, some patients think that their doctor agrees with their opinion about prognosis but, in fact, the doctor doesn't."

"When people think they'll live a very long time with cancer despite evidence to the contrary, they may end up taking more aggressive chemotherapy and agreeing to be placed on ventilators or dialysis, paradoxically reducing their quality of life, keeping them from enjoying time with family and sometimes even shortening their lives," Epstein added. "So it's very important for doctors and patients to be on the same page."

Researchers surveyed 236 patients with stage 3 or 4 cancer whose doctors "would not have been surprised" if they died within a year and half of whom died within 16 months. Fewer than five percent would be alive in five years, according to medical evidence.

The 38 oncologists who treated these patients independently completed similar questionnaires to measure their own opinions about the patients' survival.

Doctors were asked: "What do you believe are the chances that this patient will live for 2 years or more?" Whereas the patients were asked: "What do you believe are the chances that you will live for 2 years or more?"

Additional survey questions gauged whether patients knew their prognosis opinions differed from their doctors, and to what extent treatment options were discussed in the context of life expectancy.

Among the 236 patients, 68 percent rated their survival prognosis differently than their oncologists. In nearly all cases the patients were more optimistic than their doctors. Of the 68 percent, only one in 10 realized that their opinions differed from their oncologists.

The study results highlight a difficult communications issue that arises often when the conversation is about cancer. Discordance almost always leans toward patients being overly optimistic, Epstein said.

"Of course, it's only possible for doctors to provide a ball-park estimate about life expectancy--and some people do beat the odds," Epstein said.

"Positive thinking by patients can improve quality of life. But when a patient with very advanced cancer says that he has a 90-100% chance of being alive in two years and his oncologist believes that chance is more like 10%, there's a problem."

The challenge, according to the researchers, is that talking about a cancer prognosis is not a straightforward exchange of information.

It occurs in the context of fear, confusion, and uncertainty, and in the best cases it should be carried out in several conversations about personal values and treatment goals.

But when doctor-patient communication is poor, it can result in mutual regret about end-of-life circumstances. For example, nearly all of the survey participants said they wanted to be involved in treatment decisions. And 70 percent said they preferred supportive care at the end of their lives as opposed to aggressive therapy--but, the study authors pointed out, making an informed decision requires knowing when death is approaching.

Another important finding was that non-white patients were much more likely than white patients to have expectations about their prognosis that were out of synch with their doctors.

However, the sample of non-white patients was small and included individuals from many different racial groups, which limited the researchers from drawing any conclusions.

The study had other limits, too, according to the authors. Researchers reported that they do not understand why discordant patients didn't know their oncologists' opinions and why it differed by race.

The scientists believe several factors could have been at play, such as patients not wanting to discuss prognosis, or having poor recall, or avoiding talk of death because of personal beliefs.

The study concluded that having differing opinions--especially when both sides don't realize they differ--is a marker for inadequate communication and calls for an "urgent clinical and societal need" to better understand what it means to communicate well.

The University of Rochester Center for Communication and Disparities Research in the Department of Family Medicine is among the few academic centers to extensively study this issue and propose improvements. Previously the group pinpointed and studied compassionate words and actions by doctors that could be used to guide medical education.

The Center is currently funded by the National Institutes of Health (NIH) to continue studying how to improve communication between physicians and patients with cancer.

Lead author of the JAMA paper, Robert E. Gramling, M.D., is a former associate professor at URMC who recently left to join the University of Vermont Medical Center as the Holly and Bob Miller Chair in Palliative Medicine at UVM. Gramling had been co-director of URMC's division of palliative care.

Other co-authors from the UR and the Wilmot Cancer Institute include Paul Duberstein, Ph.D.; Kevin Fiscella, M.D., M.P.H.; Supriya Mohile, M.D.; Sandy Plumb, B.S.; and collaborators from the University of California, Davis, and Tulane University in New Orleans.

http://www.eurekalert.org/pub_releases/2016-07/jgum-gfz071416.php

Genomes from Zagros mountains reveal different Neolithic ancestry of Europeans & South Asians

International research team led by Mainz palaeogeneticists demonstrates that populations in the ancient Fertile Crescent are the ancestors of modern day South Asians but not of Europeans

Sedentism, farming, and agriculture was invented some 10,000 years ago in a region between southeastern Anatolia, Iran, Iraq, and Syria, an area traditionally labeled as the Fertile Crescent. Most of the technology and culture associated with farming including domestic sheep, goat, cattle, and pig originated here. The transition from a hunter-gatherer lifestyle to agriculture and sedentism was considered such a radical change in human ecology that the term Neolithic revolution was coined for it. Some 2,000 years later, the new Neolithic lifestyle appeared in southeastern Europe and shortly afterwards in Central and Mediterranean Europe.

This is an approximately 10,000 year old skull from the Neolithic Tepe Abdul Hossein. **Courtesy Fereidoun Biglari, National Museum of Iran**

This week, an international research team led by palaeogeneticists of Johannes Gutenberg University Mainz (JGU) published a study in the journal Science showing that the earliest farmers from the Zagros mountains in Iran, i.e., the eastern part of the Fertile Crescent, are neither the main ancestors of Europe's first farmers nor of modern-day Europeans. "This came as a surprise," said Farnaz Broushaki, first author of the study and a member of the JGU Palaeogenetics Group. "Our team had only recently shown that early farmers from across Europe have an almost unbroken trail of ancestry leading back to northwest Anatolia. But now it seems that the chain of migration into Europe breaks somewhere in eastern Anatolia."

According to the team's previous study, Neolithic settlers from northern Greece and the Marmara Sea region of western Turkey reached central Europe via a Balkan route and the Iberian Peninsula via a Mediterranean route. These colonists brought sedentary life, agriculture, and domestic animals and plants to Europe. New research shows that some of the world's earliest farmers from Iran were a genetically distinct group and only very distantly related to the first farmers of western Anatolia and Europe.

"It is interesting that people who are genetically so different, who almost certainly looked different and spoke different languages adopted the agricultural lifestyle almost simultaneously in different parts of Anatolia and the Near East," said Professor Joachim Burger, senior author of the study. "The group of prehistoric inhabitants of the Zagros region separated more than 50,000 years ago from other people of Eurasia and were among the first who invented farming."

Professor Joachim Burger, his Mainz palaeogeneticist team, and international collaborators have pioneered palaeogenetic research of the Neolithization process in Europe over the last decade. In 2005, they presented the first ancient DNA study on prehistoric European farmers, and in 2009 and 2013 they analyzed their complex interactions with hunter-gatherers. Now they demonstrate that the idea of "ex oriente lux" is true in cultural but not in genetic terms.

The Fertile Crescent (shaded) on a political map of the Near and South East. In blue are the the archaeological sites in Iran with genomes from the Neolithic period that are ancestral to modern-day South Asians. In red are Neolithic sites with genomes that are ancestral to all European early farmers. **Ill./©: Joachim Burger, JGU**

Marjan Mashkour, an Iranian archaeozoologist who works at the CNRS in Paris and initiated the study with Burger and Fereidoun Biglari, a prehistoric archaeologist at the National Museum of Iran, added: "The Neolithic way of life originates in the Fertile Crescent, maybe also some Neolithic pioneers started

moving from there. But the majority of ancient Iranians did not move west as some would have thought."

However, they did move east, as the study shows. The research team found that the Iranian genomes represent the main ancestors of modern-day South Asians. Whilst sharing many segments of their genome with Afghani and Pakistani populations, the almost 10,000 year old genomes from the Iranian Zagros mountains were found to be most similar to modern-day Zoroastrians from Iran. "This religious group probably mixed less with later waves of people than others in the region and therefore preserved more of that ancient ancestry," said Broushaki.

In sum, it seems like at least two highly divergent groups became the world's first famers: the Zagros people of the Neolithic eastern Fertile Crescent that are ancestral to most modern South Asians and the Aegeans that colonized Europe some 8,000 years ago. "The origin of farming was genetically more complex than we thought and instead of speaking of a single Neolithic center, we should start adopting the idea of a Federal Neolithic Core Zone", emphasized Burger.

Farnaz Broushaki et al. Early Neolithic genomes from the eastern Fertile Crescent
Science, 14 July 2016 DOI: 10.1126/science.aaf7943
http://science.sciencemag.org/content/early/2016/07/13/science.aaf7943

http://www.eurekalert.org/pub_releases/2016-07/aaft-itz071116.php

Is the Zika epidemic in Latin America at its peak?

Model of virus transmission suggests that it may have already peaked

In this Policy Forum, Neil Ferguson et al. use results from a model of virus transmission to analyze the current Zika epidemic in Latin America, suggesting that it may have already peaked. Evidence increasingly suggests a causal link between Zika infection and microcephaly, as well as other serious congenital anomalies, prompting the World Health Organization to declare the Zika epidemic an international health concern in February 2016. Here, using a model incorporating factors that determine the scale and speed of emerging viral infection in naïve populations, Ferguson and colleagues estimate that the current epidemic in Latin America will be over in three years; they base this estimate largely on the transmissibility of Zika and the time between cycles of infection. After these three years have passed, herd immunity - a phenomenon by which a large percentage of a population becomes immune to an infection - will likely delay the next large Zika epidemic for more than a decade, the authors say. They also note that targeting mosquitos, the main culprit behind Zika spread, could actually be counterproductive, because this would interfere with herd immunity. As a key means to reduce fetal complications associated with Zika, health authorities are advising women to delay having children for several years, which the authors note is not feasible for all women; they recommend detailed local monitoring of the epidemic, so that local advisories and delayed pregnancies are more relevant and feasible.

In a Review also on Zika, Justin Lessler et al. summarize research to date on the virus, particularly that relevant to the latest outbreak in Latin America. As of June 2016, more than 35 countries throughout the Americas have reported local circulation of Zika. While Zika symptoms tend to be mild, the greatest concern surrounding the virus is its effects on a growing fetus. Microcephaly was the first fetal abnormality recognized, but there is increasing evidence that Zika may be responsible for other fetal complications, such as intracranial calcifications, ventriculomegaly, ocular impairment, brainstem hypoplasia, intrauterine growth restriction and fetal demise. The authors highlight studies in pregnant women infected with Zika who are symptomatic or asymptomatic, noting at what trimester they became infected; longer-term studies are ultimately required to understand Zika's impact on expectant mothers though, they say. The authors also discuss ways in which Zika may be expected to spread, but note that this can be difficult to predict. Dengue, a virus that is also transmitted by the same type of mosquito, has caused epidemics throughout the Americas, but has not achieved sustained transmission in the continental U.S., despite widespread vector presence. The reasons for dengue's limited spread in America may include not only climate but also differences in built environments and social factors, all of which are likely to affect Zika transmission as well. Human and mosquito genetics may play a role in how the current epidemic pans out. A Zika vaccine may be the best way to protect at-risk populations over the long term, the authors say.

http://www.eurekalert.org/pub_releases/2016-07/cioe-air071216.php

Artificial intelligence reveals undiscovered bat carriers of Ebola and other filoviruses

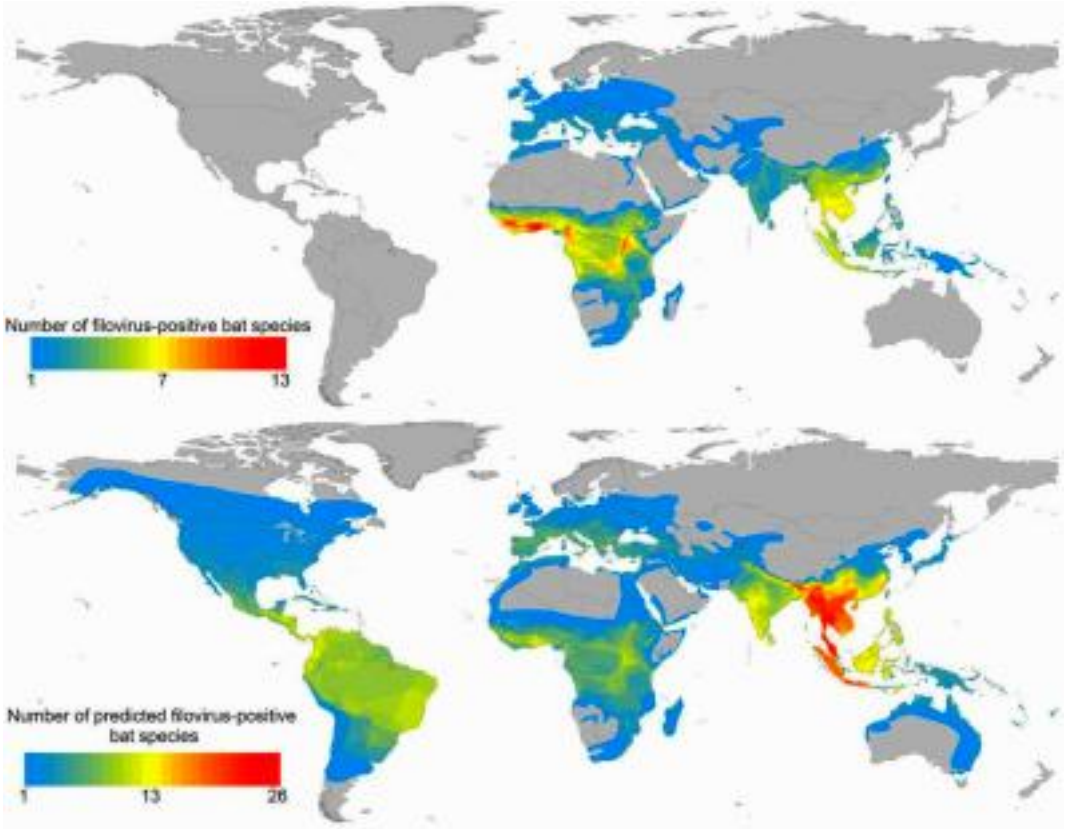
Maps pinpoint hotspots, can guide surveillance and virus discovery

Millbrook, NY - A team of scientists has developed a model that can predict bat species most likely to transmit Ebola and other filoviruses. Findings highlight new potential hosts and geographic hotspots worthy of surveillance. So reports a new paper in the journal PLoS Neglected Tropical Diseases.

Filoviruses have devastating effects on people and primates, as evidenced by the 2014 Ebola outbreak in West Africa. For nearly 40 years, preventing spillover events has been hampered by an inability to pinpoint which wildlife species harbor and spread the viruses. To date, outbreaks have occurred in areas with exceptionally high biodiversity.

Barbara Han, a disease ecologist at the Cary Institute of Ecosystem Studies and the paper's lead author, comments, "Using machine learning methods developed for artificial intelligence, we were able to bring together data from ecology, biogeography, and public health to identify bat species with a high probability of harboring Ebola and other filoviruses. Understanding which species carry these viruses, and where they are located, is essential to preventing future spillovers."

The research team included scientists from the University of Georgia, Massey University, and the University of California. They focused on bats - primary suspects in the search for Ebola reservoirs. While Ebola virus has never been isolated from a live African mammal in the wild, several bat species have tested positive for filovirus antibodies. In lab inoculations, three bat species have replicated Ebola. And, unlike great apes and humans, bats infected with filoviruses are largely symptom-free.



This is a map of known and predicted bat hosts of filoviruses, showing hotspots in Southeast Asia. **PLOS Neglected Tropical Diseases by Han et al. from the Cary Institute of Ecosystem Studies**

First, the team developed a 'profile' of filovirus-positive bat species by looking at life history, physiological, and ecological attributes of the 21 bat species known to harbor filoviruses. Using 57 variables, from diet and reproductive behavior to migratory patterns and species density, an algorithm learned features that distinguish bats that have tested positive for filoviruses from other bat species with 87% accuracy.

David Hayman of Massey University notes, "The model allows us to move beyond our own biases and find patterns in the data that only a machine can. Instead of predicting where Ebola and other filovirus outbreaks will occur by looking at the last spillover event, it forecasts risk based on the intrinsic traits of filovirus-positive bat species."

Those traits include: early maturity, having more than one pup per year (most bats only have one), offspring that are large at birth, and a tendency to live in large groups. Compared to other bats, filovirus-positive species also have broader geographic ranges that overlap with a higher diversity of mammal species per square kilometer.

When data on the world's 1116 bat species were searched using this filovirus-positive bat profile, machine learning identified new potential hosts based on their traits. Once mapped, these bats were more widely distributed than the team expected. While many potential bat hosts are found in sub-Saharan Africa, they also range across Southeast Asia and Central and South America.

Han explains, "Our results corroborate studies in Africa that have predicted the environmental niche of Ebola spans the primary tropical rainforest. But in a departure from past research, we identified several hotspots in Southeast Asia where up to 26 potential reservoir species overlap, notably in Thailand, Burma, Malaysia, Vietnam, and northeast India."

John Drake of the University of Georgia concludes, "Maps generated by the algorithm can help guide targeted surveillance and virus discovery projects. We suspect there may be other filoviruses waiting to be found. An outstanding question for future work is to investigate why there are so few filovirus spillover events reported for humans and wildlife in Southeast Asia compared to equatorial Africa."

Research is part of an ongoing effort to merge Big Data and machine learning to prioritize the surveillance and management of emerging infectious diseases globally. To access full text of the paper Undiscovered bat hosts of filoviruses visit: http://dx.plos.org/10.1371/journal.pntd.0004815.

http://www.eurekalert.org/pub_releases/2016-07/dumc-sto071316.php

Scientists trace origin cell of bone and soft tissue tumors, test drug target

Scientists at Duke Health are part of a team that has discovered a type of cell surrounding blood vessels can also serve as a starting point for sarcoma, a form of cancer that occurs in bones and connective tissues.

DURHAM, N.C. - The findings, made through studies of mice, offer insights that could aid in the development of potential new treatments for the rare but devastating cancer, which has 15,000 new diagnoses annually in the U.S.

In an article to be published online July 14 in the journal Cell Reports, the international team of researchers describe tracing the lineage of the cancer back to the pericyte, a cell that supports the body's blood vessels. According to the findings, genetic mutations in these cells led to osteosarcoma and soft-tissue sarcoma, as well as non-cancerous tumors.

"About half of all sarcomas in the U.S. affect people under 35," said senior author Benjamin Alman, M.D., chair of the Department of Orthopedic Surgery at Duke. "This cancer is difficult to treat, and for those who survive, they are living with the effects for decades. With new chemotherapies and surgery, we have seen long-term survival improve to about 60 to 65 percent, but advances have leveled off in recent years. We hope that by looking at the biological development of the tumor, we can come up with new ways to intervene."

Alman and fellow authors -- who represent Duke as well as the Hospital for Sick Children and Mount Sinai Hospital in Toronto, Tokyo Medical and Dental University Graduate School and Faculty of Medicine, and Seoul National University Hospital -- found that cancer cells contained less of a protein called beta catenin compared to the pericytes from which they originated. Alman said this suggests that at some point, the beta catenin was "turned off" in the cell.

When the researchers activated beta catenin in cells using lithium, a drug already used in patients, this appeared to limit the size and growth of the cancers that formed.

Previous studies of beta catenin in sarcoma cells lacked any means of comparison for determining whether levels were high or low, Alman said. By identifying the pericyte as a cell of origin, scientists now have baseline levels for comparison.

The researchers hope to further investigate the use of lithium to regulate beta catenin.

"Lithium has been tried in lung cancer treatments, so perhaps we could see it being used down the road to suppress sarcomas," Alman said. "It's premature to do clinical trials in humans at this point. The next step is to grow larger numbers of human sarcomas in mice and treat them with lithium to see whether this can stop or even shrink existing tumors."

In addition to Alman, study authors are Shingo Sato; Yuning J. Tang; Qingxia Wei; Makoto Hirata; Angela Weng; Ilkyu Han; Atsushi Okawa; Shu Takeda; Heather Whetstone; Puvindran Nadesan; David G. Kirsch; and Jay S. Wunder.

The research was supported by the National Institutes of Health (R01 CA183811), the Canadian Institutes for Health Research (FRN 123493), the Restracomp fellowship of the Hospital for Sick Children Research Training Centre, and grants for foreign study of KANAE Foundation for the Promotion of Medical Science. The authors also received assistance from Canada's Michael Smith Genome Sciences Center in Vancouver, which performed RNA sequencing analysis. The authors cited no conflicts of interest related to this work.

http://bit.ly/29Sr40X

Study points to fast-acting drug for OCD

Brain receptor acts as switch for OCD symptoms in mice

DURHAM, N.C. -- A single chemical receptor in the brain is responsible for a range of symptoms in mice that are reminiscent of obsessive-compulsive disorder (OCD), according to a Duke University study that appears online in the journal Biological Psychiatry.

The findings provide a new mechanistic understanding of OCD and other psychiatric disorders and suggest that they are highly amenable to treatment using a class of drugs that has already been investigated in clinical trials.

"These new findings are enormously hopeful for considering how to approach neurodevelopmental diseases and behavioral and thought disorders," said the study's senior investigator Nicole Calakos, M.D., Ph.D., an associate professor of neurology and neurobiology at the Duke University Medical Center.

OCD, which affects 3.3 million people in the United States, is an anxiety disorder that is characterized by intrusive, obsessive thoughts and repeated compulsive behaviors that collectively interfere with a person's ability to function in daily life.

In 2007, Duke researchers (led by Guoping Feng, who is now at the Massachusetts Institute of Technology) created a new mouse model of OCD by deleting a gene that codes for Sapap3, a protein that helps organize the connections between neurons so that the cells can communicate.

Similar to the way some people with OCD wash their hands excessively, the Sapap3-lacking mouse grooms itself excessively and shows signs of anxiety. Although researchers praised the new model for its remarkable similarity to a human psychiatric disorder, and have begun using it to study OCD, questions remain about how the loss of the Sapap3 gene leads to the grooming behaviors.

In the new study, Calakos's team found that overactivity of a single type of receptor for neurotransmitters -- mGluR5, found in a brain region involved in compulsive behaviors -- was the major driver for the abnormal behaviors. When

researchers gave Sapap3-lacking mice a chemical that blocks mGluR5, the grooming and anxiety behaviors abated.

"The reversibility of the symptoms was immediate -- on a minute time frame," Calakos said. In contrast, the original study describing Sapap3-lacking mice found that antidepressants could help treat symptoms but on the time scale of weeks, as is typical with these drugs in patients.

The immediate effects seen in the new study were also surprising, given that the brains of these mice appear developmentally immature and neurodevelopmental diseases are not typically thought of as being easily reversible, Calakos said.

Intriguingly, by taking normal laboratory mice and giving them a drug that boosted mGluR5 activity, Calakos's team could instantaneously recreate the same excessive grooming and anxiety behaviors they saw in the Sapap3-lacking mice.

The researchers found that without a functioning Sapap3 protein, the mGluR5 receptor is always on. That, in turn, makes the brain regions involved in compulsion overactive. In particular, a group of neurons that give the "green light" for an action, like face-washing, is working overtime. (These same neurons can promote a habit, such as eating sweets, according to a study published by Calakos's team earlier this year.)

Calakos said that mGluR5 should be considered for the treatment of compulsive behaviors. "But which people and which compulsive behaviors? We don't know yet," she added.

Other lines of research have explored targeting mGluR5 with drugs to move its activity up or down in the brain. For example, mGluR5-blockers are being considered for the treatment of Parkinson's disease. But because mGluR5 inhibitors have not always panned out in clinical trials, it may make sense to target different parts of the mGluR5 pathway or identify specific patient subsets, Calakos said. New non-invasive imaging technologies now make it possible to measure mGluR5 activity in humans.

Other authors on the study are Kristen Ade, Yehong Wan, Harold Hamann, Justin O'Hare, Weirui Guo, Anna Quian, Sunil Kumar, Srishti Bhagat, Ramona M. Rodriguiz, William Wetsel, P. Jeffrey Conn, Kafui Dzirasa, and Kimberly Huber.

The study was supported by the National Institutes of Health (NS064577, ARRA supplement to NS064577, NS04571, T32NS051156), the Brain and Behavioral Research Foundation, and the FRAXA Research Foundation.

CITATION: "Increased mGluR5 Signaling Underlies OCD-Like Behavioral And Striatal Circuit Abnormalities In Mice," Kristen K. Ade, Yehong Wan, Harold C. Hamann, Justin K. O'Hare, Weirui Guo, Anna Quian, Sunil Kumar, Srishti Bhagat, Ramona M. Rodriguiz, William C. Wetsel, P. Jeffrey Conn, Kafui Dzirasa, Kimberly M. Huber, and Nicole Calakos. Biological Psychiatry. DOI: 10.1016/j.biopsych.2016.04.023 Online: http://www.biologicalpsychiatryjournal.com/article/S0006-3223(16)32380-0/fulltext

http://www.eurekalert.org/pub_releases/2016-07/dmon-dmo071416.php

Denver Museum of Nature & Science curator discovers real reason turtles have shells

Dr. Tyler Lyson co-authors paper about turtle shells as a burrowing tool, not for protection as previously thought

DENVER, Colo. - It is common knowledge that the modern turtle shell is largely used for protection. No other living vertebrate has so drastically altered its body to form such an impenetrable protective structure as the turtle. However, a new study by an international group of paleontologists suggests that the broad ribbed proto shell on the earliest partially shelled fossil turtles was initially an adaptation, for burrowing underground, not for protection. Paleontologist Tyler Lyson from the Denver Museum of Nature & Science is among the scientists that helped make this discovery.

"Why the turtle shell evolved is a very Dr. Seuss-like question and the answer seems pretty obvious - it was for protection," said Dr. Lyson, lead author of Fossorial Origin of the Turtle Shell, which was released today by Current Biology. But just like the bird feather did not initially evolve for flight, the earliest beginnings of the turtle shell was not for protection but rather for digging underground to escape the harsh South African environment where these early proto turtles lived."

The early evolution of the turtle shell had long puzzled scientists. "We knew from both the fossil record and observing how the turtle shell develops in modern turtles that one of the first major changes toward a shell was the broadening of the ribs," said Dr. Lyson. While distinctly broadened ribs may not seem like a significant modification, it has a serious impact on both breathing and speed in quadrupedal animals. Ribs are used to support the body during locomotion and play a crucial role in ventilating the lungs. Distinctly broadened ribs stiffen the torso, which shortens an animals stride length and slows it down, interfering with breathing.

"The integral role of ribs in both locomotion and breathing is likely why we don't see much variation in the shape of ribs," said Dr. Lyson. "Ribs are generally pretty boring bones. The ribs of whales, snakes, dinosaurs, humans, and pretty much all other animals look the same. Turtles are the one exception, where they are highly modified to form the majority of the shell."

A big breakthrough came with the discovery of several specimens of the oldest (260- million-year-old) partially shelled proto turtle, Eunotosaurus africanus, from the Karoo Basin of South Africa. Several of these specimens were discovered by two of the study's coauthors, Drs. Roger Smith and Bruce Rubidge from the

University of Witwatersrand in Johannesburg. But the most important specimen was found by a then 8-year-old South African boy on his father's farm in the Western Cape of South Africa. This specimen, which is about 15 cm long, comprises a well preserved skeleton together with the fully articulated hands and feet.

"I want to thank Kobus Snyman and shake his hand because without Kobus both finding the specimen and taking it to his local museum, the Fransie Pienaar Museum in Prince Albert, this study would not have been possible," said Dr. Lyson.

The study includes authors from the United States, South Africa, and Switzerland.

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Man Gets Zika from Sex with Female Partner, in First

A woman in New York City who was infected with Zika passed the virus to her male partner during sex, marking the first report of female-to-male sexual transmission of this virus.

By Rachael Rettner, Senior Writer | July 15, 2016 03:32pm ET

Previously, all reports of sexual transmission of the Zika virus have been cases of men passing it to their sexual partners, according to the Centers for Disease Control and Prevention (CDC).

The new report "adds to the growing body of knowledge about the sexual transmission of Zika," the CDC said. "Ongoing surveillance is needed to determine the risk for transmission of Zika virus infection from a female to her sexual partners," the report said. [Zika Virus News: Complete Coverage of the 2016 Outbreak]

The woman, who is in her 20s and is not pregnant, had recently traveled to an area with ongoing Zika transmission, according to the report. (The Zika virus is currently spreading in many countries in Central and South America, as well as the Caribbean.)

The day the woman returned to New York City, she had sex with her male partner without using a condom. The next day, she had a fever, rash and joint pain, which are all symptoms of infection with Zika. The woman also started her period that day, and she reported it was heavier than usual. She soon went to the doctor, and a test detected the Zika virus in her blood and urine samples.

Six days after having sex, the woman's partner also developed symptoms of Zika, and he went to the same doctor that the woman had seen. Tests showed that the man also had Zika, and the doctor suspected that the man may have contracted the infection during sex.

An interview with the man confirmed that he had not been exposed to Zika in any other way; he had not traveled to a country where Zika is spreading, he had not been bitten by a mosquito (which can spread the virus), and he did not have any other recent sexual partners, the report said. The Zika virus is not known to spread through casual contact with an infected person, such as touching or hugging.

"The timing and sequence of events support female-to-male Zika-virus transmission through condomless, vaginal intercourse," the report said. Virus in either the vaginal fluids or menstrual blood could have infected the man during sex, the report said.

The CDC currently recommends that pregnant women either use condoms or abstain from sex if their partners have traveled to areas where Zika is spreading. Zika virus infection during pregnancy can cause a birth defect called microcephaly, or an abnormally small head and brain.

People who are not pregnant but who want to reduce their risk of contracting Zika through sex should use condoms or abstain from sex, the CDC said. The agency also said it is updating its guidelines on preventing Zika transmission through sex.

http://bit.ly/29Eomqw

First evidence that GM mosquitoes reduce disease

Releasing genetically modified mosquitoes appears to have helped reduce cases of dengue in a town in Brazil.

By Michael Le Page

The news comes as the US is considering whether to approve the use of the same mosquitoes. The trial involved *Aedes* mosquitoes that had been modified to kill off wild mosquitoes of the same species, and was carried out in the town of Piracicaba. Just by eliminating the standing water where the mosquitoes that carry dengue and other diseases like Zika breed, Piracicaba was able to halve the number of dengue cases during the 2015-16 dengue season, compared with last year. But in the areas where the GM mosquitoes were released too, cases of dengue fell by more than 90 per cent.

This result is significant because regulators have been demanding evidence that this control method not only reduces wild mosquito numbers – as previous trials have shown – but also brings down disease incidence.

Piracicaba has a population of 400,000 people, and the areas where the GM mosquitoes were trialed are home to only around 5,000. Although this small trial doesn't provide rigorous evidence of the standard that epidemiologists require, it shows potential, says Hadyn Parry, chief executive of Oxitec, the UK firm that developed the mosquitoes.

Florida next?

Independent experts agree. "It is very encouraging," says Philip McCall of the Liverpool School of Tropical Medicine in the UK. However, it is not a randomised controlled trial, he adds.

Oxitec is now working with the World Health Organisation to plan a much larger trial that will provide more rigorous evidence.

Their method involves releasing millions of mosquitoes – all of which are male, as these do not bite. These males seek out and mate with wild females, but have been genetically modified to ensure that any offspring they produce then die. Unlike with methods like insecticide fogging, no other wildlife is harmed.

Brazil is set to start commercially licensing this method for wider use, Parry says. The US Food and Drug Administration is considering whether to approve the technology. If it does, the Florida Keys will hold a referendum in November to decide whether to use it.

http://bit.ly/29EsKvK

Dinosaurs Literally Reshaped The Planet

Dinos didn't just leave behind footprints and fossil bones—they also changed the landscapes in which they lived

By Brian Switek

For over 130 million years, dinosaurs dominated life on land. They came in every shape and size, from feathery little carnivores the size of a pigeon to titans that stretched over 120 feet in length. But dinosaurs did far more than merely inhabit prehistoric floodplains, deserts and forests. Unbeknownst to them, dinosaurs permanently altered the face of our planet.

One of the best places to see the echoes of dinosaurs is in the Broome Sandstone of western Australia. Back in the Early Cretaceous, between 135 and 130 million years ago, this part of the continent's northern coast was covered in streams, swamps and lagoons. Large sauropod dinosaurs—think distant cousins of Apatosaurus—had to take care navigating between these mucky habitats, and as they did so they unknowingly changed the landscape around them.

The evidence is in the tracks. The Broome Sandstone, paleontologist Tony Thulborn pointed out in 2012, is dotted with foot-shaped potholes made by the trundling dinosaurs. In fact, the weight of these giants was so great that they deformed the sediment right beneath their feet to create what paleontologists call undertracks—think of them like ripples from each footfall pressed into stone. Many of these tracks and traces appear to cluster together, a sign of big dinosaurs following the same route around the edges of the lagoons, and in these places the dinosaurs made channels through the sand as they moved along the beach towards places where they might find more food. In a matter of weeks to months, flat shorelines were turned into stomping grounds cut through with dinosaur-made troughs.

The idea that dinosaurs were ancient landscapers shouldn't come as a surprise. Large animals alive today, such as elephants and giraffes, can change entire environments merely by walking and eating. Given that elephants often push over trees during their foraging, for example, a habitat with elephants will be more open and sparse-looking than a place where trees aren't regularly being toppled. And as animals walk along the same routes to water or food sources, they trample down paths that wouldn't otherwise exist.

Still, knowing that dinosaurs changed their world and understanding how they did so are two different things. Detecting these clues often fall in the realm of ichnology, or the study of trace fossils made by the activities of living animals, and Emory College paleontologist Anthony Martin is one of the experts looking at these clues.

Not all the transformations are as massive as huge herbivores warping the ground beneath their feet. A dinosaur simply trying to climb a steep hill could have made significant changes. "Dinosaurs are blamed for causing small avalanches by walking on dunes in the Early Jurassic," Martin says, fossils of which are preserved in the rocks of Utah. Tracks in petrified dunes, Martin says, "show where each step taken by dinosaurs on the sides of dunes triggered a collapse of sand underneath." Maybe not a big deal to a dinosaur, but enough to alter the shape of the dunes that plants, invertebrates, and other organisms lived in.

A reproduction Maiasaura nest. Dino nests like these would have, over time, transformed flat floodplains into bumpy landscapes.

Walking wasn't the only way dinosaurs changed the land. Some dinosaur species—including the famous "good mother lizard" Maiasaura—deposited their eggs in vast nesting grounds. These places, Martin says, "likely turned river floodplains and other formerly flat places into very bumpy ones," especially if dinosaurs returned season after season to make bowls to cradle their eggs. The appropriately-named Egg Mountain is a perfect place to see this. This 76-million-year-old spot in the Montana badlands was home to dozens of nests made by Maiasaura, each one dug out of the earth to nestle a clutch of eggs. Other nesting sites made by other dinosaurs—such as those found in Patagonia and India—would also have transformed level places into open, bumpy swaths of land as dinosaurs returned season after season to the same nests, as stacked nests at some sites show.

Even dinosaur dance moves could have changed the surface of the planet. Earlier this year paleontologists reported on strange fossil scratch marks that the researchers interpreted as possible signs of mating dances that theropod dinosaurs akin to Allosaurus used to woo each other, like some modern birds do. The changes all the strutting caused wouldn't have been quite so dramatic as a nesting ground or sauropod herd navigating the edge of a lagoon. Yet, Martin says, "I

suppose these might have locally increased soil erosion if any of those theropods were really bad dancers."

We might think of Earth-changing forces as large-scale phenomena like earthquakes thrusting up rock towards the surface, tsunamis changing the shape of coastlines, and even the slow grind of continental drift. Yet the dinosaurs remind us that life itself has helped to make our planet what it is. Whether scratching at the soil, trodding over the sand in search of greener pastures or slipping on sand dunes, dinosaurs changed the shape of Earth.

http://medicalxpress.com/news/2016-07-world-alzheimer-vaccine.html

Progress in world's first Alzheimer's vaccine

Breakthrough discovery of a new and potentially effective vaccine targeting the pathological proteins associated with Alzheimer's disease

With more than 7.5 million new cases of Alzheimer's disease a year, the race to find a vaccine and effective treatment for dementia is growing by the day.

Now, researchers in the U.S. and Australia have made a breakthrough discovery in the international quest to discover a new and potentially effective vaccine targeting the pathological proteins associated with Alzheimer's disease (AD), the most common cause of dementia in the elderly.

In research findings just released in Nature's Scientific Reports journal, Flinders University experts, as part of a high-level U.S. research team at the Institute of Molecular Medicine (IMM) and University of California, Irvine (UCI), have made a successful vaccine formulation that targets the abnormal beta-amyloid and tau proteins that signal Alzheimer's disease. With more than 48 million dementia cases in 2015, Alzheimer's is emerging as one of the costliest to the world's health care systems, especially in mature economies in Western countries.

The World Health Organisation has projected the total global societal cost of dementia-related illnesses and care at more than $US600 billion a year.

"If we are successful in pre-clinical trials, in three to five years, we could be well on the way to one of the most important developments in recent medical history," says Flinders University School of Medicine Professor Nikolai Petrovsky, director of South Australian vaccine research company Vaxine Pty Ltd.

"Along with our rapidly aging populations, we now know that the explosion in type 2 diabetes in the West is likely to further dramatically fuel the projected rise in the number of cases of dementia globally, with diabetes being the major risk factor for Alzheimer's disease," Professor Petrovsky says.

The scale of the dementia problem has seen the U.S. Congress commit a further $US350 million to the National Institutes of Health (NIH) for research into Alzheimer's disease, taking research funding in the US to more than $US1.3 billion this year.

With NIH and Alzheimer's Association funding, the U.S. researchers say they have developed an "exceptional" universal vaccine platform, called MultiTEP, to target the hallmark proteins, aberrant forms of AB and tau proteins.

β-amyloid (AB) is a protein found to be prominent in driving Alzheimer's disease, but the accumulation of pathological tau also correlates with the formation of dementia in Alzheimer's patients.

Using a combination of anti-amyloid-beta and anti-tau vaccines with powerful and safe adjuvant technology called Advax developed by Vaxine Pty Ltd "shows promise for both preventive and therapeutic approaches in AD," Professor David Cribbs told Bloomberg news agency in the U.S.

Professor Michael Agadjanyan, head of IMM Department of Molecular Immunology, says the MultiTEP platform-based vaccines "do not induce potentially harmful auto-reactive cellular immune responses, while still generating antibodies that bind strongly to the amyloid and tau pathological molecules in brain tissue from AD patients."

Co-author of the latest paper, IMM Department of Molecular Immunology, Associate Professor Anahit Ghochikyan, says, "This study suggests that we can immunise patients at the early stages of AD, or even healthy people at risk for AD, using our anti-amyloid-beta vaccine, and, if the disease progresses, then vaccinate with another anti-tau vaccine to increase effectiveness."

She says the cooperative studies with National Institute of Aging IMM scientists and collaborators from UCI and the University of Southern California are working with experts from four companies to conduct non-clinical safety-toxicology studies to fulfil US Government safety standards for the Investigational New Drug application. After completion of these pre-clinical studies, they plan to test the immunogenicity and efficacy of the new vaccines in human trials.

Cutting-edge research company Vaxine Pty Ltd is internationally renowned for developing the world's first swine flu vaccine during the 2009 pandemic and is active on other fronts including Ebola and Zika virus research.

The vaxine is funded by the U.S. NIH to develop novel compounds called adjuvants that play a critical role in maximising vaccine effectiveness. The Vaxine Advax adjuvant technology is a key component in the development of IMM's Alzheimer's vaccine.

Explore further: Alzheimer's vaccine cures memory of mice

More information: Hayk Davtyan et al. Alzheimer's disease AdvaxCpG- adjuvanted MultiTEP-based dual and single vaccines induce high-titer antibodies against various forms of tau and Aβ pathological molecules, Scientific Reports (2016). DOI: 10.1038/srep28912

Journal reference: Scientific Reports search and more info

http://bit.ly/29FWrZQ

Cinnamon converts poor learning mice to good learners—implications for memory improvement

New study suggests cinnamon might improve learning ability

July 15, 2016 by Deb Song

Cinnamon is a delicious addition to toast, coffee and breakfast rolls. Eating the tasty household spice also might improve learning ability, according to new study results published online in the July issue of the Journal of Neuroimmune Pharmacology.

The study by neurological scientists at Rush University Medical Center found that feeding cinnamon to laboratory mice determined to have poor learning ability made the mice better learners.

"This would be one of the safest and the easiest approaches to convert poor learners to good learners," said Kalipada Pahan, PhD, the lead researcher of the study and the Floyd A. Davis Professor of Neurology at Rush.

Some people are born naturally good learners, some become good learners by effort, and some find it hard to learn new tasks even with effort. Little is known about the neurological processes that cause someone to be a poor learner and how to improve performance in poor learners.

"Understanding brain mechanisms that lead to poor learning is important to developing effective strategies to improve memory and learning ability," Pahan said.

Cinnamon role reversal

The key to gaining that understanding lies in the hippocampus, a small part in the brain that generates, organizes and stores memory. Researchers have found that the hippocampus of poor learners has less CREB (a protein involved in memory and learning) and more alpha5 subunit of GABAA receptor or GABRA5 (a protein that generates tonic inhibitory conductance in the brain) than good learners.

The mice in the study received oral feedings of ground cinnamon, which their bodies metabolized into sodium benzoate, a chemical used as a drug treatment for brain damage. When the sodium benzoate entered the mice's brains, it increased CREB, decreased GABRA5, and stimulated the plasticity (ability to change) of hippocampal neurons.

These changes in turn led to improved memory and learning among the mice.

"We have successfully used cinnamon to reverse biochemical, cellular and anatomical changes that occur in the brains of mice with poor learning," Pahan said.

The researchers used a Barnes maze, a standard elevated circular maze consisting of 20 holes, to identify mice with good and bad learning abilities. After two days of training, the mice were examined for their ability to find the target hole. They tested the mice again after one month of cinnamon feeding.

The researchers found that after eating their cinnamon, the poor learning mice had improved memory and learning at a level found in good learning mice. However, they did not find any significant improvement among good learners by cinnamon.

"Individual difference in learning and educational performance is a global issue," Pahan said. "We need to further test this approach in poor learners. If these results are replicated in poor learning students, it would be a remarkable advance."

Cinnamon also may aid against Parkinson's disease

Cinnamon has been a sweet spot for Pahan's research. He and his colleagues previously that cinnamon can reverse changes in the brains of mice with Parkinson's disease.

These studies have made the researchers spice connoisseurs: They used mass spectrometric analysis to identify the purer of the two major types of cinnamon widely available in the United States—Chinese cinnamon (Cinnamonum cassia) and original Ceylon cinnamon.

"Although both types of cinnamon are metabolized into sodium benzoate, we have seen that Ceylon cinnamon is much more pure than Chinese cinnamon, as the latter contains coumarin, a hepatotoxic (liver damaging) molecule," Pahan said.

The study of cinnamon and learning ability was supported by grants from National Institutes of Health, the U.S. Department of Veterans Affairs and the Alzheimer's Association.

Explore further: Potential impact of cinnamon on multiple sclerosis studied

More information: Khushbu K. Modi et al. Cinnamon Converts Poor Learning Mice to Good Learners: Implications for Memory Improvement, Journal of Neuroimmune Pharmacology (2016). DOI: 10.1007/s11481-016-9693-6

http://wapo.st/2a83Zcb

One striking chart shows why pharma companies are fighting legal marijuana

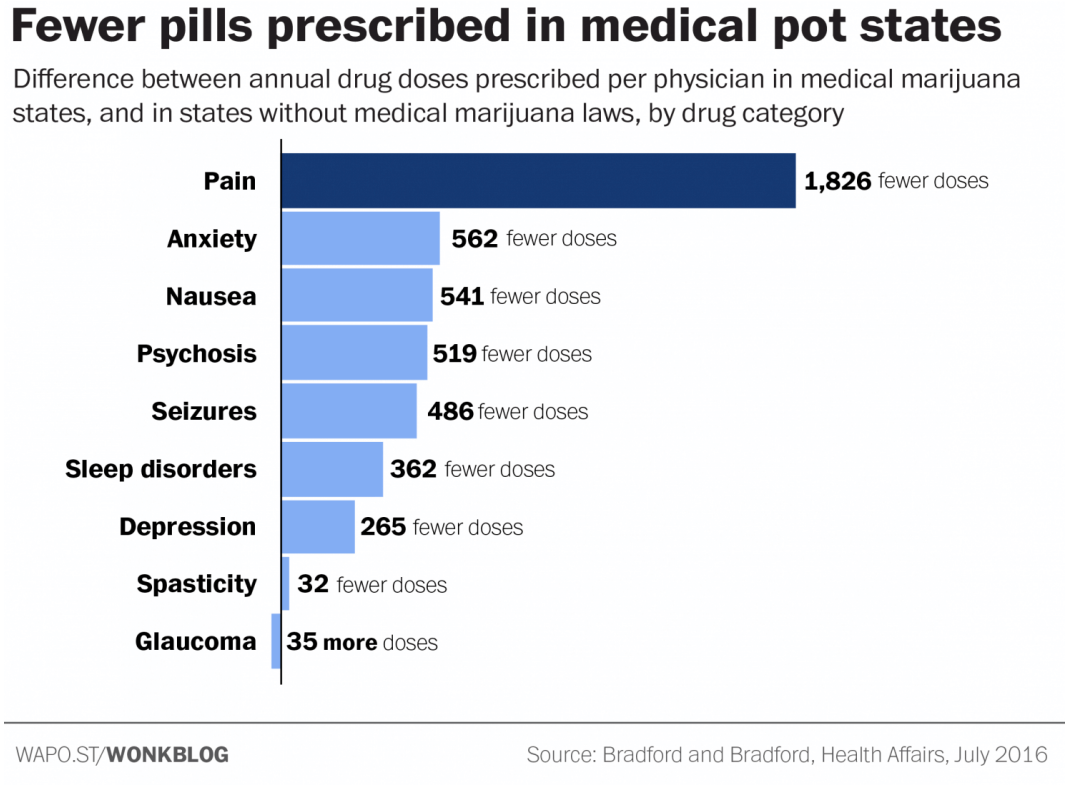
There's a body of research showing that painkiller abuse and overdose are lower in states with medical marijuana laws.

By Christopher Ingraham July 13

These studies have generally assumed that when medical marijuana is available, pain patients are increasingly choosing pot over powerful and deadly prescription narcotics. But that's always been just an assumption.

Now a new study, released in the journal Health Affairs, validates these findings by providing clear evidence of a missing link in the causal chain running from medical marijuana to falling overdoses. Ashley and W. David Bradford, a daughter-father pair of researchers at the University of Georgia, scoured the database of all prescription drugs paid for under Medicare Part D from 2010 to 2013.

They found that, in the 17 states with a medical-marijuana law in place by 2013, prescriptions for painkillers and other classes of drugs fell sharply compared with states that did not have a medical-marijuana law. The drops were quite significant: In medical-marijuana states, the average doctor prescribed 265 fewer doses of



antidepressants each year, 486 fewer doses of seizure medication, 541 fewer anti-nausea doses and 562 fewer doses of anti-anxiety medication.

But most strikingly, the typical physician in a medical-marijuana state prescribed 1,826 fewer doses of painkillers in a given year.

These conditions are among those for which medical marijuana is most often approved under state laws. So as a sanity check, the Bradfords ran a similar analysis on drug categories that pot typically is not recommended for — blood thinners, anti-viral drugs and antibiotics. And on those drugs, they found no changes in prescribing patterns after the passage of marijuana laws.

"This provides strong evidence that the observed shifts in prescribing patterns were in fact due to the passage of the medical marijuana laws," they write.

In a news release, lead author Ashley Bradford wrote, "The results suggest people are really using marijuana as medicine and not just using it for recreational purposes."

One interesting wrinkle in the data is glaucoma, for which there was a small increase in demand for traditional drugs in medical-marijuana states. It's routinely listed as an approved condition under medical-marijuana laws, and studies have shown that marijuana provides some degree of temporary relief for its symptoms.

The Bradfords hypothesize that the short duration of the glaucoma relief provided by marijuana — roughly an hour or so — may actually stimulate more demand in traditional glaucoma medications. Glaucoma patients may experience some short-term relief from marijuana, which may prompt them to seek other, robust treatment options from their doctors.

The tanking numbers for painkiller prescriptions in medical marijuana states are likely to cause some concern among pharmaceutical companies. These companies have long been at the forefront of opposition to marijuana reform, funding research by anti-pot academics and funneling dollars to groups, such as the Community Anti-Drug Coalitions of America, that oppose marijuana legalization.

Pharmaceutical companies have also lobbied federal agencies directly to prevent the liberalization of marijuana laws. In one case, recently uncovered by the office of Sen. Kirsten Gillibrand (D-N.Y.), the Department of Health and Human Services recommended that naturally derived THC, the main psychoactive component of marijuana, be moved from Schedule 1 to Schedule 3 of the Controlled Substances Act — a less restrictive category that would acknowledge the drug's medical use and make it easier to research and prescribe. Several months after HHS submitted its recommendation, at least one drug company that manufactures a synthetic version of THC — which would presumably have to compete with any natural derivatives — wrote to the Drug Enforcement Administration to express opposition to rescheduling natural THC, citing "the abuse potential in terms of the need to grow and cultivate substantial crops of marijuana in the United States."

The DEA ultimately rejected the HHS recommendation without explanation.

In what may be the most concerning finding for the pharmaceutical industry, the Bradfords took their analysis a step further by estimating the cost savings to Medicare from the decreased prescribing. They found that about $165 million was saved in the 17 medical marijuana states in 2013. In a back-of-the-envelope

calculation, the estimated annual Medicare prescription savings would be nearly half a billion dollars if all 50 states were to implement similar programs.

"That amount would have represented just under 0.5 percent of all Medicare Part D spending in 2013," they calculate.

Cost-savings alone are not a sufficient justification for implementing a medical-marijuana program. The bottom line is better health, and the Bradfords' research shows promising evidence that medical-marijuana users are finding plant-based relief for conditions that otherwise would have required a pill to treat.

"Our findings and existing clinical literature imply that patients respond to medical marijuana legislation as if there are clinical benefits to the drug, which adds to the growing body of evidence suggesting that the Schedule 1 status of marijuana is outdated," the study concludes.

One limitation of the study is that it only looks at Medicare Part D spending, which applies only to seniors. Previous studies have shown that seniors are among the most reluctant medical-marijuana users, so the net effect of medical marijuana for all prescription patients may be even greater.

The Bradfords will next look at whether similar patterns hold for Medicai