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Focused ultrasound shows promise for treating Parkinson's tremor

Study examines potential of scalpel-free surgery to manage tremor

An initial test to determine if a scalpel-free form of brain surgery can reduce tremor caused by Parkinson's disease has produced encouraging results. Further research is warranted, the researchers conclude in a paper published today by the scientific journal JAMA Neurology.

The small pilot study was led by Jeff Elias, MD, of the University of Virginia School of Medicine, and also was conducted at Swedish Neuroscience Institute in Seattle.

Twenty-seven participants with tremor-dominant Parkinson's disease were enrolled in the study; the research team randomly assigned 20 to be treated with focused ultrasound waves on their brains, while the others received a fake procedure, to account for any potential placebo effect. (They were later offered the opportunity to have the actual procedure). All had tremor that had resisted medical treatment, and all continued taking their existing Parkinson's medication.

The trial participants who received the focused ultrasound procedure had a 62 percent median improvement in their hand tremor three months later. Those who underwent a sham procedure also improved to a lesser degree, however, suggesting some placebo effect. Additional testing is needed to better establish the effectiveness of focused ultrasound for Parkinson's tremor, the researchers concluded.

The median age of trial participants was 67.8 years, and 26 were male. The most significant side effects reported were mild numbness on one side of the body, which improved, and numbness of the face and finger, which were persistent. Two subjects also experienced partial weakness that recovered or improved during the study. (The procedure has since been modified to mitigate this risk of weakness, the researchers say.)

The full paper is available to read at JAMA Neurology for free.

About Focused Ultrasound

Focused ultrasound already has been approved by the U.S. Food and Drug Administration for the treatment of essential tremor, the most common movement disorder. That approval came after Elias and his colleagues at UVA pioneered the approach. Other researchers are also evaluating focused ultrasound's potential for treating many other conditions, including breast cancer, brain tumors, epilepsy and pain.

The technology works by focusing sound waves inside the body to generate a tiny hot spot, much like a magnifying glass focuses light. By carefully controlling this process, researchers can interrupt faulty brain circuits or destroy unwanted tissue. Unlike traditional brain surgery, there is no need to drill or cut into the skull.

Magnetic resonance imaging lets them monitor the location and intensity of the procedure in real time, an important safety feature when making permanent changes to the brain.

Next Steps

The researchers believe that a larger, multicenter study is needed to better define the potential role of focused ultrasound in managing Parkinson's disease.

"Our findings suggest that the patients likely to benefit from this approach are those for whom tremor reduction is enough to improve their quality of life," said UVA researcher Binit Shah, MD.

To learn more about focused ultrasound at UVA, visit uvahealth.com/focusedultrasound. To keep up with all the latest developments and research breakthroughs from UVA, subscribe to the Making of Medicine blog at makingofmedicine.virginia.edu.

About the Parkinson's Research

The research team consisted of Aaron E. Bond, Shah, Diane S. Huss, Robert F. Dallapiazza, Amy Warren, Madaline B. Harrison, Scott A. Sperling, Xin-Qun Wang, Ryder Gwinn, Jennie Witt, Susie Ro and Elias.

The research was supported by the Focused Ultrasound Foundation, the Commonwealth of Virginia, Diane and David Heller, Robert and Molly Hardie and the Prince Charitable Trust.

http://bit.ly/2zplroq

Wait a minute! Clamping the umbilical cord later saves preterm babies' lives

Preterm babies could be saved by waiting before clamping the umbilical cord after birth instead of clamping it immediately

Thousands of preterm babies could be saved by waiting 60 seconds before clamping the umbilical cord after birth instead of clamping it immediately - according to two international studies coordinated by the University of Sydney's National Health and Medical Research Council Clinical Trials Centre.

Approved for publishing in the American Journal of Obstetrics and Gynecology, the review led by University of Sydney researchers, assessed morbidity and mortality outcomes from 18 trials comparing delayed versus immediate cord clamping in nearly 3,000 babies born before 37 weeks' gestation. It found clear evidence that delayed clamping reduced hospital mortality by a third and is safe for mothers and pre-term infants.

The review also reported that delayed clamping reduced subsequent blood transfusions and increased neonatal hematocrit, confirming that placental transfusion occurred. "The review shows for the first time that simply clamping the cord 60 seconds after birth improves survival," said the University of Sydney's Professor William Tarnow-Mordi, senior author. "It confirms international guidelines recommending delayed clamping in all preterm babies who do not need immediate resuscitation."

"We estimate that for every thousand very preterm babies born more than ten weeks early, delayed clamping will save up to 100 additional lives compared with immediate clamping," said the University of Sydney's Associate Professor David Osborn, the review's lead author and a neonatal specialist at Royal Prince Alfred Hospital. "This means that, worldwide, using delayed clamping instead of immediate clamping can be expected to save between 11,000 and 100,000 additional lives every year."

The systematic review confirms new findings from the Australian Placental Transfusion Study, published this week in the New England Journal of Medicine, reporting that delayed clamping might reduce mortality before 36 weeks - tentative evidence that required confirmation by an updated review of all relevant trials.

The Australian Placental Transfusion Study enrolled 1,566 babies born over ten weeks early in 25 hospitals in seven countries. The authors reported a 6.4 percent mortality rate in the delayed clamping group compared to 9 percent mortality rate in the immediate clamping group (p=0.03 in unadjusted analyses; p=0.39 after post-hoc adjustment for multiple secondary outcomes).

The University of Sydney's Professor Jonathan Morris, co-author of the Australian Placental Transfusion Study said: "This is so significant as it is such a simple technique, suitable for almost all preterm babies that helps saves lives".

Co-author of the Australian Placental Transfusion Study, Professor Roger Soll of the University of Vermont College of Medicine, added "About 15 million babies are born before 37 weeks gestation annually and one million die. This procedure costs nothing and will make a difference to families worldwide."

Chancellor of the University of Sydney, Belinda Hutchinson AM said the research is a breakthrough for families like hers who have experienced the emotional and physical impact of preterm birth. "This is a cause which is very important to me, with my own granddaughter born at 28 weeks. She is now a vibrant three year old but I know many others don't have such a great outcome which is why research in this area is so vital."

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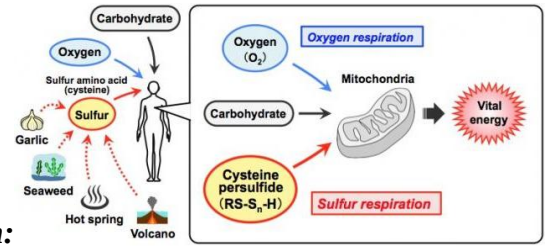
Sulfur respiration in mammals

Common sulfur metabolite with antioxidant activity appears to be formed with the help of an enzyme found in mitochondria

A common sulfur metabolite having antioxidant activity appears to be formed with the help of an enzyme found in mitochondria,

highlighting a potential area of research for future treatments of various diseases.

Researchers have gained new insight into the formation of a group of compounds found in almost all organisms, which are reportedly shown to be a powerful antioxidant that protects cells from damage by free radicals. They found that these compounds were also essential in supporting the mitochondrial energy metabolism, which is known as sulfur respiration, and identified it for the first time in humans and other mammals.



This is a diagram of sulfur respiration: oxygen-independent energy production system in mammals. **Takaaki Akaike**

The compounds, such as cysteine hydropersulfide (CysSSH) and other persulfides, are widely present in the cells of most organisms, from single-celled to humans, and even in the natural environment and foodstuffs. They are believed to act as an antioxidant that protects cells from harmful free radicals, which are byproducts of normal cell activity or pollutants, and can cause various diseases such as cancer. However, how these reactive sulfur molecules are formed, or what role they play exactly within these cells, has not been well understood.

A team of researchers from Tohoku University, working with colleagues in Japan, Hungary, the United Kingdom, and the United States, homed in on one pathway for the formation of CysSSH inside cells, publishing their findings in Nature Communications. They found that the amino acid L-cysteine acted as a starting building block for the synthesis of CysSSH, through a reaction catalyzed by cysteinyl-tRNA synthetases (CARSs), a family of enzymes present in most mammalian cells.

There are two different types of CARS enzymes: one is present in the cytoplasm of the cells and the other within mitochondria. The researchers inactivated genes that produce the enzyme variants in both mice and humans. They found that the enzyme within the mitochondria is responsible for producing the majority of CysSSH and other persulfides.

After the enzyme is produced inside the mitochondria, it travels outside to the cell's cytoplasm where it catalyzes the reaction that produces CysSSH, the researchers found. The enzyme inside the mitochondria is also responsible for producing energy and maintaining mitochondria, which is often called the powerhouse of the cells.

By identifying the dual roles that CARSs play, the researchers revealed their importance in antioxidant defense and energy production. They allow a pathway within the cells that support sulfur respiration without the need for oxygen. This could possibly pave the way for research on how the enzymes could help treat diseases resulting from an increase in oxidants or through mitochondria dysfunction, such as diabetes, chronic obstructive pulmonary disease (COPD), atherosclerosis, and cardiovascular disease. This could prolong life and increase the quality of life and may even provide new venues for cancer diagnosis, prevention and treatment.

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Alzheimer's disease might be a 'whole body' problem

Amyloid-beta can travel, cancer-like, to brain from other parts of body

Alzheimer's disease, the leading cause of dementia, has long been assumed to originate in the brain. But research from the University of British Columbia and Chinese scientists indicates that it could be triggered by breakdowns elsewhere in the body.

The findings, published today in Molecular Psychiatry, offer hope that future drug therapies might be able to stop or slow the disease without acting directly on the brain, which is a complex, sensitive and often hard-to-reach target. Instead, such drugs could target the kidney or liver, ridding the blood of a toxic protein before it ever reaches the brain. The scientists demonstrated this cancer-like mobility through a technique called parabiosis: surgically attaching two specimens together so they share the same blood supply for several months.

UBC Psychiatry Professor Dr. Weihong Song and Neurology Professor Yan-Jiang Wang at Third Military Medical University in Chongqing attached normal mice, which don't naturally develop Alzheimer's disease, to mice modified to carry a mutant human gene that produces high levels of a protein called amyloid-beta. In people with Alzheimer's disease, that protein ultimately forms clumps, or "plaques," that smother brain cells.

Normal mice that had been joined to genetically modified partners for a year "contracted" Alzheimer's disease. Song says the amyloid-beta traveled from the genetically-modified mice to the brains of their normal partners, where it accumulated and began to inflict damage.

Not only did the normal mice develop plaques, but also a pathology similar to "tangles" - twisted protein strands that form inside brain cells, disrupting their function and eventually killing them from the inside-out. Other signs of Alzheimer's-like damage included brain cell degeneration, inflammation and microbleeds. In addition, the ability to transmit electrical signals involved in learning and memory - a sign of a healthy brain - was impaired, even in mice that had been joined for just four months.

Besides the brain, amyloid-beta is produced in blood platelets, blood vessels and muscles, and its precursor protein is found in several other organs. But until these experiments, it was unclear if amyloid-beta from outside the brain could contribute to Alzheimer's disease. This study, Song says, shows it can.

"The blood-brain barrier weakens as we age," says Song, a Canada Research Chair in Alzheimer's Disease and the Jack Brown and Family Professor. "That might allow more amyloid beta to infiltrate the brain, supplementing what is produced by the brain itself and accelerating the deterioration."

Song, head of UBC's Townsend Family Laboratories, envisions a drug that would bind to amyloid-beta throughout the body, tagging it biochemically in such a way that the liver or kidneys could clear it.

"Alzheimer's disease is clearly a disease of the brain, but we need to pay attention to the whole body to understand where it comes from, and how to stop it," he says.

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Mini-strokes can be 'ominous prelude' to catastrophic strokes

Each year, more than 200,000 Americans experience mini-strokes called transient ischemic attacks (TIAs).

MAYWOOD, IL - Patients suffer stroke-like symptoms such as paralysis on one side or difficulty speaking. While symptoms typically go away in less than a few minutes and there's no brain damage, TIAs often are followed by severe strokes.

TIAs are an "ominous prelude" to an impending cerebrovascular catastrophe, but also the opportunity to prevent a disabling event," Loyola Medicine neurologists Camilo R. Gomez, MD, Michael J. Schneck, MD and José Biller, MD report in the journal F1000 Research. However, the neurologists add that rapid evaluation and treatment can reduce the risk of stroke by about 80 percent during the dangerous first week following a TIA.

Most strokes are ischemic, meaning they are caused by blood clots that block blood flow to a part of the brain. TIAs also are caused by blood clots, but the clots quickly dissolve or are dislodged. However, there's a 5 to 10 percent risk of suffering a stroke during the 30 days following a TIA, and 15 to 20 percent of ischemic stroke patients report having experienced an earlier TIA.

A TIA requires urgent management, but there is controversy about how to accomplish this: Should patients be temporarily hospitalized, which may be safer, or should they be evaluated on an outpatient basis, which may be more convenient and cost effective? The existing literature is inconclusive. "Both approaches have advantages and disadvantages," the Loyola neurologists wrote.

Traditionally, TIA patients have been admitted for a 23-hour observation period after they come to the emergency department. A

recent alternative is to refer patients to a "TIA clinic", where they are quickly seen by a stroke neurologist, undergo diagnostic tests and have access to a multidisciplinary network of cardiologists, neurosurgeons, vascular surgeons and other relevant specialists.

Therapeutic strategies include antiplatelet therapy (aspirin and other drugs that stop blood cells called platelets from sticking together and forming a clot); Coumadin and other blood thinners; surgery or stent placement to open clogged arteries; therapy to control blood pressure and cholesterol; diabetes screening; and patient education.

"Patients must be counselled about smoking cessation, proper diet (preferably Mediterranean), regular exercise, maintenance of appropriate BMI (body mass index) and limiting alcohol consumption," Drs. Gomez, Schneck and Biller wrote.

The Loyola neurologists, who all specialize in stroke care, concluded: "The diagnosis of a TIA represents the recognition of a medical emergency and an opportunity to reduce the risk of stroke by decisively evaluating the patient and applying any combination of the currently available therapeutic strategies. The future is likely to show additional methods of early diagnosis, better algorithms for stroke risk stratification and enhanced systems of care for these patients."

Drs. Gomez and Schneck are professors and Dr. Biller is professor and chair of Loyola Medicine's department of neurology. Their paper is titled, "Recent advances in the management of transient ischemic attacks."

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Smallpox-Related Viruses Are Still a Threat to Humans, Experts Warn

Smallpox has been eradicated for decades, but other, related "poxviruses" are still around and continue to pose a risk to humans, experts say.

By Rachael Rettner, Senior Writer | October 31, 2017 12:46pm ET

In fact, cases of human infection with viruses in the same family as the smallpox virus are appearing in growing numbers.

What's more, in recent years, researchers have discovered several never-before-seen poxviruses that cause illness in people. In one case, a woman in Alaska who thought she had a spider bite turned out to have an infection with a new poxvirus, and doctors never determined exactly how she became infected.

"Poxviruses continue to pose a threat," Dr. Brett Petersen, a medical officer at the Centers for Disease Control and Prevention (CDC) Poxvirus and Rabies Branch, said during a talk at an infectious disease conference called IDWeek, held in San Diego earlier this month. For this reason, there is a "need for continued vigilance and increased surveillance" for cases of poxviruses, Petersen said.

Poxviruses are oval or brick-shaped viruses with large genomes, according to the CDC. Infections with poxviruses typically cause skin lesions or rashes. Perhaps the most famous poxvirus, the variola virus, causes smallpox, a highly contagious and sometimes fatal disease that was declared eradicated from the world in 1980 thanks to a global vaccination campaign, according to the World Health Organization. (Eradication means that cases of the disease no longer occur naturally anywhere in the world.)

But after the eradication of smallpox, researchers saw an increase in cases of some other diseases caused by poxviruses. In particular, there has been a rise in cases of monkeypox, which is closely related to smallpox; both belong to the poxvirus family called orthopoxvirus. (The two diseases have similar symptoms, but monkeypox is less deadly than smallpox: The fatality rate for monkeypox is 10 percent, versus 30 percent for smallpox.)

Human cases of monkeypox occur primarily in Central and West Africa, and the virus is transmitted to humans from the fluids of animal carriers, including rodents and primates.

In a study published in 2010 in the Proceedings of the National Academy of Sciences, researchers found that since the eradication of smallpox, cases of monkeypox had increased 20-fold in the Democratic Republic of the Congo, from less than 1 case per 10,000 people in the 1980s to about 14 cases per 10,000 people in 2006-2007.

Other African countries have seen rises in monkeypox as well. In just the last month, 36 suspected cases of monkeypox have been reported in Nigeria, according to The Conversation. If confirmed, the cases would be the first in the country since 1978.

Doctors in the western world also have reason to be on the lookout for monkeypox and related poxviruses. In 2003, the United States experienced an outbreak of monkeypox tied to a shipment of animals from Ghana. In total, nearly 50 confirmed or probable cases of monkeypox were reported in six U.S. states during the outbreak, according to the CDC. "These diseases are never as far away as we think," Petersen said.

Researchers also continue to discover new types of poxviruses in various parts of the world. In the Alaska case, which occurred in 2015, the woman went to the doctor because she had a lesion on her right shoulder, along with fever, fatigue and tender lymph nodes, according to a report of the case, published in June. Her doctors thought she might have chicken pox or shingles, but testing revealed that she had a type of orthopoxvirus that had never been seen before.

It took six months for the lesion to fully disappear, but the woman eventually recovered and did not transmit the infection to anyone else, the report said. That case shows that there are "previously undiscovered, unrecognized, unknown poxviruses ... that are still being discovered to this day," Petersen said during his talk.

Efforts to discover exactly how the woman contracted the virus turned up empty. She had not traveled out of state, but her partner had traveled to Azerbaijan about four months earlier. Azerbaijan is next to the republic of Georgia, where another new orthopoxvirus was discovered, in 2013. But testing of her partner's items from the trip, such as clothes and souvenirs he brought back, did not show any evidence of orthopoxvirus DNA.

Testing of small mammals near the woman's home (such as shrews, voles and squirrels, which can carry orthopoxviruses), and testing of household areas that the small mammals may have touched, also came back negative. Still, the researchers said they were able to collect only a limited number of mammals from around the home. At this time, the most likely explanation for the patient's infection is that she was exposed to the virus around where she lived, near Fairbanks, Alaska, the report said.

"This discovery of a novel orthopoxvirus is the latest in a growing number of reports of human poxvirus infection published in recent years," the researchers said in their report. One hypothesis for the increase in such infections is the cessation of smallpox vaccination, because such vaccination may have provided protection against other poxviruses, the researchers said. "Continued emergence and re-emergence of orthopoxviruses is expected," the researchers wrote.

Petersen also noted that even though smallpox has been eradicated, the virus that causes the disease has not been completely wiped off the planet. Some stocks of the virus still exist in labs in the United States and Russia. And there's also concern that the virus could be used as a bioweapon. Earlier this year, scientists in Canada announced that they had re-created the horsepox virus, a relative of smallpox, in a lab using DNA fragments. The findings suggest scientists could also make the smallpox virus in a lab.

"Unfortunately, we're still talking about smallpox," Petersen said. "[But] hopefully, we'll never see another case."

http://bit.ly/2lMzjD6

Slow flow of human immigration may have doomed Neanderthals

What killed off the Neanderthals? It's a big debate, and now a study says that no matter what the answer, they were doomed anyway.

October 31, 2017 by Malcolm Ritter

Our close evolutionary cousins enjoyed a long run in Europe and Asia, but they disappeared about 40,000 years ago after modern humans showed up from Africa. The search for an explanation has produced many theories including climate change, epidemics, or inability to

compete with the modern humans, who may have had some mental or cultural edge.

The new study isn't intended to argue against those factors, but just to show that they're not needed to explain the extinction, says Oren Kolodny of Stanford University.

He and colleague Marcus Feldman present their approach in a paper released Tuesday by the journal Nature Communications.

They based their conclusion on a computer simulation that represented small bands of Neanderthals and modern humans in Europe and Asia. These local populations were randomly chosen to go extinct, and then be replaced by another randomly chosen population, with no regard for whether it represented the same species.

Neither species was assumed to have any inherent advantage, but there was one crucial difference: Unlike the Neanderthals, the modern humans were supplemented by reinforcements coming in from Africa. It wasn't a huge wave, but rather "a tiny, tiny trickle of small bands," Kolodny said.

Still, that was enough to tip the balance against the Neanderthals. They generally went extinct when the simulation was run more than a million times under a variety of assumptions.

If survival was a game of chance, "it was rigged by the fact that there's recurring migration," Kolodny said. "The game was doomed to end with the Neanderthals losing."

Kolodny said the evidence that such migrations actually occurred is suggestive rather than conclusive. Such migrations would not be expected to leave much of an archaeological trace, he said.

Experts in human origins said the paper could help scientists pin down the various factors that led to the Neanderthals' demise. It fits in with other recent attempts to explain the extinction without assuming behavioral differences between Neanderthals and our ancestors, said Wil Roebroeks of the University of Leiden in the Netherlands. The notion of such differences is largely disproven, he said.

Katerina Harvati of the University of Tuebingen in Germany said while the new work could be useful in solving the extinction mystery, it doesn't address the question of why modern humans dispersed from Africa into Europe and Asia. It's important to figure out what was behind that, she said in an email.

Oren Kolodny et al. A parsimonious neutral model suggests Neanderthal replacement was determined by migration and random species drift, Nature Communications (2017). DOI: 10.1038/s41467-017-01043-z

http://bit.ly/2Afxf9L

Many viruses activate a single RNA to enable successful infections

Viruses co-opt one of a cell's long noncoding RNAs to replicate.

Diana Gitig - 11/1/2017, 3:22 AM

A gene is a DNA sequence that encodes the instructions for when and where to make a particular protein. But most of the DNA in our genome—well over ninety percent—is not composed of genes.

The argument over the role of this seemingly extraneous DNA has swung back and forth. In the 1970s, it was thought to be generally useless junk. But in 2012, the ENCODE consortium (the ENCyclopedia Of DNA Elements—cute, right?) posited that most of the DNA had some sort of activity. Earlier this year, a new analysis insisted again that it's just junk.

Even as that debate was raging among researchers, viruses have used some of the noncoding DNA for their own purposes: to hijack our cellular metabolism and promote their own replication. Results are reported in Science.

ENCODE concluded that a lot of noncoding DNA may be functional because much of it is transcribed into RNA, even if that RNA isn't translated into proteins. There's evidence that some of these RNAs are functional, as they play a role in controlling other genes (though clearly not every RNA plays this role). Some of these RNAs, especially those that are relatively long (over two hundred bases) but still don't get made into proteins, have been shown to be induced by viral infection.

New work done in China has determined that viruses actually take advantage of one of these RNA molecules. The long noncoding RNA in question is made by both mice and men. It is induced by a variety of viruses, and when it's eliminated, these viruses cannot replicate. How all these different viruses activate the same gene isn't clear at this point.

The RNA binds to and activates an enzyme (glutamic-oxaloacetic transaminase) involved in many important metabolic processes, including amino acid metabolism, long-chain fat use, and a basic respiratory cycle. By inducing the production of this long noncoding RNA, viruses shift the metabolic enzyme into hyperdrive in order to spur viral replication. That suggests that the enzyme itself might make a useful drug target.

We know a fair amount about the different tricks viruses use to enter cells and the means they use to get out. Less clear are the molecular mechanisms underlying how viruses subvert a cell's metabolism toward their own nefarious ends. This work suggests that viruses, unlike biologists, are not especially interested in the evolutionary necessity and purpose of noncoding DNA. They just use it.

Science, 2017. DOI: 10.1126/science.aao0409 (About DOIs).

http://bit.ly/2zbfOqI

New research shows where in the brain the earliest signs of Alzheimer's occur

Researchers at Lund University in Sweden have for the first time convincingly shown where in the brain the earliest signs of Alzheimer's occur.

The discovery could potentially become significant to future Alzheimer's research while contributing to improved diagnostics.

In Alzheimer's, the initial changes in the brain occur through retention of the protein, β-amyloid (beta-amyloid). The process begins 10-20 years before the first symptoms become noticeable in the patient.

In Nature Communications, a research team headed by Professor Oskar Hansson at Lund University has now presented results showing where in the brain the initial accumulation of β-amyloid occurs. It is in the inner parts of the brain, within one of the brain's most important functional networks - known as the default mode network.

"A big piece of the puzzle in Alzheimer's research is now falling into place. We previously did not know where in the brain the earliest stages of the disease could be detected. We now know which parts of the brain are to be studied to eventually explain why the disease occurs", says Sebastian Palmqvist, associate professor at Lund University and physician at Skåne University Hospital.

The default mode network is one of several networks, each of which has a different function in the brain. It is most active when we are in an awake quiescent state without interacting with the outside world, for example, when daydreaming. The network belongs to the more advanced part of the brain. Among other things, it processes and links information from lower systems.

The study, conducted in collaboration with Michael Schöll, associate senior lecturer at the University of Gothenburg, and William Jagust, professor at the University of California, is based on data from more than 400 people in the United States who have an increased risk of developing Alzheimer's, and about as many participants from the Swedish research project, BioFINDER. The brain status of all the participants was monitored for two years, and compared to a control group without any signs of Alzheimer's.

The difficulty of determining which individuals are at risk of developing dementia later in life, in order to subsequently monitor them in research studies, has been an obstacle in the research world. The research team at Lund University has therefore developed a unique method to identify, at an early stage, which individuals begin to accumulate β-amyloid and are at risk.

The method combines cerebrospinal fluid test results with PET scan brain imaging. This provides valuable information about the brain's tendency to accumulate β-amyloid.

In addition to serving as a roadmap for future research studies of Alzheimer's disease, the new results also have a clinical benefit:

"Now that we know where Alzheimer's disease begins, we can improve the diagnostics by focusing more clearly on these parts of the brain, for example in medical imaging examinations with a PET camera", says Oskar Hansson, professor at Lund University, and medical consultant at Skåne University Hospital.

Although the first symptoms of Alzheimer's become noticeable to others much later, the current study shows that the brain's communication activity changes in connection with the early retention of β-amyloid. How, and with what consequences, will be examined by the research team in further studies.

The current study was funded by the European Research Council (ERC), the Swedish Research Council (VR), the Swedish Alzheimer's Foundation and Region of Skåne (through ALF funding).

http://bit.ly/2h86NdB

Why do some obese people have 'healthier' fat tissue than others?

One little understood paradox in the study of obesity is that overweight people who break down fat at a high rate are less healthy than peers who store their fat more effectively.

ANN ARBOR - That's because when fat breaks down, many of the fatty acids released from the adipose tissue (body fat) can take up residence elsewhere. Too much of this and fat can accumulate to harmful levels in other tissues and organs, which can fuel insulin resistance, a hallmark of type 2 diabetes and heart disease.

A pair of studies from the University of Michigan identifies key characteristics in fat tissue that may allow some obese adults to store their body fat more healthily and suggests that aerobic exercise may lead to healthier fat storage, said principal investigator Jeffrey Horowitz, professor of movement science at the U-M School of Kinesiology.

Most obese people develop insulin resistance, which can lead to type 2 diabetes and other chronic diseases. However, Horowitz and his team found that about one-third of the 30 obese adults in their study did not develop insulin resistance.

This begged the question: What protected these people?

Adipose tissue samples revealed that the healthier group broke down fat at slower rates, and they had fewer proteins involved in fat breakdown and more involved in fat-storing. They also had fewer fibrotic cells in the adipose tissue, which allows tissue to be more flexible, and lower activation of certain inflammatory pathways.

"It sounds counterintuitive, but if we can better understand how to store fat more effectively, and why some people are better at this than others, perhaps we can design therapies and preventions that will improve some of these obesity-related metabolic conditions," Horowitz said.

In the second study, researchers collected fat tissue after a session of aerobic exercise from two groups of overweight people: one group exercised regularly, and the other group didn't. For both groups, just one session of exercise triggered signals that led to the growth of new blood vessels in fat tissue.

Researchers also found indications that the regular exercisers had more blood vessels in their fat tissue than non-exercisers.

That's important because the health of most tissues hinges, in large part, on blood flow and nutrients, Horowitz said. When we gain weight, our fat cells expand, but if blood flow to fat tissue doesn't increase in parallel, it could become unhealthy or even necrotic.

Horowitz stressed that the two studies are relevant mainly to obese people at risk for metabolic disease. However, there's a takeaway here for everyone. "We believe that the regular exercise we do now may create a healthier fat-storing environment for those times when we do overeat and gain weight," Horowitz said.

Taken together, the studies also support the notion that clinicians must redefine their view of fat, said Horowitz. "Adipose tissue is scorned because most people see it as causing disease and obesity, but in general adipose tissue doesn't cause people to gain weight and become

obese, it's just where we store our extra energy when we do overeat," Horowitz said. "Our studies aren't suggesting it is healthy to be obese or to overeat--but when we do overeat, it is important to have a safe place to store that extra energy.

"When people gain the same amount of body fat, those with adaptations to their fat tissue that can more healthfully accommodate the extra fat may be protected from developing insulin resistance and obesity-related diseases. We have identified some of these adaptations."

Doug Van Pelt, a former doctoral student in the Horowitz lab, conducted this work as part of his dissertation. Van Pelt is currently a postdoctoral fellow at the University of Kentucky's College of Health Sciences.

The two studies are: "Factors regulating subcutaneous adipose tissue storage, fibrosis, and inflammation may underlie low fatty acid mobilization in insulin-sensitive obese adults" and "Aerobic exercise elevates markers of angiogenesis and macrophage IL6 gene expression in the subcutaneous adipose tissue of overweight to obese adults."

http://bit.ly/2zeGxW3

New theory addresses how life on Earth arose from the primordial muck

American and New Zealand researchers use experimental evidence to overturn widely-accepted theory on the dawn of life on Earth

CHAPEL HILL, NC - Life on Earth originated in an intimate partnership between the nucleic acids (genetic instructions for all organisms) and small proteins called peptides, according to two new papers from biochemists and biologists at the University of North Carolina at Chapel Hill and the University of Auckland. Their "peptide-RNA" hypothesis contradicts the widely-held "RNA-world" hypothesis, which states that life originated from nucleic acids and only later evolved to include proteins.

The new papers - one in Molecular Biology and Evolution, the other in Biosystems - show how recent experimental studies of two enzyme superfamilies surmount the tough theoretical questions about how complex life emerged on Earth more than four billion years ago.

"Until now, it has been thought to be impossible to conduct experiments to penetrate the origins of genetics," said co-author Charles Carter, PhD, professor of biochemistry and biophysics at the UNC School of Medicine. "But we have now shown that experimental results mesh beautifully with the 'peptide-RNA' theory, and so these experiments provide quite compelling answers to what happened at the beginning of life on Earth."

The special attributes of the ancestral versions of these enzyme superfamlies, and the self-reinforcing feedback system they would have formed with the first genes and proteins, would have kick-started early biology and driven the first life forms toward greater diversity and complexity, the researchers said.

Co-author Peter Wills, PhD, professor of physics at the University of Auckland, said, "Compared to the RNA-world hypothesis, what we've outlined is simply a much more probable scenario for the origin of life. We hope our data and the theory we've outlined in these papers will stimulate discussion and further research on questions relevant to the origins of life."

The two scientists are fully aware that the RNA-world hypothesis still dominates the origin-of-life research field. "That theory is so alluring and expedient that most people just don't think there's any alternative," Carter said. "But we are very confident there is."

Before there was life on Earth, there were simple chemicals. Somehow, they produced both amino acids and nucleotides that eventually became the proteins and nucleic acids necessary to create single cells. And the single cells became plants and animals. Research this century has revealed how the primordial chemical soup created the building blocks of life. There is also widespread scientific

consensus on the historical path by which cells evolved into plants and animals.

But it's still a mystery how the amino acid building blocks were first assembled according to coded nucleic acid templates into the proteins that formed the machinery of all cells.

The widely accepted RNA-world theory posits that RNA - the molecule that today plays roles in coding, regulating, and expressing genes - elevated itself from the primordial soup of amino acids and cosmic chemicals, eventually to give rise first to short proteins called peptides and then to single-celled organisms.

Carter and Wills argue that RNA could not kick-start this process alone because it lacks a property they call "reflexivity." It cannot enforce the rules by which it is made. RNA needed peptides to form the reflexive feedback loop necessary to lead eventually to life forms.

At the heart of the peptide-RNA theory are enzymes so ancient and important that their remnants are still found in all living cells and even in some sub-cellular structures, including mitochondria and viruses. There are 20 of these ancient enzymes called aminoacyl-tRNA synthetases (aaRSs).

Each of them recognizes one of the 20 amino acids that serve as the building blocks of proteins. (Proteins, considered the machines of life, catalyze and synchronize the chemical reactions inside cells.) In modern organisms, an aaRS effectively links its assigned amino acid to an RNA string containing three nucleotides complementary to a similar string in the transcribed gene. The aaRSs thus play a central role in converting genes into proteins, a process called translation that is essential for all life forms.

The 20 aaRS enzymes belong to two structurally distinct families, each with 10 aaRSs. Carter's recent experimental studies showed that the two small enzyme ancestors of these two families were encoded by opposite, complementary strands of the same small gene. The simplicity of this arrangement, with its initial binary code of just two kinds of amino acids, suggests it occurred at the very dawn of biology. Moreover, the tight, yin-yang interdependence of these two related but highly distinct enzymes would have stabilized early biology in a way that made inevitable the orderly diversification of life that followed.

"These interdependent peptides and the nucleic acids encoding them would have been able to assist each other's molecular self-organization despite the continual random disruptions that beset all molecular processes," Carter said. "We believe that this is what gave rise to a peptide-RNA world early in Earth's history," Carter said.

Related research by Carter and UNC colleague Richard Wolfenden, PhD, previously revealed how the intimate chemistries of amino acids enabled the first aaRS enzymes to fold properly into functional enzymes, while simultaneously determining the assignments in the universal genetic coding table.

"The enforcement of the relationship between genes and amino acids depends on aaRSs, which are themselves encoded by genes and made of amino acids," Wills said. "The aaRSs, in turn, depend on that same relationship. There is a basic reflexivity at work here. Theorist Douglas Hofstadter called it a 'strange loop.' We propose that this, too, played a crucial role in the self-organization of biology when life began on Earth. Hofstadter argued that reflexivity furnishes the force driving the growth of complexity."

Carter and Wills developed two additional reasons why a pure RNA biology of any significance was unlikely to have predated a peptide-RNA biology. One reason is catalysis - the acceleration of chemical reactions involving other molecules.

Catalysis is a key feature of biology that RNA cannot perform with much versatility. In particular, RNA enzymes cannot readily adjust their activities to temperature changes likely to have happened as the earth cooled, and so cannot perform the very broad range of catalytic accelerations that would have been necessary to synchronize the biochemistry of early cell-based life forms. Only peptide or protein enzymes have that kind of catalytic versatility, Carter said.

Secondly, Wills has shown that impossible obstacles would have blocked any transition from a pure-RNA world to a protein-RNA world and onward toward life.

"Such a rise from RNA to cell-based life would have required an out-of-the-blue appearance of an aaRS-like protein that worked even better than its adapted RNA counterpart," Carter said. "That extremely unlikely event would have needed to happen not just once but multiple times - once for every amino acid in the existing gene-protein code. It just doesn't make sense."

Thus, because the new Carter-Wills theory actually addresses real problems of the origin of life that are concealed by the expediency of the RNA-world hypothesis, it is actually a far simpler account of how things probably happened just before life on Earth rose from the primordial soup.

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http://bit.ly/2hK1bDE

Miracle cure costs less than a budget airline flight

Restrictions and patent issues around the world mean that hardly any patients can access generic drugs at these low costs

The revolution in generic drugs means that a 12-week course of drugs to cure hepatitis C can be manufactured for just US$50 - as low as the cost of a plane ticket on many low-cost airlines. Furthermore, new data shows that these generic copies are just as effective as the branded medicines. Yet restrictions and patent issues around the world mean that hardly any patients can access the drugs at these low costs, say experts speaking at the World Hepatitis Summit in Sao Paulo, Brazil (1-3 November).

"As there are around 70 million people infected with hepatitis C worldwide, the basic cost of the drugs to treat everyone infected globally, at $50 each, would be around US $3.5 billion," explains Dr Andrew Hill, a pharmacology expert from the University of Liverpool, UK. This represents less than a fraction of 1% of the global health budget of some US$ 8 trillion. "Much more must be done to enable all countries -- but especially developing countries -- to produce or buy drugs for these lower prices. Without significant changes to pricing structures, the battle against the global hepatitis C epidemic simply can't be won."

In his presentation, Dr Hill will present data on the hugely varying cost of a 12-week course of sofosbuvir and daclatasvir, a common combination of the new directly acting antiviral drugs (DAAs) that have revolutionised hepatitis C treatment by providing rapid cure with few or no side effects. The list price for this combination of drugs ranges from close to cost price in India ($78) and Egypt ($174) to $6,000 in Australia, $77,000 in the UK, and a staggering $96,404 the USA. Yet the basic cost of the active ingredients, including formulation and packaging costs and even allowing a small profit margin for the generic companies brings the basic cost down to under $50 per course.

In high-income countries, most of which have treatment restrictions allowing only those with advanced disease to be treated first, some infected patients have resorted to buying generic drugs from international buyers' clubs (who buy in bulk from developing countries) or directly from countries where they are manufactured. For example, in the UK, those not wanting to wait for advanced disease to be treated have been able to legally purchase a 12-week generic course for prices ranging from US $1000 to $1200. Research studies on these patients show that cure rates are as high as for the branded medicines, ranging from 90% to 95%.

An analysis presented at the summit on the efficacy of generic DAAs looked at 1160 patients who have imported DAAs for personal use into 88 countries on 5 continents. Data from these patients show that

cure rates are well over 90%, the same as for the branded products, but at a fraction of the cost.

"In 2016, for every person cured of hepatitis C globally (1.76 million), another person was newly infected (1.5 million). We simply cannot eliminate this epidemic unless we treat more people. And we can only do this if the prices of the drugs come down," explains Dr Hill.

He adds that the manufacturers of DAAs must do more to provide voluntary licences in countries that do not currently have them for generic companies to produce cheaper (but just as effective) generic DAAs. This is what has happened in Egypt, which had nearly 7 million people to treat, but now have fewer than 5 million. However, more than half of those people infected globally live in countries with no voluntary licence to allow generic production. "For example, China and Russia, two countries with very large hepatitis C epidemics, have no voluntary licence in place to produce cheap generic drugs," explains Dr Hill.

However, Dr Hill makes clear that any efforts to reduce drug prices and enable mass generic DAA production worldwide will be futile unless countries also step up their efforts to find and diagnose their infected populations. "We cannot treat people if we do not know who they are," explains Dr Hill. "Countries must massively step up their screening efforts, or they will simply run out of people to treat - a diagnostic 'burn-out'. The proportion of patients with hepatitis C who know they have it ranges from 44% in high-income countries to just 9% in low-income countries."

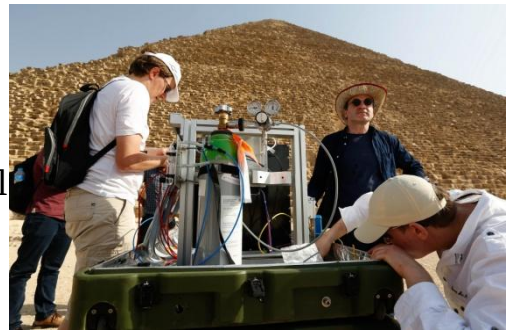
He concludes that lessons can and should be learned from the HIV epidemic to successfully end the hepatitis C epidemic worldwide. "It has taken the world 15 years to get 19 million people globally on antiretroviral treatments for HIV," he says. "We already have the drugs necessary to eliminate hepatitis C. Let's learn from the past, and repeat the medical success story of global HIV treatment."

http://nyti.ms/2Am48lw

Inside Giza's Great Pyramid, Scientists Discover a Void

The Great Pyramid of Giza has towered over Egypt for more than 4,500 years.

By NICHOLAS ST. FLEUR



Built during the reign of Pharaoh Khufu, the monument was a testament to the ruler's architectural prowess and is thought to have been a home for his mummified remains.

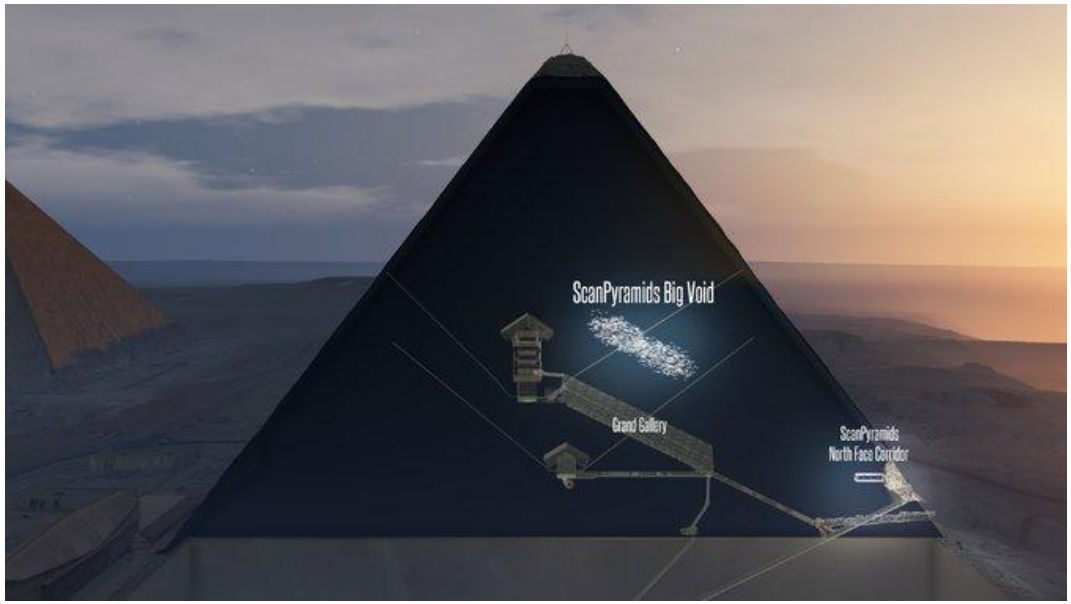
Researchers set up a muon telescope in front of the Great Pyramid of Giza's north face. Borrowing a technique from particle physics, they discovered a 100-foot "void" inside the pyramid. **ScanPyramids mission**

For centuries, archaeologists have ventured into the Pyramid of Khufu, as it is also known, and marveled at the King's chamber, the Queen's chamber and the Grand Gallery. Now, using a technique from the field of particle physics, an international team of researchers has harnessed cosmic-ray collisions to peek inside and uncover a hidden "void" within the pyramid's stones that is roughly 100 feet long, similar to the Statue of Liberty from her heel to her head.

"We don't know if it's a chamber, a tunnel, a big gallery or things like that," said Mehdi Tayoubi, co-director of the ScanPyramids project, which published the finding Thursday in the journal Nature. "We have chosen the word 'void' and nothing else because we don't know what this void is."

Many archaeologists questioned whether the study offered any new information about the ancient Egyptians, and were quick to note that the team had most likely not found a hidden room filled with the pharaoh's riches. They said the so-called void was probably empty space designed by the pyramid's architects to lessen the weight on its chambers and prevent them from collapsing, an example of features that were already documented in the construction of the ancient monuments.

However, the study may suggest that advances in technology can offer a richer understanding of wonders of the ancient world that have long fascinated the human imagination.



***A rendering by the researchers at ScanPyramids show the "Big Void" relative to known structures in the Great Pyramid of Giza*. ScanPyramids mission**

Khufu, also known by his Greek name Cheops, is thought to have ruled from 2509 B.C. to 2483 B.C., during Egypt's fourth dynasty. Though he constructed the largest pyramid Egypt has ever seen, the only intact three-dimensional figure of him that archaeologists have found measures a mere three inches tall. Very little is known about him, so his pyramid offers one of the few looks into his life and reign. The site at Giza where his pyramid was built also contains two other major pyramids and the Sphinx.

Since 2015, Dr. Tayoubi and his colleagues, now consisting of three separate teams of physicists and engineers, have investigated the pyramid using a particle physics technique known as muon tomography to see through to its core. "We tried to do for the pyramid what a doctor can do with X-rays," Dr. Tayoubi said.

Instead of X-rays, the team used muons, the heavy cousins of electrons that form when cosmic rays from outer space collide with particles in Earth's atmosphere. The fallout from the collisions creates a constant bombardment of harmless particles that can penetrate deep into the planet. As the muons pass through matter they lose energy and decay, so if the team detected a small number of muons, that means they were passing through matter. But if they detected more muons, it suggests the particles were passing through empty space or less dense material.

The technology was previously used by Luis Alvarez, a Nobel Prize-winning physicist, to investigate whether there were hidden chambers in the Pyramid of Khafre in the 1960s. As muon detector resolution has greatly improved over the decades, it has since been used to see the inner structures of volcanoes as well as the irradiated Fukushima nuclear reactor.

In 2016, Dr. Tayoubi's colleagues stood in the Queen's chamber and used muon detectors capable of making improved measurements to study particles as they passed through the pyramid. When they analyzed their data from a region above the Grand Gallery, a long inclined passageway that leads to the King's Chamber, they found something strange: an unexpected excess of muons.

***Researchers using a muon detector inside the Queen's chamber of the Great Pyramid.* ScanPyramids mission**

They found a void.

The first measurements were made by researchers from Nagoya University in Japan who were a part of the project. Then two more teams associated with ScanPyramids, one from France and another from Japan, also confirmed the anomaly with muon tomography, even from outside the pyramid. The discovery comes on the footsteps of the

team's previous work, which detected a small void behind the north face of the pyramid in 2016.

Christopher Morris, a physicist who conducts research using muon tomography at Los Alamos National Laboratory and was not involved in the study, called the findings "pretty amazing," adding that all the team needed to do was set up their muon detectors and reap the rewards. "All the other physicists who could have done it, and didn't, are jealous," he said.

Arturo Menchaca-Rocha, a physicist from the National Autonomous University of Mexico who has used muon detection to investigate the Pyramid of the Sun in Mexico, echoed Dr. Morris's sentiments and said the project's physics supported its claims.

But archaeologists were more critical of the work.

Mark Lehner, an Egyptologist from Ancient Egypt Research Associates, said that previous work had shown that the ancient Egyptians most likely constructed gaps in their pyramids and that the voids the team found are nothing special, or new.

"The great pyramid of Khufu is more Swiss cheese than cheddar," he said. He added that the steep incline of the void also casts doubts on whether it was some sort of room. "At that angle, it doesn't make much sense for it to be a chamber that would contain artifacts, burials and objects and that sort of thing."

Zahi Hawass, an Egyptologist, former Egyptian government minister and head of the scientific committee appointed by the Egyptian Ministry of Antiquities to review the work, was more critical of the finding. "They found nothing," said Dr. Hawass, noting that such construction gaps had been known of for at least two decades. "This paper offers nothing to Egyptology. Zero."

Both Dr. Lehner and Dr. Hawass agreed that the scanning work should continue in hopes that the teams can retrieve higher resolution data about the inner workings of the pyramid, specifically the shape and size of the anomaly.

Hany Helal, who is also a co-director of the ScanPyramids project, responded to the criticism, saying that from an engineering perspective, it would not make sense to have such a big void above the Gallery if its purpose was to relieve pressure.

He said the next steps are to have an international discussion with archaeologists to figure out the structure's purpose. In the future, he added that scientists may use drones to explore the void once they have more information about it. "We are sure there is a void," he said. "Now let us continue our research."

http://bit.ly/2y2CAjw

The Subatomic Discovery That Physicists Considered Keeping Secret

A pair of physicists announced the discovery of a subatomic event so powerful that the researchers wondered if it was too dangerous to make public.

By Rafi Letzter, Staff Writer | November 2, 2017 01:46pm ET

The explosive event? The duo showed that two tiny particles known as bottom quarks could theoretically fuse together in a powerful flash. The result: a larger subatomic particle, a second, spare particle known as a nucleon, and a whole mess of energy spilling out into the universe. This "quarksplosion" would be an even more powerful subatomic analog of the individual nuclear fusion reactions that take place in the cores of hydrogen bombs.

Quarks are tiny particles that are usually found clinging together to make up the neutrons and protons inside atoms. They come in six versions or "flavors": up, down, top, bottom, strange and charm.

Energetic events at the subatomic level are measured in megaelectronvolts (MeV), and when two bottom quarks fuse, the physicists found, they produce a whopping 138 MeV. That's about eight times more powerful than one of the individual nuclear fusion events that takes place in hydrogen bombs (a full-scale bomb blast consists of billions of these events). H-bombs fuse together tiny hydrogen nuclei known as deuterons and tritons to create helium

nuclei, along with the most powerful explosions in the human arsenal. But each of those individual reactions inside the bombs releases only about 18 MeV, according to the Nuclear Weapon Archive, a website devoted to collecting research and data about nuclear weapons. That's far less than the fusing bottom quarks' 138 MeV.

"I must admit that when I first realized that such a reaction was possible, I was scared," co-researcher Marek Karliner of Tel Aviv University in Israel told Live Science. "But, luckily, it is a one-trick pony."

As powerful as fusion reactions are, a single instance of fusion on its own isn't at all dangerous. Hydrogen bombs derive their enormous power from chain reactions — the cascading fusion of lots and lots of nuclei all at once.

Karliner and Jonathan Rosner, of the University of Chicago, determined that such a chain reaction wouldn't be possible with bottom quarks, and, before publishing, privately shared their insight with colleagues, who agreed.

"If I thought for a microsecond that this had any military applications, I would not have published it," Karliner said.

To spark a chain reaction, nuclear bomb makers need large stockpiles of particles. And an important property of bottom quarks makes them impossible to stockpile: They wink out of existence just 1 picosecond after they're created, or in about the time it takes light to travel half the length of a single grain of salt. After that time span, they decay into a far more common and less energetic kind of subatomic particle, known as the up quark.

It might be possible to generate single fusion reactions of bottom quarks inside miles-long particle accelerators, the scientists said. But even inside an accelerator, one couldn't assemble a large enough mass of quarks to do any damage out in the world, the researchers said. So there's no need to worry about bottom quark bombs.

The discovery is exciting, though, because it's the first theoretical proof that it's possible to fuse subatomic particles together in ways that release energy, Karliner said. That's brand-new territory in the physics of very tiny particles, made possible by an experiment in the Large Hadron Collider at CERN, the massive particle-physics laboratory near Geneva.

Here's how the physicists made this discovery.

At CERN, particles zip around a 17-mile-long (27 kilometers) underground ring at near light speed before smashing into one another. The scientists then use powerful computers to sift through the data from those collisions, and strange particles sometimes emerge from that research. In June, something especially strange turned up in the data from one of those collisions: a "doubly charmed" baryon, or a bulky cousin of the neutron and proton, itself made up of two cousins of the "bottom" and "top" quarks known as "charm" quarks.

Now, charm quarks are very heavy compared to the more common up and down quarks that make up protons and neutrons. And when heavy particles bind together, they convert a large chunk of their mass into binding energy, and in some cases, produce a bunch of leftover energy that escapes into the universe.

When two charm quarks fuse, Karliner and Rosner found, the particles bind with an energy of about 130 MeV and spit out 12 MeV in leftover energy (about two-thirds of the energy of deuteron-triton fusion). That charmed fusion was the first reaction of particles on this scale ever found to emit energy in this way, and is the headline result of the new study, published yesterday (Nov. 1) in the journal Nature.

The even more energetic fusion of two bottom quarks, which bind with an energy of 280 MeV and spit out 138 MeV when they fuse, is the second, and more powerful of the two reactions discovered.

So far, these reactions are entirely theoretical and haven't been demonstrated in a lab. That next step should come soon though. Karliner said he expects to see the first experiments showing this reaction at CERN within the next couple years.

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University of Guelph study first to identify the cells driving gecko's ability to re-grow its tail

University of Guelph researcher's discovery of which cells are behind the gecko's ability to re-grow its tail has implications for spinal cord treatment in humans

A U of G researcher is the first to discover the type of stem cell that is behind the gecko's ability to re-grow its tail, a finding that has implications for spinal cord treatment in humans.

Many lizards can detach a portion of their tail to avoid a predator and then regenerate a new one. Unlike mammals, the lizard tail includes a spinal cord. Prof. Matthew Vickaryous found that the spinal cord of the tail contained a large number of stem cells and proteins known to support stem cell growth.

"We knew the gecko's spinal cord could regenerate, but we didn't know which cells were playing a key role," said Vickaryous, lead author of the study recently published in the Journal of Comparative Neurology. "Humans are notoriously bad at dealing with spinal cord injuries so I'm hoping we can use what we learn from geckos to coax human spinal cord injuries into repairing themselves."

Geckos are able to re-grow a new tail within 30 days - faster than any other type of lizard. In the wild, they detach their tails when grabbed by a predator. The severed tail continues to wiggle, distracting the predator long enough for the reptile to escape.

In the lab, Vickaryous simulates this by pinching the gecko's tail causing the tail to drop. Once detached, the site of the tail loss begins to repair itself, eventually leading to new tissue formation and a new spinal cord. For this study, the biomedical sciences professor, along with PhD student Emily Gilbert, investigated what happens at the cellular level before and after detachment.

They discovered that the spinal cord houses a special type of stem cell known as the radial glia. These stem cells are normally fairly quiet.

"But when the tail comes off everything temporarily changes," he said. "The cells make different proteins and begin proliferating more in response to the injury. Ultimately, they make a brand new spinal cord. Once the injury is healed and the spinal cord is restored, the cells return to a resting state."

Humans, on the other hand, respond to a spinal cord injury by making scar tissue rather than new tissue, he added. The scar tissue seals the wound quickly, but sealing the injury prevents regeneration. "It's a quick fix but in the long term it's a problem." "This may play a role in why we have a limited ability to repair our spinal cords. We are missing the key cells types required."

This study is part of a series of investigations into the regenerative abilities of the gecko's central nervous system. The next step is to examine how the gecko is able to make new brain cells, said Vickaryous.

"Geckos are able to regenerate many tissues throughout their bodies, making them ideal models for studying wound healing and tissue re-development. We can learn a lot from them."

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Shifting bacterial communities in the stomach may influence cancer risk

Microbe changes linked with specific conditions could explain differences in risk and type of tumor

Different changes to the microbial community of the stomach may explain why related conditions are associated with different risk levels and types of gastric tumor, according to a new study in PLOS Pathogens.

Autoimmune disease or infection with Helicobacter pylori bacteria can damage the stomach and reduce gastric acid secretion. Despite their similar effects, each of these conditions is associated with higher risk of a different type of gastric tumor. Meanwhile, widely used medications known as proton pump inhibitors (PPIs) also reduce gastric acid secretion, but they do not increase cancer risk.

Bryony Parsons of the University of Liverpool, U.K., and colleagues hypothesized that microbes living in the stomach could explain differences in tumor risk associated with the different causes of reduced gastric acid. Every healthy stomach is known to be home to bacterial communities, but reduced gastric acid can alter the stomach environment and cause changes in amount and type of microbes.

To investigate how changes in these microbial communities might influence tumor risk, the researchers analyzed stomach biopsies from 95 people with different conditions. They used a genetic technique known as 16S rRNA sequencing to determine which bacterial species were living in the stomachs of healthy people, people receiving PPIs, and people with reduced gastric acid secretion as a result of H. pylori infection or autoimmune disease.

They found that that people receiving PPIs had similar microbial communities in their stomachs as those seen in healthy people, despite reduced gastric acid secretion. However, people with H. pylori infection had lower amounts and fewer types of bacteria than seen in healthy people, while those with autoimmune disease had higher amounts of bacteria and equal diversity as seen in healthy people (but with different types of bacteria dominating the community).

The researchers also identified dominant biochemical processes associated with the microbial communities seen in each type of patient. Differences in these processes and their effects on the stomach could help explain why H. pylori is more commonly associated with a cancer type known as gastric adenocarcinoma, while autoimmune disease is linked with neuroendocrine tumors.

Future research that confirms and builds on these findings could eventually lead to development of new ways to prevent cancer by manipulating the microbial community of the stomach.

My quote can be found below (and I would be grateful if you could name me in association with this quote. I would ideally like to be referred to as):

"Our work has excitingly shown that three specific conditions which all result in the stomach producing less acid cause different changes to the composition of the bacteria which live in the stomach," claims author Mark Pritchard, Professor of Gastroenterology at the University of Liverpool. "We now hope to move on to investigate how these bacteria contribute to the development of the characteristic stomach tumor types that are associated with each of these conditions."

Citation: Parsons BN, Ijaz UZ, D'Amore R, Burkitt MD, Eccles R, Lenzi L, et al. (2017) Comparison of the human gastric microbiota in hypochlorhydric states arising as a result of Helicobacter pylori-induced atrophic gastritis, autoimmune atrophic gastritis and proton pump inhibitor use. PLoS Pathog 13(11): e1006653.
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Competing Interests: The authors have declared that no competing interests exist.

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New system for treating colorectal cancer can lead to complete cure

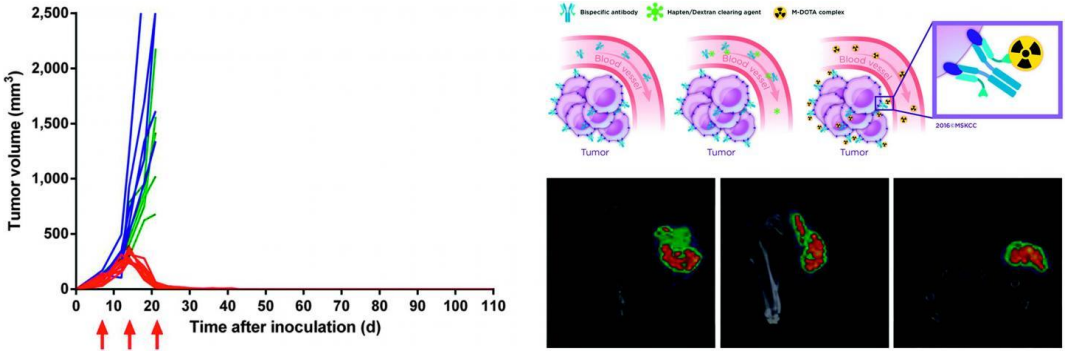
Novel three-step pretargeted radioimmunotherapy offers safe, effective treatment

RESTON, Va. - Researchers at Memorial Sloan Kettering Cancer Center in New York City and Massachusetts Institute of Technology in Boston have developed a new, three-step system that uses nuclear medicine to target and eliminate colorectal cancer. In this study with a mouse model, researchers achieved a 100-percent cure rate--without any treatment-related toxic effects. The study is reported in the November featured article in The Journal of Nuclear Medicine.

Until now, radioimmunotherapy (targeted therapy) of solid tumors using antibody-targeted radionuclides has had limited therapeutic success. "This research is novel because of the benchmarks reached by the treatment regimen, in terms of curative tumor doses, with non-toxic secondary radiation to the body's normal tissues," explains

Steven M. Larson, MD, and Sarah Cheal, PhD, of Memorial Sloan Kettering Cancer Center. "The success in murine tumor models comes from the unique quality of the reagents developed by our group, and the reduction to practice methodology, including a theranostic approach that can be readily transferred, we believe, to patients."

Efficacy of DOTA-PRIT Evaluated as Tumor Growth and Survival in Mice Bearing SW1222 Subcutaneous Xen (image)



Left: Tumor growth presented as the change in tumor volume for each individual mouse over time (green: no treatment; blue: 177Lu-DOTA-Bn only; red: DOTA-PRIT). Top right: Schematic representation of the three-step anti-GPA33 DOTA-PRIT protocol. Bottom right: Representative SPECT/CT images obtained from mouse at 24 hours post-injection of cycle 1. **S Cheal et al., Memorial Sloan Kettering Cancer Center, New York, NY**

Theranostics, a term derived from therapy and diagnostics, is the use of a single agent to both diagnose and treat disease. The theranostic agent first finds the cancer cells, then destroys them, leaving healthy cells unharmed--minimizing side effects and improving quality of life for patients.

In this study, the glycoprotein A33 (GPA33), an antigen found on over 95 percent of primary and metastatic human colorectal cancers, was targeted with a bispecific antibody for A33 tumor antigen and a second antibody for a small-molecule radioactive hapten, a complex of lutetium-177 (^{177}Lu) and S-2-(4-aminobenzyl)1,4,7,10-tetraazacyclododecane tetra-acetic acid (^{177}Lu-DOTA-Bn).

The DOTA-pretargeted radioimmunotherapy (PRIT) strategy was tested on a mouse model. In randomly selected mice undergoing treatment, serial SPECT/CT imaging was used to monitor treatment response and calculate radiation-absorbed doses to tumors. All the DOTA-PRIT-treated animals tolerated the treatment well, and all 9 assessed mice had no trace of cancer remaining upon microscopic examination. There was also no detectable radiation damage to critical organs, including bone marrow and kidneys.

The 100-percent cure rate in the mouse model is a promising preliminary finding that suggests that anti-GPA33-DOTA-PRIT will be a potent radioimmunotherapy regimen for GPA33-positive colorectal cancer tumors in humans.

According to the Centers for Disease Control and Prevention, colorectal cancer is the third most common cancer affecting both men and women. Each year, approximately 140,000 new cases are diagnosed in the United States and 50,000 people die of the disease.

The applications of this nuclear medicine treatment protocol could extend to other cancers as well. Larson and Cheal state, "If clinically successful, our approach will expand the repertoire of effective treatments for oncologic patients. The system is designed as a 'plug and play' system, which allows for the use of many fine antibodies targeting human tumor antigens and is applicable, in principle, to virtually all solid and liquid tumors in man." They add, "There is a huge unmet need in oncology, especially for the solid tumors, for curative treatments for advanced disease. This includes, colon, breast, pancreas, melanoma, lung, and esophageal, to name a few."

Authors of "Curative multicycle radioimmunotherapy monitored by quantitative SPECT/CT-based theranostics, using bispecific antibody pretargeting strategy in colorectal cancer" include Sarah M. Cheal, Edward K. Fung, Mitesh Patel, Hong Xu, Hong-fen Guo, Pat B. Zanzonico, Nai-Kong V. Cheung, and Steven M. Larson of Memorial Sloan Kettering Cancer Center, New York, NY; Sebastien Monette of the Tri-Institutional Laboratory of Comparative Pathology, Memorial Sloan Kettering Cancer Center, Weill Cornell Medicine, and The Rockefeller University, New York, NY; and K. Dane Wittrup, Massachusetts Institute of Technology, Cambridge, MA.

This study was supported in part by the Donna & Benjamin M. Rosen Chair; Enid A. Haupt Chair; The Center for Targeted Radioimmunotherapy and Theranostics, Ludwig Center for Cancer Immunotherapy of Memorial Sloan Kettering Cancer Center; NIH R01 CA101830,

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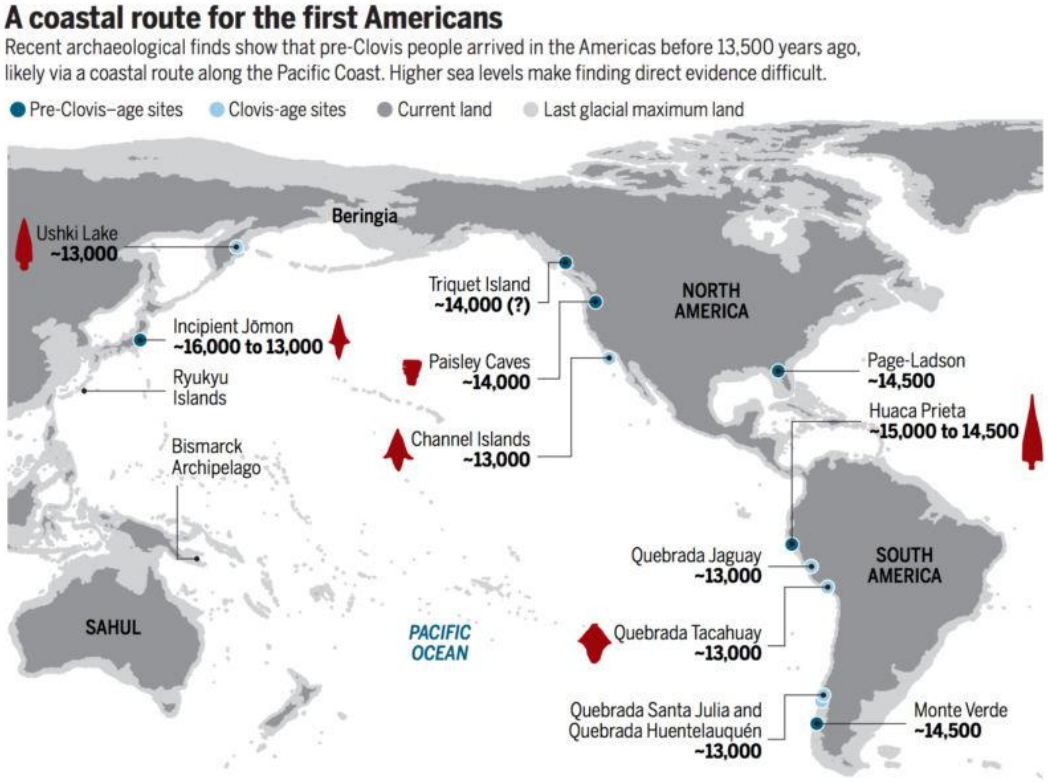
http://bit.ly/2h5ZFuv

Most scientists now reject the idea that the first Americans came by land

Researchers embrace the kelp highway hypothesis in "a dramatic intellectual turnabout."

Annalee Newitz - 11/5/2017, 5:50 AM



It's been one of the most contentious debates in anthropology, and now scientists are saying it's pretty much over. A group of prominent anthropologists have done an overview of the scientific literature and declare in *Science* magazine that the "Clovis first" hypothesis of the peopling of the Americas is dead.

For decades, students were taught that the first people in the Americas were a group called the Clovis who walked over the Bering land bridge about 13,500 years ago. They arrived (so the narrative goes) via an ice-free corridor between glaciers in North America. But evidence has been piling up since the 1980s of human campsites in North and South America that date back much earlier than 13,500 years. At sites ranging from Oregon in the US to Monte Verde in Chile, evidence of human habitation goes back as far as 18,000 years.

In the 2000s, overwhelming evidence suggested that a pre-Clovis group had come to the Americans before there was an ice-free passage connecting Beringia to the Americas. As Smithsonian anthropologist Torben C. Rick and his colleagues put it, "In a dramatic intellectual turnabout, most archaeologists and other scholars now believe that the earliest Americans followed Pacific Rim shorelines from northeast Asia to Beringia and the Americas."

Now scholars are supporting the "kelp highway hypothesis," which holds that people reached the Americas when glaciers withdrew from the coasts of the Pacific Northwest 17,000 years ago, creating "a possible dispersal corridor rich in aquatic and terrestrial resources." Humans were able to boat and hike into the Americas along the coast due to the food-rich ecosystem provided by coastal kelp forests, which attracted fish, crustaceans, and more.

No one disputes that the Clovis peoples came through Beringia and the ice free corridor. But the Clovis would have formed a second wave of immigrants to the continent.

Despite all the evidence for human habitation, ranging from tools and butchered animal bones to the remains of campfires, scientists are still uncertain who the pre-Clovis peoples were. We have many examples of Clovis technology, with characteristic shapes for projectile points and pottery. But we have no recognizable pre-Clovis toolkit.

That may be about to change, however. The pre-Clovis people traveled along a now-drowned coastline, submerged after the last of the ice-age glaciers melted. New techniques in marine archaeology, ranging from ROVs to underwater lasers, are helping scientists

explore ancient submerged villages. A team even turned up a 14,500-year-old campsite in Florida in a blackwater sinkhole last year.

Rick and his colleagues write that the big question now is when pre-Clovis people actually arrived in the Americas. They suggest the arrival could be as early as 20,000 years ago on the verdant kelp highway. Other researchers, however, say people could have arrived during a temperate period about 130,000 years ago. A recent paper in *Nature* describes what appear to be the 130,000-year-old butchered remains of mastodons in California, along with sharp stones used to deflesh the animals. There is plenty of skepticism in the scientific community about this discovery, but the evidence can't be ignored.

To the best of our knowledge, the kelp highway brought humans to the Americas. Using boats and fishing tools, humans made it all the way from Asia to the Americas, founding many coastal communities along the way. And now for the next debate: who were they, and when exactly did they arrive?

Science, *2017. DOI: 10.1126/science.aao5473 (About DOIs).*

http://bit.ly/2yx4qsb

Science confirms you should stop and smell the roses

Short nature intervention can bring out the best in people

Is it any wonder that most happiness idioms are associated with nature? Happy as a pig in muck, happy as a clam, happy camper.

A UBC researcher says there's truth to the idea that spending time outdoors is a direct line to happiness. In fact, Holli-Anne Passmore says if people simply take time to notice the nature around them, it will increase their general happiness and well-being.

Passmore, a PhD psychology student at UBC's Okanagan campus, recently published research examining the connection between taking a moment to look at something from the natural environment and personal well-being.

A recent study involved a two-week 'intervention' where participants were asked to document how nature they encountered in their daily routine made them feel.

They took a photo of the item that caught their attention and jotted down a short note about their feelings in response to it.

Other participants tracked their reactions to human-made objects, took a photo and jotted down their feelings, while a third group did neither.

Passmore explains that examples of nature could be anything not human built: a house plant, a dandelion growing in a crack in a sidewalk, birds, or sun through a window.

"This wasn't about spending hours outdoors or going for long walks in the wilderness," Passmore says. "This is about the tree at a bus stop in the middle of a city and the positive effect that one tree can have on people."

Passmore, who studies wellness, says she was 'overwhelmed' not only by the response of her 395 study participants--more than 2,500 photos and descriptions of emotions were submitted--but also by the impact that simply noticing emotional responses to nearby nature had on personal well-being.

And their prosocial orientation--a willingness to share resources and the value they placed on community.

There is scientific documentation that people who live in greenspaces generally seem to be happier, and may live longer than those who don't.

Passmore is taking that research further. This study is one of a series by a research team in UBC Okanagan's psychology department known as the "Happy Team" which is providing evidence that nature can increase happiness.

"The difference in participants' well-being--their happiness, sense of elevation, and their level of connectedness to other people, not just nature--was significantly higher than participants in the group noticing how human-built objects made them feel and the control group."

Passmore's research, recently published in the Journal of Positive Psychology, is supported by the Social Sciences and Humanities Research Council of Canada.

http://bit.ly/2j5sPhX

Caffeine consumption may help kidney disease patients live longer

In patients with chronic kidney disease, there was a dose-dependent inverse association between caffeine consumption and early death.

New Orleans, LA -- Caffeine consumption may prolong the lives in patients with chronic kidney disease (CKD), according to a study that will be presented at ASN Kidney Week 2017 October 31-November 5 at the Ernest N. Morial Convention Center in New Orleans, LA.

Coffee consumption has been linked to a longer life in the general population. To see if this holds true for individuals with CKD, Miguel Bigotte Vieira, MD (Centro Hospitalar Lisboa Norte, in Portugal), and his colleagues examined the association of caffeine consumption with mortality among 2328 patients with CKD in a prospective US cohort, using the continuous National Health and Nutrition Examination Survey (NHANES) 1999-2010.

The team found a dose-dependent inverse association between caffeine and all-cause mortality. Compared with those in the lowest quartile of caffeine consumption, those in the second, third, and highest quartiles had 12%, 22%, and 24% lower risks of dying.

"Our study showed a dose-dependent protective effect of caffeine consumption on mortality among patients with CKD. This association was independent of potential confounders including age, gender, race, annual family income, education level, estimated GFR, albumin/creatinine ratio, hypertension, smoking status, dyslipidemia, body mass index, previous cardiovascular events and diet: consumption of alcohol, carbohydrates, polyunsaturated fatty acids, and fibers," said Dr. Bigotte Vieira.

"These results suggest that advising patients with CKD to drink more caffeine may reduce their mortality.

This would represent a simple, clinically beneficial, and inexpensive option, though this benefit should ideally be confirmed in a randomized clinical trial." Dr. Bigotte Vieira stressed that this observational study cannot prove that caffeine reduces the risk of death in patients with CKD, but only suggests the possibility of such a protective effect.

Study: "Caffeine consumption and mortality in chronic kidney disease" (Abstract 2784081)

http://bit.ly/2zzeNvW

Solar greenhouses generate electricity and grow healthy crops

Magenta panes also help plants save water

The first crops of tomatoes and cucumbers grown inside electricity-generating solar greenhouses were as healthy as those raised in conventional greenhouses, signaling that "smart" greenhouses hold great promise for dual-use farming and renewable electricity production.

"We have demonstrated that 'smart greenhouses' can capture solar energy for electricity without reducing plant growth, which is pretty exciting," said Michael Loik, professor of environmental studies at the University of California, Santa Cruz, and lead author on a paper that appears in the current issue of the American Geophysical Union's journal Earth's Future.

Electricity-generating solar greenhouses utilize Wavelength-Selective Photovoltaic Systems (WSPVs), a novel technology that generates electricity more efficiently and at less cost than traditional photovoltaic systems. These greenhouses are outfitted with transparent roof panels embedded with a bright magenta luminescent dye that absorbs light and transfers energy to narrow photovoltaic strips, where electricity is produced. WSPVs absorb some of the blue and green wavelengths of light but let the rest through, allowing the plants to grow. WSPV technology was developed by coauthors Sue Carter and Glenn Alers, both professors of physics at UC Santa Cruz, who founded Soliculture in 2012 to bring the technology to market.

Loik's team monitored photosynthesis and fruit production across 20 varieties of tomatoes, cucumbers, lemons, limes, peppers, strawberries,

and basil grown in magenta glasshouses at two locations on campus and one in Watsonville, California.

"Eighty percent of the plants weren't affected, while 20 percent actually grew better under the magenta windows," said Loik. Tomatoes and cucumbers are among the top greenhouse-produced crops worldwide, he said.

In additional experiments, small water savings were associated with tomato photosynthesis inside the magenta glasshouses. "Plants required 5 percent less water to grow the same amount as in more conventional glasshouses," he said.

"I thought the plants would grow more slowly, because it's darker under these pink panels. The color of the light makes it like being on the Red Planet," said Loik. "Plants are sensitive not just to the intensity of light but also to color. But it turns out the plants grow just as well."

Reducing the energy consumed by greenhouses has become a priority as the global use of greenhouses for food production has increased six-fold over the past 20 years to more than 9 million acres today--roughly twice the size of New Jersey, according to Loik. "It's big and getting bigger," he said. "Canada relies heavily on greenhouses for vegetable production, and their use is growing in China, too." Plastic greenhouses are becoming popular for small-scale commercial farming, as well as for household food production, he added.

Greenhouses use electricity to control temperature and power fans, lights, and other monitoring systems. "This technology has the potential to take greenhouses offline," said Loik, who specializes in climate change, plant physiology, water resources, and sustainable technologies. Cost per panel of WSPV technology is 65 cents per watt--about 40 percent less than the per-watt cost of traditional silicon-based photovoltaic cells.

"If greenhouses generate electricity on site, that reduces the need for an outside source, which helps lower greenhouse gas emissions even more," said Loik. "We're moving toward self-sustaining greenhouses."

Additional coauthors include Catherine Wade, who participated as a graduate student, Carley Corrado, who participated as a postdoctoral researcher, and undergraduates David Shugar and Devin Jokerst, all of UC Santa Cruz; and Carol Kitayama, senior grower at Kitayama Brothers Growers.

http://bit.ly/2yx0qrM

Elderly doctor: I lost my license because I don't know how to use a computer

Doc says her paper records are just fine—state medical board disagrees.

Cyrus Farivar - 11/5/2017, 7:30 PM

An 84-year-old doctor in New London, New Hampshire, appeared in state court Friday in an effort to regain her medical license, less than a week after closing her office on October 28.

Close-up of an opened prescription bottle, labelled as containing the opioid hydrocodone, as a number of its pills lie on a white surface, March 14, 2017.

Tom Kelley/Getty Images

State authorities claim that—because Dr. Anna Konopka doesn't have a computer, much less know how to use one—her organizational skills are lacking, according to the Associated Press.

"The problem now is that I am not doing certain things on a computer," she told the news service. "I have to learn that. It is time consuming. I have no time."

Specifically, Konopka is unable to access the state's required online drug monitoring program—it mandates that prescribers tell state authorities what quantities of opioids they're issuing.

These issues, authorities claim, are seemingly harming her ability to practice medicine and abide by state law.

Earlier this year, one of her patient's family members complained to the state medical board, which sparked an investigation.

Konopka was formally reprimanded in May 2017, but then received more complaints. However, Konopka said she was forced to give up her medical license in October 2017.

The *New Hampshire Union Leader* reported Friday that Senior Assistant Attorney General Lynmarie Cusack said Konopka "surrendered her license after Board of Medicine investigators confronted her with the results of four separate investigations. Cusack would not discuss the investigations, saying they remain confidential under state law."

Neither Konopka, the New Hampshire Board of Medicine, nor the Office of the Attorney General immediately responded to Ars' requests for comment.

Online state records show her license is set to expire on June 30, 2018, but that there is a "settlement agreement" dated May 12, 2017. Ars was not able to find any other publicly-available documentation.

Simple, country doctor

Konopka graduated from medical school in her native Poland in 1960 and moved to the United States shortly thereafter. She has been a licensed physician since 1968.

The Associated Press described her now-shuttered office in this small town of just 4,000 people as containing "two file cabinets in a tiny waiting room inside a 160-year-old clapboard house [that] hold most of her patient records. The only sign of technology in the waiting room is a landline telephone on her desk."

According to the *Union Leader*, Konopka appeared in court on Friday without an attorney and pressed the Merrimack County Superior Court judge to order the state's medical board to reinstate her.

Konopka told the court that the Board of Medicine threatened to revoke her license if she did not give it up voluntarily—which allowed her to keep practicing for another month.

"I had no choice," she told Judge John Kissinger, who did not issue a ruling. The AP also noted that Konopka will see any patient who can pay her $50 in cash.

"If I close my office, they will be without medical care," she also told the court. "Some of them need medications. Who will prescribe for them if I don't have a license? I worry what will happen to them."

http://wb.md/2zmwXjk

Oral HPV in Men: On the Rise

Incidence of HPV-related mouth and throat cancers in men is now higher than cervical cancer in women

Arefa Cassoobhoy, MD, MPH

Hello. I'm Dr Arefa Cassoobhoy, a practicing internist, Medscape advisor, and senior medical director for WebMD. Welcome to Morning Report, our 1-minute news story for primary care.

Oral HPV Rates Higher in Men

New data point to an alarming trend: 1 in 9 men have an oral human papillomavirus (HPV) infection. And when the focus is on HPV 16, the high-risk type associated with oropharyngeal cancer, the prevalence is six times higher among men than women.

To put this in context, the incidence of HPV-related mouth and throat cancers in men is now higher than cervical cancer in women.

The prevalence of oral HPV infection peaks at age 50-54 years and is particularly high among men who have had more than 16 lifetime oral sex partners, men who have had sex with men, and men with concurrent genital HPV infection.

Smoking and marijuana use also increased the risk for infection.

The authors recommend looking at the value of vaccinating middle-age men. But for now, to reverse this trend, we must encourage males, as well as females, to get vaccinated against HPV according to the guidelines, as children or young adults.

http://bit.ly/2AakTPw

It's mostly mothers who pass on mitochondria – and a new theory says it's due to the first sexual conflict

Different kind of sexual conflict identified possibly dating back 1.5 billion years when the most complex organisms were single cells

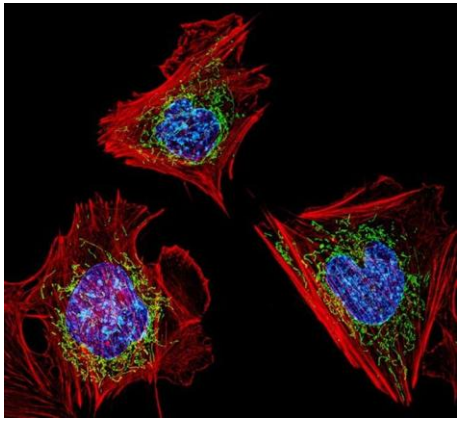
1. Arunas L. Radzvilavicius

Postdoctoral Researcher of Evolutionary Biology, University of Pennsylvania

Evolutionary interests of males and females do not always coincide. This is known as sexual conflict: male innovations that allow them to reproduce more sometimes hurt females, and vice versa.

Male fruit flies, for instance, inject their partners with toxic chemicals during sex. These toxins destroy sperm of the female's previous mates, improving his own chances for becoming the sole father of her offspring. But the toxins also make female flies sick and reduce their lifespan. Females, in turn, have evolved defenses to counter the chemicals, sometimes at the expense of males' success.

Biologists believe that sexual conflicts are rooted in the size and number of reproductive cells – eggs and sperm. Males typically produce large numbers of sperm that can fertilize multiple eggs. Females, on the other hand, produce a small number of large reproductive cells, and so invest more energy and resources in each.

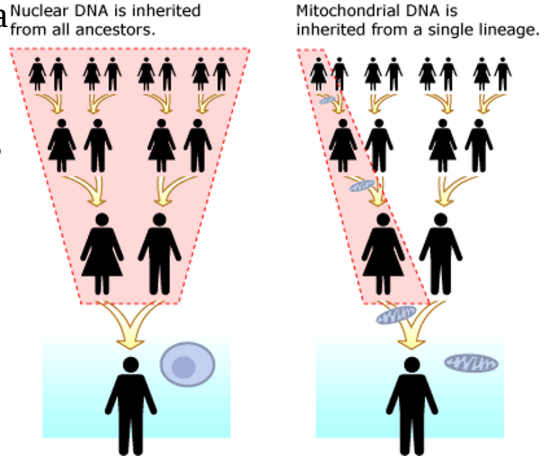


Eukaryotic cells have a nucleus (blue) and numerous mitochondria (green). Dylan Burnette and Jennifer Lippincott-Schwartz, Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health, CC BY-NC

My team of evolutionary biologists at University College London has now identified a different kind of sexual conflict, dating back to the days when the most complex organisms were made of single cells, possibly as far as 1.5 billion years ago. This ancient sexual conflict – before the two sexes even existed – had to do with whose mitochondria would be passed on to offspring.

Whose mitochondria will be passed on?

We studied inheritance of genes located in mitochondria – the structures inside our cells that breathe and produce energy. In many animals and plants, when the egg is fertilized, only the mother's mitochondrial genes survive, while the father's mitochondria are lost. This is not by accident: Females have evolved many mechanisms to recognize a partner's mitochondria entering the egg. Once detected, an army of enzymes is sent to digest them. Previous research has shown that getting rid of male mitochondria is a way to keep descendents' mitochondrial genes mutation-free. In the long run, inheritance of healthy maternal mitochondria is good news for the offspring.



For the most part mitochondria come from the mother's line. But there are exceptions. University of California Museum of Paleontology and the National Center for Science Education, CC BY-SA

But there are many exceptions that remain unexplained. In some species, paternal mitochondria remain undigested, as if the father had found a way to protect them from being detected. Stranger still, in organisms such as fruit flies and many plants, it is the father that destroys most of his own mitochondria during production of sperm.

If maternal inheritance is as beneficial as previous research shows, why are there so many exceptions?

Taking the long or the short view

In our new study, we show that these exceptions arise because of a sexual conflict over the control of mitochondrial inheritance.

Using mathematical modeling, we found that evolution in females tends to focus on long-term effects. Destroying paternal mitochondria makes it easier to weed out harmful mutations in the future, but this effect unfolds over many generations. This strategy works well in females, because the same healthy set of maternal mitochondria is passed down the female line over and over again.

But males don't have a long evolutionary time horizon to deal with in this case. Since most of their mitochondria are replaced by maternal ones at the start of every generation, evolution cannot detect long-term benefits from males' mitochondrial genes. Because there's no long-term link, they can benefit only in the immediate future, and that often means passing on some of their mitochondria right now. Males therefore seek to improve the fitness of their offspring in the short-term, even if the long-term effects are harmful.

It's these different interests of males and females that can lead to an evolutionary arms race, as selection in the two sexes acts in opposite directions. Evolution in females strives to keep the future generations free of male mitochondria, while males make every effort to get some of theirs into the mix.

"Over and over again, males have come up with ways to subvert female destruction of their mitochondria," said my co-author, geneticist Andrew Pomiankowski. "So females had to develop new ways to block male mitochondria. Our model explains nicely why there are so many different mechanisms used to exclude male mitochondria, and why males sometimes do it themselves."

It's all about the control of mitochondrial inheritance – and for males it's better to be in the driver's seat to decide how many mitochondria they contribute to the mix than be completely excluded.

A sexual conflict that led to the sexes

There is evidence that this conflict dates back to the days when all organisms were made of single cells. Male and female sexes did not exist, because all reproductive cells were of the same size.

"One of the strategies an organism can use to win in this conflict is to simply have more mitochondria than their partner, for example, by increasing the size of their sex cells," Andrew Pomiankowski said. "Strikingly, this might have been the impetus to evolve two sexes in the first place." Larger sex cells – the future eggs – garnered an advantage in the battle over mitochondrial inheritance, simply by swamping smaller sex cells – the forerunners of sperm – that had fewer mitochondria to contribute.

Most biologists currently think that two sexes evolved through division of labor – a so-called "disruptive selection" theory. Large female sex cells can survive longer but cannot move much, while smaller sperm are fragile but move faster and can find more mating partners.

Our hypothesis on the origin of sexes, if true, adds a new angle to this origins story, tracing it back to an ancient conflict over mitochondrial inheritance. Females may have won this ancient battle by simply producing larger sex cells packed with mitochondria, ensuring that mitochondrial transmission is effectively one-sided (and reaping the long-term fitness benefits). But ultimately, as with all scientific hypotheses, this one will have to stand the test of thorough experimental verification.

Disclosure statement

Arunas L Radzvilavicius receives funding from David and Lucille Packard Foundation.

http://bit.ly/2hfjSlm

Périgord black truffle cultivated in the UK for the first time

The Mediterranean black truffle, one of the world's most expensive ingredients, has been successfully cultivated in the UK, as climate change threatens its native habitat.

Researchers from the University of Cambridge and Mycorrhizal Systems Ltd (MSL) have confirmed that a black truffle has been successfully cultivated in the UK for the first time: the farthest north that the species has ever been found. It was grown as part of a

programme in Monmouthshire, South Wales, run by MSL in collaboration with local farmers. The results of the programme, reported in the journal Climate Research, suggest that truffle cultivation may be possible in many parts of the UK.

After nine years of waiting, the truffle was harvested in March 2017 by a trained dog named Bella. The aromatic fungus was growing within the root system of a Mediterranean oak tree that had been treated to encourage truffle production. Further microscopic and genetic analysis confirmed that Bella's find was indeed a Périgord black truffle (Tuber melanosporum).

The black truffle is one of the most expensive delicacies in the world, worth as much as £1,700 per kilogram. Black truffles are prized for their intense flavour and aroma, but they are difficult and time-consuming to grow and harvest, and are normally confined to regions with a Mediterranean climate. In addition, their Mediterranean habitat has been affected by drought due to long-term climate change, and yields are falling while the global demand continues to rise. The truffle industry is projected to be worth £4.5 billion annually in the next 10-20 years.

Black truffles grow below ground in a symbiotic relationship with the root system of trees in soils with high limestone content. They are found mostly in northern Spain, southern France and northern Italy, where they are sniffed out by trained dogs or pigs. While they can form naturally, many truffles are cultivated by inoculating oak or hazelnut seedlings with spores and planting them in chalky soils. Even through cultivation, there is no guarantee that truffles will grow.

"It's a risky investment for farmers - even though humans have been eating truffles for centuries, we know remarkably little about how they grow and how they interact with their host trees," said paper co-author Professor Ulf Büntgen of Cambridge's Department of Geography. "Since the system is underground, we can't see how truffles are affected by different environmental conditions, or even when the best time to water them is. There's been no science behind it until now, so progress is slow."

In partnership with local farmers, Büntgen's co-author Dr Paul Thomas from MSL and the University of Stirling has been cultivating truffles in the UK for the past decade. In 2015, MSL successfully cultivated a UK native Burgundy truffle, but this is the first time the more valuable black Périgord truffle has been cultivated in such a northern and maritime climate. Its host tree is a Mediterranean oak that was planted in 2008. Before planting, the tree was inoculated with truffle spores, and the surrounding soil was made less acidic by treating it with lime.

"This is one of the best flavoured truffle species in the world and the potential for industry is huge," said Thomas. "We planted the trees just to monitor their survival, but we never thought this Mediterranean species could actually grow in the UK - it's an incredibly exciting development."

The researchers have attributed the fact that black truffles are able to grow so far outside their native Mediterranean habitat to climate change. "Different species respond to climate change on different scales and at different rates, and you often get an ecological mismatch," said Büntgen. "For instance, insects can move quickly, while the vegetation they depend on may not. It's possible that truffles are one of these fast-shifting species."

"This cultivation has shown that the climatic tolerance of truffles is much broader than previously thought, but it's likely that it's only possible because of climate change, and some areas of the UK - including the area around Cambridge - are now suitable for the cultivation of this species," said Thomas. "While truffles are a very valuable crop, together with their host trees, they are also a beneficial component for conservation and biodiversity."

The first harvested truffle, which weighed 16 grams, has been preserved for posterity, but in future, the truffles will be distributed to restaurants in the UK.

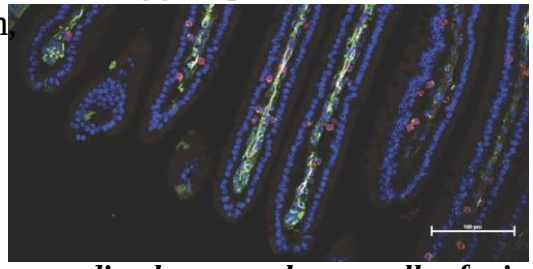
http://bit.ly/2ixFGp9

Gut bacteria may make or break your chances of cancer treatment working

Bacteria in the intestines may prime immune cells to run down tumors.

Beth Mole - 11/6/2017, 12:00 AM

New, potent cancer therapies can act like daggers pressed into the hindquarters of the immune system, prodding it to lunge at any cancerous cells in the body. When the drugs work, the immune system tramples tumors into oblivion.



Enlarge / After fecal transplants from responding humans, the gut cells of mice (blue) were flooded with cancer-fighting immune cells (red, green) Dr. Luigi Nezi]

But they don't always work—in fact, cancer drugs can fail 60 to 70 percent of the time. The drugs might not give the immune system a sharp enough sticking in every patient. But according to a pair of new studies, it may not be the immune system that needs a swift kick—it may be the gut.

Some intestinal-dwelling bacteria appear to corral and train immune cells to fight off cancer cells—prior to any spurring from cancer immunotherapies. Without such microbial priming, the drugs may only offer a futile prod. In both studies, published this week in *Science*, researchers found that the cancer patients who saw no benefit from the drugs (non-responders) were the ones who lacked certain beneficial gut bugs, particularly after taking antibiotics. Meanwhile, cancer patients who did respond to the drugs had bacteria that could prompt the immune system to release chemicals that get cancer-killing immune cells—T cells—to chomp at the bit.

When the researchers transferred the gut microbes from their human cancer patients into germ-free mice with cancer, the rodents mirrored the patients' fates. That is, mice that got gut microbes from non-responding humans also did not respond to immunotherapies. But, the mice that got microbes from responders responded. And when researchers swapped responder gut microbes into non-responding mice, the mice converted and fought back the cancer.

"Our studies in patients and subsequent mouse research really drive home that our gut microbiomes modulate both systemic and anti-tumor immunity." That's according to Jennifer Wargo, a surgical oncologist and geneticist at the University of Texas MD Anderson Cancer Center and the senior author of one of the studies. Dr. Wargo is planning clinical trials to see if fecal transplants in cancer patients could improve immunotherapy success rates.

"You can change your microbiome," she added. "It's really not that difficult, so we think these findings open up huge new opportunities."

Charging ahead

In Dr. Wargo's study and the other—led by immunologist Laurence Zitvogel of the Gustave Roussy Cancer Campus in Villejuif, France—researchers focused on a type of "checkpoint" inhibitor cancer treatment called "PD-1 inhibitors." Generally, PD-1 is a protein on the surface of T cells that—in non-cancerous scenarios—acts as a checkpoint to guard against over-zealous immune responses and auto-immune diseases. PD-1 does this by latching onto proteins on healthy cells, namely PD-L1, which basically signals to the T-cell to stand down and not attack the healthy cell.

Crafty cancer cells often don PD-L1, though, allowing them to escape a T cell blitz. That's where the PD-1 inhibitors come in. If the drugs get in the way of PD-1 binding to PD-L1 on cancer cells, they can help unleash the wrath of T cells on those tumors. But, as mentioned, PD-1 inhibitor therapies often don't work.

Prior to the new study, Zitvogel and colleagues noticed that recent mouse studies were showing that gut microbes play a role in regulating immune responses to cancers. If that's true, they hypothesized, then bacteria-killing antibiotics could squash the effects

of PD-1 inhibitors. To see if that held up, they simply looked at the outcomes of 249 patients with either lung, kidney, or bladder cancer, some of whom received antibiotics around the time of their PD-1 inhibitor treatments. The researchers found a clear link between antibiotic use and immunotherapy failures. Specifically, the 69 patients taking antibiotics had shorter survival times and periods without their cancers progressing compared with patients with the same cancers and similar health factors.

Next, the researchers examined the communities of microbes in the poop of 100 responding and non-responding cancer patients. They found big differences in the abundance of certain types of bacteria. Specifically, those who responded to PD-1 inhibitors were more likely to carry *Akkermansia muciniphila*, an intestinal bacterium hypothesized to have anti-inflammatory effects. In mouse experiments, *A. muciniphila* spurred immune cells to release a chemical signal called IL-2, which is known to regulate T-cells and prime them to attack. Likewise, treatments of *A. muciniphila* could convert non-responding gut microbes into responding microbes in mice with cancer.

Wargo's study had similar findings. In their work with 112 skin cancer patients undergoing PD-1 inhibitor treatments, they, too, found that a patient's gut microbiomes linked with the success or failure of their immunotherapy. Though they didn't pick out *A. muciniphila* specifically, they noted that responders tended to have more diverse communities and more of certain types of bacteria. And again, when they transferred the patients' gut microbiomes into germ-free mice with cancer, the mice met the same fate as their human microbe donors. The researchers also found evidence of beneficial microbes priming T cells.

Together, the studies suggest a big role for gut microbes in determining the cancer-killing potential of immunotherapies. But there are still plenty of questions, namely how, exactly, certain bacteria may spur the immune system to fight cancer and if there are side-effects or potential dangers of manipulating the microbiomes of cancer patients. Still, as Wargo and colleagues conclude:

These findings highlight the therapeutic potential of modulating the gut microbiome in patients receiving checkpoint blockade immunotherapy, and [they] warrant prompt evaluation in cancer patients through clinical trials.

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Science, 2017. DOI: 10.1126/science.aan3706 (About DOIs).

http://bbc.in/2h8Q5r3

Australia gonorrhoea cases surge 63%

The number of cases of gonorrhoea in Australia has soared by 63% in the past five years, a new study has found.

Australian researchers say the rise in gonorrhoea diagnoses was led by an increase in infection in young heterosexual city dwellers. However the reasons for the dramatic increase are unclear, researchers say.

Changes in sexual behaviour or a particular strain of the infection could be behind the rise, researchers told AAP. Gonorrhoea can infect the genitals, rectum and throat, and is treatable with antibiotics.

"Up until recently, gonorrhoea had been uncommon in young heterosexual people living in major cities," said associate professor at the University of New South Wales, Rebecca Guy, one of the study's authors. "Rising rates in this group highlight the need for initiatives to raise awareness among clinicians and young people about the importance of testing."

An annual report on Australia's sexual health was released by the university's Kirby Institute on Monday. It found that other sexually transmissible infections (STIs), such as syphilis, had also increased, particularly among Indigenous Australians. Meanwhile the number of HIV diagnoses remained steady for a fifth consecutive year at about 1,000 cases. Chlamydia was the most common STI in Australia, with nearly 72,000 cases last year. Three quarters of the sufferers were aged 15-29.

Mostly men affected

Between 2012 and 2016, rates of gonorrhoea jumped from 62 per 100,000 people to 101 per 100,00 people. Rates soared 72% for men and 43% for women. The rise suggested "suggests increasing transmission through heterosexual sex", the report said.

Young people saw the biggest increase, with males aged between 25 and 29, and females aged 20 and 24 experiencing the steepest rises. However the majority of cases still affect men. In 2016, men experienced three-quarters of the near 24,000 cases of gonorrhoea.

The rate of infection among Aboriginal and Torres Strait Islander people were also almost seven times that of the non-Indigenous population.

Gonorrhoea has no symptoms in about 80% of women and 50% of men. The World Health Organization warned earlier this year that the disease is rapidly developing resistance to antibiotics.

What is gonorrhoea?

The disease is caused by the bacterium called Neisseria gonorrhoea.

The infection is spread by unprotected vaginal, oral and anal sex.

Symptoms can include a thick green or yellow discharge from sexual organs, pain when urinating and bleeding between periods.

However, of those infected, about one in 10 heterosexual men and more than three-quarters of women, and gay men, have no easily recognisable symptoms.

Untreated infection can lead to infertility, pelvic inflammatory disease and can be passed on to a child during pregnancy.

http://nyti.ms/2heTGHL

If You Tear a Knee Ligament, Arthritis Is Likely to Follow in 10 Years

Reviewing available data shows over 50% chance of getting arthritis within a decade of tearing a knee tendon or a ligament

By GINA KOLATA NOV. 6, 2017

When Jason Lalli tore his left anterior cruciate ligament at age 26, he thought he would be fine as soon as he had his knee repaired. As a soccer player who competed through college and then on recreational teams, he knew that A.C.L. injuries could be debilitating but also that orthopedists could fix them.

He figured that he would miss a season, but that he could play and coach the game he loved for the rest of his life.

Four years later, his knee began to ache, and the pain became more constant over time, nagging almost “like a toothache,” he said. Within about another year, Lalli’s doctor did more work on the knee and gave him bad news: He had arthritis.

And, Lalli eventually learned, it was almost predictable.

Orthopedists have believed for years that torn tendons or ligaments put patients, no matter how young, at risk for arthritis. But quantifying the long-term risk has been difficult because most orthopedic patients are not studied for extended periods after their injuries.

Dr. Mininder Kocher, an orthopedics professor at Harvard Medical School, has reviewed the available data and determined that the chance of getting arthritis within a decade of tearing a tendon or a ligament in the knee is greater than 50 percent.

Lalli, now 39 and a resident of Canonsburg, Pa., is hobbled by knee pain. He gave up soccer. Then he had to give up running. He has tried swimming and cycling, but he said, “My heart is not in it.” Some days he can barely walk. And he has no memory of any doctor warning him that he could get arthritis.

“It’s like a dirty little secret,” said Kocher, who is also the associate director of the division of sports medicine at Boston Children’s Hospital. “It’s not that anyone is covering up. It’s just that it’s not well known.”

But as someone who spends his days repairing torn knee ligaments in teenagers, he is worried. He has written a paper, soon to be published, that says the number of A.C.L. operations at 26 children’s hospitals in the United States has soared as more children and adolescents play sports that involve twisting the knee, like soccer and basketball, and often participate year-round.

In 2004, there were about 500 A.C.L. operations at those hospitals; in 2014, there were more than 2,500, he reports. “This is a major issue for me,” said Kocher, who does more than 150 A.C.L. reconstructions a year, mostly in adolescents. “If a 15-year-old gets arthritis in 10 years, knee replacement is not a great option at age 25.”

One of the few long-term studies was done carried out by Britt Elin Oiestad, a physical therapy researcher at Oslo and Akershus University College of Applied Sciences, who followed 181 people for 10 to 15 years after A.C.L. surgery. Seventy-four percent developed arthritis that could be seen on X-rays. Some of those patients had yet to feel arthritic pain; 41 percent of those studied had reported knee pain that indicated arthritis. “It’s scary,” Oiestad said.

While knee injuries have received the most attention in research on arthritis risk, other joints are not immune, said Dr. Brett Owens, a professor of orthopedic surgery at Brown University Alpert Medical School. People who repeatedly sprain an ankle are at risk, he said. And up to 40 percent of those who dislocate a shoulder get arthritis within about 15 years, he said.

What researchers want to know is this: Why do these injuries precipitate arthritis? Is the answer a bone bruise that injures cartilage? Chemical changes that happen as the body tries to repair the injury? An intrinsic instability of the knee?

And would surgical methods that more closely reproduce an individual’s original knee anatomy reduce the risk?

Research is not definitive but seems to support all of the hypotheses, as well as a strong hunch among investigators that there are genetic factors. Owens mentioned “A.C.L. families,” explaining, “I have operated on multiple siblings in a family.”

Doctors say they struggle with telling adolescents who just tore an A.C.L. that arthritis might follow. Owens says that he mentions arthritis but not in his initial conversations with young injured athletes. “Most young athletes just want to focus on the problem at hand,” he said. “Yesterday in my office, I saw a 17-year-old soccer player. ‘Yes, you tore your A.C.L.’ The tears start to come. It is hard to talk to a 17-year-old about what their knee will be like in 20 years.”

Although Lalli, the former soccer player, said his arthritis diagnosis was a shock, he also said that knowing that it might happen would not have made much difference. He might have a genetic predisposition toward knee arthritis. His father took up soccer in his late 40s and had to have surgery at 50 when he tore the A.C.L. in his left knee.

Then he tore the meniscus — a piece of cartilage that acts as a cushion between the shinbone and the thighbone — in his right knee. He got arthritis later but thought it was because of his age, not his injuries.

Lalli’s arthritis progressed despite his receiving a second A.C.L. reconstruction that was more tailored to the anatomy of his knee. His initial operation had been done by a surgeon who did not position the new ligament in the exact place it had been before.

Lalli had the subsequent operation done by Dr. Freddie Fu, the chairman of the Department of Orthopedic Surgery at the University of Pittsburgh School of Medicine. Fu is a leader in A.C.L. operations that are more anatomically specific, and his procedure stabilized Lalli’s knee. Nonetheless, Lalli has faced years of disabling pain.

Four years ago, when his arthritis got so bad that he gave up playing soccer, Lalli asked for a knee replacement. Fu refused, telling him that artificial knees last only 10 or 15 years in younger and active people and that each knee replacement is more problematic than the one before.

A person can have only two or three knee replacements in a lifetime, Fu told Lalli, and so it was best to wait until he was 50.

Now Lalli is trying to decide whether to let his children play soccer. He has a 5-year-old and 3-year-old twins, and he said they “seem to naturally gravitate toward soccer.”

Lalli, who loves the sport, is torn and has been talking it over with his wife. “I’m not sure what we will do,” he said.