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Herbal medicine shows potential to treat cancer

Three plants used for traditional medicine in Saudi Arabia are shown to be worthy of further investigation for anticancer properties

Researchers from KAUST have been searching locally for plants that have potential for use to combat cancer. Now, three plants used for traditional medicine in Saudi Arabia are shown to be worthy of further investigation for anticancer properties.

Cancer is a leading cause of illness and death worldwide. In 2015, the World Health Organization (WHO) recorded 8.8 million cancer-related deaths, but almost twice as many cases are diagnosed each year. And the WHO predict that the number of cancer diagnoses is likely to continue to increase by about 70% for at least the next two decades due to growing longevity.

Seeking to expand the armory of cancer treatments -- especially ones that are simple and inexpensive to manufacture -- a team led by Timothy Ravasi and Christian Voolstra from KAUST has investigated the biological potential (bioactivity) of a range of plants used locally in traditional medicine.

Use of herbal medicines is common in Saudi Arabia, explains Ravasi's PhD student, Dina Hajjar. "However, there are almost no scientific studies," says Hajjar. "Saudi people tend to use information inherited from their families to decide about these plants without validated knowledge of their biological or chemical activity."

The team initially investigated 52 plants before they homed in on three plants that showed promise -- Juniperus phoenicea (known in herbal medicine as Arar or Phoenican juniper), Anastatica hierochuntica (known as Kaff Maryam or the Jericho rose) and Citrullus colocynthis (known as Hanzal or bitter cucumber).

The team used cell-based phenotypic profiling via imaging-based high-content screening to assess anticancer activity. This approach followed a technique developed in 2016 by Stephan Kremb and Christian Voolstra that uses a comprehensive marker panel with standardized settings -- an efficient process that could potentially be easily adopted by other laboratories. This meant the team compared the cytological profiles of fractions taken from the plants with a set of reference compounds with established mechanisms of action.

This enabled the team to show, for the first time, that these three plants contain potent anticancer substances -- topoisomerase inhibitors, which are compounds that can block the topoisomerase enzymes that control changes in DNA -- that could be used to develop novel anticancer inhibitors.

There are many steps, however, before these compounds are properly tested and available for clinical treatments for cancer. "The active compounds identified in the study will need to be evaluated and better characterized," says Hajjer. "Also, active compounds need to be synthesized and tested in vivo."

This study proves the power of using imaging-based high-content screening in revealing information about the bioactivity of unknown natural resources. Hajjar adds that it also highlights the opportunity for more exciting discoveries amongst the natural resources of Saudi Arabia.

http://bit.ly/2vlBD5m

Man loses feeling in legs after long-term denture fixative use

Zinc in fixative to blame for development of rare neurological disorder

A 62-year-old man lost the feeling in both his legs after the regular long term use of a denture fixative containing zinc, reveal doctors writing in the online journal BMJ Case Reports.

The man was referred to a neurology clinic after developing numbness, pain and weakness in his legs. The symptoms, which had lasted for more than six months, stopped him from leaving the house.

An MRI (magnetic resonance imaging) scan revealed spinal cord abnormalities and after several tests he was diagnosed with copper deficiency myelopathy (CDM).

CMD is a neurological disorder which can cause loss of feeling and numbness in the arms and legs.

The man explained that he had been using 2-4 tubes of denture fixative that contained zinc every week for the past 15 years because of his ill-fitting false teeth. Excess zinc intake can interfere with the absorption of copper, leading to neurological problems, in rare cases.

The man was advised to stop using the fixative and given copper supplements to treat his symptoms. But he didn't recover completely, and the doctors warn that irreversible nerve damage may be a consequence of a delayed diagnosis of CDM.

http://bit.ly/2vOum0O

How a chemo drug can help cancer spread from the breast to the lungs

Mouse study helps explain the paradoxical pro-cancer effects of paclitaxel

COLUMBUS, Ohio -The very same treatment that thwarts breast cancer has a dark side -- it can fuel the spread of the disease to the lungs.

Researchers at The Ohio State University studied the cascade of events that lead to metastatic cancer and found clues to why it happens, opening up the possibility of one day interfering with the medication's downsides while preserving its cancer-fighting properties in breast tissue.

The front-line chemotherapy drug paclitaxel sets off a variety of molecular-level changes that allow breast cancer cells to escape from the tumor. At the same time, it creates an environment in the lung that is more hospitable to the cancer cells, facilitating the spread of the disease, the researchers found in a mouse model of breast cancer.

The study, which appears in the journal Proceedings of the National Academy of Sciences, includes an analysis of data from women with breast cancer that suggest the findings from mouse models could be relevant to breast cancer metastasis in humans.

"That chemotherapy can paradoxically promote cancer progression is an emerging revelation in cancer research. However, a molecular-level understanding of this devastating effect is not clear," said Tsonwin Hai, the study's senior author and a professor of biological chemistry and pharmacology.

The changes in both the tumor and the lung documented in the study depend on a gene called Atf3, which is turned on by stress. In human data, the researchers found higher Atf3 gene expression in patients who had chemotherapy than those who did not.

"This gene seems to do two things at once: essentially help distribute the 'seeds' (cancer cells) and fertilize the 'soil' (the lung)," Hai said.

First, the chemo appears to send signals to increase the number of molecular doors through which the cancer cells can escape from the primary tumor into the bloodstream, freeing them to travel to other organs, the researchers found.

"I think it's an active process -- a biological change in which the cancer cells are beckoned to escape into the blood -- rather than a passive process in which the cancer cells get into the bloodstream because of leaky vessels," said Hai, a member of The Ohio State University Comprehensive Cancer Center.

This finding is bolstered by another recent study conducted at the Albert Einstein College of Medicine and published in Science Translational Medicine, which showed a similar result using imaging techniques to observe the tumor in mice, Hai said.

Second, the Ohio State researchers found that, beyond aiding cancer cell escape, paclitaxel creates a cascade of events that makes the tissue environment in the lung fertile ground for circulating cancer cells. "There are signals that help cancer cells enter the lungs and set up shop, that make the environment more immunologically tolerant to cancer cells," Hai said.

A molecular-level understanding of why chemotherapy sometimes increases risk of metastatic cancer is in the early stages, Hai said.

She said it's important to recognize that the cancer cells in the study's mouse model are very aggressive and that it would be interesting to

test whether paclitaxel also enhances the escape of cancer cells at earlier stages in cancer progression.

Hai cautioned that much more work is required before extrapolating the findings in mice to human cancer treatment.

"At this point, what our study and the recent literature on chemotherapy taught us is that it is prudent to keep our mind open, realizing that chemo can help treat cancer, but at the same time may increase the possibility of the spread of that cancer," she said.

What set their study apart from other research in this area is the identification of the stress gene Atf3. They showed that paclitaxel -- a stressor -- exerts its pro-cancer effect at least in part by turning on Atf3.

"It's possible there could be a treatment given in conjunction with the chemo that would inhibit this problem by dampening the effect of the stress gene Atf3," Hai said.

And that will be a focus of Hai's work in this area going forward, she said.

The U.S. Department of Defense supported this study.

Other Ohio State researchers who worked on the study were Yi Seok Chang, Swati Jalgaonkar and Justin Middleton.

http://bit.ly/2vNinjt

Largest-ever study of pets and kids' health finds no link

Findings dispute widely held beliefs about positive effects of pet ownership

Contrary to popular belief, having a dog or cat in the home does not improve the mental or physical health of children, according to a new RAND Corporation study.

The findings are from the largest-ever study to explore the notion that pets can improve children's health by increasing physical activity and improving young people's empathy skills.

Unlike earlier smaller studies on the topic, the RAND work used advanced statistical tools to control for multiple factors that could contribute to a child's wellbeing other than pet ownership, such as belonging to a family that has higher income or living in a more affluent setting. The results are published online by the journal Anthrozoos.

"We could not find evidence that children from families with dogs or cats are better off either in terms of their mental wellbeing or their physical health," said Layla Parast, a co-author of the study and a statistician at RAND, a nonprofit research organization. "Everyone on the research team was surprised -- we all have or grew up with dogs and cats. We had essentially assumed from our own personal experiences that there was a connection."

The study analyzed information from more than 2,200 children who lived in pet-owning households in California and compared them to about 3,000 households without a dog or cat. The information was collected as a part of the 2003 California Health Interview Survey, an annual survey that for one year also asked participants about whether they had pets, along with an array of other health questions.

Researchers did find that children from pet-owning families tended to have better general health, have slightly higher weight and were more likely to be physically active compared to children whose families did not have pets. In addition, children who had pets were more likely to have ADD/ADHD, were more likely to be obedient and were less likely to have parents concerned about their child's feelings, mood, behavior and learning ability.

But when researchers adjusted the findings to account for other variables that might be associated with both the likelihood that a family has a pet and the child's health, the association between pet ownership and better health disappeared. Overall, researchers considered more than 100 variables in adjusting their model of pet ownership and health, including family income, language skills and type of family housing.

While many previous studies have suggested a link between pet ownership and better emotional and physical health, RAND researchers say their analysis has more credibility because it analyzed a larger sample than previous efforts.

Researchers say future research could examine associations involving pet ownership over longer periods of time and in more experimental settings.

The ultimate test of the pet-health hypothesis would require a randomized trial where some people are given pets and other are not, with the groups being followed for 10 to 15 years to see if there are differences in their health outcomes.

"Such a study would likely be too costly and/or infeasible to implement, and I'm afraid it's not likely to be funded by anybody," Parast said.

Support for the study was provided by the National Institute of Child Health and Human Development. Other authors of the study are Jeremy N. V. Miles, Beth Ann Griffin and Jessica M. Saunders, all of RAND, and Susan H. Babey of the UCLA Center for Health Policy Research.

http://bit.ly/2frQUO2

Bacterial plasmids readily pick up new genes and spread them to new species

An increasing concern for transfer of antibiotic resistance between bacterial species

New research from the University of Sheffield has found that bacterial plasmids readily pick up new genes and spread them to new species – something which is an increasing concern for transfer of antibiotic resistance between bacterial species.

Plasmids are circular molecules of DNA which can copy themselves between neighbouring bacteria. They can be beneficial to bacteria when they carry useful genes, but where the genes they carry aren't useful, plasmids are often burdensome, acting a bit like parasites as they spread between bacteria.

Scientists from the University's Department of Animal and Plant Sciences discovered that plasmids may be best at spreading genes between species when they act like parasites, rather than when they are beneficial.

In the study, published in Nature Ecology and Evolution, the Sheffield team in collaboration with scientists from the Universities of York and Liverpool, set up bacterial populations in soil 'microcosms'. These consisted of a small volume of soil inoculated with bacteria carrying a plasmid that was beneficial in the presence of mercury.

By adding small amounts of mercury, the researchers could control whether the plasmid was beneficial or parasitic. The researchers allowed the bacteria and plasmids to evolve under these conditions for hundreds of generations, before sequencing their genomes.

Dr Jamie Hall, lead researcher on the study from the University of Sheffield, said: "We were really surprised by the sequencing results.

"In several populations the plasmid had picked up genes from one species and spread them to another. We knew this could happen but we weren't expecting to see so much of it. Most interestingly, the plasmid was best at picking up genes and transferring them between species when it acted like a parasite.

"If the plasmid is useful, then bacteria tend to inherit it from their parent. But if the plasmid is not useful then bacteria are more likely to pick it up from their neighbours—and thus are more prone to picking up their neighbours' other genes too."

He added: "If we imagine that bacteria are like PC computers from the 1990s the genes they swap are programs and plasmids are like floppy disks – able to copy themselves as well as any other genes they might carry between neighbouring bacteria."

Bacterial evolution, particularly resistance to antibiotics, is an emerging public health threat. Plasmids can also pick up and transfer antibiotic resistance genes, so the results of this study indicate concern for places like hospital plumbing and waste-water treatment plants which may provide opportunities for plasmids to move genes between species.

"Our research shows that bacteria can evolve rapidly, particularly by picking up genes from their neighbours, and that plasmids may play an important role in this process," said Dr Hall.

"Understanding the conditions that favour plasmid spread is an important piece in this puzzle."

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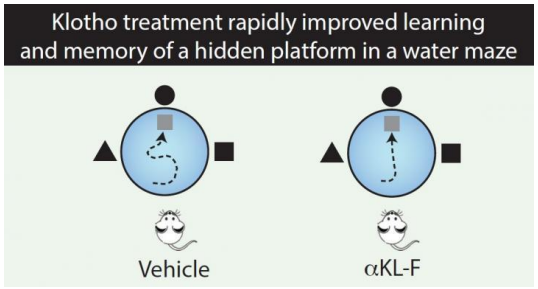
Longevity hormone klotho boosts memory and protects against brain aging in mice

Klotho treatment in mice rapidly improved learning and memory of a hidden platform in a water maze

A single injection of a fragment of the longevity hormone klotho into both young and old mice improved spatial and working memory and strengthened connections between neurons in the hippocampus rapidly, and these cognitive benefits lasted for several weeks, according to a study published August 8 in Cell Reports. Moreover, short-term treatment with the klotho fragment countered cognitive and motor deficits in mice with diseased brains. Clinical studies are needed to test whether this approach is safe and effective in humans.



This illustration shows how klotho treatment in mice rapidly improved learning and memory of a hidden platform in a water maze. **Leon et al.**

"With our new aging demographic, cognitive dysfunction and lack of mobility are now emerging as our biggest biomedical challenges, and there are no truly effective medical therapies for these debilitating problems," says senior author Dena Dubal (@DenaDubal), associate professor of neurology and the David A. Coulter Endowed Chair in Aging and Neurodegenerative Disease at the University of California, San Francisco. "Our findings suggest that treatment with a klotho fragment enhances brain function across the lifespan and could represent a new therapeutic strategy to boost brain resilience against neurodegenerative diseases like Alzheimer's and Parkinson's disease."

High levels of the naturally occurring hormone klotho, which regulates multiple signaling pathways and cellular processes, are associated with longer lifespan in worms, mice, and humans. In model organisms and humans, klotho levels decline with age, chronic stress, cognitive aging, and neurodegenerative disease. In recent studies, Dubal and her team discovered that life-long exposure to high levels of klotho enhances normal cognition in genetically engineered mice and protects against brain dysfunction in a mouse model of Alzheimer's disease. But until now, a major open question was whether short-term klotho treatment could rapidly enhance brain functions.

In this study, Dubal and her team treated mice with injections of the α-klotho protein fragment (αKL-F), which resembles the secreted form of the hormone. Young mice that received daily αKL-F treatment for four days showed improved spatial learning and memory performance in a classic test called the Morris water maze, which assesses the ability to find and remember the location of a hidden platform submerged in a pool of water. Similarly, a single injection of αKL-F improved working memory performance four hours later in the small Y-maze, which measures alternations between exploring arms of the maze. These cognitive benefits lasted at least two weeks after the last treatment.

Moreover, old mice that received a single injection of αKL-F showed improved spatial and working memory performance two days later in the two-trial Y-maze, which measures the natural preference to explore the novel arm of the maze. Additional experiments demonstrated that αKL-F treatment for several days counters motor and cognitive deficits in mice engineered to produce high levels of a pathogenic protein called α-synuclein, which contributes to Alzheimer's and Parkinson's disease.

"Since αKL-F resembles the circulating endogenous form of klotho that we all normally produce, we believe that elevating klotho in humans could be an effective therapy to enhance brain resilience," says first author Julio Leon, a postdoctoral scholar in the Dubal lab. "In this way, our findings could potentially pave paths to human therapy for a wide range of neurodegenerative diseases, including

Parkinson's and Alzheimer disease, and also for cognitive decline and decreased mobility due to aging."

During the same time frame that αKL-F enhanced cognition, it also increased signaling through the NMDA glutamate receptor and thereby strengthened the connections between neurons in a brain region called the hippocampus, which plays a critical role in learning and memory. Surprisingly, αKL-F treatment exerted its benefits without entering the brain or altering levels of toxic molecules associated with neurodegenerative diseases, suggesting that it enhances neural resilience against these pathogenic proteins. In future studies, Dubal and her team will explore how αKL-F transmits signals into the brain to improve neural resilience and cognitive function.

This study was funded by grants from NINDS, the National Center for Advancing Translational Sciences, the National Institutes of Health, the American Federation for Aging Research, the Glenn Medical Foundation, and the Dr. Miriam and Sheldon G. Adelson Medical Research Foundation. Additional funding was provided by gifts from Unity Biotechnology, the Bakar Foundation, the Bradley Foundation, and the Coulter-Weeks Foundation.

Cell Reports, Leon et al.: "Peripheral Elevation of a Klotho Fragment Enhances Brain Function and Resilience in Young, Aging, and α-Synuclein Transgenic Mice" http://www.cell.com/cell-reports/fulltext/S2211-1247(17)30990-7

http://bit.ly/2viVQdv

Blocking enzyme linked to Alzheimer's may reverse memory loss

MIT study suggests a new approach to developing treatments for Alzheimer's disease.

In the brains of Alzheimer's patients, many of the genes required to form new memories are shut down by a genetic blockade, contributing to the cognitive decline seen in those patients.

MIT researchers have now shown that they can reverse that memory loss in mice by interfering with the enzyme that forms the blockade. The enzyme, known as HDAC2, turns genes off by condensing them so tightly that they can't be expressed.

For several years, scientists and pharmaceutical companies have been trying to develop drugs that block this enzyme, but most of these drugs also block other members of the HDAC family, which can lead to toxic side effects. The MIT team has now found a way to precisely target HDAC2, by blocking its interaction with a binding partner called Sp3.

"This is exciting because for the first time we have found a specific mechanism by which HDAC2 regulates synaptic gene expression," says Li-Huei Tsai, director of MIT's Picower Institute for Learning and Memory and the study's senior author.

Blocking that mechanism could offer a new way to treat memory loss in Alzheimer's patients. In this study, the researchers used a large protein fragment to interfere with HDAC-2, but they plan to seek smaller molecules that would be easier to deploy as drugs.

Picower Institute postdocs Hidekuni Yamakawa, Jemmie Cheng, and Jay Penney are the lead authors of the study, which appears in the Aug. 8 edition of Cell Reports.

Memorable interactions

In 2007, Tsai first discovered that blocking HDAC activity could reverse memory loss in mice. There are several classes of HDACs, and their primary function is to modify histones -- proteins around which DNA is spooled, forming a structure called chromatin. These modifications condense chromatin, making genes in that stretch of DNA less likely to be expressed.

Human cells have about a dozen forms of HDAC, and Tsai later found that HDAC2 is responsible for the blockade of memory-linked genes. She also discovered that HDAC2 is elevated in human Alzheimer's patients and in several mouse models of the disease.

"We think that HDAC2 serves as a master regulator of memory gene expression, and during Alzheimer's disease it's elevated so it causes an epigenetic blockade of the expression of those memory genes," she says. "If we can remove the blockade by inhibiting HDAC2 activity or reducing HDAC2 levels, then we can remove the blockade and restore expression of all these genes necessary for learning and memory."

Most of the existing HDAC inhibitors that block HDAC2 also affect HDAC-1, which can have toxic side effects because HDAC1 is necessary for cell proliferation, especially in the production of white and red blood cells.

To find a way to more specifically target HDAC2, Tsai set out to identify proteins that help the enzyme bind to genes required for memory formation. First, she analyzed gene expression data from postmortem brain samples taken from people who did not have Alzheimer's disease, including 28 brains with high HDAC-2 levels and 35 with low levels. This search yielded more than 2,000 genes whose levels closely matched HDAC2 levels, suggesting that those genes might work in tandem with HDAC2.

Based on what they already knew about these genes' functions and how they physically interact with HDAC2, the researchers then picked out three of those genes for further testing. Those tests revealed that a gene called Sp3 is necessary to recruit HDAC2 to chromatin to enact its blockade of memory-linked genes.

The researchers also examined gene expression data from postmortem brains of Alzheimer's patients and found a nearly perfect correlation between levels of HDAC2 and Sp3.

Specific targets

The researchers then explored what would happen if they lowered Sp3 levels in a mouse model of Alzheimer's disease. In these mice, the same type in which they previously studied the effects of blocking HDAC2, they found that deactivating Sp3 also restored the mice's ability to form long-term memories.

The researchers used a type of short RNA strand to perform the genetic "knockdowns" in these experiments, but for this approach to be useful for potentially restoring memory function in human patients, scientists would likely need to develop a drug in the form of a small protein or chemical compound.

To that end, the researchers identified the section of the HDAC2 protein that binds to Sp3. When they engineered neurons to overproduce that HDAC2 fragment, the fragment sopped up most of the available Sp3, blocking it from binding HDAC2 and releasing the blockade of memory-linked genes. Furthermore, the fragment did not interfere with cell proliferation, suggesting that this more targeted approach would not have the adverse side effects of more general HDAC inhibitors.

The protein fragment that the researchers used to block the interaction in this study has about 90 amino acids, which would likely be too large to use as a drug, so the researchers hope to either identify a smaller segment that would still be effective, or find a chemical compound that would also disrupt the Sp3-HDAC2 interaction.

Tsai also hopes to further investigate some of the other genes that were found to correlate with HDAC2, in hopes of identifying other drug targets. She also plans to explore whether this approach could be useful in treating other disorders that involve elevated levels of HDAC2, such as posttraumatic stress disorder.

The research was funded by the Robert and Renee Belfer Family Foundation.

http://bit.ly/2vP5WED

Amateur collectors in Japan discover country's first and oldest fossil diving bird

Journal of Systemic Palaeontology publishes paper detailing remarkable discovery of Chupkaornis keraorum, an iconic marine diving bird heralded as the best-preserved hesperornithiform specimen from Asia

HOKKAIDO, JAPAN - During a walk near a reservoir in a small Japanese town, amateur collectors made the discovery of their lives - the first and oldest fossil bird ever identified in their country.

After sharing their mysterious find with paleontologists at Hokkaido University, brothers Masatoshi and Yasuji Kera later learned the skeletal remains were that of an iconic marine diving bird from the Late Cretaceous Period, one that is often found in the Northern Hemisphere but rarely in Asia.

The remarkable specimen - which includes nine skeletal elements from one individual, including the thoracic vertebrae and the femoral bones - is being heralded as the "best preserved hesperornithiform material from Asia" and to be "the first report of the hesperorinthiforms from the eastern margin of the Eurasian Continent."

Amateur collectors in Japan are credited with the discovery of the country's first and oldest fossil diving bird. Identified as a new species, it has been named Chupkaornis keraorum. **Illustration by Masato Hattori**

Identified as a new species, it has been named Chupkaornis keraorum - Chupka is the Ainu word used by indigenous people from Hokkaido for 'eastern,' and keraorum is named after Masatoshi and Yasuji Kera, who discovered the specimen. The bird would have lived during the time when dinosaurs roamed the land.

The scientific paper describing the find - entitled "The oldest Asian Hesperornithiform from the Upper Cretaceous of Japan, and the phylogenetic reassessment of Hesperornithiformes" - has been posted today on the Journal of Systematic Palaeontology website, an internationally renowned, peer-reviewed journal published by the Trustees of the Museum of Natural History, London.

The co-authors of the report are Tomonori Tanaka, Ph.D. student, Department of Natural History Sciences, Hokkaido University; Yoshitsugu Kobayashi, Ph.D., Hokkaido University Museum; Ken'ichi Kurihara, Ph.D., Hokkaido Museum; Anthony R. Fiorillo, Ph.D., Perot Museum of Nature and Science, Dallas, Texas, USA; and Manabu Kano, Ph.D., Mikasa City Museum. To read their entire manuscript and view renderings, go to http://www.tandfonline.com/doi/full/10.1080/14772019.2017.1341960 or perotmuseum.org/press.

"This amazing find illustrates the special relationship paleontologists and other scientists have with ordinary citizens who come upon interesting and unusual objects," said Tanaka. "Thanks to the wisdom and willingness of Masatoshi and Yasuji Kera to share their discovery with us at Hokkaido University, they have made a major contribution to science, and we are very grateful."

The bones, estimated to be anywhere from 90 million to 84 million years old, were unearthed from the Upper Cretaceous Kashima Formation of the Yezo Group in Mikasa City, Hokkaido. The fossil bird consists of four cervical vertebrae, two thoracic vertebrae, the distal end of the left and right femora, and the middle part of the right fibula. The specimen is currently housed in the collection of the Mikasa City Museum in Hokkaido, Japan.

"Hespeornithiforms is the oldest group of birds that succeeded to adapt for diving in ocean. This study provides better understanding in the early evolution of this group and the origin of diving in birds," added Tanaka.

Chupkaornis has a unique combination of characteristics: finger-like projected tibiofibular crest of femur; deep, emarginated lateral excavation with the sharply defined edge of the ventral margin of that the thoracic vertebrae (those vertebrae in the upper back); and the heterocoelous articular surface of the thoracic vertebrae. Phylogenetic analysis of this study revealed that Chupkaornis is one of the basal hesperornithiforms, thereby providing details of the evolution of this iconic group of diving birds.

"In Japan, many important vertebrate fossils have been discovered by amateurs because most of the land is covered with vegetation, and there are few exposures of fossil-bearing Cretaceous rocks. This research is a result of collaboration with amateurs, and I am thankful to their help and understanding of science," said Kobayashi.

Hesperornithiformes were toothed, foot-propelled diving birds and one of the most widely distributed groups of birds in the Cretaceous of the northern hemisphere. These birds had extremely reduced forelimbs and powerful hind limbs, suggesting that they were flightless sea-going predatory birds. Most of hesperornithiform fossils have been discovered from North America so far. The discovery of Chupkaornis, the oldest Asian hesperornithiform, suggests that basal hesperornithiform had dispersed to the eastern margin of Asia no later than 90 million to 84 million years old.

The discovery has broader aspects - and that's why Dr. Fiorillo, curator and vice president of research and collections at the Perot Museum of Nature and Science, is involved. Dr. Fiorillo is considered one of the world's preeminent experts on arctic dinosaurs for his decades of research in Alaska. He has deep interest in the Beringia land bridge that connects North America to Asia. He was asked to collaborate on this discovery because several of the co-authors of the paper, including Kobayashi and lead-author Tanaka, have been members of his field team during past Alaska expeditions.

"This study not only tells important new information about the evolution of this unusual group of birds, it also helps further our understanding of life in the ancient northern Pacific region, more specifically what was going on in the ocean while dinosaurs walked the land" said Fiorillo.

http://bit.ly/2w0voXz

Spider peptides battle superbugs and cancer

Improving the antimicrobial -- and anticancer -- properties of an antimicrobial peptide from a spider

As antibiotic resistance rises and fears over superbugs grow, scientists are looking for new treatment options. One area of focus is antimicrobial peptides (AMPs), which could someday be an alternative to currently prescribed antibiotics, many of which are becoming increasingly useless against some bacteria.

Now, a team reports in ACS Chemical Biology that they have improved the antimicrobial -- and anticancer -- properties of an AMP from a spider.

According to the U.S. Centers for Disease Control and Prevention, 2 million people become infected with antibiotic-resistant bacteria in the U.S. each year.

Because no known antibiotics work against these bacteria, patients simply have to hope that their natural defenses eventually overcome the infection. But some patients experience severe symptoms, landing them in a hospital, and in extreme cases, they could die.

Researchers are trying to find alternatives to traditional antibiotics, and one such possibility is a group of peptides called AMPs. These peptides are found in all plants and animals as a type of immune response and have been shown to be potent antibiotics in the laboratory.

Gomesin, an AMP from the Brazilian spider Acanthoscurria gomesiana can function as an antibiotic, but it also has anticancer activity. When gomesin was synthesized as a circle instead of as a linear structure, these characteristics were enhanced. Sónia Troeira Henriques and colleagues wanted to further boost the peptide's traits.

The team made several variations of the cyclic gomesin peptide and found that some of these were 10 times better at killing most bacteria than the previously reported cyclic form.

In other experiments, the new AMPs specifically killed melanoma and leukemia cells, but not breast, gastric, cervical or epithelial cancer cells. The researchers determined that the modified peptides killed bacteria and cancer cells in a similar way -- by disrupting the cells' membranes. The group also notes that the modified AMPs were non-toxic to healthy blood cells.

The authors acknowledge funding from the Australian Research Council and the National Health and Medical Research Council.

The abstract that accompanies this study is available here.

http://bit.ly/2hVefIJ

Moon's magnetic field lasted far longer than once believed

Rutgers and MIT experts lead lunar rock study with implications for life and habitability on other moons and planetary bodies

Video

The moon's magnetic field lasted 1 billion to 2.5 billion years longer than once thought - a finding with important implications for habitability on other moons and planets throughout the universe, a Rutgers University-New Brunswick professor says.

"The Earth's magnetic field is a shield that protects us from dangerous solar wind particles and ionizing radiation, so magnetic fields play a key role in the habitability of planets and, possibly, moons," said Sonia Tikoo, lead author of a study published online today in Science Advances and an assistant professor in Rutgers' Department of Earth and Planetary Sciences.

"Without this shield, we'd have more radiation, we'd have lots of mutations and who knows how life would respond in an unstable environment like that," said Tikoo, who began working on the study in 2013 while she was a graduate student at the Massachusetts Institute of Technology and who has examined more than 10 moon rocks. "It would be a harsher place to survive in."

In their study, the researchers -- for the first time -- successfully heated a lunar rock brought to Earth during an Apollo space mission to retrieve an accurate intensity for the lunar magnetic field, she said. The energetic cores of planets and moons generate magnetic fields, and rocks can record magnetic fields to which they were exposed.

Tikoo reanalyzed a moon rock collected by the Apollo 15 crew on Aug. 1, 1971, on the southern rim of Dune Crater within eastern Mare Imbrium. The small, young rock -- partially coated with melted glass -- likely formed during a meteor impact on the lunar surface.

Tikoo used a rock magnetometer to analyze the lunar rock. The device measures the strength and direction of magnetic fields in rocks. She slowly demagnetized the rock to reveal its original magnetization, heating it to 1,436 degrees Fahrenheit in a controlled atmosphere chamber at MIT to keep the heat from altering the rock.

The researchers think the moon's magnetic field declined by about 90 percent from its high point 3.56 billion years ago or earlier. That's when the moon's magnetic field was about the same strength as the Earth's is today -- an average of about 50 microtesla, a measure of magnetism. The lunar rock Tikoo tested, which is about 1 billion to 2.5 billion years old, recorded 5 microtesla. The moon has no core-generated magnetic field today, and scientists don't know when it turned off. Lingering questions include trying to figure out when the field ceased and what the field was like between 3.56 billion and 2.5 billion years ago, she said.

"We didn't think that small planetary bodies could generate magnetic fields for a very long time because they have smaller cores that would cool quickly and crystallize early in their lifetimes," she said. "Because the rate of crystallization depends on the core composition, our finding may challenge what we think the lunar core is made of. It's mostly made of iron, but something must be mixed in with it: sulfur, carbon or another element."

When a planet's magnetic field dies, ionizing particles from its sun can lead to the loss of its water over hundreds of millions of years, Tikoo said. "That's a big deal in terms of habitability," she said, adding that Mars once had lots of water but lost nearly all of it after its magnetic field died about 4 billion years ago.

"Whenever we look at exoplanets or the moons of exoplanets that could be in the habitable zone, we can consider the magnetic field as an important player in habitability," she said. "Then the question becomes what size planets and moons should we be considering as possibly habitable worlds."

Study coauthors include Benjamin P. Weiss of MIT; David L. Shuster of the University of California, Berkeley; and Clément Suavet, Huapei Wang and Timothy L. Grove of MIT.

http://nyti.ms/2hW02eH

When Dinosaurs Ruled the Earth, Mammals Took to the Skies

New fossil discoveries show that prehistoric "squirrels" glided through forests at least 160 million years ago, long before scientists had thought.

Carl Zimmer MATTER AUG. 9, 2017

The Mesozoic Era, from 252 million years ago to 66 million years ago, is often called the Age of Dinosaurs. To generations of paleontologists, early mammals from the period were just tiny nocturnal insect-eaters, trapped in the shadows of leviathans.

In recent years, scientists have significantly revised the story. Mammals already had evolved into a staggering range of forms, fossil evidence shows, foreshadowing the diversity of mammals today.

In a study published on Wednesday, a team of paleontologists added some particularly fascinating new creatures to the Mesozoic Menagerie. These mammals did not lurk in the shadows of dinosaurs.

Instead, they glided far overhead, avoiding predatory dinosaurs on the ground — essentially flying squirrels of the Jurassic Period, from an extinct branch of mammals that probably still laid eggs.

The fossils "are most primitive-known mammal forerunners that took to air," said Zhe-Xi Luo, a paleontologist at the University of Chicago who led the research.

The first Mesozoic mammal fossils came to light in the early 1800s, but for generations, paleontologists struggled to find more than teeth and bits of bone. In the late 1990s, they hit the jackpot.

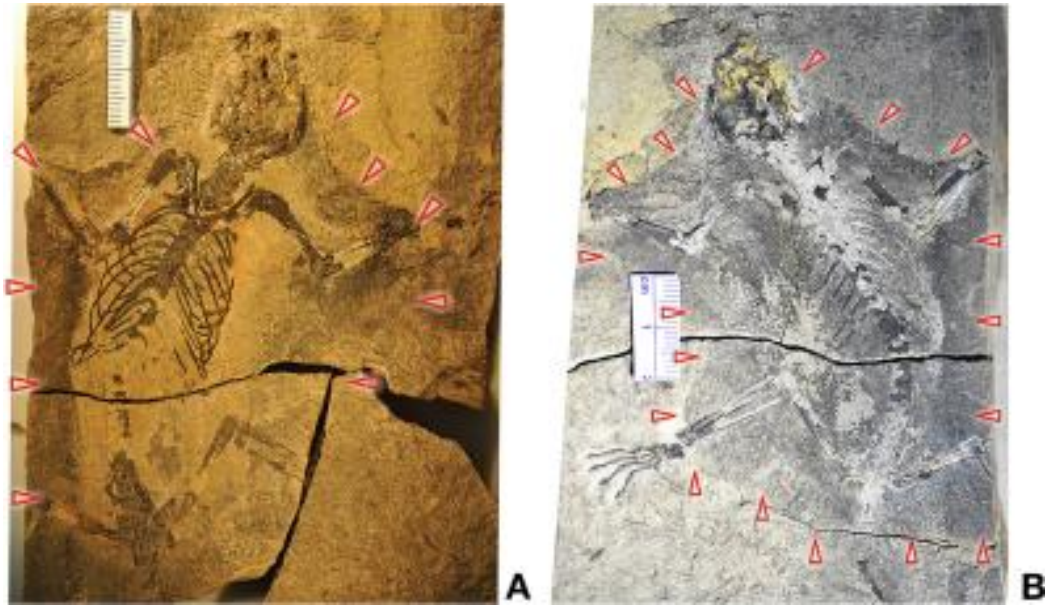
A rendering of a mother climbing on a tree branch with a baby in a suspended roosting position. **April I. Neander/University of Chicago**

At a site in northeastern China, hillside after hillside turned out to contain stunning mammal fossils, most dating back about 160 million years. Researchers were suddenly able to examine entire skeletons, some still bearing impressions of skin and hair.

As new fossils get unearthed, scientists are using them to draw in many previously unknown branches on the mammal family tree.

All living mammals are divided into three main branches. Platypuses, which still lay eggs, belong to the oldest; their ancestors split off from those of other living mammals roughly 170 million years ago.

Millions of years later, the other branch split. One lineage produced the marsupials, such as kangaroos and opossums, which finish development in a pouch.



Vilevolodon fossils with arrows indicating the winglike skin membrane that allowed it to glide. **Zhe-Xi Luo/University of Chicago**

The other lineage, our own, makes up the vast majority of living mammal species. Placental mammals all develop inside a uterus, drawing nutrients and oxygen from their mothers.

Some of the newly discovered mammal fossils belong to these three groups. Others belong to branches no one knew about before. Of those,

some diverged from the common ancestors of living mammals, but more primitive mammals split off even earlier.

When paleontologists looked at the size and shape of these fossils, they found that many did not fit the simple picture of early mammals as tiny insect-eaters. To the researchers' surprise, a number of extinct species independently evolved bodies resembling those of living mammals.

Some swam like otters, for example. Others scavenged, like raccoons, or dug into insect nests like today's aardvarks.

In 2007, Jin Meng, a paleontologist at the American Museum of Natural History, and his colleagues reported finding the fossil of a 160-million-year-old mammal, called Volaticotherium, that looked as if it could glide.

Today, placental mammals like flying squirrels and marsupials like sugar gliders travel through the air from tree to tree. But Volaticotherium belonged to a different lineage and independently evolved the ability to glide.

They were not the only mammals to do so, it turns out. Dr. Luo and his colleagues have now discovered at least two other species of gliding mammals from China, which they described in the journal Nature.

http://bit.ly/2fCspO5

Hepatitis A vaccination for Alaskan children has wiped out the virus

Established in Alaska in the 1990s, the program has virtually wiped out the virus in the native peoples of Alaska

A comprehensive hepatitis A vaccination program established in Alaska in the 1990s, which became a requirement for school entry in 2001, has virtually wiped out the virus in the native peoples of Alaska, where it had been endemic.

Data from the program is being presented at this year's World Indigenous Peoples' Conference on Viral Hepatitis in Anchorage, Alaska, USA (8-9 August) by Stephanie Massay, Epidemiology Specialist with the Alaska Division of Public Health, Section of Epidemiology, Anchorage, AK, USA, and colleagues.

Hepatitis A is an acute (short-term but severe) infection of the liver caused by the hepatitis A virus. Fever, weakness, nausea, aches and pains, and jaundice can be among the symptoms experienced. The hepatitis A virus can survive in the environment on and in food. It is also relatively resistant to detergents but can be inactivated by high temperature (85°C or higher) and by chemicals such as chlorine. Although it occurs worldwide, HAV occurs more commonly in populations with poor sanitation, such as poor populations in developed countries (e.g. Indigenous populations) and also in developing countries more generally.

Alaska experienced epidemics of hepatitis A every 10-15 years during the 1950s to the 1990s, resulting in thousands of cases. Alaska Native (AN) people living in rural communities were disproportionately impacted.

Hepatitis A virus (HAV) vaccines were licensed in 1995 and recommended by the Advisory Committee on Immunization Practice (ACIP) for routine vaccination of US children in populations with high HAV infection rates. Alaska began universal vaccination for children aged 2-14 years in 1996? HAV vaccination became required for school entrance in 2001. In 1997, following ACIP recommendations, this was expanded to include all children age 2 - 18 years, and in 2006 this was further expanded to include children age 1 - 18 years.

The data showed that during 1972-1995, Alaska's average annual incidence of hepatitis A was 60 per 100,000 population. Rates by race were substantially higher for AN people compared to non-AN people (244 vs 19 per 100,000 respectively, with AN people being 13 times more likely to be infected than non-AN people).

Compared to 1972-1995 (pre-vaccine), 2002-2007 (post-vaccine) statewide hepatitis A incidence fell by 98% (0.9 vs. 60 per 100,000); among AN peoples the incidence fell by 99.9% (0.3 vs. 243.8 per

100,000). During 2008-2016, 23 HAV cases were reported in Alaska? 5 among AN, 11 among non-AN, and 7 among people of unknown race/ethnicity.

The 2008-2016 statewide incidence of hepatitis A was 0.35 cases per 100,000 people? the incidence in children aged <14 years was 0.14 cases per 100,000 children. Of the 17 cases with documentation on travel, 15 (88%) had recent travel outside of Alaska. In 2015, National Immunization Survey data estimated that among children aged 19-35 months, HAV vaccine coverage was similar in Alaska (84%) and all US children (86%).

The authors conclude: "Dramatic declines in the incidence of hepatitis A occurred after HAV vaccine was recommended as a routine childhood vaccine and after it was required for school entry. Prior to routine vaccination, most the reported HAV cases were associated with outbreaks occurring within Alaska. Since 2008 however, 88% of reported hepatitis A cases have been imported, many of which were acquired during travel outside of the United States."

http://bit.ly/2vy8F1W

Use of common heart drugs dropped after price increases, Cleveland Clinic study finds

Findings disprove the notion that rising prices do not reduce patient access and utilization of certain medications

Cleveland - Following major price increases, the use of two cardiac medications - nitroprusside and isoproterenol -- decreased by one-half and one-third between 2012 and 2015, according to a Cleveland Clinic study published in the August 10th issue of the New England Journal of Medicine as a Letter to the Editor.

From 2012 to 2015, nitroprusside prices increased 30-fold from $27.46 to $880.88, while isoproterenol prices increased nearly 70-fold from $26.20 to $1,790.11.

These medications are used only in the hospital, with no external patient demand and no direct-to-consumer advertising. Therefore, researchers were able to objectively examine the effect of the price increases on physician prescribing behavior.

To analyze the impact, researchers analyzed utilization data for nitroprusside and isoproterenol in 47 hospitals between 2012 and 2015. They also obtained data for nitroglycerin and dobutamine -- two intravenous cardiovascular drugs with stable pricing -- for use as controls.

During this period, the number of patients treated with nitroprusside fell 53 percent and with isoproterenol fell 35 percent. In comparison, the number of patients treated with nitroglycerin increased 118 percent and those treated with dobutamine increased 7 percent.

"In public testimony, it had been stated that these price increases would not decrease patient access or utilization of these two critical drugs, both of which have been used for decades in patient care," said Umesh Khot, M.D., vice chairman of Cardiovascular Medicine at Cleveland Clinic and lead author of the study.

"However, our research shows that these price hikes are not benign. Further research will determine if there has been any effect on patient outcomes, but it's clear that utilization has been impacted."

Nitroprusside lowers blood pressure and is used in the treatment of critical hypertension and congestive heart failure, as well as to keep blood pressure low during surgery.

Isoproterenol is used primarily for treating bradycardia (low heart rate) and heart block. It's also used during electrophysiology procedures and specific cardiothoracic surgery cases to increase heart rate or contractility.

"These are medications that physicians are very familiar with, and for which there are no direct alternatives. As a result, hospitals have had to reevaluate use of these drugs and potentially bring in other therapies," said Michael Militello, PharmD.

"Understanding how physicians, pharmacists and health systems have addressed their use of these medications is an important area of further study."

http://bit.ly/2vuAU3n

First Organ-Specific Tissue Sheets

The material is durable, flexible, and can serve as a scaffold for cell growth, a study shows.

By Ashley Yeager | August 9, 2017

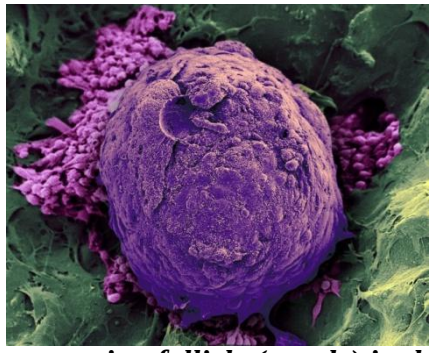
An accidental spill in the lab has led to the development of bioactive "tissue papers" that could act as a scaffold to grow cells and repair wounds. Described August 7 in Advanced Functional Materials, the cellular scaffolds are the first of their kind to be organ-specific, and researchers have made six different kinds.

Materials engineer Adam Jakus, a postdoc at Northwestern University, discovered the scaffolds after spilling a 3-D printable ovary ink, which is made of decellularized ovarian tissue. He'd previously developed similar materials to repair and regenerate bone, muscle, and nerve tissue. "I knew the spill would be easier to clean up if I let the ink dry," he tells The Scientist in a phone interview. When Jakus went to wipe up the dried ink, he found it had spread and hardened into a thin, pliable, yet durable sheet.

Having worked in the past with surgeons on biomaterials, Jakus thought the flexibility and stability of the "tissue paper" had the potential to be used in surgeries, wound healing and possibly cell growth. He decided to try to make the paper out of other organs.

Jakus chopped cow and pig organs into little pieces, then washed them with a detergent to dissolve all of the cells, leaving behind structural proteins, such a collagens and elastins, along with bioactive agents, such as growth factors. The material looks like translucent jelly, which Jakus and colleagues then freeze-dried and ground into a powder. Mixing the powder with a polymer allowed the team to create thin, flexible sheets.

Making the sheets, called extracellular matrices, isn't new, but making them organ-specific is. Past studies have tried, but doing so is challenging because the sheets weren't strong enough to be bent, cut, or folded without losing their utility, or they didn't have a lot of organ-specific material, or the method wasn't reproducible, Yale School of Medicine bioengineer and postdoc Yifan Yuan tells The Scientist in an email. He was not involved in the new study but says the team's "relatively simple technique," which generates sheets composed of 35 percent biocompatible polymer PLGA with 65 percent organ-specific extracellular matrix, could be used in drug screening and disease modeling.



A tissue paper (green) supports the growth of an ovarian follicle (purple) in this SEM image **Adam Jakus/Northwestern University**

To test if the tissue papers could provide a scaffold for cells, Jakus and his colleagues seeded the sheets with human adult stem cells and showed the scaffolds could support the growth and proliferation of the cells over four weeks. Yuan says it would interesting to see how the cells' phenotype changes after long-term culture on the tissue papers.

Jakus and colleagues also tested the ovarian tissue paper to see if it could allow ovarian follicles to grow. These tissue are vulnerable to chemotherapy and radiation, but preserving ovarian follicles is challenging because it has been hard to find a material to put the follicles on that will support their growth. The sheets keep them alive and seemingly healthy for several weeks, the team found.

"The results are pretty convincing," tissue engineer Stephen Badylak of the University of Pittsburg tells The Scientist. The development of organ-specific sheets shows an appreciation for the biology that goes on within these extracellular matrices. There's cell signaling and other processes that are hard to replicate in matrices built from synthetic materials, he says.

Badylak notes that one surprising feature of the technique used to generate the tissue paper is the extent of decellularization. It's significant compared to other techniques to make extracellular matrices, and it's about the same amount of decellularization for all

the different organs, he says. Such a loss of cellular organization, along with the composition of the tissue papers, is something that will have to be tested in animals to see if the body can tolerate it, Badylak says. Still, he says, the innovativeness and versatility of the tissue papers is impressive, and he encourages the researchers to continue to explore their utility.

Jakus has started a company, Dimension Inx, with his advisor Ramille Shah to continue development of the tissue papers.

http://bit.ly/2uCavh2

Biohackers Encoded Malware in a Strand of DNA

When DNA is analyzed, the resulting data becomes a program that corrupts gene-sequencing software, taking control of the computer

Andy Greenberg

When biologists synthesize DNA, they take pains not to create or spread a dangerous stretch of genetic code that could be used to create a toxin or, worse, an infectious disease. But one group of biohackers has demonstrated how DNA can carry a less expected threat—one designed to infect not humans nor animals but computers.

In new research they plan to present at the USENIX Security conference on Thursday, a group of researchers from the University of Washington has shown for the first time that it's possible to encode malicious software into physical strands of DNA, so that when a gene sequencer analyzes it the resulting data becomes a program that corrupts gene-sequencing software and takes control of the underlying computer. While that attack is far from practical for any real spy or criminal, it's one the researchers argue could become more likely over time, as DNA sequencing becomes more commonplace, powerful, and performed by third-party services on sensitive computer systems. And, perhaps more to the point for the cybersecurity community, it also represents an impressive, sci-fi feat of sheer hacker ingenuity.

"We know that if an adversary has control over the data a computer is processing, it can potentially take over that computer," says Tadayoshi Kohno, the University of Washington computer science professor who led the project, comparing the technique to traditional hacker attacks that package malicious code in web pages or an email attachment. "That means when you're looking at the security of computational biology systems, you're not only thinking about the network connectivity and the USB drive and the user at the keyboard but also the information stored in the DNA they're sequencing. It's about considering a different class of threat."

A Sci-Fi Hack

For now, that threat remains more of a plot point in a Michael Crichton novel than one that should concern computational biologists. But as genetic sequencing is increasingly handled by centralized services—often run by university labs that own the expensive gene sequencing equipment—that DNA-borne malware trick becomes ever so slightly more realistic. Especially given that the DNA samples come from outside sources, which may be difficult to properly vet.

If hackers did pull off the trick, the researchers say they could potentially gain access to valuable intellectual property, or possibly taint genetic analysis like criminal DNA testing. Companies could even potentially place malicious code in the DNA of genetically modified products, as a way to protect trade secrets, the researchers suggest. "There are a lot of interesting—or threatening may be a better word—applications of this coming in the future," says Peter Ney, a researcher on the project.

Regardless of any practical reason for the research, however, the notion of building a computer attack—known as an "exploit"—with nothing but the information stored in a strand of DNA represented an epic hacker challenge for the University of Washington team. The researchers started by writing a well-known exploit called a "buffer overflow," designed to fill the space in a computer's memory meant for a certain piece of data and then spill out into another part of the memory to plant its own malicious commands.

But encoding that attack in actual DNA proved harder than they first imagined. DNA sequencers work by mixing DNA with chemicals that

bind differently to DNA's basic units of code—the chemical bases A, T, G, and C—and each emit a different color of light, captured in a photo of the DNA molecules. To speed up the processing, the images of millions of bases are split up into thousands of chunks and analyzed in parallel. So all the data that comprised their attack had to fit into just a few hundred of those bases, to increase the likelihood it would remain intact throughout the sequencer's parallel processing.

When the researchers sent their carefully crafted attack to the DNA synthesis service Integrated DNA Technologies in the form of As, Ts, Gs, and Cs, they found that DNA has other physical restrictions too. For their DNA sample to remain stable, they had to maintain a certain ratio of Gs and Cs to As and Ts, because the natural stability of DNA depends on a regular proportion of A-T and G-C pairs. And while a buffer overflow often involves using the same strings of data repeatedly, doing so in this case caused the DNA strand to fold in on itself. All of that meant the group had to repeatedly rewrite their exploit code to find a form that could also survive as actual DNA, which the synthesis service would ultimately send them in a finger-sized plastic vial in the mail.

The result, finally, was a piece of attack software that could survive the translation from physical DNA to the digital format, known as FASTQ, that's used to store the DNA sequence. And when that FASTQ file is compressed with a common compression program known as fqzcomp—FASTQ files are often compressed because they can stretch to gigabytes of text—it hacks that compression software with its buffer overflow exploit, breaking out of the program and into the memory of the computer running the software to run its own arbitrary commands.

A Far-Off Threat

Even then, the attack was fully translated only about 37 percent of the time, since the sequencer's parallel processing often cut it short or—another hazard of writing code in a physical object—the program decoded it backward. (A strand of DNA can be sequenced in either direction, but code is meant to be read in only one. The researchers suggest in their paper that future, improved versions of the attack might be crafted as a palindrome.)

Despite that tortuous, unreliable process, the researchers admit, they also had to take some serious shortcuts in their proof-of-concept that verge on cheating. Rather than exploit an existing vulnerability in the fqzcomp program, as real-world hackers do, they modified the program's open-source code to insert their own flaw allowing the buffer overflow. But aside from writing that DNA attack code to exploit their artificially vulnerable version of fqzcomp, the researchers also performed a survey of common DNA sequencing software and found three actual buffer overflow vulnerabilities in common programs. "A lot of this software wasn't written with security in mind," Ney says. That shows, the researchers say, that a future hacker might be able to pull off the attack in a more realistic setting, particularly as more powerful gene sequencers start analyzing larger chunks of data that could better preserve an exploit's code.

Needless to say, any possible DNA-based hacking is years away. Illumina, the leading maker of gene-sequencing equipment, said as much in a statement responding to the University of Washington paper. "This is interesting research about potential long-term risks. We agree with the premise of the study that this does not pose an imminent threat and is not a typical cyber security capability," writes Jason Callahan, the company's chief information security officer "We are vigilant and routinely evaluate the safeguards in place for our software and instruments. We welcome any studies that create a dialogue around a broad future framework and guidelines to ensure security and privacy in DNA synthesis, sequencing, and processing."

But hacking aside, the use of DNA for handling computer information is slowly becoming a reality, says Seth Shipman, one member of a Harvard team that recently encoded a video in a DNA sample. (Shipman is married to WIRED senior writer Emily Dreyfuss.) That storage method, while mostly theoretical for now, could someday

allow data to be kept for hundreds of years, thanks to DNA's ability to maintain its structure far longer than magnetic encoding in flash memory or on a hard drive. And if DNA-based computer storage is coming, DNA-based computer attacks may not be so farfetched, he says.

"I read this paper with a smile on my face, because I think it's clever," Shipman says. "Is it something we should start screening for now? I doubt it." But he adds that, with an age of DNA-based data possibly on the horizon, the ability to plant malicious code in DNA is more than a hacker parlor trick.

"Somewhere down the line, when more information is stored in DNA and it's being input and sequenced constantly," Shipman says, "we'll be glad we started thinking about these things."

http://bbc.in/2uRDr4d

Pioneering type 1 diabetes therapy safe

The first trial of a pioneering therapy to retrain the immune system and slow the advance of type 1 diabetes has shown it is safe.

By James Gallagher Health and science reporter, BBC News website

The disease is caused by the body destroying cells in the pancreas that control blood sugar levels. The immunotherapy - tested on 27 people in the UK - also showed signs of slowing the disease, but this needs confirming in larger trials. Experts said the advance could one day free people from daily injections.

Aleix Rowlandson, from Lancashire, was diagnosed in 2015 aged 18.

"Your blood sugars affect how much energy you have," she told the BBC. "If they're high, they can make you feel tired. If they're low, you can feel shaky. "I'm more optimistic knowing that the study has gone well and they can use that to find further treatments. "Even if it doesn't help me, myself, and it might help other people in the future, I'm very happy."

Aleix's immune system is attacking her beta cells, which release the hormone insulin to keep blood sugar levels stable. As a result, she has to inject insulin several times a day.

Balance

Aleix is taking part in the trials of immunotherapy at the National Institute for Health Research Biomedical Research Centre at Guy's and St Thomas'. It is an attempt to stop her diabetes by tapping into the immune system's natural checks and balances.

The body's defence system is primed to attack hostile invaders. But it also has "regulatory T cells", which calm the immune response and prevent it attacking the body's own tissues.

Immunotherapies try to get regulatory T cells on-side by exposing them to fragments of proteins found in beta cells.

Prof Mark Peakman, from King's College London, told the BBC News website: "This is a landmark in the sense it's the first time it has been done. "Importantly, [the trial] shows the overall safety is good and there is some evidence we're restoring the balance and getting some regulatory T cells activated."

Patients given the therapy did not need to increase their dose of insulin during the trial. However, it is too soon to say this therapy stops type 1 diabetes and larger clinical trials will be needed. And further types of immunotherapy that should deliver an even stronger reaction are already underway.

Beta cell saver

The trial focused on patients newly diagnosed with type 1 as they still have about a fifth of their beta cells left. Even retaining these cells would make it easier to manage the condition, but the ultimate goal is to intervene even earlier to hopefully prevent the disease starting. However, it is not likely to help people diagnosed with type 1 years ago.

Prof Peakman added: "At that stage, most of the beta cells have gone and we don't find, with any therapies tried, any evidence of regeneration so it seems unlikely to help someone who has had the disease for a while."

All the volunteers were injected either every two or four weeks for six months.

Karen Addington, the UK chief executive of the type 1 diabetes charity JDRF, said: "Exciting immunotherapy research like this increases the likelihood that one day insulin-producing cells can be protected and preserved. "That would mean people at risk of type 1 diabetes might one day need to take less insulin, and perhaps see a future where no-one would ever face daily injections to stay alive."

Diabetes

There are two main types of diabetes:

type 1 - where the pancreas does not produce any insulin

type 2 - where the pancreas does not produce enough insulin or the body's cells do not react to insulin

Type 1 diabetes can develop at any age, but usually appears before the age of 40, particularly in childhood.

About 10% of all diabetes is type 1, but it is the most common type of childhood diabetes, so it is sometimes called juvenile diabetes or early onset diabetes

Type 2 diabetes tends to develop later in life and is linked to lifestyle and being overweight.

Source: NHS Choices

http://bit.ly/2uRXoHR

New hope for endangered eels, Japanese summer delicacy

"Dr. Eel" thinks he's unlocked the secrets to eventually farming eels sustainably and profitably

August 10, 2017 by Sherry Zheng

The Japanese summer delicacy of roasted eel, braised with a tangy sauce and sprinkled with prickly mountain pepper, is in question as the creatures with their mysterious migrations become increasingly endangered.

Soaring demand for Japanese eel, or Anguilla japonica, helped put the creatures on the International Union of Conservation of Nature's "Red List" of endangered species in 2014. It's spurring poaching of similar species off the U.S. east coast.

But Katsumi Tsukamoto, "Dr. Eel" of the only "Eel Science Laboratory" at Nihon University in Japan, thinks he's unlocked the secrets to eventually farming the eels, known as unagi, sustainably and profitably. Tsukamoto found out where the eels are spawning, and that helped researchers study conditions needed to raise them from the egg stage to adulthood.

In this Aug. 2, 2017 photo, unajyu is served at Hashimoto, a Michelin one-star unagi restaurant in Tokyo. Known as "unajyu," the grilled "kabayaki" eel delicacy served on hot steaming rice in a neat lacquer box is what many Japanese people indulge in during the summer to celebrate the Day of the Ox. The endangered Japanese summer delicacy may get a new lease on life with commercial farming. **(AP Photo/Sherry Zheng)**

The possibility of extinction, and soaring prices for grilled eel believed to help build stamina for enduring sweltering summer days, have dismayed many Japanese gourmands and the restaurants that specialize in the dish.

Despite their important role in Japanese food culture, until recently very little was known about the life cycles of eels, such as where they spawned and how tiny, nearly transparent glass eels manage to travel back to their freshwater habitats in Asia and elsewhere.

Supplies depend on wild-catching the juveniles and farm raising them until adulthood, a practice that has spread from Japan to Taiwan and mainland China as demand has surged.

Tsukamoto says his discovery of Japanese eel larvae and spawning adults west of the Mariana Ridge, near Guam, in 2009 has enabled him and other researchers to figure out the right diet and environmental conditions for spawning eels and their offspring.

Despite skepticism about the potential for such farming to work, Tsukamoto says three Japanese state-owned laboratories already are able to raise the eels from the larval stage and get them to spawn, completing their life cycle. But for now each lab can raise only about 3,000-4,000 a year. A lack of funds is hindering construction of the

infrastructure needed to make such operations commercially viable by producing tens of thousands of eels a year.

The complete farming of eels and some other endangered species as a way to help them survive by relieving the pressure from soaring demand.

Fisherman Masataka Uchida, who sells wild caught "blue eel," or ao-unagi, shrugs off any potential competition from farming.

Depending on the environment, some eels have a tough texture and pungent, muddy taste that even unagi aficionados may find off-putting.

Uchida's eels, with their pale blue-gray skin and soft pink bellies, have a highly sought-after, light and clean flavor that fetches premium prices even in the pricey unagi market.

Depending on the restaurant, Yuta Maruyama, an intermediate wholesaler who handles wild blue eel at Tokyo's famous Tsukiji Fish market, says a multi-course menu including grilled blue eel can cost up to 30,000 yen ($270) per person at exclusive restaurants, mainly in the flashy Ginza shopping and dining district.

The choice eels are often served in different styles to the traditional "kabayaki" eels which are grilled in a coating of dark soy sauce marinade. Restaurants that specialize in kabayaki, often handed down generation to generation, may offer both wild and farmed eels—with supply depending on what is available that day at the market.

At Hashimoto, a Michelin one-star kabayaki restaurant in Tokyo that first opened in 1835, the eels are all farm-raised the conventional way on the southern island of Kyushu, after being caught as glass eels.

Like farmed salmon, the farmed eels raised from wild-caught glass eels tend to be fattier. "They have a flavor that is preferred by most customers," says Shinji Hashimoto, the sixth-generation owner.

Hashimoto says his kabayaki sauce is "light," to allow the eel's flavor to come through.

"The Tokyo palette has traditionally disliked sweet flavors," he says.

To manage with fewer catches and higher prices, Hashimoto tries to get two servings out of larger eels.

After cleaning and slicing them open, the cooks skewer them to ensure they will stay together while cooking. They are grilled directly over hot charcoal, then steamed to soften the flesh. Afterwards they are coated in a sauce of soy sauce boiled with sweet rice wine, or mirin and then returned to the grill and basted three times before being served as "unajyu," steaming hot over rice in a neat lacquer box.

The busiest days tend to be the Day of the Ox in the lunar calendar, the first of which in 2017 was Tuesday, July 25th. Hashimoto served about 150 customers that day.

"Even if the price rose to 10,000 yen (about $90) for one box of unajyu, Japanese people would still eat it once a year," Tsukamoto said. "Why do Japanese people like unagi? Because we like soy sauce. The salty-sweet sauce, made from a mixture of soy sauce and mirin, is brushed on, is singed and grilled on the eel over charcoal - and that smell makes it irresistible."

http://bit.ly/2fBXa5G

'Vitamin B3 prevents miscarriage, defects'

In a finding bringing hope to thousands of Australian couples, preventing birth defects and miscarriage could be as simple as supplementing a pregnant woman's diet with Vitamin B3.

Sarah Wiedersehn, Australian Associated Press

A landmark Australian study undertaken at the Victor Chang Cardiac Research Institute has identified a new cause of miscarriages and multiple types of congenital birth defects. More importantly, though, it has identified a way to prevent them.

It comes in the form of niacin, otherwise known as Vitamin B3 and typically found in meats, leafy green vegetables and Vegemite.

Lead researcher Professor Sally Dunwoodie says the ramifications of the double breakthrough - hailed as the biggest since folic acid was identified as a preventative of neural tube birth defects and spina bifida in babies - are likely to be "huge". "This has the potential to significantly reduce the number of miscarriages and birth defects around the world," she said on Thursday.

"Some 15,000 women in Australia every year have a child with a birth defect or they suffer from multiple miscarriages. This discovery brings hope to many of those women."

Using whole exome sequencing technology, researchers looked for gene variants in families that had experienced multiple congenital malformations. Identified was a gene mutation that caused a deficiency in a molecule critical to all living cells, known as nicotinamide adenine dinucleotide (NAD).

They found low levels of NAD crippled the growth of the embryo and led to miscarriage and birth defects in mice engineered with the same gene mutations as the study participants. However the deficiency was cured through the supplementation of Vitamin B3 which is required to make NAD. After the dietary change, both the miscarriages and birth defects were completely prevented, with all offspring born healthy.

"The science is not simple and it took 12 years but the beauty is the simplicity of the prevention, it's cheap and its available," said Prof Dunwoodie. The findings are published in the prestigious New England Journal of Medicine and the research team is confident they will translate to humans.

Professor David Winlaw, a paediatric surgeon at The Children's Hospital at Westmead says families affected by congenital heart disease should be encouraged by this "blockbuster" breakthrough. "This is the biggest finding in congenital heart disease for at least 20 years," Prof Winlaw said. "The impact for the population will mean a very significant reduction in human misery in the early years of life, a very significant decrease in hospital admissions and cost of care," he said.

Previous research has shown that at least a third of pregnant women have low levels of vitamin B3 in the first trimester of pregnancy. Currently, the National Medical Research Council only recommends pregnant women take folic acid.

Prof Dunwoodie hopes Vitamin B3 will eventually be added to that list, but acknowledges more research is needed. "We need to identify women at risk and then work out what would be a safe level of niacin for them to take to prevent miscarriages and birth defects," she said.

In the meantime, women contemplating pregnancy are advised to take just the recommended multivitamins.

http://bit.ly/2w0qH02

Using alternative medicine only for cancer linked to lower survival rate

Patients receiving alternative therapy as treatment for curable cancers rather than conventional cancer treatment have a higher risk of death

New Haven, Conn. -- Patients who choose to receive alternative therapy as treatment for curable cancers instead of conventional cancer treatment have a higher risk of death, according to researchers from the Cancer Outcomes, Public Policy and Effectiveness Research (COPPER) Center at Yale School of Medicine and Yale Cancer Center. The findings were reported online by the Journal of the National Cancer Institute.

There is increasing interest by patients and families in pursuing alternative medicine as opposed to conventional cancer treatment. This trend has created a difficult situation for patients and providers. Although it is widely believed that conventional cancer treatment will provide the greatest chance at cure, there is limited research evaluating the effectiveness of alternative medicine for cancer.

While many cancer patients use alternative therapy in addition to conventional cancer treatments, little is known about patients who use alternative therapy as their only approach to treating their cancer.

"We became interested in this topic after seeing too many patients present in our clinics with advanced cancers that were treated with ineffective and unproven alternative therapies alone," said the study's senior author, James B. Yu, M.D., associate professor of therapeutic radiology at Yale Cancer Center.

To investigate alternative medicine use and its impact on survival compared to conventional cancer treatment, the researchers studied

840 patients with breast, prostate, lung, and colorectal cancer in the National Cancer Database (NCDB) -- a joint project of the Commission on Cancer of the American College of Surgeons and the American Cancer Society.

The NCDB represents approximately 70% of newly diagnosed cancers nationwide. Researchers compared 280 patients who chose alternative medicine to 560 patients who had received conventional cancer treatment.

The researchers studied patients diagnosed from 2004 to 2013. By collecting the outcomes of patients who received alternative medicine instead of chemotherapy, surgery, and/or radiation, they found a greater risk of death.

This finding persisted for patients with breast, lung, and colorectal cancer. The researchers concluded that patients who chose treatment with alternative medicine were more likely to die and urged for greater scrutiny of the use of alternative medicine for the initial treatment of cancer.

"We now have evidence to suggest that using alternative medicine in place of proven cancer therapies results in worse survival," said lead author Skyler Johnson, M.D. "It is our hope that this information can be used by patients and physicians when discussing the impact of cancer treatment decisions on survival."

Cary Gross, M.D., co-author of the study, called for further research, adding, "It's important to note that when it comes to alternative cancer therapies, there is just so little known -- patients are making decisions in the dark. We need to understand more about which treatments are effective -- whether we're talking about a new type of immunotherapy or a high-dose vitamin -- and which ones aren't, so that patients can make informed decisions."

Henry Park, M.D., MPH, was also a study author.

The American College of Surgeons and the Commission on Cancer have not verified and are not responsible for the analytic or statistical methodology employed, or the conclusions drawn from these data by the researchers.

http://bit.ly/2hWcJWU

Here's What the Last Common Ancestor of Apes and Humans Looked Like

Last common ancestor of all living apes and humans likely resembled a baby gibbon

By Charles Q. Choi, Live Science Contributor

The most complete extinct-ape skull ever found reveals what the last common ancestor of all living apes and humans might have looked like, according to a new study. The 13-million-year-old infant skull, which its discoverers nicknamed "Alesi," was unearthed in Kenya in 2014. It likely belonged to a fruit-eating, slow-climbing primate that resembled a baby gibbon, the researchers said.

This skull belongs to a 16-month-old ape, now called Nyanzapithecus alesi, that died about 13 million years ago. **Fred Spoor**

Among the living primates, humans are most closely related to the apes, which include the lesser apes (gibbons) and the great apes (chimpanzees, gorillas and orangutans). These so-called hominoids — that is, the gibbons, great apes and humans — emerged and diversified during the Miocene epoch, approximately 23 million to 5 million years ago. (The last common ancestor that humans had with chimpanzees lived about 6 million to 7 million years ago.)

Much remains unknown about the common ancestors of living apes and humans from the critical time when these branches diverged. Fossil evidence from this part of the primate family tree is scarce, and consists mostly of isolated teeth and broken jaw fragments. As such, researchers were not sure what the last common ancestors of living apes and humans might have looked like, and even whether they

originated in Africa or Eurasia. The extinct primate may have looked like a baby gibbon (shown here in a stock image).

"The living apes are found all across Africa and Asia — chimps and gorillas in Africa, orangutans and gibbons in Asia — and there are many fossil apes found on both continents, and Europe as well," study co-author Christopher Gilbert, a paleoanthropologist at Hunter College in New York, told Live Science.

The extinct primate may have looked like a baby gibbon (shown here in a stock image). **trato/Shutterstock**

"So, as you can imagine, there are numerous possibilities for how that distribution came to be, and different researchers have suggested different hypotheses for where the common ancestor of the living apes and humans might be found."

Great timing

Kenyan fossil hunter John Ekusi discovered the skull in 2014 in the Napudet area, west of Lake Turkana in northern Kenya. He suggested its nickname, "Alesi," because "ales" means "ancestor" in the local Turkana language.

"The Napudet locality offers us a rare glimpse of an African landscape 13 million years ago," study co-author Craig Feibel, chair of the anthropology department at Rutgers University in New Jersey, said in a statement. "A nearby volcano buried the forest where the baby ape lived, preserving the fossil and countless trees. It also provided us with the critical volcanic minerals by which we were able to date the fossil."

This is the first ape cranium unearthed from between 10 million and 14 million years ago, and the most complete one discovered from between 7 million and 17 million years ago.

"Alesi came from exactly the right time and place to show us what the ancestors of all the modern apes and humans might have looked like," study co-author Ellen Miller, a primatologist and paleoanthropologist at Wake Forest University in Winston-Salem, North Carolina, told Live Science. "We never had information on that before — it was always a mystery."

It remains uncertain how Alesi died. However, perhaps the infant was killed by the thick layers of ash from huge volcanic eruptions that covered the fossil, the researchers said.

Baby primate looked like gibbon

The lemon-size skull still had the roots of its baby teeth, and none of the adult teeth had erupted from the jaw yet. The three-dimensional X-ray images taken of these adult teeth were so detailed that researchers could count their enamel layers, which were laid down over time like rings inside a tree, helping the scientists estimate that the baby primate was 16 months old when it died.

"From the teeth, we can tell it generally ate fruits," Miller said.

The shape of the unerupted adult teeth revealed that Alesi belonged to a genus, or group of species, known as Nyanzapithecus, a sister group to the hominoids that was discovered about 30 years ago. However, Alesi's teeth were much larger than those of other members of this genus, so the scientists declared that Alesi belonged to a new species, Nyanzapithecus alesi. ("Nyanza" is the province in western Kenya where the first specimen of Nyanzapathecus was found, and "pithecus" comes from the Greek word for "ape.")

"Nyanzapithecus alesi was part of a group of primates that existed in Africa for over 10 million years," lead study author Isaiah Nengo, of Stony Brook University in New York, said in the statement. "What the discovery of Alesi shows is that this group was close to the origin of living apes and humans, and that this origin was African."

Determining that the last common ancestors of living apes and humans originated in Africa is important because it helps scientists better understand how ancient climate, ecology, geography and other factors were key to their evolution. "It helps us understand and

reconstruct how and why a certain lineage might have evolved," Gilbert said.

The researchers cannot tell if Alesi was male or female, as the infant was too young for the features of the skull that distinguish the sexes to have emerged, the researchers said. However, the size of the skull and teeth do suggest that if Alesi had reached adulthood, it would have weighed about 24.9 lbs. (11.3 kilograms) at maturity. The researchers also noted that Alesi's 6.16-cubic-inch (101 cubic centimeters) brain was about as big as that of a modern lemur of the same size.

The small snout of the skull would have made Alesi look like a baby gibbon. "Because they are probably close to the ancestor of all living apes, the specimen may help give us some sort of idea of what the common ancestor of all living apes and modern humans might have looked like, and because our specimen looks most similar to gibbons among living apes, it would potentially support the idea that the common ancestor of living apes and humans looked like a gibbon," Gilbert said.

However, the shape of Alesi's inner ear, which contains the balance organ of primates, suggests that Alesi was not capable of the rapid, acrobatic tree-swinging associated with gibbons. "It probably had a more slow-climbing form of locomotion, more like [that of] a chimpanzee," Miller said. The scientists detailed their findings in the Aug. 10 issue of the journal Nature.

http://bit.ly/2uRMjH1

Scientists reveal how goldfish make alcohol to survive without oxygen

Scientists at the Universities of Oslo and Liverpool have uncovered the secret behind a goldfish's remarkable ability to produce alcohol as a way of surviving harsh winters beneath frozen lakes.

Humans and most other vertebrate animals die within a few minutes without oxygen. Yet goldfish and their wild relatives, crucian carp, can survive for days, even months, in oxygen-free water at the bottom of ice-covered ponds.

During this time, the fish are able to convert anaerobically produced lactic acid into ethanol, which then diffuses across their gills into the surrounding water and avoids a dangerous build-up of lactic acid in the body.

The molecular mechanism behind this highly unusual ability, which is unique among vertebrates and more commonly associated with brewer's yeast, has now been uncovered and is published in the journal Scientific Reports.

The international team has shown that muscles of goldfish and crucian carp contain not just the usual one, but two sets of the proteins normally used to channel carbohydrates towards their breakdown within a cell's mitochondria - a key step for energy production.

While one set of these proteins appears very similar to that in other species, the second set is strongly activated by the absence of oxygen and shows a mutation that allows channelling of metabolic substrates to ethanol formation outside the mitochondria.

Further genetic analyses suggest that the two sets of proteins arose as part of a whole genome duplication event in a common ancestor of goldfish and crucian carp some 8 million years ago.

Dr Michael Berenbrink, an evolutionary physiologist at the University of Liverpool, said: "During their time in oxygen-free water in ice-covered ponds, which can last for several months in their northern European habitat, blood alcohol concentrations in crucian carp can reach more than 50 mg per 100 millilitres, which is above the drink drive limit in these countries.

"However, this is still a much better situation than filling up with lactic acid, which is the metabolic end product for other vertebrates, including humans, when devoid of oxygen."

Lead author Dr Cathrine Elisabeth Fagernes, from the University of Oslo, said: "This research emphasises the role of whole genome duplications in the evolution of biological novelty and the adaptation of species to previously inhospitable environments.

"The ethanol production allows the crucian carp to be the only fish species surviving and exploiting these harsh environments, thereby avoiding competition and escaping predation by other fish species with which they normally interact in better oxygenated waters.

"It's no wonder then that the crucian carp's cousin the goldfish is arguably one of the most resilient pets under human care."

The work is the result of a collaboration between scientists at the University of Liverpool, UK, and the University of Oslo, Norway. The work was funded by the Research Council of Norway.

http://wb.md/2wUcnTe

Melanoma and Parkinson's: A Surprising Connection

Linked Diseases: Parkinson's and Melanoma

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.

This week's news story is about a surprising connection between two seemingly unrelated diseases: Parkinson's disease and melanoma.

A Mayo Clinic study[1] looked at a cohort of almost 1000 patients with Parkinson's disease and found a fourfold increased risk for preexisting melanoma. Next, they assessed the prevalence of Parkinson's in more than 1500 skin and ocular melanoma patients. They also had a fourfold increased risk for Parkinson's.

Researchers don't yet know which environmental, genetic, or immunologic abnormality is linking these two diseases, but it doesn't seem to be the Parkinson's drug levodopa. For now, it's too early to recommend changing routine screening. However, it's still important for clinicians to be aware of the link-to be vigilant for one disease in patients who have the other, and to counsel those patients about their increased risk.

Follow Dr Cassoobhoy on Twitter at @ArefaMD

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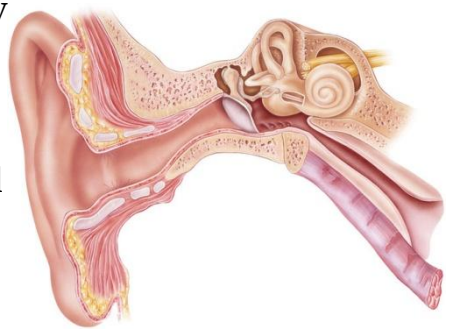
http://bit.ly/2uCRJq3

A Sonic Attack in Cuba? How an Acoustic Weapon Might Work

Supersecret sonic weapon used to attack diplomats may sound like the start of a sci-fi novel

By Tia Ghose, Senior Writer | August 11, 2017 10:39am ET

A supersecret sonic weapon being used to attack diplomats in a foreign country may sound like the start of a sci-fi novel, but that's exactly what several U.S. diplomats in Cuba may have been exposed to, the U.S. State Department recently announced.



Credit: Shutterstock

The physical symptoms, which the State Department would not confirm, but which some news reports have suggested included hearing loss, got so bad that some of these officials had to be recalled from their duties in Havana.

"Some U.S. government personnel who were working at our embassy in Havana, Cuba, on official duties — so they were there working on behalf of the U.S. embassy there — they've reported some incidents which have caused a variety of physical symptoms," Heather Nauert, a spokeswoman for the State Department, said in a news briefing Aug. 9.

After an extensive investigation, U.S. officials determined that a secret sonic weapon was to blame.

But what exactly could that weapon be, and how could it cause hearing loss without any of the people involved noticing a painful audible sound?

While the mysterious story has a lot of holes, one possibility is that the workers were exposed to infrasound, or low-frequency sound waves that are below the audible hearing range, said Charles Liberman, a hearing loss researcher at Harvard Medical School and Massachusetts Eye and Ear in Boston.

What we know

The strange symptoms emerged in the fall of 2016, when several employees at the U.S. embassy in Havana began complaining of physical symptoms. Many of the individuals were new to the embassy and some had to return to the United States because of the severity of their symptoms — the details of which have yet to be disclosed.

An investigation by the U.S. government concluded that the symptoms could be attributed to a device that operated outside the audible hearing range and was used somewhere, possibly in their houses, Time magazine reported.

Right now, there's no word on whether these devices were deliberately used. In retaliation, the U.S. government expelled two Cuban diplomats on May 23, Nauert said. Cuba denied any involvement in the bizarre scenario.

"Cuba has never permitted, nor will permit, that Cuban territory be used for any action against accredited diplomatic officials or their families, with no exception," according to a statement from the Cuban government. Another possibility is that some other hostile group (such as Russian agents) may have initiated the attack, Time reported.

Hard of hearing

There are so many details missing in this story that it's hard to explain exactly what the device could be, Liberman said. However, sound-induced hearing loss requires that the mechanical part of the ear that senses audible sound be overloaded. "You overstimulate the part of the ear that's mechanically tuned to those frequencies and it falls apart," Liberman.

If the people in the embassy didn't hear anything, that suggests the weapon probably didn't operate in the normal hearing range, or else it would have caused pain and been distracting, Liberman said. (Human audible hearing range is typically between 20 hertz, or cycles per second, and 20 kilohertz). If so, there's little possibility for it to damage the mechanical parts of the ear that are tuned to those frequencies, he said.

Infrasound

However, it's possible the devices somehow generate infrasound — the type of low-frequency sound given off by windmills or wind generators with the beating of the blades. Infrasound is below the human hearing range.

And yet, many people claim these machines are making them sick, and there are several lawsuits from people who live or work near wind farms, claiming they make them sick, according to Liberman.

"There is a growing controversy about people who live near these windmills who start feeling bad," Liberman told Live Science. "They get headaches, they get dizzy, they get nausea."

For instance, a 2014 study in the journal Royal Society Open Science found that low-frequency sounds below the audible range could disrupt little whistles made by the ear, called spontaneous optoacoustic emissions, in response to noise. (How that mapped to symptoms, however, wasn't clear.)

In this instance, one possibility is that the infrasound stimulated the part of the ear not dedicated to hearing — the vestibular system that controls balance, Liberman said. In that instance, the symptoms wouldn't appear immediately. "You could imagine them being very slow onset and very persistent," Liberman said. "It might take days before you even notice any funny sensations."

That may explain why the State Department refused to describe the symptoms experienced by their employees as including hearing loss, Liberman said.

High-frequency ultrasound

The other type of sound humans can't hear is ultrasound, which is above 20 khz. That's a less likely possibility because high-frequency sound dissipates quickly with distance and in tissue such as the ear. However, high-intensity, focused ultrasound has been used for everything from breaking kidney stones to cauterizing tissues in the body.

But the fact that it doesn't work well across long distances means it's tough to imagine a device could get close enough to the people to work, without them suspecting, Liberman said.

What's more, if a covert acoustic device using ultrasound produced enough energy to permeate and damage the ear from far away, it would probably heat the head up, too, Liberman said.

However, it's theoretically possible that high-frequency ultrasound may have somehow damaged the blood vessels in the ear canal, thereby leading to damage, he said. That seems less likely, but "I've been in science long enough to not discount as impossible things that seem improbable," Liberman said.

Sonic weapons

While the idea of a silent sonic weapon sounds like something out of James Bond, Inspector Gadget or the reject pile of DARPA, the idea of using sound as a weapon has a long history.

For instance, studies show that animals exposed to high-intensity, focused ultrasound can experience lung and brain damage. And a cruise line circling the pirate-infested waters off the Somali coast has taken to using a military-grade "sonic weapon" to deter would-be hijackers, the BBC reported. This long-range device, also known as a sound cannon, can cause permanent hearing loss at distances of up to 984 feet (300 meters), according to the BBC. Other companies have developed a magnetic acoustic device, commonly referred to as a sound laser, that deploys incredibly painful, focused beams of sound to deter people from an area, NPR reported. The Israeli army has also used a device known as "The Scream," which damages the inner ear, causing nausea and dizziness, Wired reported.

http://nyti.ms/2fBL0dq

We Need to Talk Some More About Your Dirty Sponges

You don't have to be afraid of your sponge, experts say, but it's wise to take a few precautions in the kitchen, including discarding it when it starts to stink.

By JOANNA KLEIN AUG. 11, 2017

A kitchen sponge is not your enemy. But it can be very dirty. Last week, scientists published a study revealing how densely packed your dirty kitchen sponge is with microscopic bacteria. After I wrote an article about their work, readers flooded my inbox with good questions, so I asked around for some answers.

First, let's examine what the study did and didn't do.

The study was designed to establish improved measurements of the bacterial populations that live inside this common household item. Previous measurements had mainly looked at those from sponges dirtied in the lab, growing the bacteria in a petri dish. But because not all bacteria will grow in that medium, their numbers may have been underestimated, said Markus Egert, the microbiologist at the University of Furtwangen in Germany who led the study.

"Our study was mainly thought to create awareness, and not fear," Dr. Egert wrote in a follow-up email.

But what they found alarmed many readers. Although not designed to evaluate disinfection methods, the researchers collected additional data from the sponge donors (a sample of 14 sponges, which the researchers concede was limited). And to their surprise, sponges regularly cleaned in soapy water or the microwave actually harbored more of a bacteria called Moraxella osloensis. This bacteria is generally common and harmless, but it can cause infections in people with compromised immune systems.

Nonetheless, Dr. Egert suggested that in most cases it may be best to throw away your sponge when it starts to stink — a sign that the nasty bacteria may be there — even if it may not harm you. This decision to toss, said Dr. Egert, means balancing hygiene and sterility, thriftiness and a sustainable environment. The United States Department of Agriculture also suggests buying new sponges frequently, as they are "difficult to clean."

"You should not become hysteric and afraid of your kitchen sponge now," said Dr. Egert in our original interview. Even sterile

environments can make a person ill, he added. “But if you’re already ill or have ill people at home, you should be more careful.”

And that brings us to talking about risk, which the study was not designed to assess.

Kitchens are hot spots for cross-contamination, and immune systems differ. You could just as easily contract an illness from poorly prepared food or your cellphone as you could from a dirty sponge, many experts say. And two bodies’ responses to the same pathogen can differ, just like a pothole might damage one car but not another, said Kevin Sauer of Kansas State University, who has studied cross-contamination in the kitchen.

But if you’re still worried, here are three tips from Solveig Langsrud, a microbiologist at Nofima, an applied research institution in Norway, who has examined how different hygiene procedures can reduce bacterial contamination in kitchens.

Don’t feed your sponge with dangerous bacteria

Don’t use your sponge to scrub off chunky food debris or wipe up fresh meat juices, dirt from fruits and veggies, unpasteurized milk stuff, vomit or your pet’s droppings. Just use a paper towel, cleanser or running water. Keep sick people away from food preparation areas. (And for those who asked, a vegan kitchen full of raw vegetables is not immune.)

To avoid cross-contamination, wash your hands (properly) and give different sponges their own jobs — like cleaning only your counter, floor or dishes. A proper handwashing means removing jewelry and using soapy water for 20 seconds before drying with a clean towel, said Argyris Magoulas, an information specialist at the Office of Public Affairs and Consumer Education at the U.S.D.A. Food Safety and Inspection Service.

Keep your sponge clean

Dr. Langsrud says that you should wash your sponge after each use, which doesn’t quite jibe with Dr. Egert’s study. But Dr. Egert doesn’t think his donors gave their sponges a correct washing. With some effort, you can disinfect your sponges and get rid of most of their bacteria, although this may not be practical for many of us.

In a 2008 study, Manan Sharma, a microbiologist who studies foodborne pathogens with the U.S.D.A., and his colleagues soaked sponges in ground beef at room temperature for two days to get them extra bacteria-y and then compared common cleaning methods. He found that microwaving and running them through the dishwasher were the most effective killers of some bacteria, mold and yeast.

But there were caveats: A synthetic, metallic or dry sponge can catch fire in the microwave. Microwaves and dishwasher models can vary — you must watch temperatures. Too little heat, time or steam can put your sponge in what Mr. Magoulas calls “the danger zone,” a place where bacteria proliferate. Also make sure your sponge is wet — the steam kills many microbes, experts say.

Dr. Langsrud says drying is also is “a simple, cheap, environmentally friendly and effective way to keep bacterial numbers down.” That’s because moisture-loving bacteria can’t multiply on a dry sponge — for the most part — which brings us to Dr. Langsrud’s final piece of advice and our original conundrum.

Don’t be too attached to your sponge

Even with prevention, washing and drying, some bacteria that live in kitchens can accumulate in the sponge, Dr. Langsrud said. “These bacteria are tolerable to drying and protect themselves in food debris and a self-produced slime,” she said. “They will be impossible to fight.”

She agrees with Dr. Egert: Dispose of sponges at least once a week, or when they smell bad. And if someone is sick in your house, like with cancer, she says to throw away sponges daily. Reuse disinfected sponges in less hygiene-sensitive spots if you must.

This all may make you wonder if you even need a sponge, if some are better than others and if alternatives exist.

Plenty of companies offer solutions — like bacteria-killing baths for sponges, water-repellent surfaces or antimicrobial materials. But

without peer-reviewed scientific studies, it's difficult to evaluate their effectiveness. Also, consider instead brushes, paper towels and washcloths (which are washed more often and used in restaurants).

"Tools that soak less water, dry faster, have smaller inner surfaces might indeed be better for regular cleaning," Dr. Egert wrote in a follow-up email.

Dr. Sauer says the problem with sponges is that they're easy to ignore. They inhabit the sink. They stay wet. They get nasty. But can you really blame them? "A lot of us have been brought up to grab that sponge because it takes care of the surface, cleaning what we see," he said. "I don't think sponges are the enemy, but they provide a great medium to grow bacteria."

http://nyti.ms/2hV8cnr

A Cancer Conundrum: Too Many Drug Trials, Too Few Patients

A problem without precedent in medical research

By GINA KOLATA AUG. 12, 2017

With the arrival of two revolutionary treatment strategies, immunotherapy and personalized medicine, cancer researchers have found new hope — and a problem that is perhaps unprecedented in medical research.

There are too many experimental cancer drugs in too many clinical trials, and not enough patients to test them on.

Dr. Wassim Abida, a medical oncologist at Memorial Sloan Kettering Cancer Center, examined Bruce Fenstermacher, a patient taking part in a clinical trial. **George Etheredge for The New York Times**

The logjam is caused partly by companies hoping to rush profitable new cancer drugs to market, and partly by the nature of these therapies, which can be spectacularly effective but only in select patients.

In July, an expert panel of the Food and Drug Administration approved a groundbreaking new leukemia treatment, a type of immunotherapy. Companies are scrambling to develop other drugs based on using the immune system itself to attack cancers.

Many of these experimental candidates in trials are quite similar. Yet each drug company wants to have its own proprietary version, seeing a potential windfall if it receives F.D.A. approval.

As a result, there are more than 1,000 immunotherapy trials underway, and the number keeps growing. "It's hard to imagine we can support more than 1,000 studies," said Dr. Daniel Chen, a vice president at Genentech, a biotechnology company.

In a commentary in the journal Nature, he and Ira Mellman, also a vice president at the company, wrote that the proliferating trials "have outstripped our progress in understanding the basic underlying science."

"I think there is a lot of exuberant rush to market," said Dr. Peter Bach, director of the Center for Health Policy and Outcomes at Memorial Sloan Kettering Cancer Center. "And we are squandering our most precious resource — patients."

Take melanoma: There are more than 85,000 cases a year in the United States, according to Dr. Norman Sharpless, director of the Lineberger Comprehensive Cancer Center at the University of North Carolina, who was recently named director of the National Cancer Institute.

Memorial Sloan Kettering is testing a drug that attacks a tumor with a mutation found in just 1 percent of cancer patients. **George Etheredge for The New York Times**

Most melanomas are cured by surgery, leaving about 10,000 patients who have had relapses and could be candidates for an experimental treatment. But nearly all will be treated by doctors outside of

academic medical centers, who are not part of the clinical trials network and so do not offer patients experimental treatments.

Companies therefore must compete for the few patients with relapsed melanoma who are at centers offering clinical trials. Many end up struggling to find enough subjects to determine whether a treatment actually works — and if so, for whom.

And these drugs often are not so different from one another.

Immunotherapy drugs that attack a protein known as PD-1 are approved for treatment of lung cancer, renal cell cancer, bladder cancer and Hodgkin's disease, noted Dr. Richard Pazdur, director of the F.D.A.'s Oncology Center of Excellence.

Yet many pharmaceutical companies want their own anti-PD-1. Companies are hoping to combine immunotherapy drugs with other cancer drugs for added effect, and many do not want to have to rely on a competitor's anti-PD-1 drug along with their own secondary drugs.

So in new trials, additional anti-PD-1 drugs are being tested all over again against the same cancers — a me-too business strategy taken to multibillion-dollar extremes.

"How many PD-1 antibodies does Planet Earth need?" wondered Dr. Roy Baynes, a senior vice president at Merck, which received approval for its first such drug in 2014.

Immunotherapy trials have proliferated so quickly that major medical centers are declining to furnish patients to them. The Yale Cancer Center participates in fewer than 10 percent of the immunotherapy trials it is asked to join.

The problem is that many of the trials are uninteresting from a scientific view, said Dr. Roy Herbst, the center's chief of medical oncology. The companies sponsoring these trials are not addressing new research questions, he said; they are trying to get proprietary drugs approved.

If the struggle to find patients for immunotherapy trials is challenging, finding patients for another new type of cancer treatment can be next to impossible.

These are drugs that attack mutations that tumors need to grow and thrive — so-called targeted therapies. The idea is that tumors can be reliant on certain gene mutations. Block those mutations and the tumors will die.

Mr. Fenstermacher at the start of a trial of an experimental drug, which has since shown signs of helping fight his cancer. **George Etheredge for The New York Times**

The problem is that the mutations can be extraordinarily rare. Most patients who have cancers with the mutation in question have no idea; to find them, large groups of cancer patients must have their tumors genetically tested.

That's expensive: Genetic sequencing costs about $5,000, and insurers rarely pay. Most cancer patients treated outside of academic centers do not have their tumors sequenced.

So what to do if you're a company with a drug that seems to be dramatically effective, but only in a few patients?

You may be forced to undertake a worldwide search for subjects that can last for years.

To test a two-drug combination against lung cancer, GlaxoSmithKline searched the United States, Japan, South Korea and Europe for 13 months just to find 59 patients whose tumors shared a rare mutation.

It took Pfizer three years to locate 50 lung cancer patients who carried a rare aberration called ROS1, found in just 1 percent of patients.

Clinical trials with patient searches like these are "not for the faint of heart," said Dr. Mace Rothenberg, a senior vice president at Pfizer.

It helps that the F.D.A. has not insisted on large trials with control groups in instances of targeted therapies with few who qualify.

Instead the agency is looking for drugs with effects so powerful there is no question that they work — studies in which patients went into remission, for example, when all evidence suggested they would die.

"We used to have trials not long ago that had 700 patients per arm," Dr. Sharpless said, referring to the treatment groups in a study. "That's almost undoable now."

Today, "trials can be eight patients."

To test a drug that attacks a tumor with a mutation found in just 1 percent of cancer patients, researchers at Memorial Sloan Kettering fanned out to the nonacademic medical centers where the majority of patients are treated, offering to pay for most of the cost of genetic testing, seeking patients at practices in the Lehigh Valley of Pennsylvania; Hartford, Conn.; and Miami.

That is how Bruce Fenstermacher, 67, a retired long-distance truck driver who lives in Allentown, Pa., discovered he had the rare mutation that the drug's manufacturer, Loxo Oncology, had been looking for.

He had been receiving immunotherapy for his melanoma, but it had stopped working and his cancer was spreading again. Discovering that mutation was like hitting the jackpot for Mr. Fenstermacher, said Dr. Suresh Nair, an oncologist with Lehigh Valley Health Network.

The experimental drug seems to be working for Mr. Fenstermacher. But since so few patients have tumors that might respond, oncologists wonder how they will find them.

Is it worth it? Is it even possible?

"If, God forbid, I had a family member with cancer, I would insist on this type of testing," said Dr. David Hyman, chief of the Early Drug Development Service at Memorial Sloan Kettering Cancer Center. "But I don't know what the rate has to be for society to say, 'We can't afford to miss these people.'"

And trials involving limited numbers of patients can be perilous. The smaller the study and the shorter its duration, the more likely that what looks like an effect in a trial might simply be a result of chance, Dr. Bach of Memorial Sloan Kettering said.

"That leaves some of us evidence geeks wondering if it works," he said.

Some of the new cancer drugs have had such impressive results that their effectiveness was not in doubt, said Dr. Vinay Prasad, an oncologist at Oregon Health and Sciences University.

But, there also were drugs approved without control groups that did not provide such stunning benefits, and others that markedly slowed the growth of tumors but did not extend life.

In tiny studies, serious side effects can be missed, said Dr. Scott Ramsey, an oncologist at the Fred Hutchinson Cancer Research Center.

He worries about the expense of the new drugs, including out-of-pocket costs to patients. They may want the new cancer drugs reaching the market, he said, "but you wonder if you are doing them any favors."