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## **Yeast model reveals Alzheimer's drug candidate and its mechanism of action**

*A yeast model of Alzheimer's disease, helped researchers identify a drug that reduces levels of amyloid- $\beta$  and prevents some of the cellular damage caused when  $A\beta$  accumulates in the brains of AD patients*

Written by Nicole Giese Rura

CAMBRIDGE, Mass. - Using a yeast model of Alzheimer's disease (AD), Whitehead Institute researchers have identified a drug that reduces levels of the toxic protein fragment amyloid- $\beta$  ( $A\beta$ ) and prevents at least some of the cellular damage caused when  $A\beta$  accumulates in the brains of AD patients.

"We can use this yeast model to find small molecules that will address the underlying cellular pathologies of Alzheimer's, an age-related disease whose burden will become even more significant as our population grows older," says Kent Matlack, a former staff scientist in Whitehead Member Susan Lindquist's lab. "We need a no-holds-barred approach to find effective compounds, and we need information about their mechanism of action quickly. Our work demonstrates that using a yeast model of  $A\beta$  toxicity is a valid way to do this."

The U.S. National Institute on Aging estimates that 5.1 million Americans may have AD, the most common form of dementia, which progressively robs patients of their memories, thinking, and reasoning skills. Research focused on the disease has been hampered by the affected cells' location in the brain, where they cannot be studied until after an AD patient's death. To explore the cellular processes compromised by AD, researchers in Lindquist's lab created a yeast model, first described in the journal *Science* in 2011, that mimics in vivo the accumulation of  $A\beta$  that occurs in the human disease.

In the current research, which is described in this week's issue of the journal *Proceedings of the National Academy of Sciences (PNAS)*, a team of scientists in Lindquist's lab used the yeast model to screen approximately 140,000 compounds to identify those capable of rescuing the cells from  $A\beta$  toxicity. One of the more promising classes of compounds has previously shown efficacy in animal models of AD and is about to complete a second phase II trial for AD. The mechanism by which the best-studied member of this class, clioquinol, targets  $A\beta$  within the cell – where a large portion of it is produced in neurons – was unclear.

"Our work in the yeast model shows that clioquinol decreases the amount of  $A\beta$  in the cells by 90%," says Daniel Tardiff, a scientist in Lindquist's lab. "That's a strong decrease, and it's dose-dependent. I've tested a lot of compounds before, and I've never seen anything as dramatic."

Clioquinol chelates copper, meaning that it selectively binds the metal. In many AD patients,  $A\beta$  aggregates have higher concentrations of copper and other metals than normal, healthy brain tissue. Biochemical experiments also show that copper makes  $A\beta$  more toxic.

With clioquinol's chelation capabilities in mind, Tardiff and Matlack, co-authors of the *PNAS* paper, tested clioquinol's effect on  $A\beta$ -expressing cells in the presence of copper. The drug dramatically increased the degradation of  $A\beta$  in a copper-dependent manner, and even restored the cellular protein-trafficking process known as endocytosis, which is disrupted in both the yeast model and in AD-affected neurons.

"The clioquinol probably has a slightly higher affinity for copper than  $A\beta$  does, but it is not a strong enough chelator to strip the cell's normal metalloproteins of the copper they need," says Matlack. "From what we've seen in the yeast model, we think the drug pulls the copper away from  $A\beta$ . That would alter  $A\beta$ 's structure and likely make it more susceptible to degradation, thus shortening its half-life in the cell."

The results from clioquinol in yeast and the clinical potential of closely related compounds are promising. While these compounds are not yet ready to serve as AD drugs in the clinic, the identification of an AD-relevant compound and cellular pathology – along with the Lindquist lab's previous identification of human AD risk alleles that reduce  $A\beta$  toxicity in yeast – suggests that this discovery platform will continue to yield information and lead to more compounds with equal or greater effectiveness, some of which will hopefully make a difference in human disease.

"It is important to remember that this class of compounds was shown to work in mouse models and in a limited human trial," says Lindquist, who is also a professor of biology at MIT and an investigator of the Howard Hughes Medical Institute. "We have validated the yeast model and shown that we can find such compounds at a speed that was inconceivable before—indeed we found some compounds that look even more effective."

*This work is supported by the Howard Hughes Medical Institute, National Institutes of Health (R03 Grant DA032472), the Ellison Foundation, National Research Service Award (NRSA F32NS061419), the JPB Foundation, and the Edward N. and Della L. Thome Memorial Foundation.*

*Susan Lindquist's primary affiliation is with Whitehead Institute for Biomedical Research, where her laboratory is located and all her research is conducted. She is also a professor of biology at Massachusetts Institute of Technology and an investigator of the Howard Hughes Medical Institute.*

*"Clioquinol promotes the degradation of metal-dependent amyloid- $\beta$  ( $A\beta$ ) oligomers to restore endocytosis and ameliorate  $A\beta$  toxicity" *PNAS*, March 3, 2014.*

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## **Experimental stroke drug also shows promise for people with Lou Gehrig's disease**

*New Keck School of Medicine of USC research finds vascular damage in mice with ALS contributes to early development of the neurodegenerative disease, while repairing damage delays disease progression*

Keck School of Medicine of USC neuroscientists have unlocked a piece of the puzzle in the fight against Lou Gehrig's disease, a debilitating neurological disorder that robs people of their motor skills. Their findings appear in the March 3, 2014, online edition of the Proceedings of the National Academy of Sciences of the United States of America, the official scientific journal of the U.S. National Academy of Sciences.

"We know that both people and transgenic rodents afflicted with this disease develop spontaneous breakdown of the blood-spinal cord barrier, but how these microscopic lesions affect the development of the disease has been unclear," said Berislav V. Zlokovic, M.D., Ph.D., the study's principal investigator and director of the Zilkha Neurogenetic Institute at USC. "In this study, we show that early motor neuron dysfunction related to the disease in mice is proportional to the degree of damage to the blood-spinal cord barrier and that restoring the integrity of the barrier delays motor neuron degeneration. We are hopeful that we can apply these findings to the corresponding disease mechanism in people. "

In this study, Zlokovic and colleagues found that an experimental drug now being studied in human stroke patients appears to protect the blood-spinal cord barrier's integrity in mice and delay motor neuron impairment and degeneration. The drug, an activated protein C analog called 3K3A-APC, was developed by Zlokovic's start-up biotechnology company, ZZ Biotech.

Lou Gehrig's disease, also called amyotrophic lateral sclerosis, or ALS, attacks motor neurons, which are cells that control the muscles. The progressive degeneration of the motor neurons in ALS eventually leads to paralysis and difficulty breathing, eating and swallowing.

According to The ALS Association, approximately 15 people in the United States are diagnosed with ALS every day. It is estimated that as many as 30,000 Americans live with the disease. Most people who develop ALS are between the ages of 40 and 70, with an average age of 55 upon diagnosis. Life expectancy of an ALS patient averages about two to five years from the onset of symptoms.

ALS's causes are not completely understood, and no cure has yet been found. Only one Food and Drug Administration-approved drug called riluzole has been shown to prolong life by two to three months. There are, however, devices and therapies that can manage the symptoms of the disease to help people maintain as much independence as possible and prolong survival.

*The international research team included scientists from the The Scripps Research Institute, University of Rochester Medical Center, Sichuan University's West China Hospital, and Ludwig Institute for Cancer Research at the University of California, San Diego. Grants from The ALS Association (1859) and National Institutes of Health (AG039452, AG23084, NS34467, HL031950, HL052246, NS27036) supported their research.*

*Winkler, E. A., Sengillo, J. D., Sagare, A. P., Zhao, Z., Ma, Q., Zuniga, E., ... & Zlokovic, B. V. (2014). PNAS Early Edition, 1-8. Published online March 3, 2014; doi:10.1073/pnas.1401595111*

<http://bit.ly/1eV04jG>

## **Machines Moored to the Seafloor Harness Ocean Power**

*Waves and tides offer some of the most predictable, consistent, and just generally big energy resources available.*

by Dave Levitan, IEEE Spectrum

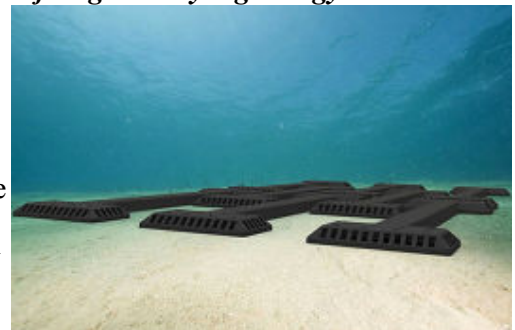
Rollouts of actual wave and tidal power installations, however, have been slow and generally limited to pilot projects so far. Part of the reason for this, along with straightforward but difficult problems like transmission, is that there is no consensus at all on what represents the best device designs to actually harness waves and tides.

A couple of interesting ideas -- one wave, one tidal -- were on display this week at the ARPA-E Innovation Summit in Washington, D.C., that offer some clear advantages over many of the other attempts at drawing energy from the oceans.

*M3 Wave A simple device moored to the ocean floor captures wave energy as it passes over the top.*

Iceland is leading the way when it comes to using magma as an alternative source of fuel. Trace explains how this new power plant is changing how we heat our homes in hopes for a more sustainable future.

The wave power idea is closer than the tidal energy one to rollout, with a planned open-water test for this summer. M3 Wave dispenses with all the problems that come with buoys or other above-and-below-the-surface designs by mooring a simple device to the ocean floor.



The device, pictured above, involves two air chambers: as a wave passes over the top of the first chamber, the pressure inside increases, forcing air through a passageway to the second chamber. Inside the passageway is a turbine, so the passing air is actually what generates the electricity. As the wave continues on, it raises the pressure inside the second chamber, pushing the air back through the turbine -- importantly, it is a bidirectional turbine -- and back into the first chamber. Another wave, another cycle. Repeat.

The primary selling point here is its simple and small footprint. There is no impact on ocean view, on shipping or fishing traffic, and rough seas above won't endanger the system in any way. M3 is selling it as "expeditionary" wave power, meaning it might be brought along on a ship and deployed for things like disaster relief; the company suggests such a deployment could produce 150 to 500 kilowatts. The system will undergo open-water testing at a U.S. National Guard facility, Camp Rilea in Oregon, in August.

On the other side of the country, a group at Brown University has developed what they call an oscillating hydrofoil, intended to minimize some of the impacts of tidal power devices and increase efficiency. The hydrofoil is mounted on to the sea floor and resembles a car's spoiler attached to a pole, essentially. As the water flows past that spoiler it oscillates, generating electricity.

It's designed so that the pole can actually fold down and out of the way if necessary, allowing for ships or even wildlife (detected with sensors on the device) to pass by without incident. The team received US \$750,000 in funding from ARPA-E in 2012, and will soon move to a phase II involving a medium-scale, 10-kw prototype. They have calculated that the device can achieve much better energy conversion efficiencies in tides flowing very slowly than any of the devices that are on or close to market.

The National Renewable Energy Laboratory has estimated that in the United States alone there are wave power resources totaling 252 terawatt-hours/year, with tidal power adding another 17 Twh/year. Those are big numbers, and they come without the intermittency complaints that plague wind and solar power. Any new way to catch the ocean's energy is worth a look.

<http://www.wired.com/wiredscience/2014/03/dark-matter-galactic-center/#rssowlmlink>

### Strange Signal From Galactic Center Is Looking More and More Like Dark Matter

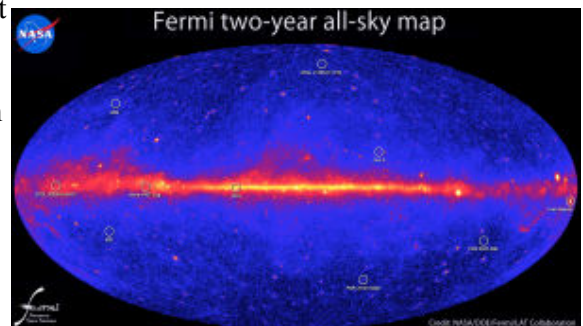
*The more that scientists stare at it, the more a strange signal from the center of the Milky Way galaxy appears to be the result of dark matter annihilation. If confirmed, it would be the first direct evidence for dark matter ever seen.*

By Adam Mann

Dark matter is a mysterious, invisible substance making up roughly 85 percent of all matter in the universe. It floats throughout our galaxy, but is more concentrated at its center. There, a dark matter particle can meet another dark matter particle flying through space. If they crash into one another, they will annihilate each other (dark matter is its own antiparticle) and give off gamma rays.

To search for a dark matter signal, astronomers use NASA's Fermi Gamma-Ray Telescope to map the gamma radiation throughout the galaxy. Then, they try to account for all known sources of light within this map. They plot the location of gas and dust that could be emitting radiation and subtract that signal from their gamma-ray map. Then they determine where all the stars are and subtract out that light, and so on for every object that might be emitting radiation. Once all those sources are gone, there remains a tiny excess of gamma radiation in the data that no known process can account for.

"The more we scrutinize it, the more it looks like dark matter," said astrophysicist Dan Hooper of Fermi National Accelerator Laboratory, co-author of a paper that appeared Feb. 26 on arXiv, a website that hosts scientific papers that have yet to go through peer-review.



*The sky as seen in gamma rays from the Fermi telescope. The red line through the center is the disk of our galaxy.*

Image: NASA/DOE/Fermi LAT Collaboration

Since 2009, Hooper has been claiming that this bright signal is evidence of dark matter. According to his team's latest data, the gamma radiation could be produced by dark matter particles with a mass of 30 to 40 giga-electronvolts (GeV) crashing into one another. A proton is roughly 1 GeV for comparison.

But the galactic center is a tricky place. There are many other gamma ray sources that could be mimicking a dark matter signal as well as yet undiscovered phenomena that might account for the radiation. For the most part, few other researchers have been convinced of Hooper's data. One oft-used counterargument is that the excess gamma ray signal could come from millisecond pulsars — dead star cores that spin extremely fast and



beam out a huge amount of energy. Astronomers don't yet have a good understanding of how these objects work.

"If you need to explain something weird in the galactic center, you wave your hands and say, 'Millisecond pulsars,'" said astronomer Doug Finkbeiner of Harvard, another co-author of the new work.

Finkbeiner has long been a skeptic that the excess Fermi telescope signal represents dark matter annihilation. He knows that the galactic center is a strange place full of unexpected phenomena, having discovered in 2010 two gigantic structures spanning 50,000 light-years emanating from the Milky Way, which had gone unnoticed until then. But a more careful look at Hooper's data has started to convince Finkbeiner that there might be something there.

When a galaxy forms, gravitational attraction brings together a huge mass that begins spinning. As they spin, large galaxies cool down and flatten out like a pizza, forming the familiar spiral shape seen in many telescope images. Dark matter, which actually makes up the bulk of a galaxy's mass, can't flatten out because it doesn't interact with the electromagnetic force, which would allow it to radiate away thermal energy. It stays in a spherical halo circling the galaxy. So any dark matter signal should come not just from within the galactic plane, but also from above and below it, where stars are few and far between but dark matter is abundant.

The problem is that the galactic center is extremely bright. Its billions of stars give off an incredible amount of light that shines far above and below the plane of the Milky Way. Showing that the gamma ray signal comes from dark matter and nothing else requires extremely precise mapping. But the Fermi telescope's data also happens to be a little blurry at the energy ranges where the dark matter signal shows up. Working with physicist Tracy Slatyer of MIT, Finkbeiner combed through the Fermi data and found a way to throw out the blurriest parts. This left a very sharp map showing exactly that the excess gamma ray signal was coming from areas where few stars should exist.

"The answers just got a lot better," said Finkbeiner. "It looked more like dark matter and less like pulsars."

The newly sharpened data is making other researchers take notice. "We may in the future say this was when dark matter was discovered," said theoretical physicist Neal Weiner of New York University.

A particle mass of 30 to 40 GeV would make this form of dark matter quite interesting, he added, because it is something that could have shown up at the Large Hadron Collider. The fact that it didn't might suggest that dark matter is more complicated than our simplest models predict.

But others remain more skeptical. "If the question is, 'Have we really discovered dark matter?' I would really caution to set the burden of proof as high as we can," said physicist Stefano Profumo of the University of California, Santa Cruz. There are many things that our Earth-bound perspective might not be taking into account, such as differences in the density or energies of cosmic rays in the galactic center, he added.

Even though he is a co-author of the new work, Finkbeiner also remains cautious. Of all the options he is aware of, he thinks dark matter annihilation remains the best explanation for the Fermi telescope's excess signal. But the universe is vast and there likely remain many unknown objects for astronomers to find.

To definitively answer this question, scientists will likely have to study dwarf galaxies, which are up to 99 percent dark matter and contain few other odd phenomena that could mimic a dark matter signal. The Fermi telescope will have to stare at these objects for a few more years before it has enough data to confirm or deny the latest results.

<http://bit.ly/1fHkTUM>

## **Scientists revive largest virus yet from 30,000-year-old permafrost**

*And it's a very strange beast. Fortunately, it only affects amoebas. We think.*

by John Timmer - Mar 4 2014, 5:08am TST

Up until recently, the line between viruses and cells seemed pretty simple: cells were big and carried everything they needed to live and grow. Viruses were tiny and only carried the genes they needed to take over their host cells; they relied on their hosts for most essential proteins.

That line got a bit blurry as we found parasitic and symbiotic cells with very stripped-down, minimalist genomes that wouldn't let them survive outside their hosts. But it's nearly been obliterated by the discovery of giant viruses—some of these have genomes that are larger than those of bacteria and carry many of the genes needed to copy DNA and translate it into proteins.

Scientists have now identified yet another giant virus, this time using a technique that sounds like it's straight out of a sci-fi horror flick: they thawed some 30,000-year-old permafrost and allowed any viruses present to infect some cells. Fortunately, the cells were amoebas, and this virus is overwhelmingly unlikely to present a threat to human health. But the fact that viruses could apparently survive so many centuries in the Siberian permafrost does lead the authors to suggest that the melting Arctic may pose an emerging disease risk.

The authors of the new paper, a mix of French and Russian researchers, identified the virus using a procedure that's incredibly simple: take a culture of amoebas (a strain that has been found in the permafrost) and put a bit of permafrost in with the culture. After that, it was a matter of waiting for something bad to happen to the amoebas.

The something bad in this case happened to be the explosion, or lysis, of the cells. A check of the culture showed the presence of a giant virus particle, shaped similarly to the Pandoravirus described in the article linked above. In terms of the sheer physical size of the virus, it's the largest one we've yet discovered. Because of its jug-like shape, the authors named it Pithovirus after a type of amphora used by Pandora (the namesake of the second largest virus).

However, there were some clear differences with Pandoravirus from the start. For example, the cork of the jug (their term, not mine) appears to contain some specialized fibers that are unlike anything seen in Pandoravirus. And the Pithovirus reproduces in a virus factory it sets up inside infected cells; the Pandoravirus takes over a cell's nucleus. (Viral factories are also set up by the first giant virus identified, Mimivirus, which looks physically distinct from these other two.)

Despite its giant physical size, Pithovirus carries a relatively small genome at only 600,000 DNA bases long. Some of the extra space inside the virus is taken up by the proteins needed to get the virus' replication started after infection (RNA transcription machinery). But the authors are at a bit of a loss to explain what all the extra space inside the virus' capsule might be used for.

The genome is also small in another sense: gene content. It encodes only 467 proteins, far fewer than the 1,000 to 2,500 genes carried by other giant viruses. Missing are the sorts of things that make the other giants unique among viruses: genes for translating RNA into proteins and others involved in energy metabolism. Also unusual is the presence of repetitive DNA. Viruses normally get rid of any unused DNA sequences, leaving most of their DNA taken up by protein-coding genes. Pithovirus has a large collection of nearly identical, non-protein coding sequences.

The authors suggest two options: either that the virus just needs the extra DNA as padding to make it large enough to work in its giant shell, or it has recently been invaded by some parasitic DNA and hasn't had the chance to get rid of it via evolution. (Although they can't rule out other possibilities right now.)

As far as the genes themselves, only a third are similar to anything we've ever seen before. And that third is divided roughly equally among similarities to genes from bacteria, the virus' eukaryotic host, and other viruses. All of which means that Pithovirus is a distinct type of virus from anything we've ever seen before. It does seem to be distantly related to some other viruses we've previously identified, but those aren't giants like this one. So far, all of the giant viruses we've identified infect amoebas, and the authors chose to go this route when searching permafrost explicitly because it seemed safe. Anything that came out of the search was very unlikely to infect humans. But they consider the search itself a proof-of-principle: they took care not to contaminate the permafrost, which was still frozen when it was obtained. That means that the virus is very likely to have survived 32,000 years of deep freeze, which is how old the layer it came from appears to be.

All of which, the authors suggest, should be a warning. There are already humans living in areas with permafrost, and many more are expected to arrive there as the thawing Arctic makes exploitation of natural resources there much easier. The new find suggests that some of the new arrivals may potentially come in contact with infectious agents that have been out of circulation for tens of thousands of years. This doesn't mean the permafrost will necessarily be a hotbed of emerging diseases, but the authors argue that we might want to take the possibility seriously.

*PNAS, 2014. DOI: 10.1073/pnas.1320670111 (About DOIs).*

<http://nyti.ms/1nbXMZ8>

### **A Powerful New Way to Edit DNA**

***In the late 1980s, scientists at Osaka University in Japan noticed unusual repeated DNA sequences next to a gene they were studying in a common bacterium.***

**By ANDREW POLLACK MARCH 3, 2014**

They mentioned them in the final paragraph of a paper: "The biological significance of these sequences is not known." Now their significance is known, and it has set off a scientific frenzy.

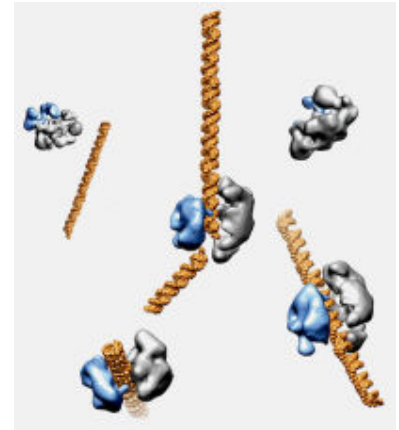
The sequences, it turns out, are part of a sophisticated immune system that bacteria use to fight viruses. And that system, whose very existence was unknown until about seven years ago, may provide scientists with unprecedented power to rewrite the code of life.

In the past year or so, researchers have discovered that the bacterial system can be harnessed to make precise changes to the DNA of humans, as well as other animals and plants. This means a genome can be edited, much

as a writer might change words or fix spelling errors. It allows “customizing the genome of any cell or any species at will,” said Charles Gersbach, an assistant professor of biomedical engineering at Duke University. Already the molecular system, known as Crispr, is being used to make genetically engineered laboratory animals more easily than could be done before, with changes in multiple genes. Scientists in China recently made monkeys with changes in two genes.

Scientists hope Crispr might also be used for genomic surgery, as it were, to correct errant genes that cause disease. Working in a laboratory — not, as yet, in actual humans — researchers at the Hubrecht Institute in the Netherlands showed they could fix a mutation that causes cystic fibrosis.

But even as it is stirring excitement, Crispr is raising profound questions. Like other technologies that once wowed scientists — like gene therapy, stem cells and RNA interference — it will undoubtedly encounter setbacks before it can be used to help patients. It is already known, for instance, that Crispr can sometimes change genes other than the intended ones. That could lead to unwanted side effects.



*The enzyme Cas9, shown in blue and gray, can cut DNA, in gold, at selected sites, as seen in this model from electron microscope images. Credit David Taylor and Jennifer Doudna*

The technique is also raising ethical issues. The ease of creating genetically altered monkeys and rodents could lead to more animal experimentation. And the technique of altering genes in their embryos could conceivably work with human embryos as well, raising the specter of so-called designer babies.

“It does make it easier to genetically engineer the human germ line,” said Craig C. Mello, a Nobel laureate at the University of Massachusetts Medical School, referring to making genetic changes that could be passed to future generations.

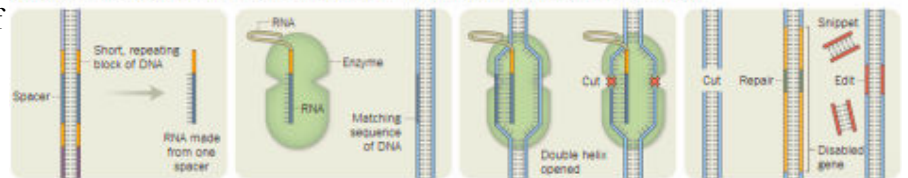
Still, Crispr is moving toward commercial use. Five academic experts recently raised \$43 million to start Editas Medicine, a company in Cambridge, Mass., that aims to treat inherited disease. Other start-ups include Crispr Therapeutics, which is being formed in London, and Caribou Biosciences in Berkeley, Calif.

Agricultural companies might use Crispr to change existing genes in crops to create new traits. That might sidestep the regulations and controversy surrounding genetically engineered crops, which generally have foreign DNA added.

The development of the new tool is an example of the unanticipated benefits of basic research. About 15 years ago, after it became possible to sequence the entire genomes of bacteria, scientists noticed that many species had those repeated DNA sequences that were first noticed a decade earlier in Osaka. They were called “clustered regularly interspaced short palindromic repeats” — Crispr for short.

#### Breaking the Chain

A complex immune system found in bacteria is already proving useful in editing DNA and may lead to future therapies.



**STORAGE** Researchers in the 1980s noticed that bacteria had small blocks of palindromic DNA repeated many times, with nonrepeated spacers of DNA stored in between. This pattern is a sophisticated immune system known by the acronym Crispr, for “clustered regularly interspaced short palindromic repeats.”

**RECOGNITION** These spacers match pieces of DNA from viral invaders that bacteria or their ancestors have faced before. When needed, the DNA, contained in the spacer is converted to RNA. An enzyme and a second piece of RNA latch on, forming a structure that will bind to strands of DNA that match the spacer’s sequences.

**CUTTING** When a matching strand of DNA is found, the enzyme opens the double helix and cuts both sides. The double cut breaks the strand and disables the viral DNA. If a bacterium survives an attack by an unfamiliar virus, it will make and store a new spacer, which can be inherited by future generations.

**EDITING** Researchers are learning how to use synthetic RNA sequences to control the cutting of any piece of DNA they choose. The cell will repair the cut, but an imperfect repair may disable the gene. Or a snippet of different DNA can be inserted to fill the gap, effectively editing the DNA sequence.

**By The New York Times Sources: Nature; Addgene**

But what was their purpose? In 2007, researchers at Danisco, a company that supplies bacterial cultures used in making cheese and yogurt, confirmed hypotheses that Crispr protects bacteria from viruses.

It is part of an adaptive immune system — one that remembers a pathogen so it is ready the next time that same invader appears. The human adaptive immune system is why people get measles only once and why vaccines work. But it was not imagined that single-cell organisms like bacteria had such systems.

Here is how it works. The repeated DNA sequences in the bacterial genome are separated from one another by other sequences. These “spacers” are excerpts from the sequences of viruses that have attacked the bacterium or its ancestors. They are like genetic mug shots, telling the bacterium which bad guys to watch for. The Crispr defense system will slice up any DNA with that same sequence, so if the same virus invades again, it will be destroyed.

If a previously unseen virus attacks, a new spacer, a new mug shot, is made and put at the end of the chain.

That means the Crispr region “is like a tape recording of exposure to prior invaders,” said Erik J. Sontheimer, a Northwestern University professor who helped unravel the mechanism.

And it provides a way to tell two bacterial strains apart, because even two strains from the same species are likely to have encountered different viruses. This is already being used to identify sources of food-poisoning outbreaks. Cheese and yogurt companies can examine Crispr regions to see if their bacterial cultures are immunized against particular viruses that could slow production.

“Now you can extend the shelf life of that great strain,” said Rodolphe Barrangou of North Carolina State University, who previously worked at Danisco and was the lead author on the 2007 paper. “That has changed the game quite a bit for the dairy industry.”

The real frenzy, however, started in 2012, when a team led by Emmanuelle Charpentier, then at Umea University in Sweden, and Jennifer A. Doudna of the University of California, Berkeley, demonstrated a way for researchers to use Crispr to slice up any DNA sequence they choose.

Scientists must synthesize a strand of DNA’s chemical cousin RNA, part of which matches the DNA sequence to be sliced. This “guide RNA” is attached to a bacterial enzyme called Cas9. When the guide RNA binds to the corresponding DNA sequence, Cas9 cuts the DNA at that site. The cell tries to repair the cut but often does so imperfectly, which is enough to disable, or knock out a gene. To change a gene, scientists usually insert a patch — a bit of DNA similar to where the break occurred but containing the desired change. That patch is sometimes incorporated into the DNA when the cell repairs the break.

Would this work in organisms besides bacteria? “I knew it was like firing a starting gun in a race,” Dr. Doudna said, but sure enough, by early 2013 scientists had shown it would work in human cells, and those of many other animals and plants, even though these species are not known to have Crispr-based immune systems.

“I don’t know any species of plant or animal where it has been tried and it failed,” said George Church, a professor of genetics at Harvard Medical School. “It allows you to do genome engineering on organisms that are very hard to do otherwise.”

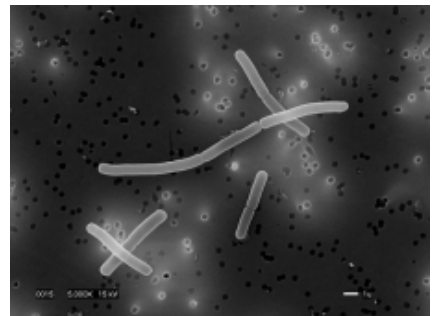
In the past, making an animal with multiple genetic changes usually required creating separate animals with single changes and then crossbreeding them to produce offspring with multiple changes. With Crispr, multiple genetic changes can be made in one step, by putting multiple guide RNAs into the cell.

“It just completely changes the landscape,” Dr. Doudna said. Berkeley scientists used to farm out that work to specialized laboratories or companies. Now, she said, “people are able to make mice in their own labs.”

There are other techniques that can do what Crispr does, though Crispr is “the easiest by far,” Dr. Church said.

RNA interference, for instance, can silence particular genes. It is similar to Crispr in that it also uses RNA that matches the gene to be silenced.

But RNA interference works by inhibiting messenger RNA, which translates a gene into a protein. That usually provides only a partial and temporary disabling of the gene, because the cell can make new messenger RNA. Crispr disables the gene itself, potentially a more complete and permanent inactivation.



***The dairy industry can use the Crispr immune system to protect important bacteria like *Lactobacillus acidophilus*, which is widely used in yogurts and dietary supplements, from viruses. Credit Todd Klaenhammer/North Carolina State University***

There are also already ways to change genes, namely zinc-finger nucleases and transcription activator-like effector nucleases, or Talens. The biotechnology company Sangamo BioSciences is already conducting a clinical trial of a treatment for H.I.V. that uses zinc fingers to alter patients’ immune cells to make them resistant to the virus.

Both techniques use proteins to guide where the DNA is cut; it is more difficult to develop a protein that binds to a specific DNA sequence than it is to make a piece of RNA with the matching sequence.

With zinc fingers “it might take you months or years to get something to work well for one gene,” said Dr. Gersbach at Duke. With Crispr, “it takes days to weeks.”

Quick is not always accurate, however. While Crispr is generally precise, it can have off-target effects, cutting DNA at places where the sequence is similar but not identical to that of the guide RNA.

Crispr “may not yet have adequate specificity to completely displace” the older techniques, Dana Carroll, a biochemistry professor at the University of Utah, wrote in a commentary in *Nature Biotechnology* in September. Still, scientists are already figuring out how to make Crispr more specific. Another obstacle for treating diseases will be the delivery of the genetic changes to all the cells in the body that need it.

For some diseases, it may be possible to extract blood stem cells from the body, alter them using Crispr, and put them back. If that is not possible, the DNA needed to make Cas9, the guide RNA and the corrective patch might be put into a disabled virus. This technique is used for gene therapy, but does not always work well.



It is likely to be a few years before Crispr is tested in people. For now, there is a lot more to learn about it. Chase L. Beisel at North Carolina State reported that Crispr could be used to kill one strain of bacteria in a mixture of strains, by targeting a sequence unique to that strain. That might one day lead to antibiotics that can kill the bad bugs without also killing the good ones.

David S. Weiss of Emory University found that some bacteria use Cas9 to silence one of their own genes, rather than that of a virus, to help them evade detection by their host's immune system. The pace of new discoveries and applications is dizzying. "All of this has basically happened in a year," Dr. Weiss said. "It's incredible."

<http://bit.ly/MNeXCJ>

## **Scientists create accurate predictor of the next year's flu virus**

*New model takes evolutionary pressures into account to help design vaccines.*

by Sarah Cobey Mar 4 2014, 10:00am TST

Influenza viruses evolve rapidly, making it hard to develop protective vaccines against them. Despite a great deal of effort, scientists have found it difficult to forecast which way the virus' evolution would take it. Now, thanks to improvements in our ability to study viruses and a new mathematical model, anticipating influenza's next move appears possible.

### **Making the jump**

In addition to the rapid evolution of genes within human flu strains, the viruses have the ability to jump from animals to humans, a move that can spark global pandemics like the 2009 swine flu, which killed thousands from Mexico to China.

But a pandemic does not always follow from these jumps. For example, there have been numerous reports of humans being infected with the H5N1 bird flu, yet it doesn't seem to spread from human to human. Researchers are still trying to understand why some influenza viruses are unable to spread within human populations, while others have taken off.

One of the successful jumps was made by a subtype called H3N2 in 1968. H3N2 evolves quickly enough that its entire population is replaced every few years. It exemplifies the other type of evolutionary challenge: predicting, from year to year, which of the many circulating strains will take over.

Because influenza is a major cause of death (it can result in pneumonia), understanding this evolution is more than an academic exercise—developing the right vaccines can save lives. Predicting which strain will be widespread nearly a year into the future is the central challenge of the World Health Organization's vaccine strain selection committee. It meets twice a year to review the evidence on circulating viruses and pick the likeliest candidates for the next flu seasons. The challenge the committee faces is that it is difficult to build a compelling case against any one strain.

### **Slow and costly**

Measuring how well different strains have evaded the immune system has been a slow and costly process.

Traditionally, ferrets are experimentally infected with common flu strains to see whether they develop antibodies that can cross react to other circulating strains—including those targeted by vaccines. These are then compared with measures from human samples. Often, several strains show some ability to escape immunity.

For more than a decade, different groups have attempted to find genetic shortcuts to predict the winners in advance. Mutations in certain parts of the virus are more likely to lead to immune escape than others. But in the past, every time a rule based on these mutations was derived, the virus seemed to break it.

Over time, however, a pattern gradually became clear, one that's been a recurring theme in evolution: the impact of a mutation depends heavily on the genetic background in which it occurs. In other words, it's not just the new mutations; it's how they interact with the rest of the virus' genetic material. For fast-evolving viruses such as influenza, the combinatorial possibilities of mutations and backgrounds have made prediction seem like a daunting task.

### **A new model**

But a recent study, published last week in *Nature*, shows that in the case of H3N2, we perhaps can predict its evolution after all. The study's authors, Marta Łuksza and Michael Lässig, showed that the future success of related H3N2 strains, known as clades, could be predicted by a relatively simple model.

The model considers only three types of information when assessing a clade's future: mutations in sites that are targeted by antibodies (generally thought to be helpful to the virus), mutations in sites not binding antibodies (generally thought to be harmful), and the recent frequencies of the clade and competing clades. The authors showed the model can be used to predict strain frequencies on a time scale useful for creating vaccines. This could greatly increase the effectiveness of flu jabs.



In addition to its ability to identify strains, the model also reveals important information about the way influenza evolves. It reinforces that the immunity acquired by host populations shapes the virus' evolution. This suggests that widespread vaccination could also shape the evolution of influenza.

The study also supports the idea that strains emerging from Asia tend to be inordinately successful. Why this is, and whether the trend will continue, are unanswered questions. Finally, the model suggests that influenza follows a narrow path between beneficial mutations to escape immunity and harmful ones that affect its ability to stably infect the populations it targets.

How do we know the virus won't break the rules of this model too? In a way, we don't, but the authors took steps to show that their model balanced the trade-off between complexity and predictive power. Their ability to find this sweet spot comes entirely from the large and growing number of publicly available influenza genome sequences.

[http://www.eurekalert.org/pub\\_releases/2014-03/hcfe-apm030414.php#rsslmlink](http://www.eurekalert.org/pub_releases/2014-03/hcfe-apm030414.php#rsslmlink)

### **Are plants more intelligent than we assumed?**

*In the fight against parasites, the Barberry sacrifices its own seeds depending upon its chances of survival*

Tilo Arnhold

Leipzig. Plants are also able to make complex decisions. At least this is what scientists from the Helmholtz Center for Environmental Research (UFZ) and the University of Göttingen have concluded from their investigations on Barberry (*Berberis vulgaris*), which is able to abort its own seeds to prevent parasite infestation. The results are the first ecological evidence of complex behaviour in plants. They indicate that this species has a structural memory, is able to differentiate between inner and outer conditions as well as anticipate future risks, scientists write in the renowned journal *American Naturalist* — the premier peer-reviewed American journal for theoretical ecology.

The European barberry or simply Barberry (*Berberis vulgaris*) is a species of shrub distributed throughout Europe. It is related to the Oregon grape (*Mahonia aquifolium*) that is native to North America and that has been spreading through Europe for years.

Scientists compared both species to find a marked difference in parasite infestation: "a highly specialized species of tephritid fruit fly, whose larvae actually feed on the seeds of the native Barberry, was found to have a tenfold higher population density on its new host plant, the Oregon grape", reports Dr. Harald Auge, a biologist at the UFZ.



***Plants are also able to make complex decisions. At least this is what scientists have concluded from their investigations on barberry (*Berberis vulgaris*), which is able to abort its own seeds to prevent parasite infestation. Approximately 2,000 berries were collected during this study from different regions of Germany, examined for signs of piercing and then cut open to examine any infestation by the larvae of the tephritid fruit fly (*Rhagoletis meigenii*). Credit: Photo:***

**Steffen Hauser / botanikfoto**

This led scientists to examine the seeds of the Barberry more closely. Approximately 2000 berries were collected from different regions of Germany, examined for signs of piercing and then cut open to examine any infestation by the larvae of the tephritid fruit fly (*Rhagoletis meigenii*).

This parasite punctures the berries in order to lay its eggs inside them. If the larva is able to develop, it will often feed on all of the seeds in the berry. A special characteristic of the Barberry is that each berry usually has two seeds and that the plant is able to stop the development of its seeds in order to save its resources. This mechanism is also employed to defend it from the tephritid fruit fly. If a seed is infested with the parasite, later on the developing larva will feed on both seeds. If however the plant aborts the infested seed, then the parasite in that seed will also die and the second seed in the berry is saved.

When analysing the seeds, the scientists came across a surprising discovery: "the seeds of the infested fruits are not always aborted, but rather it depends on how many seeds there are in the berries", explains Dr. Katrin M. Meyer, who analysed the data at the UFZ and currently works at the University of Goettingen.

If the infested fruit contains two seeds, then in 75 per cent of cases, the plants will abort the infested seeds, in order to save the second intact seed. If however the infested fruit only contains one seed, then the plant will only abort the infested seed in 5 per cent of cases.

The data from fieldwork were put into a computer model which resulted in a conclusive picture. Using computer model calculations, scientists were able to demonstrate how those plants subjected to stress from parasite infestation reacted very differently from those without stress.

"If the Barberry aborts a fruit with only one infested seed, then the entire fruit would be lost. Instead it appears to 'speculate' that the larva could die naturally, which is a possibility. Slight chances are better than none at all", explains Dr. Hans-Hermann Thulke from the UFZ. "This anticipative behaviour, whereby anticipated losses and outer conditions are weighed up, very much surprised us. The message of our study is therefore that plant intelligence is entering the realms of ecological possibility."

But how does the Barberry know what is in store for it after the tephritid fruit fly has punctured a berry? It is still unclear as to how the plant processes information and how this complex behaviour was able to develop over the course of evolution. The Oregon grape that is closely related to the Barberry has been living in Europe for some 200 years with the risk of being infested by the tephritid fruit fly and yet it has not developed any such comparable defence strategy. These new insights shed some light on the underestimated abilities of plants, while at the same time bringing up many new questions.

*Katrin M. Meyer, Leo L. Soldaat, Harald Auge, Hans-Hermann Thulke (2014): Adaptive and selective seed abortion reveals complex conditional decision making in plants. The American Naturalist. Vol. 183, No. 3, March 2014*

<http://www.amnat.org/an/newpapers.html>

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<http://www.press.uchicago.edu/ucp/journals/journal/an.html>

[http://www.eurekalert.org/pub\\_releases/2014-03/mu-nec030414.php#rssowlmlink](http://www.eurekalert.org/pub_releases/2014-03/mu-nec030414.php#rssowlmlink)

## **New evidence confirms link between IQ and brain cortex**

### ***Montreal scientists play key role in long-term international study***

Rate of change in the thickness of the brain's cortex is an important factor associated with a person's change in IQ, according to a collaborative study by scientists in five countries including researchers at the Montreal Neurological Institute and Hospital – The Neuro, at McGill University and the McGill University Health Centre. The study has potentially wide-ranging implications for the pedagogical world and for judicial cases in which the defendant's IQ score could play a role in determining the severity of the sentence.

The cortex is the thin, outermost layer of nerve cell tissue of the brain, typically measuring a few millimeters in thickness. The cortex contains nerve cell bodies and is critical for cognitive functions such as perception, language, memory and consciousness.

"Often, small differences in IQ scores are observed when people's IQs are tested twice over a period of time. However, in some instances, dramatic changes in IQ scores are observed," said Dr. Sherif Karama, assistant professor of psychiatry at McGill University, psychiatrist at Douglas Mental Health University Institute and affiliate at The Neuro where he conducted the study published in the scientific journal, *Neuro Image*. "These dramatic changes are generally attributed to measurement errors rather than assumed to reflect real changes in general cognitive ability."

The cortex begins to thin after the age of five or six as part of the normal aging process. This study by Professor Karama and his colleagues involved 188 children and adolescents over a period of two years. MRIs of the study participants were taken at six sites across the US. This study is the first to show the association between cortical thickness and development in full scale IQ. They found that within a relatively short period of 2 years:

***people with a significant increase in IQ did not have the expected cortical thinning,***

***people whose IQ stayed the same had the normal expected cortical thinning,***

***people with a significant decrease in IQ had exaggerated cortical thinning.***

"Finding that IQ is not fixed and correlates to changes in brain anatomy has important implications as it shows that some of the changes in IQ are real and not merely due to measurement error. This finding should make people wary of sticking to an early IQ assessment given the role it plays in school entrance criteria, detection of the gifted, as well as in eligibility for social security disability income or even the death penalty. In some US states, people with an IQ below 70 are not eligible for the death penalty."

The reasons behind the changes in IQ are not clear at this point. Some of these may be due to programmed developmental trajectories or other factors such as nutrition and education, noted Professor Karama.

*The study was undertaken jointly by scientists at the Universidad Autonoma de Madrid, Fundacion CIEN/Fundacion Reina Sofia and the Universitat Pompeu Fabra in Spain, the University of Edinburgh, UK, the Boston Children's Hospital of Harvard University, USA, at the Montreal Neurological Institute and Hospital, as well as at the Douglas Mental Health University Institute, Canada. The project was conducted by the Brain Development Cooperative Group and supported by the National Institute of Child Health and Human Development, the National Institute on Drug Abuse, the National Institute of Mental Health, and the National Institute of Neurological Disorders and Stroke, the National Institutes of Health, the Fonds de recherche du Québec - Santé, the Spanish Ministry of Education and Science, and the Alianza 4 Universidades.*

*This paper was published in the January 2014 issue of NeuroImage:*

<http://www.sciencedirect.com/science/article/pii/S1053811913009749>

[http://www.eurekalert.org/pub\\_releases/2014-03/sovp-pot022514.php#rssowlmlink](http://www.eurekalert.org/pub_releases/2014-03/sovp-pot022514.php#rssowlmlink)

## **Prequel outshines the original: Exceptional fossils of 160 million year old doahugou biota** *Several Jurassic sites are linked together by shared species and can be recognized as representing a single fossil fauna and flora*

Over the last two decades, huge numbers of fossils have been collected from the western Liaoning Province and adjacent parts of northeastern China, including exceptionally preserved feathered dinosaurs, early birds, and mammals. Most of these specimens are from the Cretaceous Period, including the famous Jehol Biota. However, in recent years many fossils have emerged from sites that are 30 million years earlier, from the Middle-Upper Jurassic Period, providing an exceptional window on life approximately 160 million years ago. A new paper published in latest issue of the Journal of Vertebrate Paleontology shows that several of these Jurassic sites are linked together by shared species and can be recognized as representing a single fossil fauna and flora, containing superbly preserved specimens of a diverse group of amphibian, mammal, and reptile species.



*This is a reconstruction of the Daohugou fauna featuring feathered dinosaurs, pterosaurs, early mammals and amphibians among others. Original artwork by Dr Julia Molnar*

This fossil assemblage, newly named the Daohugou Biota after a village near one of the major localities in Inner Mongolia, China, dates from a time when many important vertebrate groups, including our own group, mammals, were undergoing evolutionary diversification. The Daohugou Biota makes an immense contribution to our understanding of vertebrate evolution during this period, with such notable creatures as the oldest known gliding mammal, another early mammal that may have swum with a beaver-like tail, the oldest dinosaurs preserved with feathers, and a pterosaur that represents an important transitional form between two major groups. As described by Dr. Corwin Sullivan, lead author of the study, "The Daohugou Biota gives us a look at a rarely glimpsed side of the Middle to Late Jurassic - not a parade of galumphing giants, but an assemblage of quirky little creatures like feathered dinosaurs, pterosaurs with 'advanced' heads on 'primitive' bodies, and the Mesozoic equivalent of a flying squirrel."

Almost more impressive than the diversity of the biota is the preservation of many of the vertebrate specimens, including complete or nearly-complete skeletons associated with preserved soft tissues such as feathers, fur, skin or even, in some of the salamanders, external gills. Dr Yuan Wang, co-author of the study, explained, "The Daohugou amphibians are crucially important in the study of the phylogeny and early radiation of modern amphibian groups."

Dr. Paul Barrett, dinosaur researcher at the Natural History Museum, London, who was not involved with the study, commented, "Daohugou is proving to be one of the key sites for understanding the evolution of feathered dinosaurs, early mammals, and flying reptiles, due largely to the fantastic levels of preservation. Many of the fossils are stunning and offer vast amounts of information. There are only a handful of similar sites elsewhere in the world and this article represents the first comprehensive attempt to draw all of the relevant information together into a single benchmark paper". Because the Daohugou Biota and the much better studied Jehol Biota are similar in preservational mode and geographic location, but separated by tens of millions of years, they give palaeontologists an outstanding, even unique, opportunity to study changes in the fauna of this region over a significant span of geological time and an important period in vertebrate evolution. As Dr. Sullivan further remarked, "The Cretaceous feathered dinosaurs of northeastern China have been astonishing palaeontologists and the public for almost two decades now, and the Daohugou Biota preserves their Jurassic counterparts in the same region. As prequels go, it's pretty exciting."

*The article appears in the Journal of Vertebrate Paleontology 34(2), published by Taylor and Francis*

*Citation: The Vertebrates of the Jurassic Daohugou Biota of Northeastern China. Corwin Sullivan, Yuan Wang, David W. E. Hone, Yuanqing Wang, Xing Xu, and Fucheng Zhang. Journal of Vertebrate Paleontology. 34(1):1.*

*Journal Web site: <http://www.tandfonline.com/toc/ujvp20/current>*

[http://www.eurekalert.org/pub\\_releases/2014-03/uosc-mac022814.php#rssowlmlink](http://www.eurekalert.org/pub_releases/2014-03/uosc-mac022814.php#rssowlmlink)

## **Meat and cheese may be as bad for you as smoking**

*A high-protein diet during middle age makes you nearly twice as likely to die and four times more likely to die of cancer, but moderate protein intake is good for you after 65*

That chicken wing you're eating could be as deadly as a cigarette. In a new study that tracked a large sample of adults for nearly two decades, researchers have found that eating a diet rich in animal proteins during middle

age makes you four times more likely to die of cancer than someone with a low-protein diet — a mortality risk factor comparable to smoking. "There's a misconception that because we all eat, understanding nutrition is simple. But the question is not whether a certain diet allows you to do well for three days, but can it help you survive to be 100?" said corresponding author Valter Longo, the Edna M. Jones Professor of Biogerontology at the USC Davis School of Gerontology and director of the USC Longevity Institute.

Not only is excessive protein consumption linked to a dramatic rise in cancer mortality, but middle-aged people who eat lots of proteins from animal sources — including meat, milk and cheese — are also more susceptible to early death in general, reveals the study to be published March 4 in *Cell Metabolism*. Protein-lovers were 74 percent more likely to die of any cause within the study period than their more low-protein counterparts. They were also several times more likely to die of diabetes.

But how much protein we should eat has long been a controversial topic – muddled by the popularity of protein-heavy diets such as Paleo and Atkins. Before this study, researchers had never shown a definitive correlation between high protein consumption and mortality risk. Rather than look at adulthood as one monolithic phase of life, as other researchers have done, the latest study considers how biology changes as we age, and how decisions in middle life may play out across the human lifespan.

In other words, what's good for you at one age may be damaging at another. Protein controls the growth hormone IGF-I, which helps our bodies grow but has been linked to cancer susceptibility. Levels of IGF-I drop off dramatically after age 65, leading to potential frailty and muscle loss. The study shows that while high protein intake during middle age is very harmful, it is protective for older adults: those over 65 who ate a moderate- or high-protein diet were less susceptible to disease. The latest paper draws from Longo's past research on IGF-I, including on an Ecuadorian cohort that seemed to have little cancer or diabetes susceptibility because of a genetic mutation that lowered levels of IGF-I; the members of the cohort were all less than five-foot tall.

"The research shows that a low-protein diet in middle age is useful for preventing cancer and overall mortality, through a process that involves regulating IGF-I and possibly insulin levels," said co-author Eileen Crimmins, the AARP Chair in Gerontology at USC. "However, we also propose that at older ages, it may be important to avoid a low-protein diet to allow the maintenance of healthy weight and protection from frailty."

Crucially, the researchers found that plant-based proteins, such as those from beans, did not seem to have the same mortality effects as animal proteins. Rates of cancer and death also did not seem to be affected by controlling for carbohydrate or fat consumption, suggesting that animal protein is the main culprit.

"The majority of Americans are eating about twice as much proteins as they should, and it seems that the best change would be to lower the daily intake of all proteins but especially animal-derived proteins," Longo said. "But don't get extreme in cutting out protein; you can go from protected to malnourished very quickly."

Longo's findings support recommendations from several leading health agencies to consume about 0.8 grams of protein per kilogram of body weight every day in middle age. For example, a 130-pound person should eat about 45-50 grams of protein a day, with preference for those derived from plants such as legumes, Longo explains.

The researchers define a "high-protein" diet as deriving at least 20 percent of calories from protein, including both plant-based and animal-based protein. A "moderate" protein diet includes 10-19 percent of calories from protein, and a "low-protein" diet includes less than 10 percent protein.

Even moderate amounts of protein had detrimental effects during middle age, the researchers found. Across all 6,318 adults over the age of 50 in the study, average protein intake was about 16 percent of total daily calories with about two-thirds from animal protein — corresponding to data about national protein consumption. The study sample was representative across ethnicity, education and health background.

People who ate a moderate amount of protein were still three times more likely to die of cancer than those who ate a low-protein diet in middle age, the study shows. Overall, even the small change of decreasing protein intake from moderate levels to low levels reduced likelihood of early death by 21 percent.

For a randomly selected smaller portion of the sample – 2,253 people – levels of the growth hormone IGF-I were recorded directly. The results show that for every 10 ng/ml increase in IGF-I, those on a high-protein diet were 9 percent more likely to die from cancer than those on a low-protein diet, in line with past research associating IGF-I levels to cancer risk.

The researchers also extended their findings about high-protein diets and mortality risk, looking at causality in mice and cellular models. In a study of tumor rates and progression among mice, the researchers show lower cancer incidence and 45 percent smaller average tumor size among mice on a low-protein diet than those on a high-protein diet by the end of the two-month experiment.



"Almost everyone is going to have a cancer cell or pre-cancer cell in them at some point. The question is: Does it progress?" Longo said. "Turns out one of the major factors in determining if it does is protein intake."

*Morgan Levine, Jorge Suarez and Pinchas Cohen of the USC Davis School of Gerontology were co-authors of the study. The research was funded by the National Institute of Aging of the National Institutes of Health (grants: AG20642, AG025135, AG034906, P30AG017265 and T32AG0037) and a USC Norris Cancer Center pilot grant to Valter Longo.*

<http://www.bbc.com/news/science-environment-26435809#rssowlmlink>

### **New magnetic material could boost electronics**

***Computer hard drives are just one possible application of the new material***

**By James Morgan Science reporter, BBC News, Denver**

A highly sensitive magnetic material that could transform computer hard drives and energy storage devices has been discovered. The metal bilayer needs only a small shift in temperature to dramatically alter its magnetism - a tremendously useful property in electronic engineering.

"No other material known to man can do this. It's a huge effect. And we can engineer it," said Ivan Schuller, of the University of California, San Diego.

He presented his findings at the American Physical Society meeting in Denver. The material combines thin layers of nickel and vanadium oxide, creating a structure that is surprisingly responsive to heat.

"We can control the magnetism in just a narrow range of temperature - without applying a magnetic field. And in principle we could also control it with voltage or current," said Prof Schuller.

"At low temperatures, the oxide is an insulator. At high temperatures it's a metal. And in between it becomes this strange material," he said.

Although it's too early to say exactly how it will be used, Prof Schuller sees an obvious opportunity in computing memory systems. "A problem with magnetic memory is reversibility - you want it to be reversible but also stable.

"Today's best systems are heat-assisted, but they use lasers, which involves a lot of heat. But with this new material, you barely need to heat it by 20 degrees (Kelvin) to get a five-fold change in coercivity (magnetic resistance)," he told the conference.

Another potential use is in electricity networks. Prof Schuller envisions a new type of transformer which can cope with sudden surges in current - such as during a lightning strike or a power surge.

But he points out that new phenomena such as this often lead to entirely unexpected technologies. He gave the example of giant magnetoresistance - a discovery that radically miniaturised hard drives in digital devices, and won the 2007 Nobel prize.

"Without it, that computer you're writing on would not work," he told the meeting. "So if you want to find the next transformative technology, this is the type of research you do. We don't know what the best application is yet," he said. "I'm not saying it's going to solve world's energy crisis but it's certainly going to help us."

<http://bit.ly/1ncrGMC>

### **Silk screws are strong enough to mend broken bones**

***Silk can also be fashioned into screws so tough that they can cut through bone.***

**16:55 04 March 2014 by Colin Barras**

Silk is tougher than it looks. Weight for weight, the shiny stuff is as strong as steel when stretched – and now it seems it can also be fashioned into screws so tough that they can cut through bone.

Metal alloy screws and plates can hold fractured bones together but if they start to corrode a second operation is required to remove them.

Biodegradable alternatives can trigger inflammation and are time-consuming to implant – the polymers are so soft that you first have to drill a hole in the bone and fashion a helical ridge around the inside - the inner thread - to hold the screw in place.



***Ditch the ironmongery (Image: Corbis)***

Samuel Lin at the Harvard Medical School and David Kaplan at Tufts University in Medford, Massachusetts, wondered if silk screws and plates could work better. To find out, they dissolved silk in alcohol, poured the solution into moulds shaped like the implants and baked them.

In rats, the team found that their silk screws were tough enough to carve their own threads into bone as they are screwed into a hole, just as metal alloy screws do. The silk naturally biodegrades with time, like the polymer alternatives but without causing inflammation.

"Clinical trials will hopefully begin in the near future," says Lin.

*Journal reference: Nature Communications, DOI: 10.1038/ncomms4385*

<http://bit.ly/1cueBNU>

## I can has cheezburger? Protein cancer risk overblown

### *Are you middle-aged and partial to cheeseburgers?*

18:54 04 March 2014 by Catherine de Lange

If so, you may be concerned by a study suggesting you have a much greater risk of dying from cancer than your peers who favour a less protein-rich diet. But not all researchers agree with the study's findings.

Morgan Levine at the University of Southern California in Los Angeles and her colleagues analysed a dietary survey of more than 6300 people in the US aged over 50. Those aged 50-65 at the time of the survey and who had a high-protein diet – one where protein supplied a fifth of calories – were 75 per cent more likely to have died over the next 18 years than peers who only got 10 per cent of their calories from protein.

The high-protein eaters had a cancer death rate four times that of their low-protein peers. Statistical analyses showed that the findings only held for animal protein diets – in other words, protein from meat and dairy rather than beans and pulses. In a follow-up study in mice, the team also found that animals fed a low-protein diet had a lower incidence of cancer than those on a high-protein diet. The low-protein mice that did develop the disease had slower-growing tumours.

#### **Lots of leaps**

But Tim Key, a Cancer Research UK epidemiologist based at the University of Oxford, says the dietary survey is too small to provide any robust conclusions.

Catherine Collins, chief dietician at St George's Hospital, London, doesn't dispute the results in mice, but says the authors make a lot of leaps when trying to apply the findings to humans. What's more, the conclusions are based on a single survey of what people reported eating in the preceding 24 hours. "As a dietician that's worrying," she says. "There are so many errors with the data collection. It implies people's diet doesn't change over 18 years."

Study co-author Valter Longo, also at the University of Southern California, counters that the participants said that the 24 hour period was representative of their diet. "Most people don't change their diet very often," he says. Different health organisations recommend consuming different amounts of protein. Longo says that people in middle age should try to eat at the lower end of these recommendations. Collins isn't convinced. "We don't need to do anything different, and nor should we be worried [on the strength of this study]," she says.

Journal reference: *Cell Metabolism*, DOI: 10.1016/j.cmet.2014.02.006

<https://www.sciencenews.org/article/hpv-vaccination-proves-its-worth-australia#rssowlmlink>

## HPV vaccination proves its worth in Australia

### *Shots are decreasing cases of abnormal cervical cells in country that has embraced vaccine program*

by Nathan Seppa

HPV vaccination is reducing the incidence of abnormal cervical cell growth in women and girls in Australia. The standard three-shot regimen against sexually spread human papillomavirus nearly halves the likelihood of developing precancerous lesions on the cervix, the forerunners of cervical cancer that a Pap smear can detect. Before these findings, reported March 4 in *BMJ*, there was a lot of clinical information but little real-world evidence to show that the vaccine protects against such abnormal growths. Researchers at the University of Queensland in Brisbane and elsewhere examined data on more than 108,000 girls and women age 12 to 26 who got their first Pap smear between 2007 and 2011 — after HPV mass vaccination had begun in Australia. Those who received all three shots were 54 percent as likely as unvaccinated women to have precancerous cervical growth and two-thirds as likely to have other abnormal cervical cell growth. Getting two HPV shots conferred less protection. The findings jibe with data suggesting that the two cancer-causing virus subtypes targeted by vaccination, HPV-16 and HPV-18, account for more than half of cervical cancers. Other HPV subtypes cause the rest. Vaccination in Australia has outpaced U.S. rates (SN: 4/20/13, p. 20).

*E. Crowe et al. Effectiveness of quadrivalent human papillomavirus vaccine for the prevention of cervical abnormalities: case-control study nested within a population based screening programme in Australia. BMJ. Vol. 348, March 4, 2014. doi: 10.1136/bmj.g1458.*

<http://www.medscape.com/viewarticle/820717?src=rss>

## Bugs in the Back: Is Lumbago an Infectious Disease?

*Perhaps beginning with a report in the early 2000s some have speculated that P acnes may explain more mundane lower back pain or sciatica or problems attributed to a herniated disk* [Video](#)

Paul G. Auwaerter, MD

Hello. I am Paul Auwaerter, from Johns Hopkins, speaking for Medscape Infectious Diseases.

I just had my first consultation with a patient who came to the ID clinic asking whether *Propionibacterium acnes* was responsible for his chronic back pain. This is a man who has had multiple back surgeries and many

previous interventions and treatments for his pain. He recently had been encouraged by family members, who had been trolling the Internet literature, to find out whether a chronic infection could be causing his back pain. *P. acnes* is often dismissed as a contaminant, but during the past decade or so it has been recognized as an indolent pathogen that can cause problems such as ventriculoatrial shunt infection and perhaps prosthetic joint problems, especially in the shoulder. In addition, a small amount of supportive literature about *P. acnes* infection in the spine has been published. This infection often is not typical; patients have no fever or elevated sedimentation rate. It seems to be fairly rare; however, one review <sup>[1]</sup> found that 97% of 29 patients with this infection had previously undergone surgery.

Perhaps beginning with a report in the early 2000s in *The Lancet*, <sup>[2]</sup> some have speculated that *P. acnes* may explain more mundane lower back pain or sciatica or problems attributed to a herniated disk, for example. A number of studies have supported <sup>[3-5]</sup> or refuted <sup>[6,7]</sup> this idea that an infectious cause may be responsible for some back ailments. A few of the studies purport to have used very careful techniques for removing disks and growing this anaerobic organism in cultures.

Recently, a group in Denmark has investigated this more thoroughly and published 2 papers of interest on the subject. <sup>[5,8]</sup> In the first, <sup>[5]</sup> they removed disks in 61 patients; *P. acnes* was cultivated from 46% of these herniated disks, and 80% of those had specific MRI findings called Modic 1 (bone edema adjacent to the disk area). There are 3 different kinds of Modic descriptions, named after the physician who described them. Modic 1 means that the disk has caused some adjacent bony trabecular problems with microfractures and resulting serum leaking into the area, which leads to radiographic changes. Thus, perhaps a certain subset of back pain could be attributed to this.

But the proof would have to come, in my mind, from repeated cultures that recover this organism from not just one but multiple areas or perhaps a therapeutic trial. Indeed, the same group has published a therapeutic trial <sup>[8]</sup> in which patients with Modic 1 MRI findings were randomly assigned to receive either amoxicillin/clavulanate or placebo. Of 162 patients enrolled, 144 completed the trial and were available for follow-up. They all had at least 6 months of chronic low back pain and Modic 1 changes. Patients were randomly assigned to receive amoxicillin/clavulanate or placebo 3 times daily for 100 days. At 1-year follow-up, there was a statistically significant difference between the antibiotic and placebo groups, with reductions in pain in the active treatment group that seemed to continue even after antibiotic cessation. In addition, the antibiotic group had more resolution of the Modic 1 changes.

These findings are intriguing. This type of antibiotic trial bears repeating in a different setting, and if it holds up, it is highly suggestive that a subset of patients with chronic low back pain may benefit more from antibiotic treatment than injections, neurosurgical interventions, and so on.

I believe this issue deserves close observation and may even be at the point where a trial of amoxicillin/clavulanate could be worthwhile in patients with back pain and Modic 1 changes. I will say that most *P. acnes* isolates are susceptible to amoxicillin alone, which might be a better tolerated regimen, and perhaps the dose could be pushed a bit higher to 1000 mg 3 times daily.

Stay tuned because this particular area of study may change a certain subset of medicine. Whether we can go by MRI findings to make treatment decisions or need some kind of microbiologic confirmation is uncertain. There is biologic plausibility; the spinal column has unique characteristics that make the environment favorable for this particular organism.

Thanks very much for listening.

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### **With flip of wrist, interventional radiologists treat uterine fibroids**

***Journal of Vascular and Interventional Radiology report highlights benefits of different access approach to treat women's noncancerous growths; could be 'game changer' for image-guided minimally invasive treatments, improving patient comfort***

FAIRFAX, Va.- Interventional radiologists have devised a new way to access a woman's fibroids—by flipping her wrist and treating via an arm not groin artery—to nonsurgically shrink noncancerous growths in the muscular wall of the uterus. Researchers found this to be less painful and traumatic for women, allowing them to immediately sit up and move after uterine fibroid embolization (UFE)—with no overnight stay, according to a March article in the Society of Interventional Radiology's flagship publication, the *Journal of Vascular and Interventional Radiology*.

"Improving patient care and providing advanced treatment options are always on the minds of interventional radiologists. And this could be a game changer for image-guided minimally invasive treatments," said Aaron M. Fischman, M.D., an interventional radiologist and assistant professor of radiology and surgery at Mount Sinai Medical Center in New York. Mount Sinai researchers studied the access treatment favored by cardiologists for coronary interventions—and applied it to a minimally invasive treatment for women's uterine fibroids.

By flipping access for treatment from the artery in the groin to the artery in the wrist, the researchers said that the women experienced less pain and trauma than the traditional groin technique—opening the door to potential savings in health care costs. Complications related to bleeding at the puncture site are also significantly reduced using this novel approach. Patients are able to walk immediately after treatment, which dramatically improves their experience. "This is just the beginning," he added, indicating that this technique may also pave the way toward improving other interventional radiology treatments—including those for cancer patients.

Fischman said that his team wanted to explore options that were more comfortable and beneficial for patients undergoing UFE, a nonsurgical interventional radiology treatment for women that cuts off blood flow to painful fibroids to kill the noncancerous tumors. "Few reports in the literature have explored this application to interventional radiology treatments. This is the first reported use of transradial access for UFE," Fischman added.

Uterine fibroids, which affect up to 40 percent of all women 35 and older, can cause prolonged, heavy menstrual bleeding that can be severe enough to cause anemia or require transfusion; disabling pelvic pain and pressure; urinary frequency; pain during intercourse; and miscarriage. Typically, interventional radiologists have delivered treatment directly to the fibroid—by threading a catheter through a woman's femoral artery in her thigh.

In this new approach, the interventional radiologists threaded a catheter through one of two arteries in a woman's left wrist. They then made a tiny nick in the skin, less than one-fourth of an inch, and inserted a catheter into the artery. Using real-time imaging, the doctor guided the catheter through the artery and then released tiny particles, the size of grains of sand, into the uterine arteries that supply blood to the fibroid tumor. This blocked the blood flow to the fibroid tumor and caused it to shrink and symptoms to subside.

Women seeking UFE at Mount Sinai were presented both access options, said Fischman. His team treated 29 women (ages 23–56, some with benign tumors the size of a grapefruit) from March through October 2013. Fischman said that their findings suggest that wrist (transradial) UFE offers a safe and effective alternative to groin (transfemoral) UFE. He indicated that a much larger prospective, randomized trial is needed to validate conclusions about specific benefits of this novel approach. He noted that interventional radiologists will need to be trained in this new access. In addition to presenting this study, Fischman will be leading workshops on this new technology at the Society of Interventional Radiology's Annual Scientific Meeting March 22–27 in San Diego.

*Nonsurgical UFE is a major advance in women's health, and women should be aware of all of their fibroid treatment options, said Fischman. UFE is widely available and covered by medical insurance. SIR identifies interventional radiologists with expertise in this area in its online doctor directory. More information about SIR, interventional radiologists, uterine fibroids and UFE can be found online at <http://www.SIRweb.org>.*

*"Uterine Artery Embolization Using a Transradial Approach: Initial Experience and Technique," which appears in the March issue of the *Journal of Vascular and Interventional Radiology*, was co-written by Fischman, along with Neil J. Resnick, M.D.; Edward Kim, M.D.; Rahul S. Patel, M.D.; Robert A. Lookstein, M.D., FSIR; and F. Scott Nowakowski, M.D., FSIR, all at Mount Sinai Medical Center, New York, N.Y. All are SIR members.*



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## **UF researchers find drug therapy that could eventually reverse memory decline in seniors**

### ***Researchers have found a drug therapy that could potentially reverse this type of memory decline***

GAINESVILLE, Fla. — It may seem normal: As we age, we misplace car keys, or can't remember a name we just learned or a meal we just ordered. But University of Florida researchers say memory trouble doesn't have to be inevitable, and they've found a drug therapy that could potentially reverse this type of memory decline.

The drug can't yet be used in humans, but the researchers are pursuing compounds that could someday help the population of aging adults who don't have Alzheimer's or other dementias but still have trouble remembering day-to-day items. Their findings will be published in today's (March 5) issue of the Journal of Neuroscience.

The kind of memory responsible for holding information in the mind for short periods of time is called "working memory." Working memory relies on a balance of chemicals in the brain. The UF study shows this chemical balance tips in older adults, and working memory declines. The reason? It could be because their brains are producing too much of a chemical that slows neural activity.

"Graduate student Cristina Banuelos' work suggests that cells that normally provide the brake on neural activity are in overdrive in the aged prefrontal cortex," said researcher Jennifer Bizon, Ph.D., an associate professor in the department of neuroscience and a member of UF's Evelyn F. & William L. McKnight Brain Institute.

This chemical, an inhibitory brain neurotransmitter called GABA, is essential. Without it, brain cells can become too active, similar to what happens in the brains of people with schizophrenia and epilepsy. A normal level of GABA helps maintain the optimal levels of cell activation, said collaborator Barry Setlow, Ph.D., an associate professor in UF's departments of psychiatry and neuroscience.

Working memory underlies many mental abilities and is sometimes referred to as the brain's mental sketchpad, Bizon said. For example, Bizon said, you use your working memory in many everyday activities such as calculating your final bill at the end of dining at a restaurant. Most people can calculate a 15 percent tip and add it to the cost of their meal without pencil and paper. Central to this process is the ability to keep multiple pieces of information in mind for a short duration — such as remembering the cost of your dinner while calculating the amount needed for the tip.

"Almost all higher cognitive processes depend on this fundamental operation," Bizon said.

To determine the culprit behind working memory decline, the researchers tested the memory of young and aged rats in a "Skinner box." In the Skinner box, rats had to remember the location of a lever for short periods of up to 30 seconds. The scientists found that while both young and old rats could remember the location of the lever for brief periods of time, as those time periods lengthened, old rats had more difficulty remembering the location of the lever than young rats.

But not all older rats did poorly on the memory test, just as not all older adults have memory problems. The study shows the older brains of some people or rats with no memory problems might compensate for the overactive inhibitory system — they are able to produce fewer GABA receptors and therefore bind less of the inhibitory chemical. Older rats with memory problems had more GABA receptors. The drug the researchers tested blocked GABA receptors, mimicking the lower number of those receptors that some older rats had naturally and restoring working memory in aged rats to the level of younger rats.

"Modern medicine has done a terrific job of keeping us alive for longer, and now we have to keep up and determine how to maximize the quality of life for seniors," Bizon said. "A key aspect of that is going to be developing strategies and therapies that can maintain and improve cognitive health."

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## **Patients have a right to know -- not a duty to know -- their diagnosis says new research**

### ***Defensive mechanisms protect patients from fully engaging with bad news say healthcare professionals from the University of Leicester***

The experiences of doctors, patients and carers of initial cancer consultations have informed new guidelines developed at the University of Leicester, in collaboration with University Hospitals of Leicester NHS Trust and Imperial College London, to help patients better understand their cancer consultations.

The research, published today (6 March 2014) in the British Journal of Health Psychology, found patients' experiences of being given their diagnosis differed both between participants and within the same participant. This means a doctor's role in communicating information in a patient-centred way can be very difficult.

A variety of defensive mechanisms were found to be employed by patients in order to protect themselves from fully engaging with the knowledge they had been given within an oncology consultation.

Semi-structured interviews were carried out with 36 patients and interpretive phenomenological analysis (IPA) was used to understand participants' meanings of their experiences in their initial consultation. They found

patients had a 'right to know' but not a 'duty to know' their diagnosis and prognosis, and as such doctors face a difficult task in ascertaining how much detail the individual patient wants at any one time.

Research lead Professor Anne Thomas, from the University of Leicester's Department of Cancer Studies and Molecular Medicine, said: "The accounts from patients of what they wished to know in the consultation could be affected by a desire to protect themselves and/or family members from the distress of bad news.

"With this in mind, the complexity of patients' needs and preferences regarding information means that the doctor's role in communicating that information in a patient-centric way is difficult, especially as we also found that patients' needs varied over time. Additionally, it is also difficult for doctors to know whether or not the information they disclosed about diagnosis, prognosis and treatments was wanted or understood."

Using information from this analysis and data from a larger study, the researchers have developed a consultation aid for doctors and patients to refer to that will identify the patients' preferences with regard to 'knowing and not knowing'.

Dr Lynn Furber, Senior Nurse Researcher from University Hospitals of Leicester NHS Trust, added: "It was imperative to us to be able to use our research findings to develop a tool based on what patients and doctors told us was important to improve their experiences and provide them with information in a timely and efficient manner. "This should provide the doctors with better information so that they are able to conduct consultations in a more patient-centred manner. Whilst an oncology consultation that involves giving bad news to patients is likely to be a difficult experience for both doctor and patient, it is hoped that the consultation aid will lead to an increase in patient satisfaction, and help inform doctors on how to meet the individual patients' needs."

The researchers now hope to expand on this pilot study to explore the acceptability and usability of their consultation support tool. Once they have proved its effectiveness in practice, it is hoped that it will be adopted into current patient pathways.

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### **Biomarkers of cell death in Alzheimer's reverse course after symptom onset**

*Three promising biomarkers being studied to detect Alzheimer's disease in its early stages appear to undergo a surprising shift as patients develop symptoms of dementia, researchers at Washington University School of Medicine in St. Louis report.*

Scientists use the biomarkers to assess brain changes linked to the disease in research volunteers. The levels of markers of neuronal injury increase in the spinal fluid for a decade or more before the onset of dementia, but in a new twist, the research shows for the first time that they later reverse course, decreasing as symptoms of memory loss and mental decline appear. The results appear online March 5 in Science Translational Medicine.

"We're not sure why this reversal occurs, but understanding it may be very important for clinical trials of drugs to treat or prevent Alzheimer's," said senior author Anne Fagan, PhD, research professor of neurology.

"Changes in the levels of these biomarkers likely will be among the criteria we use to assess the success or failure of Alzheimer's drugs, so we need to know how these biomarkers normally behave in the absence of treatment."

Motivated by the realization that Alzheimer's damages the brain for a decade or more before it causes dementia, researchers have identified several biomarkers of the disease in patients before they develop symptoms. They hope to use the biomarkers to diagnose patients and start treatment long before the onset of problems with memory and other brain functions that characterize dementia.

Fagan and her colleagues studied data from the Dominantly Inherited Alzheimer's Network (DIAN), a multinational research project led by Washington University. All DIAN participants come from families affected by genetic mutations that cause rare inherited forms of Alzheimer's. Carriers of their family's mutation can develop symptoms of mental decline as early as their 30s. DIAN participants regularly are evaluated using a variety of tests, including analyses of Alzheimer's biomarkers in their spinal fluid. For the new study, Fagan and her coauthors looked at three injury-related biomarkers in spinal fluid samples collected at multiple evaluations of 26 DIAN participants. All the participants had an Alzheimer's-causing mutation.

Two of the biomarkers, tau and p-tau, are structural proteins that form the neurofibrillary tangles seen in the brains of Alzheimer's patients; the third is a neuronal calcium sensor called VILIP-1. Levels of the three biomarkers increase after neurons are injured and are linked to decline of cognitive function. Evidence suggests that as Alzheimer's assaults the brain, dying cells release the biomarkers, freeing them to be washed into the spinal fluid. As expected, levels of the biomarkers increased over time in participants who had not yet developed dementia. But the researchers were surprised to find that in most participants who had dementia, levels of the three biomarkers decreased over time. The drop in levels was relatively small but consistent and statistically significant.

"This was very interesting, particularly given that previous studies have shown that other indicators of Alzheimer's disease, such as brain shrinkage, continue after the onset of dementia," Fagan said.

Fagan speculated that increasing levels of the biomarkers prior to dementia likely reflect an intense stage of cell death, while decreasing levels as dementia begins indicate a slowing of this process. However, it's also possible that such reductions result from a decrease in the number of remaining brain cells that have yet to be killed by Alzheimer's, she said.

To advance the research, the scientists are gathering data on new DIAN enrollees and continuing to follow participants in the current study. "Our findings are limited both by the small number of participants we studied and by the fact that we only had a few years of longitudinal follow-up," Fagan said. "Additional data taken over longer periods of time will help us draw more definitive conclusions."

Additional research also is needed to learn whether levels of the biomarkers undergo a similar change in patients with the more common sporadic forms of the disease, which are typically diagnosed later in life.

*Funding from the National Institutes of Health (NIH), the National Institute on Aging, the Dominantly Inherited Alzheimer's Network, the DIAN Pharma Consortium and other sources supported this research.*

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### **Study: Alzheimer's disease a much larger cause of death than reported**

***A new study suggests that Alzheimer's disease may contribute to close to as many deaths in the United States as heart disease or cancer.***

MINNEAPOLIS –The research is published in the March 5, 2014, print issue of Neurology®, the medical journal of the American Academy of Neurology.

Currently, Alzheimer's disease falls sixth on the list of leading causes of death in the United States according to the Centers for Disease Control and Prevention (CDC), whereas heart disease and cancer are numbers one and two, respectively. These numbers are based on what is reported on death certificates.

"Alzheimer's disease and other dementias are under-reported on death certificates and medical records," said study author Bryan D. James, PhD, of Rush University Medical Center in Chicago. "Death certificates often list the immediate cause of death, such as pneumonia, rather than listing dementia as an underlying cause." James added that attempting to identify a single cause of death does not always capture the reality of the process of dying for most elderly people, as multiple health issues often contribute.

"The estimates generated by our analysis suggest that deaths from Alzheimer's disease far exceed the numbers reported by the CDC and those listed on death certificates," said James.

For the study, 2,566 people ages 65 and older received annual testing for dementia. The average age of the participants was 78. The research found that after an average of eight years, 1,090 participants died. A total of 559 participants without dementia at the start of the study developed Alzheimer's disease. The average time from diagnosis to death was about four years. After death, Alzheimer's disease was confirmed through autopsy for about 90 percent of those who were clinically diagnosed. The death rate was more than four times higher after a diagnosis of Alzheimer's in people age 75 to 84 and nearly three times higher in people age 85 and older. More than one-third of all deaths in those age groups were attributable to Alzheimer's disease.

James said this translates into an estimated 503,400 deaths from Alzheimer's in the U.S. population over age 75 in 2010, which is five to six times higher than the 83,494 number reported by the CDC based on death certificates. "Determining the true effects of dementia in this country is important for raising public awareness and identifying research priorities regarding this epidemic," said James.

*The study was supported by the National Institute on Aging and the Illinois Department of Public Health. The authors thank the participants in the Religious Orders Study and the Rush Memory and Aging Project.*

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### **Long-lasting device protects against HIV and pregnancy**

***Intravaginal ring providing dual protection is first of its kind to enter a clinical trial***

EVANSTON, Ill. --- Women's reproductive health may never be the same, thanks to Northwestern University biomedical engineer Patrick Kiser and his first-of-its-kind intravaginal ring that reliably delivers an antiretroviral drug and a contraceptive for months. Kiser's one ring delivers two drugs that do three important things: the device is designed to protect against HIV and herpes as well as unwanted pregnancy. It will be the first device with the potential to offer this protection to be tested in women.

The easy-to-use ring delivers controlled doses of tenofovir (a common antiretroviral drug) and levonorgestrel (a contraceptive) for 90 days. The rings are being manufactured now, and the device soon will undergo its first test in women. Details of the development of the ring, a device that represents a lot of 'firsts,' will be published March 5 by PLOS ONE, a peer-reviewed, open-access online journal.

According to the World Health Organization, 35 million people around the world live with HIV, and 222 million women would like to delay or stop childbearing but are not using any method of contraception.

"I suspect women will use the ring primarily for contraception, but they also will benefit from protection against sexually transmitted diseases," said Kiser, an expert in intravaginal drug delivery. "And for women in the developing world in particular, unwanted pregnancy can have significant health, economic and cultural consequences. We want to motivate women to use this ring."

The ring, 5.5 centimeters in diameter, is simple yet complex. Kiser and his colleagues worked painstakingly for five years, engineering the three materials that make up the ring and optimizing the device to reliably deliver fixed and efficacious doses of two medicines over a long period of time.

"A lot of engineering has gone into developing the ring," said Kiser, senior author of the paper. "It represents two Ph.D. theses -- one Ph.D. for the larger section containing the antiretroviral drug and another Ph.D. for the smaller section containing the contraceptive." Kiser is a faculty member in the department of biomedical engineering at the McCormick School of Engineering and Applied Science and in the department of obstetrics and gynecology at Northwestern University Feinberg School of Medicine.

The ring is easily inserted in the vagina and stays in place for three months. And because the tenofovir is delivered at the site of transmission, the ring -- known as the tenofovir levonorgestrel IVR -- utilizes a smaller dose than pills. The levonorgestrel released by the ring is the same drug as that used in certain contraceptive pills and in an intrauterine device.

"This system represents a significant advance in vaginal drug delivery technology and is the first in a new class of long-acting multipurpose prevention drug delivery systems," say the authors in the study. They also report details of the ring's engineering, safety, stability and drug release.

"The differences between the two drugs are huge, which presented us with a design challenge," Kiser said.

"Tenofovir is highly water soluble while levonorgestrel is highly water insoluble. And the daily dose is different: the ring delivers about 10 milligrams of tenofovir and only 10 micrograms of levonorgestrel. Our scientific hurdle was finding a way to manufacture a dual-purpose ring that got the device into the clinic."

Tenofovir is taken orally by 3.5 million HIV-infected people worldwide, and it also has been studied as a gel. The drug inhibits HIV and HSV-2 (herpes simplex virus-2) replication in susceptible cells.

Previous studies have demonstrated that antiretroviral drugs can prevent HIV infection, but existing methods for delivering the drug fall short. Pills must be taken daily and require high doses; some women may prefer a longer-lasting method, such as the ring, versus methods used at the time of sex, such as a gel.

Kiser's combination ring promises much more. The strength of the device stems from its unique polymer construction: its elastomer swells in the presence of fluid (such as that found in the human body), delivering up to 100 times more of the tenofovir than current intravaginal ring technology, which have release rates that decline over time.

"Products only work when they are used," said co-author David Friend, product development director at CONRAD, which develops reproductive health technologies for low-income countries and is affiliated with Eastern Virginia Medical School.

"By having a ring that can remain in the body for up to 90 days, our hope is that this ring will offer a solution to increase adherence, and therefore provide greater protection against HIV while also preventing pregnancy," he said.

The antiretroviral drug section of the ring is made of one kind of polyurethane, and the contraceptive section of the ring is made of another polyurethane. Each material needed to be engineered with the correct diffusion rates, so the encapsulated drug is released into the body at the desired rate, providing the correct dose.

A third polyurethane material between the two sections keeps the drugs separate. All the parts are welded together to complete the ring.

*CONRAD (at the Eastern Virginia Medical School), through a cooperative agreement with USAID, supported the research. The title of the paper is "Engineering a Segmented Dual-Reservoir Polyurethane Intravaginal Ring for Simultaneous Prevention of HIV Transmission and Unwanted Pregnancy."*

*In addition to Kiser, authors of the paper are Justin T. Clark (first author), Namdev B. Shelke, Todd J. Johnson, Eric M. Smith, Andrew K. Andreasen, Joel S. Nebeker and Judit Fabian of the University of Utah, and Meredith R. Clark and David R. Friend of CONRAD, Eastern Virginia Medical School.*



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## **Pigment or bacteria? Researchers re-examine the idea of 'color' in fossil feathers**

*New research demonstrates that it is not yet possible to tell if structures are melanosomes or if they are the remnants of ancient bacteria*

Paleontologists studying fossilized feathers have proposed that the shapes of certain microscopic structures inside the feathers can tell us the color of ancient birds. But new research from North Carolina State University demonstrates that it is not yet possible to tell if these structures – thought to be melanosomes – are what they seem, or if they are merely the remnants of ancient bacteria.

Melanosomes are small, pigment-filled sacs located inside the cells of feathers and other pigmented tissues of vertebrates. They contain melanin, which can give feathers colors ranging from brownish-red to gray to solid black. Melanosomes are either oblong or round in shape, and the identification of these small bodies in preserved feathers has led to speculation about the physiology, habitats, coloration and lifestyles of the extinct animals, including dinosaurs, that once possessed them.

But melanosomes are not the only round and oblong microscopic structures that might show up in fossilized feathers. In fact, the microbes that drove the decomposition of the animal prior to fossilization share the same size and shape as melanosomes, and they would also be present in feathers during decay.

Alison Moyer, a Ph.D. candidate in paleontology at NC State, wanted to find out whether these structures could be definitively identified as either melanosome or microbe. Using black and brown chicken feathers – chickens are one of the closest living relatives to both dinosaurs and ancient birds – Moyer grew bacteria over them to replicate what we see in the fossil record.

She used three different types of microscopy to examine the patterns of biofilm growth, and then compared those structures to melanosomes inside of chicken feathers that she had sliced open. Finally, she compared both microbes and actual melanosomes to structures in a fossilized feather from *Gansus yumenensis*, an avian dinosaur that lived about 120 million years ago, and to published images of fossil "melanosomes" by others. Her findings led to more questions.

"These structures could be original to the bird, or they could be a biofilm which has grown over and degraded the feather – if the latter, they would also produce round or elongated structures that are not melanosomes," Moyer says.

"Melanosomes are embedded in keratin, which is a very tough protein, so they're hard to see unless there's been some degradation. But the bacteria are doing the degrading, and so that may be what we're seeing, rather than the melanosome itself. It's impossible to say with certainty what these structures are without more data, including fine scale chemical data."

The research appears online in *Scientific Reports*. Possible next steps for Moyer include testing for the presence of keratin or bacteria within the fossils, by looking for their molecular signals.

"The technology that we have available to us as paleontologists now is amazing, and will make it much easier to test all of the hypotheses we develop about these fossils," Moyer says. "In the meantime, perhaps we can establish some basic criteria for identifying these structures as melanosomes, such as whether they're found within the feather's interior, or externally."

*The research was funded in part by the National Science Foundation and the David and Lucille Packard foundation. The fossil feather was provided by the Gansu Geological Museum in Lanzhou, Gansu, China. An abstract of the paper follows.*

*"Melanosomes or Microbes: Testing an Alternative Hypothesis for the Origin of Microbodies in Fossil Feathers"*

*Authors: Alison Moyer, Wenxia Zheng, Mary Schweitzer, NC State University; Elizabeth Johnson, Colorado Northwestern Community College; Matthew Lamanna, Carnegie Museum of Natural History; Daqing Li, Gansu Geological Museum; Kenneth Lacovara, Drexel University Published: March 5, 2014 in Scientific Reports*

***Abstract: Microbodies associated with fossil feathers, originally attributed to microbial biofilm, have been reinterpreted as melanosomes; pigment-containing, eukaryotic organelles. This interpretation generated hypotheses regarding coloration in non-avian and avian dinosaurs. Because melanosomes and microbes overlap in size, distribution and morphology, we re-evaluate both hypotheses. We compare melanosomes within feathers of extant chickens with patterns induced by microbial overgrowth on the same feathers, using scanning (SEM), field emission (FESEM) and transmission (TEM) electron microscopy. Melanosomes are always internal, embedded in a morphologically distinct keratinous matrix. Conversely, microbes grow across the surface of feathers in continuous layers, more consistent with published images from fossil feathers. We compare our results to both published literature and new data from a fossil feather ascribed to *Gansus yumenensis* (ANSP 23403). "Mouldic impressions" were observed in association with both the feather and sediment grains, supporting a microbial origin. We propose criteria for distinguishing between these two microbodies.***

<http://bit.ly/1fcj8Ps>

## Distant Black Hole Spins at Half the Speed of Light

*Back when the universe was half its present age, supermassive black holes were feeding from a steady and plentiful diet of neighboring galaxies, the first measurement of a distant supermassive black hole's spin shows.*

Mar 5, 2014 01:00 PM ET // by Irene Klotz

A powerful NASA telescope has found not one, but 10 supermassive black holes. And it did so by accident! Taking advantage of a naturally occurring zoom lens in space, astronomers analyzed X-rays streaming from near the mouth of a supermassive black hole powering a quasar about 6 billion light years from Earth.

"The 'lens' galaxy acts like a natural telescope, magnifying the light from the faraway quasar," University of Michigan astronomer Rubens Reis explains in a paper published in this week's Nature.

Analyzing four magnified images created by the lens galaxy -- an elliptical galaxy about 3 billion light years away -- Reis and colleagues found that the quasar's black hole is spinning at half the speed of light.

The spin rate directly relates to how black holes feed and grow: The steadier the diet, the faster the spin, computer models show.

"If the mass accretion was more messy it would suggest that the black hole would have a lower spin," astronomer Mark Reynolds, also with University of Michigan, told Discovery News. "What we found in this system is that it's spinning very rapidly," Reynolds said, consuming mass equivalent to about one sun per year. That suggests that the quasar, known as RX J1131-1231, is growing primarily by what is known as "coherent accretion" such as what might happen when two galaxies merge, producing lots of gas that can funnel down toward the black hole very efficiently, Reynolds said.

Until astronomers measure the spin rates of other and even more distant supermassive black holes they won't know if RX J1131 is an odd bird or not. "This is the first time that we've been able to push out to this type of distance by using the gravitational lensing effect. We hope ... to carry out similar studies on other (more distant) galaxies. Then we can begin to really start relating the black hole to the actual galaxy it's in, how many mergers happened and things like that," Reynolds said.

Spin rates may evolve over time, reflecting changes in evolution of galaxies. "Different theories of galaxy evolution predict a different rate of mergers, and a different process of gas inflow into the center of galaxies," Guido Risaliti, with the INAF Arcetri Astrophysical Observatory in Florence, Italy, wrote in an email to Discovery News. "These processes, in turn, determine the final black hole spin. So knowing the distribution of supermassive black hole spins is a way to constrain the way they were formed, and so, ultimately, the way their host galaxies formed and evolved," Risaliti wrote.

At some distance, the black holes' spins might be even higher, approaching light speed, and then slow down to RX J1131's spin rate. "If we go back further, maybe they'll all be maximally spinning because of more mergers and more things happening. Or maybe they'll be less spinning. We can theoretically produce both scenarios at the moment," Reynolds said.

<http://bit.ly/1fNgXli>

## Huge Mexican pyramid could collapse like a sandcastle

*THE Pyramid of the Sun may fall apart. One side is dry while another side is wet, which could lead to the pyramid's collapse unless a fix can be found.*

05 March 2014 by Frank Nowikowski

Between the 1st and 7th centuries, Mexico's Pyramid of the Sun was at the heart of the largest city in the Americas. Now known as Teotihuacan, the lost city had a population of more than 125,000, making it one of the biggest in the world. The pyramid itself is among the largest on the planet. Its exterior is covered with 3 million tonnes of volcanic rock, but the interior is a mound of earth.

From 2010 to 2013, Arturo Menchaca of the National Autonomous University of Mexico (UNAM) in Mexico City and colleagues studied the interior of the pyramid using muons. These sub-atomic particles can pass through most materials, but are deflected when they hit denser ones. That means more muons reach the other side if an object has an internal cavity, filled with less dense air. So by tracking the paths of muons through the pyramid, Menchaca could create a 3D representation of its insides.



*Feeling distinctly wonky (Image: Harald Sund/Getty)*

To do this, his team placed muon detectors under the centre of the pyramid, in a tunnel that runs beneath its base. The muons originate in space as cosmic rays, which break up into smaller particles when they pass

through Earth's atmosphere. The team was looking for internal chambers, but none was apparent. In contrast, the nearby Pyramid of the Moon contains royal tombs.

Instead they found a problem: the density of the earth in the pyramid is at least 20 per cent lower on one side than the other. "The pyramid is at risk of collapsing if something isn't done," says Menchaca. He presented his results at a conference on Teotihuacan at UNAM last month.

Menchaca believes the difference is caused by the south side drying out. He compares the pyramid to a sandcastle on a beach. "I can use slightly moist sand to make a sandcastle," he says. "If I leave it exposed to the sun and touch it when it is dry, then it crumbles."

The pyramid is "not going to collapse tomorrow", Menchaca says. "But it is the same phenomenon we observe in the subsoil of Mexico City." Mexico's capital is built on a dried-out lake, and every year the city sinks by tens of centimetres as water is extracted from aquifers beneath it.

Opinion is divided on how to save the pyramid. Menchaca suggests wetting the dry side.

But the real problem may be excess water, not dryness, says Alejandro Sarabia, the site director at Teotihuacan. "Decades ago, cement was added between the covering stones. This added stability and hindered the growth of vegetation," he says. "On the other hand, it prevents evaporation of damp created by water seeping through gaps." Sarabia says archaeologists are now replacing the cement with more suitable materials like river sand.

<http://www.wired.com/wiredscience/2014/03/organic-quasicrystal/#rssowlmlink>

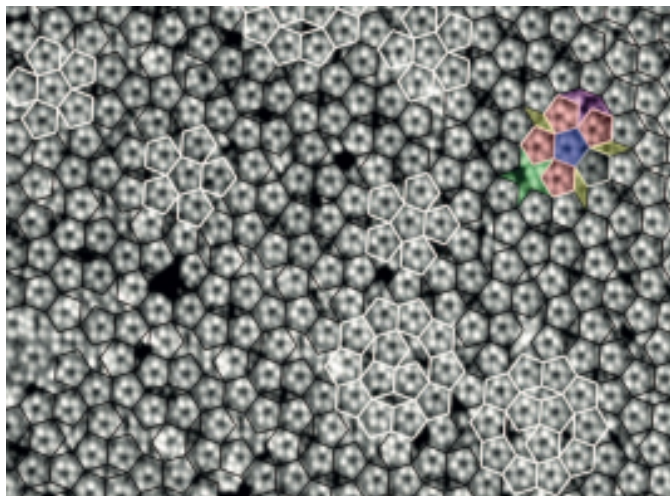
### **Bizarre Organic Quasicrystal Accidentally Created in Lab**

*Quasicrystals have teased and intrigued scientists for three decades. Now, this already strange group of materials has a bizarre new member: a two-dimensional quasicrystal made from self-assembling organic molecules.*

By Nadia Drake

This odd quasicrystal is flat, made from a single layer of molecules with five-sided rings. The molecules form groups within the layer as weak hydrogen bonds link them together. These molecular groups are assembled in a way that forces other molecules in the layer into shapes including pentagons, stars, boats, and rhombi. If this were a regular old crystal, you'd expect to see these groups and shapes repeated over and over throughout the layer in a predictable way. But in this quasicrystal, you'll see the same shapes over and over in the layer, but not in any organized pattern.

The things that set these quasicrystals apart from all the others, scientists say, are its organic materials and self-assembling parts.



*Two-dimensional quasicrystal with pentagonal crystalline units overlaid.* (Natalie Wasio et al., Nature, 2014)

"They're markedly different from just about everything else out there," said physical chemist Alex Kandel, whose lab at the University of Notre Dame described the material today in Nature. Previously known quasicrystals are mostly metallic, and tied together by strong ionic bonds rather than the weaker hydrogen bonds that can be found in complex organic molecules like DNA.

As their name suggests, quasicrystals have a structure that's part crystalline, part disorganized. In other words, they are something in between a structure with repeating, symmetric units, and one with completely random building blocks. Their atomic units are locally symmetric, but are not regularly repeated over longer distances. Because of these arrangements, quasicrystals are slippery and have been used in things like non-stick frying pans.

The first quasicrystal of any sort was also accidentally made in the lab, in 1982, by materials scientist Daniel Schechtman who won a Nobel Prize for the discovery in 2011. Up until that point, scientists thought the semi-organized structure of quasicrystals was an impossibility. Now, we know that's not true. Not only can quasicrystals be grown in the lab, they can also grow in nature. In 2012, Princeton University physicist Paul Steinhardt showed that quasicrystals found in eastern Russia had fallen to Earth in a meteorite.

Kandel's group discovered the organic quasicrystal accidentally. Instead of trying to make the thing, they were actually hoping to study how electrons are distributed in ferrocenecarboxylic acid, the molecule the quasicrystal is built from. To do that, the team needed to build a stable, linear group of molecules. But when the scientists tried, they produced a two-dimensional quasicrystal instead. "The first images were quite a shock," Kandel said.



“Certainly, 2-D quasicrystals aren’t easy to make, which is why we’re only seeing very recent reports of them now, some 30-odd years after the first quasicrystalline materials were discovered.”

Wolf Widdra of Germany’s Martin Luther University, who made the first 2-D quasicrystal, reported in October 2013, is a bit skeptical of the new research. He doesn’t think there’s enough evidence yet to prove quasicrystal structure over a large enough area. There is also disagreement among scientists about what it means to be self-assembling. Widdra thinks the term could be applied to all quasicrystal structures, not just this new one.

Kandel argues that structures assembled by way of strong chemical bonds — like the other quasicrystals — aren’t actually self-assembled. Those strong chemical bonds, he says, overwhelm the forces holding individual building blocks together and leave the material no choice but to form. In this new quasicrystal, those building blocks are joined by weak hydrogen bonds. “Self-assembly is interesting precisely because the forces that drive organization are weaker than the forces responsible for the individual structure,” Kandel said.

<http://www.medscape.com/viewarticle/821551?src=rss>

## HIV Baby Taken Off Antiretrovirals in Remission at Age 3

### *Researchers Now Reporting Second Case*

Marcia Frellick

BOSTON — The Mississippi infant born with HIV who made headlines around the world last year when physicians announced she was functionally cured 10 months after stopping combination antiretroviral therapy still has no detectable levels of the virus at age 3, researchers report.

The baby has undetectable plasma viremia (<20 copies/mL) and normal CD4+ and CD8+ T-cell counts at 39 months of age — 21 months after stopping antiretroviral therapy, explained Deborah Persaud, MD, from Johns Hopkins University School of Medicine in Baltimore.

"The child remains in remission and there's no replication combinant T-cell reservoir detectable to date," she reported here at the 2014 Conference on Retroviruses and Opportunistic Infections.

"This supports our hypothesis that very early treatment may prevent the formation of reservoirs that currently preclude a cure."

Dr. Persaud introduced the case of a second baby, in Los Angeles County, who started receiving therapy 4 hours after birth. At 8 months, that baby — whose sex has not been disclosed — no longer has detectable levels of the virus.

Four hours after the birth of this second baby, positive status was confirmed with peripheral blood HIV DNA polymerase chain reaction; 36 hours after birth, HIV RNA levels were determined to be 217 copies/mL. By the sixth day of life, HIV DNA testing was negative. The baby was born to a mother with a high viral load who had been prescribed antiretrovirals but had not taken them consistently.

### **Second Case**

"It's important for the field to identify strategies to manage these very early treatments in infants," Dr. Persaud said. In 2 to 3 months, clinical trials will begin domestically and internationally to test the effects of very early treatment in HIV-infected infants, she said.

Although the 2 cases are different, they share a positive message, said Anthony Fauci, MD, director of the National Institute of Allergy and Infectious Diseases.

"I don't think we can say much about the second baby because they have not discontinued antiretroviral therapy," he told Medscape Medical News.

However, "a very important component of any attempt to ultimately get people off therapy is to treat them as early as possible to decrease the size of the ultimate reservoir. The longer you have the virus, the greater the chance of having a substantial reservoir," Dr. Fauci explained.

This strongly suggests that they will be able to do the same thing with this baby that they did with the first. When treatment is started at the time of infection, the chances of very rapidly suppressing virus replications are very good, he explained.

With babies, you know almost exactly when they were infected - usually at birth. Adults might not be able to pinpoint the day or even month of infection.

He noted that although prospective studies will be done, retrospective studies will look back at babies who were treated extremely early. "We may have inadvertently cured some babies without even realizing it, merely with the normal practice of pediatric medicine," he speculated.

Short of knowing the outcome of the second child, because therapy continues, it is a good sign that the virus has been reduced to undetectable levels, Dr. Fauci said. "This strongly suggests that they will be able to do the same thing with this baby that they did with the first."

*Dr. Persaud and Dr. Fauci have disclosed no relevant financial relationships.*

*2014 Conference on Retroviruses and Opportunistic Infections (CROI). Presented March 5, 2014.*



[http://www.eurekalert.org/pub\\_releases/2014-03/byu-hts030514.php#rsslwmlink](http://www.eurekalert.org/pub_releases/2014-03/byu-hts030514.php#rsslwmlink)

## **Half the survivors in 1 Japanese town have PTSD symptoms**

### ***Study shows that work increases resilience among disaster survivors***

Though just two of Hirono's 5,418 residents lost their lives in Japan's mega-earthquake and tsunami, a new study shows that the survivors are struggling to keep their sanity.

One year after the quake, Brigham Young University professor Niwako Yamawaki and scholars from Saga University evaluated the mental health of 241 Hirono citizens. More than half of the people evaluated experienced "clinically concerning" symptoms of post-traumatic stress disorder. Two-thirds of the sample reported symptoms of depression. Those rates exceed levels seen in the aftermath of other natural disasters, but what happened in Japan wasn't just a natural disaster. Leaked radiation from nuclear power plants forced residents of Hirono to relocate to temporary housing far from home.

"This was the world's fourth-biggest recorded earthquake, and also the tsunami and nuclear plant and losing their homes – boom boom boom boom within such a short time," said Yamawaki, a psychology professor at BYU. "The prevalence one year after is still much higher than other studies of disasters that we found even though some time had passed."

Yamawaki got the idea for this study while shoveling mud from a damaged Japanese home one month after the tsunami flooded coastal towns. She had just arrived for a previously scheduled fellowship at Saga University. During her off-time, she traveled to the affected area and volunteered in the clean-up effort. One seemingly stoic homeowner broke down in tears when Yamawaki and her husband thanked her for the chance to help. "She said 'This is the first time I have cried since the disaster happened,'" Yamawaki said. "She just said 'Thank you. Thank you for letting me cry.'"

Back at Saga University, Yamawaki collaborated with Hiroko Kukihara to conduct a study on the mental health and resilience of survivors. Their report appears in the journal *Psychiatry and Clinical Neurosciences*.

Participants in the study lived in temporary housing provided by the Japanese government when Hirono was evacuated. With an average age of 58, the people are noticeably older than the populations of normal Japanese towns. Yamawaki suspects that young people were more likely to permanently relocate elsewhere in Japan following the disaster.

The researchers didn't just measure the rates of mental illness; they also performed a statistical analysis to learn what fostered resilience among the survivors. Eating right, exercising regularly and going to work all promoted resilience and served as a buffer against mental illness. "Having something to do after a disaster really gives a sense of normalcy, even volunteer work," Yamawaki said. As the researchers got to know survivors, they heard from so many that they missed seeing their former neighbors. The mass relocation outside the radiation zone broke up many neighborhood ties. "Japanese are very collectivistic people and their identity is so intertwined with neighbors," Yamawaki said. "Breaking up the community has so much impact on them."

While it's hard to fathom the scope of the devastation in the coastal region of Fukushima, most survivors believe something like this will happen again. If so, this new study provides a blueprint for how to help them put their lives back together again.

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## **Astronomers witness mysterious, never-before-seen disintegration of asteroid**

***Astronomers have witnessed for the first time the breakup of an asteroid into as many as 10 smaller pieces.***

***The discovery is published online March 6 in *Astrophysical Journal Letters*.***

Though fragile comet nuclei have been seen falling apart as they near the sun, nothing resembling this type of breakup has been observed before in the asteroid belt. NASA's Hubble Space Telescope photographed the demolition. "Seeing this rock fall apart before our eyes is pretty amazing," said David Jewitt, a professor in the UCLA Department of Earth, Planetary and Space Sciences and the UCLA Department of Physics and Astronomy, who led the astronomical forensics investigation.

The crumbling asteroid, designated P/2013 R3, was first noticed as an anomalous, fuzzy-looking object on Sept. 15, 2013, by the Catalina and Pan-STARRS sky-survey telescopes. A follow-up observation on Oct. 1 with the W.M. Keck telescope on Hawaii's Mauna Kea revealed three co-moving bodies embedded in a dusty envelope that is nearly the diameter of Earth. "The Keck telescope showed us that this asteroid was worth looking at with Hubble," Jewitt said. With its superior resolution, the Hubble telescope revealed that there were really 10 embedded objects, each with comet-like dust tails. The four largest rocky fragments are up to 200 yards in radius, about twice the length of a football field.

The Hubble data showed that the fragments are drifting away from each other at a leisurely pace of one mile per hour — slower than a strolling human. The asteroid began coming apart early last year, but new pieces continue

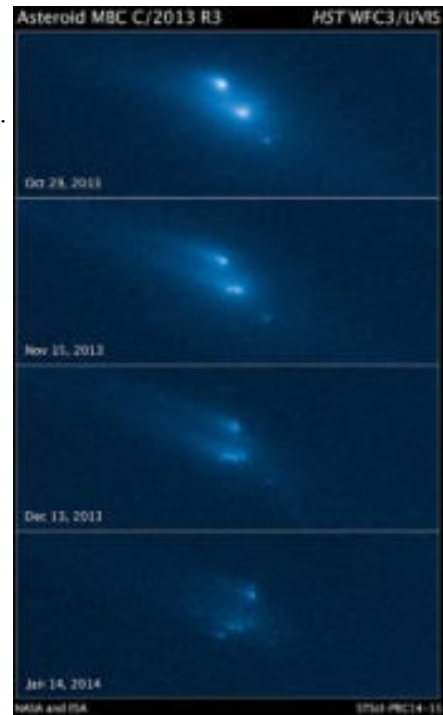
to emerge in the most recent images. This makes it unlikely that the asteroid is disintegrating because of a collision with another asteroid, which would be instantaneous and violent. Some of the debris from such a high-velocity smash-up would also be expected to travel much faster than observed.

Nor is the asteroid coming unglued due to the pressure of interior ices warming and vaporizing, Jewitt said. The asteroid is too cold for ices to significantly sublimate, and it has presumably maintained its nearly 300 million-mile distance from the sun for much of the age of the solar system, he said.

This leaves a scenario in which the asteroid is disintegrating due to a subtle effect of sunlight, which causes the rotation rate to slowly increase. Eventually, its component pieces, like grapes on a stem, gently pull apart due to centrifugal force, Jewitt said. The possibility of disruption by this so-called "YORP torque" has been discussed by scientists for several years but, so far, never reliably observed.

For this to happen, P/2013 R3 must have a weak, fractured interior, probably as the result of numerous ancient but non-destructive collisions with other asteroids. Most small asteroids, in fact, are thought to have been severely damaged in this way, giving them a "rubble pile" internal structure. P/2013 R3 itself is probably the product of collisional shattering of a bigger body some time in the last billion years.

With Hubble's recent discovery of an active asteroid spouting six tails (P/2013 P5), astronomers are seeing more circumstantial evidence that the pressure of sunlight may be the primary force that disintegrates small asteroids (less than a mile across) in the solar system. The asteroid's remnant debris, weighing in at 200,000 tons, in the future will provide a rich source of meteoroids, Jewitt said. Most will eventually plunge into the sun, but a small fraction of the debris may one day enter the Earth's atmosphere to blaze across the sky as meteors, he said.



*This series of Hubble Space Telescope images reveals the breakup of an asteroid over a period of several months in late 2013. The largest fragments are up to 200 yards in radius, each with "tails" caused by dust lifted from their surfaces and pushed back by the pressure of sunlight. The 10 pieces of the asteroid drift apart slowly and show a range of breakup times, suggesting that the disintegration cannot be explained by a collision with another asteroid. One idea for the breakup is that the asteroid was accelerated by sunlight to spin at a fast enough rate to fly apart by centrifugal force. The images were taken in visible light with Hubble's Wide-Field Camera 3. Credit: NASA, ESA, D. Jewitt/UCLA*

Jewitt, who is on the faculty of the UCLA College of Letters and Science, is a member of the National Academy of Sciences and a fellow of both the American Association for the Advancement of Science and the American Academy of Arts and Sciences. He co-discovered the Kuiper Belt beyond Neptune in 1993. The discovery of the belt, which contains more than a billion objects and was once believed to be empty space, has fundamentally changed the modern perception of the solar system.

The Hubble Space Telescope is a project of international cooperation between NASA and the European Space Agency. NASA's Goddard Space Flight Center in Greenbelt, Md., manages the telescope. The Space Telescope Science Institute (STScI) in Baltimore conducts Hubble science operations. STScI is operated for NASA by the Association of Universities for Research in Astronomy, Inc., in Washington. "Hubble's incredible resolution and sensitivity are creating a new cottage industry for planetary scientists," said Hal Weaver, of the Johns Hopkins University Applied Physics Laboratory in Laurel, Md., one of Jewitt's co-investigators.

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### **How seeing the same GP helps your health**

*Patients are more likely to raise a health problem with a doctor they've seen over time and have built-up a relationship with, new research has revealed.*

The insight comes as an increasing number of patients struggle to see the same GP. Researchers from the University of Bristol will share their findings with health practitioners and researchers at the South West Society for Academic Primary Care (SW SAPC) meeting today [07 March].

Seeing the same GP is thought to be important in ensuring quality of patient care, as the doctor will have better knowledge of the patient's history, medications, and health-related behaviours and attitudes. However, a quarter of patients find it difficult to see the doctor of their choice most of the time due to a combination of factors. Namely, a reduction in doctors' working hours, an increase in part-time working, a focus on access and rapid appointments in the 2004 GP contract, and organisational changes in out-of-hours care. Previous studies have

quantified the numbers and types of problems that are raised in GP consultations, but there is little evidence about the effect of increasing depth of patient-doctor relationships on the content of these interactions.

To shed light on this, researchers collected data from 22 practices in the Bristol area, recording consultations between 190 patients and 30 GPs. Researchers then looked at whether consultation length and the number of problems and issues raised were affected by patient-doctor continuity.

Analysis showed that almost a third of patients had a 'deep' relationship with their GP, which in turn encouraged them to raise 0.5 more problems (a topic requiring a GP to make a decision or diagnosis) and 0.9 more issues (the number of topics raised within each problem, such as symptoms) during each consultation. This may mean many more problems and issues are addressed over the course of several visits.

Dr Matthew Ridd, from Bristol University's School of Social and Community Medicine, was part of the research team and said: "Participants mostly reported a strong relationship with their GP, built-up over time. There was evidence that patients raised more problems and issues with GPs that they felt they had a deep relationship with. "This could be because patients feel more comfortable raising additional issues with a GP they feel they know well, or because more issues can be addressed within the time available as the GP knows the patient and their medical history. "This research study is the first of its kind to show how seeing the same doctor can positively affect consultations."

The study also found that the type of problem or issue raised was not related to the depth of the relationship between the patient and their doctor, except that behavioural problems or issues were less likely to be raised when a deep relationship existed.

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### Nearby star's icy debris suggests 'shepherd' planet

***An international team of astronomers exploring the disk of gas and dust around a nearby star have uncovered a compact cloud of poisonous gas formed by ongoing rapid-fire collisions among a swarm of icy, comet-like bodies.***

The researchers suggest the comet swarm is either the remnant of a crash between two icy worlds the size of Mars or frozen debris trapped and concentrated by the gravity of an as-yet-unseen planet.

Using the Atacama Large Millimeter/submillimeter Array (ALMA) in Chile, the researchers mapped millimeter-wavelength light from dust and carbon monoxide (CO) molecules in a disk surrounding the bright star Beta Pictoris. Located about 63 light-years away and only 20 million years old, the star hosts one of the closest, brightest and youngest debris disks known, making it an ideal laboratory for studying the early development of planetary systems.

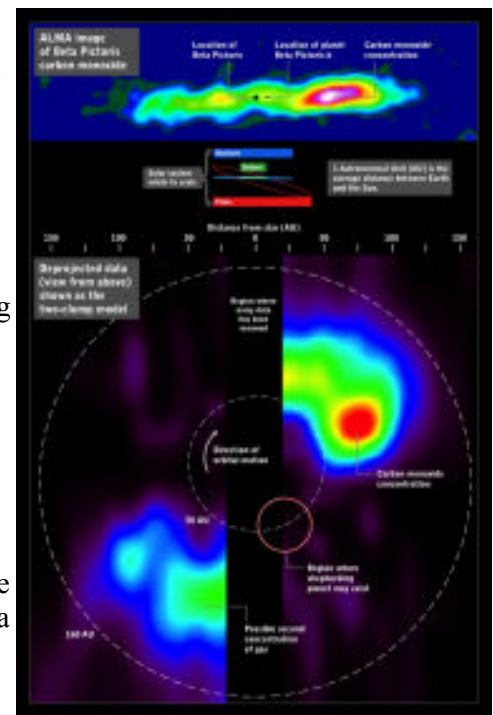
"Although toxic to us, carbon monoxide is one of many gases found in comets and other icy bodies," said team member Aki Roberge, an astrophysicist at NASA's Goddard Space Flight Center in Greenbelt, Md. "In the rough-and-tumble environment around a young star, these objects frequently collide and generate fragments that release dust, icy grains and stored gases."

The ALMA images reveal a vast belt of carbon monoxide located at the fringes of the Beta Pictoris system. Much of the gas is concentrated in a single clump located about 8 billion miles (13 billion kilometers) from the star, or nearly three times the distance between the planet Neptune and the sun. The total amount of CO observed, the scientists say, exceeds 200 million billion tons, equivalent to about one-sixth the mass of Earth's oceans.

***The ALMA image of carbon monoxide around Beta Pictoris (above) can be deprojected (below) to simulate a view looking down on the system, revealing the large concentration of gas in its outer reaches. For comparison, orbits within the solar system are shown for scale.***

***ALMA (ESO/NAOJ/NRAO) and NASA Goddard/F. Reddy***  
***VIDEO: NASA Goddard's Aki Roberge explains how observations with the Atacama Large Millimeter/submillimeter Array in Chile tell us about poison gas, comet swarms and a hypothetical planet around Beta Pictoris***

The presence of all this gas is a clue that something interesting is going on because ultraviolet starlight breaks up CO molecules in about 100 years, much faster than the main cloud can complete a single orbit around the star. "So unless we are observing Beta Pictoris at a very unusual time, then the carbon monoxide we observed must be continuously replenished," said Bill Dent, a researcher at the Joint ALMA Office in Santiago, Chile, and the lead author of a paper published by Science Express on March 6.





Dent and his team calculate that to offset the destruction of CO molecules around Beta Pictoris, a large comet must be completely destroyed every five minutes. Only an unusually massive and compact swarm of comets could support such an astonishingly high collision rate.

Because we view the disk nearly edge-on, the ALMA data cannot determine whether the carbon monoxide belt has a single concentration of gas or two on opposite sides of the star. Further studies of the gas cloud's orbital motion will clarify the situation, but current evidence favors a two-clump scenario.

In our own solar system, Jupiter's gravity has trapped thousands of asteroids in two groups, one leading and one following the planet as it travels around the sun. A giant planet located in the outer reaches of the Beta Pictoris system likewise could corral comets into a pair of tight, massive swarms.

"Detailed dynamical studies are now under way, but at the moment we think this shepherding planet would be around Saturn's mass and positioned near the inner edge of the CO belt," said coauthor Mark Wyatt, an astronomer at the University of Cambridge in England.

Astronomers have directly imaged one giant planet, Beta Pictoris b, with a mass several times greater than Jupiter, orbiting much closer to the star. While it would be unusual for a giant planet to form up to 10 times farther away, as required to shepherd the massive comet clouds, the hypothetical planet could have formed near the star and migrated outward as the young disk underwent changes.

"We think the Beta Pictoris comet swarms formed when the hypothetical planet migrated outward, sweeping icy bodies into resonant orbits," explained Wyatt. When the orbital periods of the comets matched the planet's in some simple ratio – say, two orbits for every three of the planet – the comets received a nudge from the planet at the same location every orbit. Like regular pushes on a child's swing, these accelerations amplify over time and work to confine the comets in a small region.

If, however, the gas actually turns out to reside in a single clump, the researchers suggest an alternative scenario. A crash between two Mars-sized icy planets about half a million years ago would account for the comet swarm, with frequent ongoing collisions among the fragments gradually releasing carbon monoxide gas. Either way, Beta Pictoris clearly has a fascinating story to tell, and ALMA's keen vision will help astronomers delve ever deeper into the tale.

[http://www.eurekalert.org/pub\\_releases/2014-03/p-dpm022714.php#rsslmlink](http://www.eurekalert.org/pub_releases/2014-03/p-dpm022714.php#rsslmlink)

### **Drug protects mice against malaria brain damage, raises levels of BDNF in humans**

*Cerebral malaria is a serious complication of infection with the malaria parasite, affecting approximately one in a thousand children in areas where malaria is common.*

Many of the patients die, and among those who survive, about a third have lasting cognitive and neurological disabilities, including epilepsy and learning disorders. A study published on March 6th in PLOS Pathogens shows that a known drug can prevent brain damage in a cerebral malaria mouse model and eliminate subsequent neurological deficits.

Infection with the malaria parasite elicits a strong immune response in the patient, and it is known that both parasite and host response contribute to the nervous system problems in cerebral malaria. Lena Serghides, from the Toronto General Research Institute, Canada, and colleagues are interested in modulating the host response to malaria infection, in addition to anti-parasite drugs, with the goal to improve outcomes in patients.

They focused on a drug called rosiglitazone (approved for patients with diabetes) which activates a molecule called PPAR $\gamma$  and is known to have anti-inflammatory and anti-oxidant properties. Using a mouse model of cerebral malaria, they show that when they give rosiglitazone in addition to antimalarial drugs at the onset of cerebral malaria symptoms, mice are more likely to survive, and the survivors which had received rosiglitazone did not show the brain abnormalities or cognitive defects seen in surviving mice that had only received antimalarial drugs.

When they compared both groups of mice at the molecular level, they found that rosiglitazone protects the integrity of the blood-brain-barrier and increases the level of anti-oxidant enzymes and of neuroprotective factors in the brain. One of the latter, called BDNF (for brain-derived neurotropic factor), was also increased in the blood of adult human patients with uncomplicated malaria who had participated in a clinical trial and received antimalarial drugs plus rosiglitazone, compared with other trial participants who had only taken antimalarials.

"Our results demonstrate that rosiglitazone adjunctive therapy resulted in increased survival and protection from long-term cognitive impairments in a mouse model of cerebral malaria", the authors say, "And the clinical trial data suggests that this approved drug, which has an excellent safety profile when taken for limited periods, might also induce such putative protective mechanisms in humans". They conclude that "in view of these results, testing rosiglitazone in patients with cerebral malaria is warranted."

<http://dx.plos.org/10.1371/journal.ppat.1003980> (link becomes active March 6)



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[http://www.eurekalert.org/pub\\_releases/2014-03/ason-sut022814.php#rssowlmlink](http://www.eurekalert.org/pub_releases/2014-03/ason-sut022814.php#rssowlmlink)

## **Simple urine test detects common causes of kidney dysfunction after transplantation**

### ***Test could possibly replace invasive biopsies to help guide treatment***

Washington, DC - A new noninvasive urine test can distinguish among different causes of acute kidney dysfunction after transplantation. The test, which is described in a study appearing in an upcoming issue of the Journal of the American Society of Nephrology (JASN), may allow patients to avoid invasive kidney biopsies when their transplanted organ is not functioning properly.

When creatinine levels are elevated in the blood of a kidney transplant recipient, it is an indication that the transplanted kidney is not functioning well. There are several reasons for transplant kidney dysfunction, and none of the blood or urine tests can reliably differentiate them. Because it is important to establish the exact reason for kidney dysfunction in order to determine the appropriate treatment, physicians typically perform a needle biopsy of the transplanted kidney.

Now, however, Thangamani Muthukumar, MD (Weill Medical College of Cornell University) and his colleagues have developed a urine test that measures the levels of several messenger RNAs (mRNAs) that are directly related to the disease processes that cause kidney dysfunction. The researchers measured absolute levels of mRNAs in 84 urine samples from 84 kidney transplant recipients who had undergone needle biopsy of the transplanted kidney to determine the cause of their acute kidney dysfunction.

"Using statistical methods we have combined the mRNAs to yield a diagnostic signature," explained Dr. Muthukumar. The researchers developed two such signatures from cells found in the urine that could differentiate, in a two-step approach, the common causes of acute kidney dysfunction with high accuracy.

"Our study shows that when the creatinine level is elevated in the blood of a kidney transplant recipient, use of our urine test would differentiate the common causes of kidney dysfunction that led to the elevation in creatinine, hence benefiting many patients by allowing them to avoid the need for an invasive needle biopsy," said Dr. Muthukumar.

### **Highlights**

***A new urine test can distinguish among different causes of kidney dysfunction in kidney transplant recipients.***

***If validated in larger multicenter study, the test may allow patients to avoid invasive kidney biopsies.***

***Kidney dysfunction is a common complication after transplantation.***

The first author of the study is Dr. Marie Matignon, MD. Study co-authors include Ruchuang Ding, MD, Darshana M. Dadhania, MD, Franco B. Mueller, MD, Choli Hartono, MD, Catherine Snopkowski, Carol Li, John R. Lee, MD, Daniel Sjoberg MA, Surya V. Seshan, MD, Vijay K. Sharma, PhD, Hua Yang, MD, Bakr Nour, MD, Andrew J. Vickers, PhD, and Manikkam Suthanthiran, MD. Disclosures: The authors reported no financial disclosures.

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The article, entitled "Urinary Cell mRNA Profiles and Differential Diagnosis of Acute Kidney Graft Dysfunction," will appear online at <http://jasn.asnjournals.org/> on March 6, 2014.

[http://www.eurekalert.org/pub\\_releases/2014-03/miot-pph030514.php#rssowlmlink](http://www.eurekalert.org/pub_releases/2014-03/miot-pph030514.php#rssowlmlink)

## **Plasma plumes help shield Earth from damaging solar storms**

### ***MIT scientists identify a plasma plume that naturally protects the Earth against solar storms***

Written by Jennifer Chu, MIT News Office

The Earth's magnetic field, or magnetosphere, stretches from the planet's core out into space, where it meets the solar wind, a stream of charged particles emitted by the sun. For the most part, the magnetosphere acts as a shield to protect the Earth from this high-energy solar activity. But when this field comes into contact with the sun's magnetic field — a process called "magnetic reconnection" — powerful electrical currents from the sun can stream into Earth's atmosphere, whipping up geomagnetic storms and space weather phenomena that can affect high-altitude aircraft, as well as astronauts on the International Space Station.

Now scientists at MIT and NASA have identified a process in the Earth's magnetosphere that reinforces its shielding effect, keeping incoming solar energy at bay.

By combining observations from the ground and in space, the team observed a plume of low-energy plasma particles that essentially hitches a ride along magnetic field lines — streaming from Earth's lower atmosphere up to the point, tens of thousands of kilometers above the surface, where the planet's magnetic field connects with that of the sun. In this region, which the scientists call the "merging point," the presence of cold, dense plasma slows magnetic reconnection, blunting the sun's effects on Earth.

"The Earth's magnetic field protects life on the surface from the full impact of these solar outbursts," says John Foster, associate director of MIT's Haystack Observatory. "Reconnection strips away some of our magnetic shield and lets energy leak in, giving us large, violent storms. These plasmas get pulled into space and slow down the reconnection process, so the impact of the sun on the Earth is less violent."

Foster and his colleagues publish their results in this week's issue of *Science*. The team includes Philip Erickson, principal research scientist at Haystack Observatory, as well as Brian Walsh and David Sibeck at NASA's Goddard Space Flight Center.

### **Mapping Earth's magnetic shield**

For more than a decade, scientists at Haystack Observatory have studied plasma plume phenomena using a ground-based technique called GPS-TEC, in which scientists analyze radio signals transmitted from GPS satellites to more than 1,000 receivers on the ground. Large space-weather events, such as geomagnetic storms, can alter the incoming radio waves — a distortion that scientists can use to determine the concentration of plasma particles in the upper atmosphere. Using this data, they can produce two-dimensional global maps of atmospheric phenomena, such as plasma plumes.

These ground-based observations have helped shed light on key characteristics of these plumes, such as how often they occur, and what makes some plumes stronger than others. But as Foster notes, this two-dimensional mapping technique gives an estimate only of what space weather might look like in the low-altitude regions of the magnetosphere. To get a more precise, three-dimensional picture of the entire magnetosphere would require observations directly from space.

Toward this end, Foster approached Walsh with data showing a plasma plume emanating from the Earth's surface, and extending up into the lower layers of the magnetosphere, during a moderate solar storm in January 2013. Walsh checked the date against the orbital trajectories of three spacecraft that have been circling the Earth to study auroras in the atmosphere.

As it turns out, all three spacecraft crossed the point in the magnetosphere at which Foster had detected a plasma plume from the ground. The team analyzed data from each spacecraft, and found that the same cold, dense plasma plume stretched all the way up to where the solar storm made contact with Earth's magnetic field.

### **A river of plasma**

Foster says the observations from space validate measurements from the ground. What's more, the combination of space- and ground-based data give a highly detailed picture of a natural defensive mechanism in the Earth's magnetosphere. "This higher-density, cold plasma changes about every plasma physics process it comes in contact with," Foster says. "It slows down reconnection, and it can contribute to the generation of waves that, in turn, accelerate particles in other parts of the magnetosphere. So it's a recirculation process, and really fascinating."

Foster likens this plume phenomenon to a "river of particles," and says it is not unlike the Gulf Stream, a powerful ocean current that influences the temperature and other properties of surrounding waters. On an atmospheric scale, he says, plasma particles can behave in a similar way, redistributing throughout the atmosphere to form plumes that "flow through a huge circulation system, with a lot of different consequences." "What these types of studies are showing is just how dynamic this entire system is," Foster adds.

<http://scitechdaily.com/nasas-cassini-conduct-100th-flyby-saturn-moon-titan/#rssowlmlink>

## **NASA's Cassini to Conduct Its 100th Flyby of the Saturn Moon Titan**

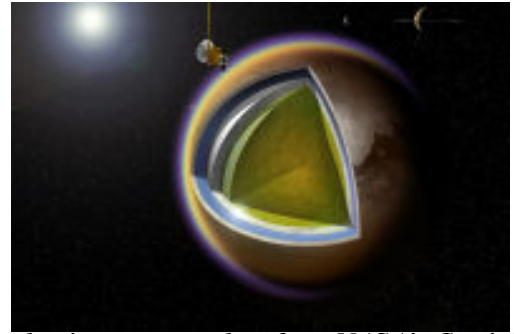
*NASA's Cassini spacecraft is ready to conduct its 100th flyby of Titan.*

Ten years ago, we knew Titan as a fuzzy orange ball about the size of Mercury. We knew it had a nitrogen atmosphere - the only known world with a thick nitrogen atmosphere besides Earth. But what might lie beneath the hazy air was still just a guess. On March 6, NASA's Cassini spacecraft will swoop down within 933 miles (1,500 kilometers) of Titan to conduct its 100th flyby of the Saturn moon. Each flyby gives us a little more knowledge of Titan and its striking similarities to our world. Even with its cold surface temperatures of minus 290 degrees Fahrenheit (94 kelvins), Titan is like early Earth in a deep freeze.

Since its 2004 arrival at Saturn, Cassini's radar instrument has identified remarkable surface features on Titan. The features include lakes and seas made of liquid methane and ethane, which are larger than North America's

Great Lakes, and an extensive layer of liquid water deep beneath the surface. Organic molecules abound in Titan's atmosphere, formed from the breakup of methane by solar radiation.

A recent innovation was the discovery that radar could be used to determine the depth of a Titan sea. "It's something we didn't think we could do before," said Michael Malaska, an affiliate of the Cassini radar team at NASA's Jet Propulsion Laboratory, Pasadena, California. "The radar can measure the depth by receiving two different bounces: one from the surface and one from the bottom of the sea. This technique was used to determine that Ligeia Mare, the second largest sea on Titan, is about 160 meters [525 feet] deep. When coupled with some laboratory experiments, it gives us information about the composition of the liquid in Ligeia Mare, too."



*This artist's concept shows a possible model of Titan's internal structure that incorporates data from NASA's Cassini spacecraft. Image Credit: A. D. Fortes/UCL/STFC*

As spring turns to summer in Titan's northern hemisphere for the first time since Cassini arrived at Saturn, scientists are looking forward to entering potentially the most exciting time for Titan weather – with waves and winds picking up. With increasing sunlight, the north polar lakes and seas can now be seen in near-infrared images, enabling scientists to learn more about their composition and giving them clues about the surrounding terrain.

"Methane is not only in the atmosphere, but probably in the crust," said Jonathan Lunine, a scientist on the Cassini mission at Cornell University, Ithaca, New York. "It's a hint there are organics not only in Titan's air and on the surface, but even in the deep interior, where liquid water exists as well. Organics are the building blocks of life, and if they are in contact with liquid water, there could be a chance of finding some form of life." Linda Spilker, Cassini project scientist at JPL, speculated on the type of life that could exist. "The astrobiological potential for Titan is two-fold," she said. "Could a unique form of methane-based life exist in Titan's liquid lakes and seas? With a global ocean of liquid water beneath its icy crust, could life exist in Titan's subsurface ocean?"

Although the official Cassini mission name for this flyby is T-99, it is, in fact, the 100th targeted Titan flyby of the mission. Why the discrepancy? An extra flyby was inserted early in the mission, after the Titan flybys had been named. For additional details on this 100th flyby, visit: <http://saturn.jpl.nasa.gov/mission/flybys/titan20140306/>.

<http://bit.ly/TjYO4rD>

## Impact Crater Origin of Mars Meteorites Discovered

*Out of the thousands of craters scarring the face of Mars, one has emerged as the likely source of most of the Martian meteorites that have been recovered on Earth, a new study shows.*

Mar 6, 2014 02:00 PM ET // by Irene Klotz

A piece of rock found its way all the way from Mars to a desert in northwest Africa. And now it has the potential to tell us all kinds of things about the Red Planet. Researchers pinpoint Mojave Crater, a 34 mile (55 kilometer) wide basin on the planet's equator, as the origin of the so-called "shergottites" meteorites, a family that includes about 75 percent of the roughly 150 known Martian meteorites. The crater is located slightly north and east of Meridian Planum, where NASA's Mars rover Opportunity landed in January 2004. Knowing where the meteorites came from would help scientists piecing together the history and evolution of Mars, the planet most like Earth in the solar system.

With clear evidence of past surface water, Mars remains a prime candidate in the search for life beyond Earth. Researchers homed in on Mojave Crater as the source of the shergottites for several reasons. First, its large size means it was created by an impact powerful enough to launch debris into space. Based on the amount of cosmic ray exposure the meteorites experience in space, scientists estimate the rocks spent 5 million years in interplanetary space before reaching Earth.

The shergottites that have cosmic ray exposures of only about 1 million years broke apart during transit, exposing fresh surfaces and new interiors to radiation, planetary scientist Stephanie Werner, with the University of Oslo in Norway, theorizes in a paper published in this week's Science.

Second, Mojave Crater is relatively young, formed from an impact that took place less than 5 million years ago on terrain that is roughly 4.3 billion years old. That's the same age, the researchers say, as when the shergottites originally crystallized. The third and final piece of evidence comes from a chemical analysis of the crater made from data collected by instruments aboard Europe's Mars Express and NASA's Mars Reconnaissance Orbiter satellites. Scientists found telltale chemical fingerprints of pyroxene and olivine in and around the crater, two minerals commonly present in the Martian meteorites.

"Only Mojave Crater combines the appropriate site mineralogy, size, and the young crater-formation age of less than 5 million years," Werner wrote in an email to Discovery News. "Additionally, the shergottite meteorites are igneous rocks which have formed at the depth of up to a few kilometers, thus most volcanic provinces can be excluded," Werner added.

Not everyone agrees with the scientists' conclusions. "The lines of evidence that they use are not widely accepted," Carl Agee, director of University of New Mexico's Institute of Meteoritics, told Discovery News. Agee points to the age of shergottites, which Werner and colleagues claim are old. "Most scientists who have studied the meteorites and done age-dating ... have data that shows they are quite young, geologically speaking," Agee said. "That's the heart of this story and that, in itself, already is a controversial position to take," he said. Combined with arguments about the chemical composition of the crater, among other factors, to conclude that it is a match "strikes me as somewhat speculative," Agee said.

<http://www.bbc.com/news/health-26466674###rssowlmlink>

### **Warning over hospital superbug linked to 16 deaths**

*Sixteen people have died in Manchester in the past four years while infected with a highly resistant superbug, figures show.*

**Michele Paduano** By Michele Paduano BBC Midlands health correspondent

Klebsiella pneumoniae carbapenemase (KPC) is causing increasing concern and a rising number of cases. Some 1,241 patients were affected within the Central Manchester University Hospitals trust area from 2009 to 2013, the figures show. Despite infection control, the numbers have increased year on year. The figures, revealed in a Freedom of Information request by the BBC, found 62 patients so far have suffered blood poisoning - with 14 confirmed deaths within 30 days of infection - at Central Manchester University Hospitals NHS Foundation Trust. Two further deaths have occurred in the current year, the hospital trust confirmed. KPC, which causes urinary tract infections and pneumonia in sick patients, is resistant to carbapenems, the last major group of antibiotics to work against multidrug-resistant bacteria.

The trust said the chemical, an enzyme, that KPC uses to render antibiotics ineffective had now entered other bacteria, including E. coli and Enterobacter. "This trust has and continues to make strenuous efforts to control and reduce this infection. We continue to work very closely with Public Health England at both a local and national level to develop solutions for the long-term management of patients," it said.

The trust stated that all the patients who had died were seriously ill. Some had diabetes, kidney problems or transplant rejection; some were suffering from leukaemia or other forms of cancer.

Central Manchester Hospitals has already had to review guidelines on antibiotics and the treatment of patients who require bowel surgery or cancer treatment that may leave their immunity compromised.

#### **'Extremely unlucky'**

Another Manchester hospital, the Christie, a specialist in cancer care, said nine patients had been colonised by KPC last year. but they had all been transferred to the cancer unit and there had been no cross-infection in the hospital. A Freedom of Information request has also revealed two cases of KPC at New Cross Hospital in Wolverhampton, with one patient dying in the past two years.

Microbiologist Dr Mike Cooper said that the patient who died was 96 and the form of KPC that had infected her was still susceptible to some drugs. "There's a huge element of luck in this. Either Manchester has been extremely unlucky or we have been extremely lucky not to have more cases," he said.

Ten patients have also been infected at the University Hospital of North Staffordshire. Two had urinary tract infections, but neither patient died of blood poisoning.

Stoke's microbiologist, George Orendi, said: "Unlike the situation in certain hospitals in Manchester and London, fortunately in our hospital and catchment area carbapenemase producers have remained rare to date."

The KPC resistance mechanism first emerged in the US and spread to Israel. In Europe, it has taken hold in Greece and has reached epidemic proportions in Italy.

Gian Maria Rossolini, of the University of Siena, said that the first case was identified in Italy in 2008, but now 4% of all infections in Italy are resistant to carbapenems.

#### **Aids epidemic**

Dr Rossolini said deaths from blood infections were running at more than 40%, but for immune-compromised patients they could be as high as 80%. Although KPC is still susceptible to an old and quite toxic antibiotic, colistin, in Florence this year more than 50% of KPC cases proved resistant to it. "Although present in the UK, the problem seems to be still much more limited as compared to Italy and Greece," he said.

Professor Laura Piddock, of Birmingham University, said: "It's clear that what has gone on in Italy is our tomorrow. We have got to start preserving what we have got and use it wisely. "If we are really serious about tackling this problem, we have to start viewing this in the same way as high-income countries viewed the Aids



epidemic in the 90s. "It's going to take that sort of level of global policymaker decision-making to really tackle this issue properly." Research published in the Journal of Antibiotics found that colonisation with KPC is long-lasting, with 39% of patients still carrying KPC in their gut a year after being released from hospital.

In Birmingham, Prof Peter Hawkey is conducting nationwide research to identify the extent of KPC resistance and that of a more widespread, but slightly less virulent superbug, ESBL.

Patients in London, Southampton, Birmingham and Shropshire are being asked to send in faeces samples so the spread of the disease can be mapped.

Prof Hawkey said: "It makes sense whilst we are looking for these ESBL that we are also able to detect how many of these KPC organisms are in the community. "I can conceive of techniques which may be able to make bacteria to kill these multidrug-resistant bacteria. It's very much at an advanced research level at the moment, but in order to drive that, we need to know how big the problem is."

Dr Rossolini said that the use of carbapenem antibiotics to control high levels of ESBL in the Midlands could actually help KPC take hold in the region.

[http://www.eurekalert.org/pub\\_releases/2014-03/ats-tap030414.php#rssowlmlink](http://www.eurekalert.org/pub_releases/2014-03/ats-tap030414.php#rssowlmlink)

### **Traffic-related air pollution associated with changes in right ventricular structure and function**

*Exposure to high levels of traffic-related air pollution may contribute to the known connection between air pollution exposure and heart disease*

Exposure to high levels of traffic-related air pollution is associated with changes in the right ventricle of the heart that may contribute to the known connection between air pollution exposure and heart disease, according to a new study. "Although the link between traffic-related air pollution and left ventricular hypertrophy, heart failure, and cardiovascular death is established, the effects of traffic-related air pollution on the right ventricle have not been well studied," said lead author Peter Leary, MD, MS, of the University of Washington Medical Center in Seattle. "Using exposure to nitrogen dioxide as a surrogate for exposure to traffic-related air pollution, we were able to demonstrate for the first time that higher levels of exposure were associated with greater right ventricular mass and larger right ventricular end-diastolic volume. Greater right ventricular mass is also associated with increased risk for heart failure and cardiovascular death."

The findings were published online ahead of print publication in the American Thoracic Society's American Journal of Respiratory and Critical Care Medicine.

The study involved 3,896 participants who were free of clinical cardiovascular disease in the Multi-Ethnic Study of Atherosclerosis and who underwent cardiac magnetic resonance imaging (MRI). Using estimated exposure to outdoor oxides of nitrogen at the homes of participants over the year preceding MRI, the authors found that increased exposure to nitrogen dioxide was associated with an approximately 1.0 g (5 percent) increase in right ventricular mass and a 4.1 mL (3%) increase in right ventricular end-diastolic volume.

These relationships remained after accounting for differences among participants in cardiovascular risk factors, left ventricular mass and volume, markers of inflammation, lung disease and socioeconomic status.

The authors note that this type of study can be limited in several ways. Specifically, estimates of air pollution exposure are not perfect and it remains possible that something related to air pollution, but not air pollution itself (known as confounding), was responsible for the association. For these reasons and others, this study cannot prove that traffic-related air pollution causes changes in the right heart, but does strongly suggest the relationship.

"The morphologic changes in the right ventricle of the heart that we found with increased exposure to nitrogen dioxide add to the body of evidence supporting a connection between traffic-related air pollution and cardiovascular disease," said Dr, Leary. "The many adverse effects of air pollution on human health support continued efforts to reduce this burden."

<http://phys.org/news/2014-03-mystery-planet-forming-disks-magnetism.html#rssowlmlink>

### **Mystery of planet-forming disks explained by magnetism**

*Astronomers say that magnetic storms in the gas orbiting young stars may explain a mystery that has persisted since before 2006.*

Phys.org - Researchers using NASA's Spitzer Space Telescope to study developing stars have had a hard time figuring out why the stars give off more infrared light than expected. The planet-forming disks that circle the young stars are heated by starlight and glow with infrared light, but Spitzer detected additional infrared light coming from an unknown source. A new theory, based on three-dimensional models of planet-forming disks, suggests the answer: Gas and dust suspended above the disks on gigantic magnetic loops like those seen on the sun absorb the starlight and glow with infrared light.

"If you could somehow stand on one of these planet-forming disks and look at the star in the center through the disk atmosphere, you would see what looks like a sunset," said Neal Turner of NASA's Jet Propulsion Laboratory, Pasadena, Calif. The new models better describe how planet-forming material around stars is stirred up, making its way into future planets, asteroids and comets.

While the idea of magnetic atmospheres on planet-forming disks is not new, this is the first time they have been linked to the mystery of the observed excess infrared light. According to Turner and colleagues, the magnetic atmospheres are similar to what takes place on the surface of our sun, where moving magnetic field lines spur tremendous solar prominences to flare up in big loops.

Stars are born out of collapsing pockets in enormous clouds of gas and dust, rotating as they shrink down under the pull of gravity. As a star grows in size, more material rains down toward it from the cloud, and the rotation flattens this material out into a turbulent disk. Ultimately, planets clump together out of the disk material.

In the 1980s, the Infrared Astronomical Satellite mission, a joint project that included NASA, began finding more infrared light than expected around young stars. Using data from other telescopes, astronomers pieced together the presence of dusty disks of planet-forming material. But eventually it became clear the disks alone weren't enough to account for the extra infrared light-especially in the case of stars a few times the mass of the sun.

One theory introduced the idea that instead of a disk, the stars were surrounded by a giant dusty halo, which intercepted the star's visible light and re-radiated it at infrared wavelengths. Then, recent observations from ground-based telescopes suggested that both a disk and a halo were needed. Finally, three-dimensional computer modeling of the turbulence in the disks showed the disks ought to have fuzzy surfaces, with layers of low-density gas supported by magnetic fields, similar to the way solar prominences are supported by the sun's magnetic field.

The new work brings these pieces together by calculating how the starlight falls across the disk and its fuzzy atmosphere. The result is that the atmosphere absorbs and re-radiates enough to account for all the extra infrared light. "The starlight-intercepting material lies not in a halo, and not in a traditional disk either, but in a disk atmosphere supported by magnetic fields," said Turner. "Such magnetized atmospheres were predicted to form as the disk drives gas inward to crash onto the growing star."

Over the next few years, astronomers will further test these ideas about the structure of the disk atmospheres by using giant ground-based telescopes linked together as interferometers. An interferometer combines and processes data from multiple telescopes to show details finer than each telescope can see alone. Spectra of the turbulent gas in the disks will also come from NASA's SOFIA telescope, the Atacama Large Millimeter/submillimeter Array (ALMA) telescope in Chile, and from NASA's James Webb Space Telescope after its launch in 2018.

<http://www.medscape.com/viewarticle/821635?src=rss>

### **NY's Mount Sinai a Lucrative PCI 'Factory' in News Report**

***Bloomberg news report digs into a hospital's drive for revenue and an edge in a rough urban market, raising questions about practices contributing to an image of the center as a "heart-surgery factory"***

Steve Stiles

NEW YORK, NY - A Bloomberg news report digs into the world of a top New York City hospital's drive for revenue and a competitive edge in a rough urban market, raising questions about practices that contribute to an image of the center as what is called a "heart-surgery factory"[1]. They include alleged case-volume-driven pay structures for interventional cardiologists, some of whom are "obscenely" well paid; stories about patients presenting to the emergency department for "acute" symptoms but who are already scheduled for the cardiac-catheterization laboratory; and the appropriateness of some procedures given its vast cath-lab volumes.

"No one has publicly accused Mount Sinai of doing anything wrong," notes the story from Bloomberg reporters David Armstrong, Peter Waldman, and Gary Putka. And there is a glowing appraisal of the Mount Sinai interventional cardiologists from highly regarded Los Angeles cardiologist Dr Sanjay Kaul (Cedars-Sinai Hospital). The story is more of an exposé of the apparent role of money in driving practice at the hospital, which it says has by far the highest interventional case volume of any hospital in the NY region.

"Hospital records show that the lab's compensation system for doctors incentivizes more procedures," according to the story. Its massive case volume owes to "thousands of patient referrals each year from a network of affiliated doctors in private practice. Among the most prolific referrers are doctors who've had financial arrangements with Mount Sinai, including agreements allowing the hospital to use their offices for a fee, according to documents reviewed by Bloomberg News."

The story describes Dr Eliscer Guzman as such a doctor, one of several cardiologists on whom the story shines a spotlight. He is said to have referred 471 patients to the Mount Sinai cath lab in 2010, "more than 23 times the average of all referring physicians that year, hospital documents show."

It continues, "Mount Sinai's dealings with Guzman also included negotiations over an employment contract for him in 2007 and a plan for the hospital to sponsor a local television show that featured the doctor."

Also garnering attention is Mount Sinai director of interventional cardiology Dr Samin Sharma, reputed to perform "more complex coronary interventions than any cardiologist in the country" and whom the hospital paid \$4.8 million in 2010, according to the story, citing tax documents. "Under Sharma's leadership, Mount Sinai's cath lab grew among some of the stiffest competition in the US," said a former member of the hospital's cath-lab personnel.

Among the story's most vivid images: 10 patients presenting to the emergency department over two Sundays in 2012 who said "they'd been instructed to arrive there before their cath-lab appointments, according to internal hospital correspondence. Two of them said they'd been coached to say they were having acute symptoms of heart disease."

Mount Sinai's cath lab, the story says, "has regularly scheduled such emergencies-by-appointment, according to three doctors and another medical professional, all of whom said they had direct knowledge of the practice." Hospital records further suggested that "reports of scheduled ER visits raised a concern internally that some cardiologists might be using the emergency department to get the costs of uninsured patients' procedures covered."

*Armstrong D, Waldman P, and Putka G. In New York, a heart surgery factory with 'obscene levels' of pay. Bloomberg News, March 6, 2014. [Available here.](#)*

<http://www.medscape.com/viewarticle/821688?src=rss>

### **Study: PAs, NPs Do Better Job of Health Education Than Docs**

*Nurses and physician assistants (PAs) are more likely than physicians to offer tips on healthy living to patients with chronic illnesses during office visits, a new study shows, although none of the 3 providers do it regularly.*

**Megan Brooks**

Health education provided to patients with asthma, diabetes, and other chronic illnesses can help them live a healthier life, but who provides this information during office visits, and how often? Few studies have looked at this issue.

Tamara S. Ritsema, MPH, MMSc, PA-C, from the University of Nebraska Medical Center in Omaha, and colleagues evaluated the rate of health education provision by physicians, PAs, and nurse practitioners (NPs). The researchers used data from the National Hospital Ambulatory Medical Care Survey spanning 2005 to 2009 on 136,432 adult patient office visits for 9 chronic conditions: asthma, chronic obstructive pulmonary disease (COPD), depression, diabetes, hyperlipidemia, hypertension, ischemic heart disease, and obesity.

They analyzed the provision of education (by provider type) on asthma, diet/nutrition, exercise, stress management, tobacco use and exposure, and weight loss. The study was published online March 6 in *Preventing Chronic Disease*, a publication of the Centers for Disease Control and Prevention.

The researchers report that health education was not routinely provided to patients with chronic conditions. In fact, they say rates of health education provision "in general are low." "The percentage of visits in which patients received health education did not reach 50% for any combination of health education and provider type," the investigators report.

The percentage of patients who did receive health advice on their chronic condition ranged from 13.0% (patients with COPD or asthma who were provided education on smoking cessation by nurse practitioners) to 42.2% (patients with diabetes or obesity who were provided education on exercise by physician assistants). In general, PAs and NPs offered health education specific to the patient's chronic condition more often than did physicians. NPs also were more apt to counsel patients on diet or nutrition (odds ratio [OR], 1.60) and stress management (OR, 2.68) than either physicians or PAs. PAs were more likely to provide counseling on tobacco use and exposure (OR, 3.62) for patients with COPD and asthma than were physicians or NPs. PAs and NPs also were more apt to counsel on exercise (OR, 3.42 and 1.72, respectively) and losing weight (OR, 2.50 and 1.96) than were physicians.

Ritsema and colleagues say it is unclear why PAs and NPs provide more health education than physicians, and their study cannot address this. Possible explanations include training differences, differing roles within a clinic by provider type, or increased clinical demands on physicians.

If physicians do not have the time, interest, or skill in providing health education to their patients, "our study may argue for increasing the mix of providers in outpatient clinics," the investigators suggest.

They say more research is needed to determine what is behind differences they uncovered and identify potential opportunities to increase the delivery of health education to patients. They suggest policymakers "consider increasing incentives for providers to deliver chronic condition-specific health education."

[Prev Chronic Dis. 2014;11:130175.](#)

[http://www.eurekalert.org/pub\\_releases/2014-03/gumc-bti030314.php#rssowlmlink](http://www.eurekalert.org/pub_releases/2014-03/gumc-bti030314.php#rssowlmlink)

### **Blood test identifies those at-risk for cognitive decline, Alzheimer's within 3 years**

***Researchers have discovered and validated a blood test that can predict with greater than 90 percent accuracy if a healthy person will develop mild cognitive impairment or Alzheimer's disease within three years.***

WASHINGTON - Described in Nature Medicine published online today, the study heralds the potential for developing treatment strategies for Alzheimer's at an earlier stage, when therapy would be more effective at slowing or preventing onset of symptoms. It is the first known published report of blood-based biomarkers for preclinical Alzheimer's.

The test identifies 10 lipids, or fats, in the blood that predict disease onset. It could be ready for use in clinical studies in as few as two years and, researchers say, other diagnostic uses are possible.

"Our novel blood test offers the potential to identify people at risk for progressive cognitive decline and can change how patients, their families and treating physicians plan for and manage the disorder," says the study's corresponding author Howard J. Federoff, MD, PhD, professor of neurology and executive vice president for health sciences at Georgetown University Medical Center.

There is no cure or effective treatment for Alzheimer's. Worldwide, about 35.6 million individuals have the disease and, according to the World Health Organization, the number will double every 20 years to 115.4 million people with Alzheimer's by 2050.

Federoff explains there have been many efforts to develop drugs to slow or reverse the progression of Alzheimer's disease, but all of them have failed. He says one reason may be the drugs were evaluated too late in the disease process.

"The preclinical state of the disease offers a window of opportunity for timely disease-modifying intervention," Federoff says. "Biomarkers such as ours that define this asymptomatic period are critical for successful development and application of these therapeutics."

The study included 525 healthy participants aged 70 and older who gave blood samples upon enrolling and at various points in the study. Over the course of the five-year study, 74 participants met the criteria for either mild Alzheimer's disease (AD) or a condition known as amnesic mild cognitive impairment (aMCI), in which memory loss is prominent. Of these, 46 were diagnosed upon enrollment and 28 developed aMCI or mild AD during the study (the latter group called converters).

In the study's third year, the researchers selected 53 participants who developed aMCI/AD (including 18 converters) and 53 cognitively normal matched controls for the lipid biomarker discovery phase of the study. The lipids were not targeted before the start of the study, but rather, were an outcome of the study.

A panel of 10 lipids was discovered, which researchers say appears to reveal the breakdown of neural cell membranes in participants who develop symptoms of cognitive impairment or AD. The panel was subsequently validated using the remaining 21 aMCI/AD participants (including 10 converters), and 20 controls. Blinded data were analyzed to determine if the subjects could be characterized into the correct diagnostic categories based solely on the 10 lipids identified in the discovery phase.

"The lipid panel was able to distinguish with 90 percent accuracy these two distinct groups: cognitively normal participants who would progress to MCI or AD within two to three years, and those who would remain normal in the near future," Federoff says.

The researchers examined if the presence of the APOE4 gene, a known risk factor for developing AD, would contribute to accurate classification of the groups, but found it was not a significant predictive factor in this study.

"We consider our results a major step toward the commercialization of a preclinical disease biomarker test that could be useful for large-scale screening to identify at-risk individuals," Federoff says. "We're designing a clinical trial where we'll use this panel to identify people at high risk for Alzheimer's to test a therapeutic agent that might delay or prevent the emergence of the disease."

*In addition to Federoff, study authors include Amrita K. Cheema, Massimo S. Fiandaca, Xiaogang Zhong, Timothy R. Mhyre, Linda H. MacArthur and Ming T. Tan of Georgetown; Mark Mapstone, William J. Hall and Derick R. Peterson of the University of Rochester School of Medicine; Susan G. Fisher of Temple University School of Medicine; James M. Haley and Michael D. Nazar of Unity Health System in Rochester; Steven A. Rich of Rochester General Hospital; Dan J. Berlau, of Regis University School of Pharmacy in Denver; and Carrie B. Peltz and Claudia H. Kawas of the University of California-Irvine.*



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*Federoff, Mapstone, Cheema and Fiandaca are named as co-inventors on a patent application that has been filed by Georgetown University and the University of Rochester related to the technology described. The other authors report no related financial interests.*

[http://www.eurekalert.org/pub\\_releases/2014-03/uoefao030614.php#rsslmlink](http://www.eurekalert.org/pub_releases/2014-03/uoefao030614.php#rsslmlink)

### **First animals oxygenated the ocean, study suggests**

***The evolution of the first animals may have oxygenated the earth's oceans – contrary to the traditional view that a rise in oxygen triggered their development.***

New research led by the University of Exeter contests the long held belief that oxygenation of the atmosphere and oceans was a pre-requisite for the evolution of complex life forms.

The study, published today in the leading journal *Nature Geoscience*, builds on the recent work of scientists in Denmark who found that sponges – the first animals to evolve – require only small amounts of oxygen.

Professor Tim Lenton of the University of Exeter, who led the new study, said: "There had been enough oxygen in ocean surface waters for over 1.5 billion years before the first animals evolved, but the dark depths of the ocean remained devoid of oxygen. We argue that the evolution of the first animals could have played a key role in the widespread oxygenation of the deep oceans. This in turn may have facilitated the evolution of more complex, mobile animals."

The researchers considered mechanisms by which the deep ocean could have been oxygenated during the Neoproterozoic Era (from 1,000 to 542 million years ago) without requiring an increase in atmospheric oxygen. Crucial to determining oxygen levels in the deep ocean is the balance of oxygen supply and demand. Demand for oxygen is created by the sinking of dead organic material into the deep ocean. The new study argues that the first animals reduced this supply of organic matter – both directly and indirectly.

Sponges feed by pumping water through their bodies, filtering out tiny particles of organic matter from the water, and thus helping oxygenate the shelf seas that they live in. This naturally selects for larger phytoplankton – the tiny plants of the ocean – which sink faster, also reducing oxygen demand in the water.

By oxygenating more of the bottom waters of shelf seas, the first filter-feeding animals inadvertently increased the removal of the essential nutrient phosphorus in the ocean. This in turn reduced the productivity of the whole ocean ecosystem, suppressing oxygen demand and thus oxygenating the deep ocean.

A more oxygen-rich ocean created ideal conditions for more mobile animals to evolve, because they have a higher requirement for oxygen. These included the first predatory animals with guts that started to eat one another, marking the beginning of a modern marine biosphere, with the type of food webs we are familiar with today.

Professor Lenton added: "The effects we predict suggest that the first animals, far from being a passive response to rising atmospheric oxygen, were the active agents that oxygenated the ocean around 600 million years ago. They created a world in which more complex animals could evolve, including our very distant ancestors."

Professor Simon Poulton of the University of Leeds, who is a co-author of the study, added: "This study provides a plausible mechanism for ocean oxygenation without the requirement for a rise in atmospheric oxygen. It therefore questions whether the long-standing belief that there was a major rise in atmospheric oxygen at this time is correct. We simply don't know the answer to this at present, which is ultimately key to understanding how our planet evolved to its current habitable state. Geochemists need to come up with new ways to decipher oxygen levels on the early Earth."

*The article, 'Co-evolution of Eukaryotes and Ocean Oxygenation in the Neoproterozoic' by Timothy M. Lenton, Richard A. Boyle, Simon W. Poulton, Graham A. Shields-Zhou and Nicholas J. Butterfield is published in Nature Geoscience doi: 10.1038/ngeo2108*

<http://phys.org/news/2014-03-dinosaur-killing-impact-acidified-oceans.html#rsslmlink>

### **Dinosaur-killing impact acidified oceans: study**

***The space rock that smashed into Earth 65 million years ago, famously wiping out the dinosaurs, unleashed acid rain that turned the ocean surface into a witches' brew, researchers said Sunday.***

11 hours ago by Richard Ingham

Delving into the riddle of Earth's last mass extinction, Japanese scientists said the impact instantly vaporised sulphur-rich rock, creating a vast cloud of sulphur trioxide (SO<sub>3</sub>) gas. This mixed with water vapour to create sulphuric acid rain, which would have fallen to the planet's surface within days, acidifying the surface levels of the ocean and killing life therein. Those species that were able to survive beneath this lethal layer eventually inherited the seas, according to the study which did not delve into the effects on land animals.

"Concentrated sulphuric acid rains and intense ocean acidification by SO<sub>3</sub>-rich impact vapours resulted in severe damage to the global ecosystem and were probably responsible for the extinction of many species," the study said.

The great smashup is known as the Cretaceous-Tertiary extinction. It occurred when an object, believed to be an asteroid some 10 kilometres (six miles) wide, whacked into the Yucatan peninsula in modern-day Mexico. It left a crater 180 kilometres (110 miles) wide, ignited a firestorm and kicked up a storm of dust that was driven around the world on high winds, according to the mainstream scenario.

Between 60 and 80 percent of species on Earth were wiped out, according to fossil surveys. Large species suffered especially: dinosaurs which had roamed the land for some 165 million years, were replaced as the terrestrial kings by mammals.

### **Extinction riddle**

Much speculation has been devoted to precisely how the mass die-out happened. A common theory is that a "nuclear winter" occurred - the dust pall prevented sunlight reaching the surface, causing vegetation to shrivel and die, and dooming the species that depended on them. Another, fiercely debated, idea adds acid rain to the mix. Critics say the collision was far likelier to have released sulphur dioxide (SO<sub>2</sub>) than SO<sub>3</sub>, the culprit chemical in acid rain. And, they argue, it would have lingered in the stratosphere rather than fallen back to Earth.

Seeking answers, a team led by Sohsuke Ohno of the Planetary Exploration Research Centre in Chiba set up a special lab rig to replicate—on a tiny scale—what happened that fateful day.

They used a laser beam to vaporise a strand of plastic, which released a high-speed blast of plasma and caused a tiny piece of foil, made of the heavy metal tantalum, to smash into a sample of rock. The heavy foil fragment replicated on a minuscule scale the mass of the asteroid, while the rock was of a similar makeup as the surface where the asteroid struck.

The team caused collisions ranging from 13 to 25 km per second (47,000-90,000 km or 29,000-55,000 miles per hour), and analysed the gas that was released. The research, reported in the journal *Nature Geoscience*, showed that SO<sub>3</sub> was by far the dominant molecule, not SO<sub>2</sub>.

The team also carried out a computer simulation of larger silicate particles that would have been ejected by the impact, and found they too played a part. The particles rapidly bound with the poisonous vapour to become sulphuric acid "aerosols" that fell to the surface. Heavily acidic waters would explain the overwhelming extinction among surface species of plankton called foraminifera. Foraminifera are single-celled creatures protected by a calcium carbonate shell, which dissolves in acidic water.

The "acid rain" scenario also helps explain other extinction riddles, including why there was a surge in the number of fern species after the impact. Ferns love acidic, water-logged conditions such as those described in the study.