

<http://bit.ly/2CXJOru>

Alzheimer's drug turns back clock in powerhouse of cell
J147 has been shown to treat Alzheimer's disease and reverse aging in mice and is almost ready for clinical trials in humans

LA JOLLA - The experimental drug J147 is something of a modern elixir of life; it's been shown to treat Alzheimer's disease and reverse aging in mice and is almost ready for clinical trials in humans.

Now, Salk scientists have solved the puzzle of what, exactly, J147 does. In a paper published January 7, 2018, in the journal *Aging Cell*, they report that the drug binds to a protein found in mitochondria, the energy-generating powerhouses of cells. In turn, they showed, it makes aging cells, mice and flies appear more youthful.

"This really glues together everything we know about J147 in terms of the link between aging and Alzheimer's," says Dave Schubert, head of Salk's Cellular Neurobiology Laboratory and the senior author on the new paper. "Finding the target of J147 was also absolutely critical in terms of moving forward with clinical trials."

Schubert's group developed J147 in 2011, after screening for compounds from plants with an ability to reverse the cellular and molecular signs of aging in the brain. J147 is a modified version of a molecule (curcumin) found in the curry spice turmeric. In the years since, the researchers have shown that the compound [reverses memory deficits, potentiates the production of new brain cells, and slows or reverses Alzheimer's progression in mice](#). However, they didn't know how J147 worked at the molecular level.

In the new work, led by Schubert and Salk Research Associate Josh Goldberg, the team used several approaches to home in on what J147 is doing. They identified the molecular target of J147 as a mitochondrial protein called ATP synthase that helps generate ATP--the cell's energy currency--within mitochondria. They showed that by manipulating its activity, they could protect neuronal cells from multiple toxicities associated with the aging brain.

Moreover, ATP synthase has already been shown to control aging in *C. elegans* worms and flies.

"We know that age is the single greatest contributing factor to Alzheimer's, so it is not surprising that we found a drug target that's also been implicated in aging," says Goldberg, the paper's first author.

Further experiments revealed that modulating activity of ATP synthase with J147 changes the levels of a number of other molecules--including levels of ATP itself--and leads to healthier, more stable mitochondria throughout aging and in disease.

"I was very surprised when we started doing experiments with how big of an effect we saw," says Schubert. "We can give this to old mice and it really elicits profound changes to make these mice look younger at a cellular and molecular level."

The results, the researchers say, are not only encouraging for moving the drug forward as an Alzheimer's treatment, but also suggest that J147 may be useful in other age-associated diseases as well.

"People have always thought that you need separate drugs for Alzheimer's, Parkinson's, and stroke" says Schubert. "But it may be that by targeting aging we can treat or slow down many pathological conditions that are old age-associated."

The team is already performing additional studies on the molecules that are altered by J147's effect on the mitochondrial ATP synthase--which could themselves be new drug targets. J147 has completed the FDA-required toxicology testing in animals, and funds are being sought to initiate phase 1 clinical trials in humans.

Other researchers on the study were A. Currais, M. Prior, W. Fischer, C. Chiruta, D. Daugherty, R. Dargusch and P. Maher of the Salk Institute; E. Ratliff and K. Finley of San Diego State University; P.B. Esparza-Molto and J.M. Cuezva of the Universidad Autonoma de Madrid; and M. Petrascheck of The Scripps Research Institute.

The work and the researchers involved were supported by grants from the National Institutes of Health, California Institute of Regenerative Medicine, the Nomis Foundation, the Della Thome Foundation, the Bundy Foundation, the Hewitt Foundation, the Paul F. Glenn Center for Aging Research at the Salk Institute and the Waitt Foundation.

<http://bit.ly/2r4fsSm>

General anesthetics do more than put you to sleep

A new understanding of the complex ways in which general anaesthetics act on the brain could eventually lead to improved drugs for surgery.

It remains unclear how general anaesthesia works, even though it is one of the most common medical procedures worldwide.

University of Queensland researcher, Associate Professor Bruno van Swinderen, said his team had overturned previous understanding of what general anaesthetics do to the brain, finding the drugs did much more than induce sleep. "We looked at the effects of propofol - one of the most common general anaesthetic drugs used during surgery - on synaptic release," the UQ Queensland Brain Institute scientist said.

Synaptic release is the mechanism by which neurons - or nerve cells - communicate with each other. "We know from previous research that general anaesthetics including propofol act on sleep systems in the brain, much like a sleeping pill," Associate Professor van Swinderen said.

"But our study found that propofol also disrupts presynaptic mechanisms, probably affecting communication between neurons across the entire brain in a systematic way that differs from just being asleep. In this way it is very different than a sleeping pill."

PhD student Adekunle Bademosi said the discovery shed new light on how general anaesthetics worked on the brain.

"We found that propofol restricts the movement of a key protein (syntaxin1A) required at the synapses of all neurons. This restriction leads to decreased communication between neurons in the brain," he said.

Associate Professor van Swinderen said the finding contributed to understanding how general anaesthetics worked, and could explain why people experienced grogginess and disorientation after coming out of surgery. "We think that widespread disruption to synaptic connectivity - the brain's communication pathways - is what makes surgery possible, although effective anaesthetics such as propofol do put you to sleep

first," he said. "The discovery has implications for people whose brain connectivity is vulnerable, for example in children whose brains are still developing or for people with Alzheimer's or Parkinson's disease.

"It has never been understood why general anaesthesia is sometimes problematic for the very young and the old. This newly discovered mechanism may be a reason."

Associate Professor van Swinderen said more research was needed to determine if general anaesthetics had any lasting effects in these vulnerable groups of people.

"Studying these effects in model systems such as rats and flies allows us to address these questions by manipulating the likely mechanisms involved, which we can't do in humans."

The research involved Professor Frederic Meunier's laboratory at QBI, where super-resolution microscopy techniques enabled the researchers to understand how the anaesthetic worked on single cells. Dr Victor Anggono, whose laboratory at QBI focusses on synaptic mechanisms, was a partner in the study.

The research is published in Cell Reports. [http://www.cell.com/cell-reports/fulltext/S2211-1247\(17\)31878-8](http://www.cell.com/cell-reports/fulltext/S2211-1247(17)31878-8)

<http://bit.ly/2D0rFcm>

Planets around other stars are like peas in a pod

Pattern suggests most planetary systems have a different formation history than the solar system

An international research team led by Université de Montréal astrophysicist Lauren Weiss has discovered that exoplanets orbiting the same star tend to have similar sizes and a regular orbital spacing. This pattern, revealed by new W. M. Keck Observatory observations of planetary systems discovered by the Kepler Telescope, could suggest that most planetary systems have a different formation history than the solar system.

Thanks in large part to the NASA Kepler Telescope, launched in 2009, many thousands of exoplanets are now known. This large sample allows researchers to not only study individual systems, but also to draw

conclusions on planetary systems in general. Dr. Weiss is part of the California Kepler Survey team, which used the W. M. Keck Observatory on Maunakea in Hawaii, to obtain high-resolution spectra of 1305 stars hosting 2025 transiting planets originally discovered by Kepler. From these spectra, they measured precise sizes of the stars and their planets.

In this new analysis led by Weiss and published in *The Astronomical Journal*, the team focused on 909 planets belonging to 355 multi-planet systems. These planets are mostly located between 1,000 and 4,000 light-years away from Earth. Using a statistical analysis, the team found two surprising patterns. They found that exoplanets tend to be the same sizes as their neighbors. If one planet is small, the next planet around that same star is very likely to be small as well, and if one planet is big, the next is likely to be big. They also found that planets orbiting the same star tend to have a regular orbital spacing.

"The planets in a system tend to be the same size and regularly spaced, like peas in a pod. These patterns would not occur if the planet sizes or spacings were drawn at random." explains Weiss.

The similar sizes and orbital spacing of planets have implications for how most planetary systems form. In classic planet formation theory, planets form in the protoplanetary disk that surrounds a newly formed star. The planets might form in compact configurations with similar sizes and a regular orbital spacing, in a manner similar to the newly observed pattern in exoplanetary systems. However, in our solar system, the inner planets have surprisingly large spacing and diverse sizes. Abundant evidence in the solar system suggests that Jupiter and Saturn disrupted our system's early structure, resulting in the four widely-spaced terrestrial planets we have today. That planets in most systems are still similarly sized and regularly spaced suggests that perhaps they have been mostly undisturbed since their formation.

To test that hypothesis, Weiss is conducting a new study at the Keck Observatory to search for Jupiter analogs around Kepler's multi-planet systems. The planetary systems studied by Weiss and her team have

multiple planets quite close to their star. Because of the limited duration of the Kepler Mission, little is known about what kind of planets, if any, exist at larger orbital distances around these systems. They hope to test how the presence or absence of Jupiter-like planets at large orbital distances relate to patterns in the inner planetary systems.

Regardless of their outer populations, the similarity of planets in the inner regions of extrasolar systems requires an explanation. If the deciding factor for planet sizes can be identified, it might help determine which stars are likely to have terrestrial planets that are suitable for life.

About the study

The article "The California-Kepler Survey V. Peas in a Pod: Planets in a Kepler Multi-planet System are Similar in Size and Regularly Spaced" is published in The Astronomical Journal. It was funded by the Trotter Family Foundation. In addition to Lauren M. Weiss (Institute for research on exoplanets iREx, Université de Montréal), the team includes Benjamin J. Fulton (Caltech, University of Hawaii), Erik A. Petigura (Caltech), Andrew W. Howard (Caltech), Howard Isaacson (UC Berkeley), Geoffrey W. Marcy (UC Berkeley), Phillip A. Cargile (Harvard), Leslie Hebb (Hobart and William Smith Colleges), Timothy D. Morton (Princeton), Evan Sinukoff (University of Hawaii, Caltech), Ian J. M. Crossfield (University of California, Santa Cruz) and Lea A. Hirsch (Caltech).

<http://bit.ly/2D9yAn9>

Hereditary facial features could be strongly influenced by a single gene variant

Variations in singular genes that have a large impact on human facial features

Do you have your grandmother's eyes? Or your father's nose?

A new study by the Universities of Oxford and Surrey has uncovered variations in singular genes that have a large impact on human facial features, paving the way to understanding what determines the facial characteristics passed on from generation to generation.

The study, which has been [published by Proceedings of the National Academy of Sciences](#), found that a single gene variant can have a large and specific effect on a person's facial features and highlighted three such examples of genetic variants.

The Centre for Vision, Speech, Signal and Processing (CVSSP) at the University of Surrey worked with Sir Walter Bodmer, Dr Dan Crouch and colleagues from the University of Oxford to analyse over 3,000 faces of participants from the People of the British Isles project, twins from the St Thomas's Hospital TwinsUK project and East Asian volunteers.

The images were taken and processed using a state-of-the-art 3dMD camera and software.

The team then registered each face image against a generic model using 14 manually annotated facial landmarks, such as the tip of the nose or the corner of the eyes, and used a series of algorithms to extract face shape information.

Using the facial analysis, the University of Oxford identified two genetic variants tied to facial profiles in females and one variant tied to shape features around the eyes in both males and females.

One variant was linked to a gene that is involved in regulating steroid biosynthesis and another may have a role in mucopolysaccharidosis type IV, a condition that occasionally involves facial dysmorphism.

Sir Walter Bodmer from the University of Oxford said: "Facial similarities tend to run in families, and genetically identical twins raised together or apart exhibit striking facial resemblances, suggesting overwhelmingly genetic control of human facial features. This new study brings us a step closer to understanding the role genetics plays in determining facial features - which is such an important part of our everyday human interactions."

Professor Josef Kittler from the University of Surrey said: "This is another example of how machine intelligence can have a positive impact and contribution to scientific discovery. We are delighted to have assisted Sir Walter and his colleagues on this project, and we look forward to future collaborations."

<http://bit.ly/2mAv1fY>

Want to make money with stocks? Never ever listen to analysts

Research by Nicola Gennaioli and colleagues shows that investing in the stocks least favored by analysts yields five times more than buying the most recommended. Here's why

Investors probably expect that following the suggestions of stock analysts would make them better off than doing the exact opposite. Nevertheless, recent research by Nicola Gennaioli and colleagues shows that the best way to gain excess-returns would be to invest in the shares least favored by analysts. They compute that, during the last thirty-five years, investing in the 10% of U.S. stocks analysts were most optimistic about would have yielded on average 3% a year. By contrast, investing in the 10% of stocks analysts were most pessimistic about would have yielded a staggering 15% a year.

Gennaioli and colleagues shed light on this puzzle with the help of cognitive sciences and, in particular, using Kahneman and Tversky's concept of representativeness. Decision makers, according to this view, overweight the representative features of a group or a phenomenon. These are defined as the features that occur more frequently in that group than in a baseline reference group.

After observing strong earnings growth - the explanation goes - analysts think that the firm may be the next Google. "Googles" are in fact more frequent among firms experiencing strong growth, which makes them representative. The problem is that "Googles" are very rare in absolute terms. As a result, expectations become too optimistic, and future performance disappoints. A model of stock prices in which investor beliefs follow this logic can account both qualitatively and quantitatively for the beliefs of analysts and the dynamics of stock returns.

In related work, the authors show that the same model can account for booms and busts in the volume of credit and interest rate spreads.

These works are part of a research project financed by the European Research Council aimed at taking robust insights from cognitive sciences and at incorporating them into economic models. Kahneman and Tversky's concept of representativeness lies at the heart of this effort.

"In a classical example, we tend to think of Irishmen as redheads because red hair is much more frequent among Irishmen than among the rest of the world", Prof. Gennaioli says. "Nevertheless, only 10% of Irishmen are redheads. In our work, we develop models of belief formation that embody this logic and study the implication of this important psychological force in different domains".

Representativeness helps describe expectations and behavior in different domains, not only in financial markets. One such domain is the formation of stereotypes about social groups. In a recent experimental paper, Gennaioli and colleagues show that representativeness can explain self-confidence, and in particular the unwillingness of women to compete in traditionally male subjects, such as mathematics. A slight prevalence of exceptional male math ability in the data is enough to make math ability un-representative for women, driving their exaggerated under-confidence in this particular subject.

Pedro Bordalo, Nicola Gennaioli, Rafael La Porta, Andrei Shleifer, Diagnostic Expectations and Stock Returns, working paper.

Pedro Bordalo, Nicola Gennaioli, Andrei Shleifer, Diagnostic Expectations and Credit Cycles, forthcoming in The Journal of Finance.

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<http://bit.ly/2D2B9Eq>

Extraterrestrial Hypatia stone rattles solar system status quo

'Hypatia' stone not part of any known types of meteorite or comet

In 2013, researchers announced that a pebble found in south-west Egypt, was definitely not from Earth. By 2015, other research teams had

announced that the 'Hypatia' stone was not part of any known types of meteorite or comet, based on noble gas and nuclear probe analyses.

(The stone was named Hypatia after Hypatia of Alexandria, the first Western woman mathematician and astronomer).

However, if the pebble was not from Earth, what was its origin and could the minerals in it provide clues on where it came from? [Micro-mineral analyses](#) of the pebble by the original research team at the University of Johannesburg have now provided unsettling answers that spiral away from conventional views of the material our solar system was formed from.

Mineral structure

The internal structure of the Hypatia pebble is somewhat like a fruitcake that has fallen off a shelf into some flour and cracked on impact, says [Prof Jan Kramers](#), lead researcher of the study published in *Geochimica et Cosmochimica Acta* on 28 Dec 2017.

"We can think of the badly mixed dough of a fruit cake representing the bulk of the Hypatia pebble, what we called two mixed 'matrices' in geology terms. The glace cherries and nuts in the cake represent the mineral grains found in Hypatia 'inclusions'. And the flour dusting the cracks of the fallen cake represent the 'secondary materials' we found in the fractures in Hypatia, which are from Earth," he says.

The original extraterrestrial rock that fell to Earth must have been at least several meters in diameter, but disintegrated into small fragments of which the Hypatia stone is one.

Weird matrix

Straight away, the Hypatia mineral matrix (represented by fruitcake dough), looks nothing like that of any known meteorites, the rocks that fall from space onto Earth every now and then.

"If it were possible to grind up the entire planet Earth to dust in a huge mortar and pestle, we would get dust with on average a similar chemical composition as chondritic meteorites," says Kramers. "In chondritic meteorites, we expect to see a small amount of carbon{C} and a good

amount of silicon (Si). But Hypatia's matrix has a massive amount of carbon and an unusually small amount of silicon."

"Even more unusual, the matrix contains a high amount of very specific carbon compounds, called polyaromatic hydrocarbons, or PAH, a major component of interstellar dust, which existed even before our solar system was formed. Interstellar dust is also found in comets and meteorites that have not been heated up for a prolonged period in their history," adds Kramers.

In another twist, most (but not all) of the PAH in the Hypatia matrix has been transformed into diamonds smaller than one micrometer, which are thought to have been formed in the shock of impact with the Earth's atmosphere or surface. These diamonds made Hypatia resistant to weathering so that it is preserved for analysis from the time it arrived on Earth.

Weirder grains never found before

When researcher [Georgy Belyanin](#) analyzed the mineral grains in the inclusions in Hypatia, (represented by the nuts and cherries of a fruitcake), a number of most surprising chemical elements showed up. "The aluminum occurs in pure metallic form, on its own, not in a chemical compound with other elements. As a comparison, gold occurs in nuggets, but aluminum never does. This occurrence is extremely rare on Earth and the rest of our solar system, as far as is known in science," says Belyanin.

"We also found silver iodine phosphide and moissanite (silicon carbide) grains, again in highly unexpected forms. The grains are the first documented to be found in situ (as is) without having to first dissolve the surrounding rock with acid," adds Belyanin. "There are also grains of a compound consisting of mainly nickel and phosphorus, with very little iron; a mineral composition never observed before on Earth or in meteorites," he adds.

Dr Marco Andreoli, a Research Fellow at the School of Geosciences at the University of the Witwatersrand, and a member of the Hypatia research team says, "When Hypatia was first found to be extraterrestrial,

it was a sensation, but these latest results are opening up even bigger questions about its origins".

Unique minerals in our solar system

Taken together, the ancient unheated PAH carbon as well as the phosphides, the metallic aluminum, and the moissanite suggest that Hypatia is an assembly of unchanged pre-solar material. That means, matter that existed in space before our Sun, the Earth and the other planets in our solar system were formed.

Supporting the pre-solar concept is the weird composition of the nickel-phosphorus-iron grains found in the Hypatia inclusions. These three chemical elements are interesting because they belong to the subset of chemical elements heavier than carbon and nitrogen which form the bulk of all the rocky planets.

"In the grains within Hypatia the ratios of these three elements to each other are completely different from that calculated for the planet Earth or measured in known types of meteorites. As such these inclusions are unique within our solar system," adds Belyanin.

"We think the nickel-phosphorus-iron grains formed pre-solar, because they are inside the matrix, and are unlikely to have been modified by shock such as collision with the Earth's atmosphere or surface, and also because their composition is so alien to our solar system", he adds.

"Was the bulk of Hypatia, the matrix, also formed before our solar system? Probably not, because you need a dense dust cloud like the solar nebula to coagulate large bodies" he says.

A different kind of dust

Generally, science says that our solar system's planets ultimately formed from a huge, ancient cloud of interstellar dust (the solar nebula) in space. The first part of that process would be much like dust bunnies coagulating in an unswept room. Science also holds that the solar nebula was homogenous, that is, the same kind of dust everywhere.

But Hypatia's chemistry tugs at this view. "For starters, there are no silicate minerals in Hypatia's matrix, in contrast to chondritic meteorites (and planets like the Earth, Mars and Venus), where silicates are

dominant. Then there are the exotic mineral inclusions. If Hypatia itself is not presolar, both features indicate that the solar nebula wasn't the same kind of dust everywhere - which starts tugging at the generally accepted view of the formation of our solar system", says Kramers.

Into the future

"What we do know is that Hypatia was formed in a cold environment, probably at temperatures below that of liquid nitrogen on Earth (-196 Celsius). In our solar system it would have been way further out than the asteroid belt between Mars and Jupiter, where most meteorites come from. Comets come mainly from the Kuiper Belt, beyond the orbit of Neptune and about 40 times as far away from the sun as we are. Some come from the Oort Cloud, even further out. We know very little about the chemical compositions of space objects out there. So our next question will dig further into where Hypatia came from," says Kramers. The little pebble from the Libyan Desert Glass strewn field in southwest Egypt presents a tantalizing piece for an extraterrestrial puzzle that is getting ever more complex.

The research was funded by University of Johannesburg Research council via the PPM Research Centre.

The researchers would like to thank Aly Barakat, Mario di Martino and Romano Serra for access to the Hypatia sample material; and Michael Wiedenbeck and his co-workers at the Geoforschungszentrum Potsdam, Germany for their collaboration.

<http://bit.ly/2FAsiuR>

Burn, Baby, Burn: Australian Birds Steal Fire to Smoke Out Prey

Grassland fires that are deadly and devastating events for many kinds of wildlife are a boon to certain types of birds known as fire foragers.

By Mindy Weisberger, Senior Writer | January 9, 2018 11:23am ET

These opportunists prey on animals fleeing from a blaze, or scavenge the remains of creatures that succumbed to the flames and the smoke.

But in Australia, some fire-foraging birds are also fire starters.

Three species of [raptors](#) — predatory birds with sharp beaks [and talons](#), and keen eyesight — are widely known not only for lurking on the

fringes of fires but also for snatching up smoldering grasses or branches and using them to kindle fresh flames, to smoke out mammal and insect prey.

Scientists recently collected and evaluated reports from Aboriginal and nonindigenous people of these so-called firehawks — black kites (*Milvus migrans*), whistling kites (*Haliastur sphenurus*) and brown falcons (*Falco berigora*) — to better understand this unusual behavior, and to evaluate its implications for fire management in regions where the birds are active, the researchers wrote in a new study.



Black kites (Milvus migrans) circle near a roadway during a fire on the Cape York Peninsula in Queensland, Australia. Dick Eussen

Aboriginal people in some parts of northern Australia referenced the fire-spreading actions of firehawks in sacred rituals and noted numerous sightings of the firehawks. In total, the study authors identified 12 Aboriginal groups in which people described firsthand sightings of raptors deliberately setting new fires with smoldering brands salvaged from [existing fires](#), acting on their own and cooperating with other birds.

"I have seen a hawk pick up a smoldering stick in its claws and drop it in a fresh patch of dry grass half a mile away, then wait with its mates for the mad exodus of scorched and frightened rodents and reptiles," an Aboriginal man named Waipuldanya recalled in "I, The Aboriginal," a 1962 autobiography ghostwritten by journalist Douglas Lockwood, according to the research article.



Fire-spreading has been observed in three species of raptors in the grasslands of northern Australia. Bob Gosford

"When that area was burnt out, the process was repeated elsewhere," he reported.

Another account also described birds intentionally starting [new fires](#) in unburned patches of grass.

"When a fire burns into a creek line and burns out, brown falcons have also been observed collecting fire brands and dropping them on the other unburnt side of the creek in order to continue the fire," according to a collection of Aboriginal accounts published in 2009, the study authors wrote.

Jump into the fire

The researchers also conducted interviews with non-Aboriginal sources and scoured prior studies for stories of the fire-seeking birds. Two of the researchers also contributed their own observations gleaned from decades of fieldwork and encounters with bushfires in the Australian grasslands.

From their reports, a behavioral pattern emerged: Firehawks (also described as kitehawks, chickenhawks and, on several occasions by non-Aboriginals, s---hawks) purposely swiped burning sticks or grasses from smoldering vegetation — or even from human cooking fires — and then made off with the brands and dropped them into unburned areas to set them alight, presumably to drive out [more prey](#).



Black kites (Milvus migrans) visit a grass fire in Borroloola, Northern Territory, Australia, in 2014. Bob Gosford

The firehawks "come out of nowhere when you start a fire because they know that the feed is on," one interview subject told the study authors. Another man described a group of birds that appeared to work together to steal embers from an existing blaze to start [a new fire](#) some distance away, according to the study.

"Certain raptors either restart extinguished fires or move fires across barriers that might otherwise hamper the fire's spread," the study's lead

author, Mark Bonta, an assistant professor of Earth sciences at Penn State Altoona, told Live Science in an email.

"In the case of co-authors Nathan Ferguson's and Dick Eussen's accounts, they saw the behavior repeatedly and at close range, including failed attempts, but also successful attempts," Bonta said.

Jump into the fire

The range of the birds' reported fire stealing spans a significant area measuring approximately 1,490 by 620 miles (2,400 by 1,000 kilometers) across part of northern Australia, the scientists reported.



A black kite carries a grass stem close by at a fire near the McArthur River mine in Northern Territory, Australia, in 2013. Bob Gosford

Photos and videos of firehawk behavior remain scarce, and it can be challenging to observe the birds while fires are blazing. Therefore, officials typically overlook firehawk activity when creating strategies for [managing fires](#), which are commonly used in Australia by Aboriginal groups and non-Aboriginal landowners for ecosystem management, the study authors wrote.

"This May, we are leading a team to Northern Territory to work with Aboriginal ranger groups who will set controlled burns for us, so we can study the dynamics of raptor behavior under semi-controlled conditions. No one has ever done this before," Bonta said.

Close collaboration with Aboriginal teams and individuals will be a critical part of studying the birds' use of fire and its relationship to the Australian [tropical grasslands](#), which indigenous people have inhabited and managed with controlled burning for at least 50,000 years. Over millennia, Aboriginal people have accumulated an unparalleled understanding of this ecosystem and the animals that inhabit it —

knowledge that is in danger of being lost as [cultural traditions](#) are abandoned by younger generations, Bonta explained.

"Our work is a collaborative effort to help valorize indigenous knowledge of birds, particularly as known to the older generations — this is not simply 'folklore' but rather intricate ecosystem knowledge that is typically unparalleled even by most outsider experts," he said.

The findings were published online in the December 2017 issue of the [Journal of Ethnobiology](#).

<http://bit.ly/2mtTQcI>

Patients react better when doctors imply uncertainty, rather than state it directly

Choice of words might matter when doctors communicate uncertainty of diagnosis to their patients.

A paper published in the *International Journal for Quality in Health Care* shows that the parents of pediatric patients may react more negatively to doctors who communicate uncertainty of diagnosis explicitly, such as directly stating they are unsure, as compared to doctors who use implicit language, such as discussing "most likely" diagnosis or providing several possible diagnoses under consideration. Diagnostic uncertainty is widespread in clinical practice and physician guidelines generally recommend that doctors explain the degree of uncertainty associated with their diagnosis.

However, how exactly doctors should communicate uncertainty is a matter of debate. This communication can lower visit satisfaction, decrease adherence to doctor instructions, lessen trust, and decrease confidence in the doctor.

The researchers here surveyed parents of pediatric patients who hypothetically received a diagnosis with an element of uncertainty. The uncertainty in the diagnosis was communicated in one of three ways; either with an explicit expression of uncertainty (such as "I'm not sure which disease this is"), an implicit expression of uncertainty using broad differential diagnoses (such as "it could be this disease or this

other disease"), or another implicit expression of uncertainty (such as "it is most likely this disease").

Researchers found that explicit expressions of uncertainty were associated with lower perceived technical competence of the doctor, less trust and confidence, and a less willingness to adhere to doctors' advice.

"Misdiagnosis is common in medical practice and to enable improvements, uncertainty of diagnosis is something both doctors and patients will need to embrace" said Hardeep Singh, MD, MPH, senior author and researcher at the Houston Veterans Affairs Center for Innovations in Quality, Effectiveness and Safety and Baylor College of Medicine. "Our study provides a foundation for future development of evidence-based guidance on how doctors can best communicate diagnostic uncertainty to patients to improve diagnosis and care outcomes."

The paper "Patient Perspectives on How Physicians Communicate Diagnostic Uncertainty: An Experimental Vignette Study" is available at: <https://academic.oup.com/intqhc/advance-article/doi/10.1093/intqhc/mzx170/4791877?preview=true>

<http://bit.ly/2DuJPEk>

Immunity May Make CRISPR-Based Therapies Ineffective

Researchers identify antibodies for two commonly used Cas9 proteins in human blood. Investors take notice.

By Jim Daley | January 10, 2018

CRISPR-Cas9 has been hailed as a breakthrough tool in genome editing that could usher in an era of precision gene therapy, and clinical trials are already [scheduled to begin this year](#). But there may be a snag: our own immune systems.

The technique relies on Cas9 nucleases found in bacteria. But the majority of humans may have preexisting immune responses to bacteria from which the most common Cas9 homologs are derived, according to a preprint published last week (January 5) on [bioRxiv](#).

The study, as [MIT Technology Review](#) first reported, examined the blood of 12 adults and 22 newborns for antibodies to Cas9 proteins

from *Staphylococcus aureus* and *Streptococcus pyogenes*. They found antibodies for *S. pyogenes* in 65 percent of donors and antibodies for *S. aureus* in 75 percent—and nearly half of the donors had CD4+ T-cells that specifically targeted Cas9 homologs from *S. aureus*.

The immunity could not only limit the effectiveness of CRISPR, but also “create safety concerns,” the researchers write in the study. However, the problem is mostly limited to therapies that seek to edit genomes in vivo, they note—those that involve removing cells and editing genes in the lab may not be affected by this discovery.

“Like any new technology, you want to identify potential problems and engineer solutions for them,” study coauthor Matthew Porteus of Stanford University tells [STAT News](#). “And I think that’s where we’re at. This is an issue that should be addressed.”

Executives at genome-editing companies, however, insist that the issues raised by this study “were either already being addressed or were not relevant to the medicines being developed,” according to [STAT News](#). Shares of Intellia Therapeutics, Editas Medicine, and CRISPR Therapeutics were down the Monday after the paper was published, *STAT News* reports.

<http://bit.ly/2EFG9Ph>

Orangutans, like people, use medicinal plants to treat joint and muscle inflammation

Scientists have discovered that the same plant used by indigenous people on Borneo is also used by wild orangutans to treat joint and muscle inflammation.

Borneo Nature Foundation scientists have been observing wild Bornean orangutans in the Sabangau Forest (Central Kalimantan, Indonesian Borneo) since 2003 and have collected over 20,000 hours of observational data.

During this time the use of the *Dracaena cantleyi* plant for self-medication by orangutans has only been observed on seven occasions. But, the team were fortunate to capture this rare behaviour on camera.

In the video, a female [orangutan](#), called 'Indy', can be seen chewing the leaves to produce a white soapy lather. This lather was then rubbed onto the upper left arm for approximately 7 minutes and the leaves were never swallowed.

Borneo Nature Foundation collaborated with an international team of scientists to analyse the properties of the plant.

"For the first time ever, self-medication activities of orangutans has been confirmed through this research," said Dr. Ivona Foitová, of Masaryk University in Brno Czech Republic and Gadjah Mada University of Yogyakarta Indonesia, and co-author of a recent *Scientific Reports* paper reporting this discovery.

"Pharmacological laboratory analyses revealed and proved leaf extracts of *Dracaena cantleyi*, which [wild orangutans](#) have been observed rubbing on their bodies, to have anti-inflammatory properties."

Dr. Helen Morrogh-Bernard, Co-Director of Borneo Nature Foundation and lead author of the *Scientific Reports* paper, said "This is very exciting news as it confirms self-medication in orangutans, the first report of self-medication in an Asian ape, and for the first time, to our knowledge, the external application of an anti-inflammatory agent in animals."

"In the Sabangau Forest, it has been primarily adult female orangutans observed performing this behaviour. We believe that females may be using this plant to soothe sore muscles and joints from the extra weight of carrying their infants while climbing through the [forest](#) canopy."

The research team added "This new finding highlights the importance of tropical forests for medicinal [plants](#), but more research into the practical uses of plants is needed.

"It also opens up the question as to what other plants orangutans may use for medicinal purposes, a topic we know very little about."

More information: H. C. Morrogh-Bernard et al. *Self-medication by orang-utans (*Pongo pygmaeus*) using bioactive properties of *Dracaena cantleyi**, *Scientific Reports* (2017). [DOI: 10.1038/s41598-017-16621-w](https://doi.org/10.1038/s41598-017-16621-w)

<http://nyti.ms/2Db8oci>

R.S.V.? She Hadn't Heard of It. Then Her Child Was Hospitalized.

It started out as a runny nose and a cough — typical cold symptoms.

Then things took a turn for the worse.

By CHRISTINA CARONJAN. 10, 2018

Courtney S. Martin noticed that her 19-month-old son, Calvin, was having coughing fits. He started breathing rapidly, his nostrils flaring. He refused to eat or drink.

“Every time he took a breath you could see he was working hard — you could see his rib cage sucking in,” said Ms. Martin, a mother of two in Rutledge, Pa. Calvin’s pediatrician advised Ms. Martin to head to the emergency room, where she learned that her son had respiratory syncytial virus, or R.S.V.

By the age of 2, nearly every child has contracted R.S.V. In most children, it presents as a bad cold. But for others, it can cause breathing problems and dangerous lung infections — and many parents have never heard of it until their child becomes ill.

What is R.S.V.?

Every winter, R.S.V. becomes a common and potentially serious illness, said Dr. Ethan S. Wiener, associate chief of pediatric emergency medicine at N.Y.U. Langone Health. While it affects both children and adults, it is most dangerous — and can even be fatal — in babies who are born prematurely and people with weak immune systems, heart disease or lung disease. But even babies who were born full-term and healthy can develop severe symptoms, like Calvin or like Andre, a toddler from Mission Viejo, Calif., who contracted the virus in 2016 when he was three weeks old.

“It was really scary seeing your son hooked up to so many monitors and not knowing what’s going on,” said Andre’s mother, Alexandria Salahshour, who [wrote about the illness](#) to raise awareness. They spent Christmas that year at the hospital, where Andre was admitted with a blood oxygen level of 70 percent. It should be close to 100 percent.

Like many parents, Ms. Salahshour was unfamiliar with R.S.V. “I remember just being in the corner, kind of hyperventilating a little bit,” she said.

In otherwise healthy patients, R.S.V. can usually be treated at home. Children who have been infected with the virus produce antibodies that help reduce its severity if they become reinfected. But R.S.V. can turn into acute lower respiratory infections such as bronchiolitis, a viral respiratory illness that is the most common cause of hospitalization in infants, Dr. Wiener said. It can also lead to pneumonia.

Each year, on average, the virus results in more than 57,000 hospitalizations among children younger than 5, according to the Centers for Disease Control.

Ms. Martin’s son was discharged after staying overnight at the hospital, where he received fluids and oxygen. “When I left it was literally a room full of tiny kids coughing, coughing, coughing,” she said.

When to worry

“When we get concerned is when we’re seeing that kids are having more trouble breathing and they’re not feeding well,” said Dr. Robert Adler, chief medical officer of the Children’s Hospital Los Angeles Health System. Other worrisome symptoms include dehydration, fever, fussiness, signs of dehydration or distress, and lethargy. Children who are managing their cold symptoms well should avoid the emergency room. “That’s where you’re going to get sick again,” Dr. Adler said.

People infected with R.S.V. can spread the virus for anywhere between three to eight days, and the virus can live on hard surfaces for as long as six hours, Dr. Adler said.

There is no antiviral therapy for R.S.V., and there isn’t a vaccine: Children are typically treated with hydration, nasal suctioning and oxygen. “Really I do not think there’s a need for unnecessary hysteria around R.S.V.,” Dr. Shari Platt, the chief of pediatric emergency medicine at NewYork-Presbyterian/Weill Cornell Medical Center, said. Other respiratory viruses, [like influenza](#), are also prevalent during this time of year, she added.

Part of the reason people are less aware of R.S.V. than the flu is because there's not a lot you can do to avoid R.S.V., said Dr. Demetre Daskalakis, the deputy commissioner for the division of disease control at the New York City Department of Health and Mental Hygiene. "We're constantly harping about the flu vaccine because we can do something to prevent it," he said.

To lessen the risk of contracting R.S.V., Dr. Platt recommends "lots of hand washing." "You walk in the house, wash your hands," she said.

Protection for \$5,000

An immunoglobulin therapy called Synagis can help protect children from R.S.V., but insurance only covers it for children who have certain lung or heart conditions.

Sam Green of New York City said his twins, who were born in 2016 at 23 weeks, were both given Synagis during their first winter. But this winter, insurance refused to cover the therapy because the children were older, Mr. Green said. So he and his husband decided to pay for the treatment out of pocket. It cost about \$5,000 per child for each of the monthly injections administered during R.S.V. season, which generally lasts from November to April. "I would rob my 401(k) to make sure that they have that extra protection," Mr. Green said.

The twins received doses of Synagis in November, but one of them, Kate, came down with R.S.V. the following month, when she was 15 months old. "She just went from mild cold symptoms to going downhill very rapidly," Mr. Green said. Kate spent seven days in the hospital, where she was treated with an IV and a bronchodilator, which stabilized her oxygen levels and increased air flow to her lungs. The Synagis most likely lessened the severity of Kate's illness, Mr. Green said. And now that she has contracted R.S.V. once, she no longer needs to take it.

Ms. Salahshour, whose son was born during the winter, is expecting her second child this month. She's on "very high alert," she said, and is planning to take a more cautious approach.

"This time around, we are not leaving the house for at least a month to two months," she said. "And in the beginning, we're only going to have our family members hold her."

In Dr. Platt's view, it's safe to go outside. "Out and about is good," she said. "But I do think you shouldn't have everybody hold the baby."

<http://bit.ly/2DqXaCk>

Mysterious explosion of a deadly plague may come down to a sugar in ice cream

C. diff kills tens of thousands each year. Its puzzling rise links to trehalose.

[Beth Mole](#) - 1/11/2018, 8:21 AM

In the early 2000s, a deadly gut infection began to surge. After decades of lurking in intestines and hospitals—more opportunistic nuisance than lethal threat—the bacterium *Clostridium difficile* abruptly exploded, spreading rapidly and causing more severe diarrheal disease than ever before. By 2011, the Centers for Disease Control and Prevention estimated that *C. diff* infected nearly half a million people in the US that year, [killing approximately 29,000](#).

Two strains led the deadly reign: RT027 and RT078 (named based on the genetic code of their ribosomes, or "ribotype"). But scientists could only speculate as to why this duo was suddenly so menacing. At least one of them [turned up with resistance](#) to a class of antibiotics called fluoroquinolones, which contains ciprofloxacin among other common antibiotics. This fact led some researchers to suggest that the bacteria's rise may have been linked to development of that drug resistance.

But scientists had identified fluoroquinolone resistance in *C. diff* back in mid-'80s. Why would it suddenly matter? There was another, cryptic factor at play, it seemed.

With [a study published in Nature](#) recently, scientists think they've finally figured out what that enigmatic element was—and it's even more obscure than anyone may have guessed. It wasn't some new weapon the bacteria acquired or a waning antibiotic. It was a boring,

harmless sugar—one often found in ice creams. And its part of the story started back in the '90s in Japan.

At the time, food scientists were trying to come up with an inexpensive way to make that sugar, called trehalose. It's a disaccharide made up of two glucose molecules linked with a sturdy α, α -1,1-glucoside bond, and it's naturally found in low levels in some bacteria, fungi, plants, and invertebrates. Its chemistry made food scientists drool. Trehalose's strong bond means it's resistant to breaking down in high temperatures and acidic conditions. It also seems to have a gel phase that stabilizes and protects cells from extreme dryness and cold. In foods, it can be used as a [mild sweetener, moisture-preserver, thickener, and stabilizer](#).

The trouble was, making it in large quantities was expensive—about \$700 per kilogram.

With tinkering, syrup scientists at Japan's Hayashibara chemistry company finally figured out a [novel enzymatic method](#) to make it on the cheap from starch. The method brought costs down to just \$3 per kilogram. By 2000—just before the rise of *C. diff*.—the company got approval from the US Food and Drug Administration to use it as an additive in food. Approval for use in Europe came the following year. Manufacturers started pouring trehalose into a variety of foods, from pasta to ground beef to ice creams.

To us, trehalose is an indistinguishable sweetener. It's about 45 percent as sweet as table sugar (sucrose) and breaks down to simple glucose. But, according to the authors of the new *Nature* study, we're not the only consumers. In a sugar-eating screen, the study authors noted that two *C. diff*. strains (out of 21) could happily survive on just a dash of trehalose. Those strains were RT027 and RT078.

Cloying killer

It's not uncommon for *C. diff* to carry the genetic blueprints for trehalose digestion. But, the study authors, led by microbiologist Robert Britton at Baylor College of Medicine, found that the two epidemic strains had genetic tricks to live on just tiny amounts. RT027 had a genetic mutation that made it more sensitive to trehalose concentrations.

RT078, on the other hand, had gotten hold of a cluster of four new genes for trehalose metabolism.

The sweet genetics helped the strains cause trouble, Britton and colleagues found. In one experiment, they infected 55 mice with either RT027 or a genetically engineered version that couldn't metabolize trehalose. When the mice drank trehalose-laced water, RT027 killed nearly 80 percent of them. But, the trehalose mutant only killed 33 percent of the mice. In a second experiment, the researchers infected another 55 mice with RT027 and gave them either trehalose-laced water or plain water. The trehalose-laced water increased mortality three-fold between the groups.

Looking closer at the rodents' infections, they found that trehalose didn't make RT027 grow more—rather, it produced more toxins, leading to more severe disease. Next, they pitted RT078 against a genetically engineered version that couldn't metabolize trehalose. In a mini-bioreactor that simulates *C. diff* infection in the bowels, the RT078 elbowed out the mutant when trehalose was present at low doses.

Together, the data suggests that trehalose metabolism gave the epidemic *C. diff* strains an advantage over their relatives and made them more deadly in the gut. Last, the researchers collected intestinal juices from three anonymous donors and found they contained enough trehalose to get RT027 to switch on trehalose metabolism.

“On the basis of these observations, we propose that the widespread adoption and use of the disaccharide trehalose in the human diet has played a significant role in the emergence of these epidemic and hypervirulent strains,” Britton and colleagues concluded.

Jimmy Ballard, a microbiologist at the University of Oklahoma Health Sciences Center, noted that there are some catches. [In an accompanying editorial](#), he pointed out that researchers need more data to know for sure if the trehalose metabolism could explain the higher death rates in people. He also noted that the gut juices the team tested were from the small intestine, not the colon where *C. diff* causes mayhem. That said, he concluded that the study is “compelling.”

"It is impossible to know all the details of events surrounding the recent *C. difficile* epidemics," he wrote. "But the circumstantial and experimental evidence points to trehalose as an unexpected culprit."

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<http://bit.ly/2D0jq08>

In 'pond scum,' scientists find answers to one of evolution's which-came-first cases

Moths and butterflies existed during Jurassic era, millions of years before flowering plants, team reports

Chestnut Hill, Mass. - Visiting a colleague in Germany in 2012, Boston College Research Professor Paul K. Strother was examining soil samples for pollen, spores, pieces of plants and insect legs - organic debris that might otherwise have been considered "pond scum" when it was trapped in sediment during cataclysmic earth events 200 million years ago.

The slides of rock samples drilled in the German countryside included some material that looked familiar to Strother, a Department of Earth and Environmental Sciences researcher at Boston College's Weston Observatory, who studies the origin and early evolution of land plants. What he saw were features similar to those found in insect wings.

The wrinkle was that these types of moths and butterflies - known as Lepidoptera - were long posited to have evolved 50 to 70 million years later, during the Cretaceous period when the first flowering plants emerged as their prime food source.

The consensus has been that insects followed flowers," said Strother, a co-author of "[A Triassic-Jurassic window into the evolution of Lepidoptera](#)," a new report published today in Science Advances. "But that would be 50 million years later than what the wings were saying. It was odd to say the least, that there would be butterflies before there were flowers." Five years later, Strother and colleagues from natural history museums in Germany and a university in the Netherlands have developed a scientific case showing the Lepidoptera evolved earlier than previously established - emerging during the Jurassic period.

Absent flowers, the researchers report, primitive moths and butterflies, known as the Glossata, developed the physical attributes - namely the sucking proboscis - to find nutrition by drawing off water droplets from the tips of immature gymnosperm seeds.

"What we've found is that these butterflies and moths with mouth parts were feeding on pollen droplets of gymnosperm seeds - from conifers related to pines, seed plants without fruits and flowers. They were feeding off the cone-borne seeds - mainly as a source of water," said Strother.

Even Charles Darwin called the mysterious evolution of flowering plants "an abominable mystery." Scientists have reckoned that flowering plants preceded the insects that fed off of them. But researchers have gradually started to piece together evidence that moths and butterflies existed earlier than the Cretaceous period, which began 145 million years ago.

The team's findings shed new light on the classic example of co-evolution: the evolutionary interplay between pollenating insects - flies, bees, wasps, butterflies and moths - and angiosperms, or flowers, Strother said.



Examples of the oldest wing and body scales of primitive moths from the Schandelah-1 core photographed with transmitted light (magnification 630x). The scales are part of palynological preparations and occur together with fossil pollen grains and other organic plant remains. Size of the images (h) approx. 85 micrometer (w) approx. 65 micrometer. Bas van de Schootbrugge, Utrecht University"

"Our discovery does not change this, but instead, it demonstrates that the Glossata - which gave rise to the Lepidoptera - evolved earlier by a feeding adaptation to the gymnospermous ovules, or the pollen droplets," said Strother. "These insects later transferred their feeding preference onto angiosperms, and, as a result, ended up co-evolving

with flowers where they function to transfer pollen as they feed on nectar."

Developing a clearer picture of insect evolution had proved elusive because much of what is learned from ancient rock, soil and fossils comes from earth once covered by oceans, said Strother. Moths and butterflies lived over land masses. In addition, their delicate features were prone to deterioration prior to fossilization.

Utrecht University paleontologist Bas van de Schootbrugge and colleagues assembled a portfolio of samples containing fossilized remains of moths and butterflies to carefully establish the presence of Lepidoptera in earth samples from a region where the cataclysmic transition between Triassic and Jurassic is preserved in rock.

The mass extinction event 201 million years ago wiped out an estimated 35 percent of all species, which makes the survival and diversification of Lepidoptera all the more remarkable.

Assembling the evidence required a team that included Strother and van de Schootbrugge, Utrecht University's Timo van Eldijk, an undergraduate at the time, Carolien Weijst, and Henk Visscher; as well as Torsten Wappler of the German natural history museum Hessisches Landesmuseum Darmstadt, and Hossein Rajaei of Museum für Naturkunde, in Stuttgart.

In 2012, Strother was examining the sample slides looking at algae, fungi and soil microorganisms. "These are organic extractions after you've dissolved away the minerals in the samples and you're looking at anything that is organic. There are pollen and spores. There are other things. Pieces of plant cuticles. Resistant organic material. Insect legs. Ninety-nine percent is plant debris.

"It's basically pond scum," said Strother, referring to the film of debris that can sit atop a pool of standing water. Part of what Strother saw looked similar to insects from another era, he said.

The project required linking a range of evidence, akin to a scientific detective story, said Strother.

"This is the old-fashioned science of discovery," said Strother. "We're looking at this microscopic world of things that lived hundreds of millions of years ago and we don't know what they are. The challenge is: can we figure out what they are? Part of it is piecing together the tree of life, or the evolution of organisms through time. It is more like a puzzle or a mystery."

<http://bit.ly/2AZNGWT>

Don't Touch the Monkeys! Florida Macaques Carry Virus Lethal to Humans

Warnings that macaques carry a strain of the herpes virus that can be fatal to humans

By Mindy Weisberger, Senior Writer | January 11, 2018 01:42pm ET

Visitors to Florida's Silver Springs State Park should avoid monkeying around with the reserve's feral macaques; officials warn that the primates carry a strain of the herpes virus that can be fatal to humans.

About 175 free-roaming rhesus macaques (*Macaca mulatta*) inhabit the park, descended from a population of around a dozen animals that were released in the 1930s to promote local tourism. Hundreds more of the macaques can be found wandering the areas adjacent to the park.

Now, researchers from the Centers for Disease Control and Prevention (CDC) report that about 25 percent of the monkeys carry macacine herpesvirus 1 (McHV-1), which causes only mild symptoms, if any, in monkeys but can be deadly in people.

The scientists also discovered that as many as 14 percent of the monkeys shed DNA from the virus in their saliva, presenting a risk of virus transmission to humans, the researchers reported in a new study, which was published online in the February 2018 issue of the journal [Emerging Infectious Diseases](#).

[Herpes viruses](#) have infected animals in the primate family for [millions of years](#). In fact, one strain of herpes — HSV-2 — appeared in early humans only after it was transmitted from chimpanzees about 1.6 million years ago, Live Science [previously reported](#).

McHV-1, which is also known as herpes B or monkey B virus, is carried by several species of macaque monkeys, which are thought to be a "natural host" for the virus, according to the [CDC](#).

Previous studies of the Silver Springs Park rhesus populations had identified herpes B in the animals, according [to a study](#) published in May 2016 by the University of Florida's Institute of Food and Agricultural Sciences (IFAS).

In the new study, scientists analyzed samples of blood, feces and saliva collected from the macaques, as well as soil samples from the monkeys' habitat. Blood samples from 317 macaques revealed that 84 monkeys carried the virus and that the odds of a monkey being infected increased with age.

To date, only 50 cases of herpes B have been documented in humans in the U.S. since the disease was first identified in 1932, and many of the infections resulted from animal scratches or bites, [according to the CDC](#). But in humans, infection with herpes B can lead to severe brain damage or death, with 70 percent of untreated patients killed by complications from infection. Of the 50 reported herpes B cases, 21 proved fatal, the CDC reported. The virus could pose a serious threat to public health and safety, the CDC said.

Visitors to Silver Springs Park risk exposure to herpes B by coming into contact with monkey urine or feces, or through the animals' saliva in scratches or bites, the researchers reported in the new study. They concluded that management plans are required to limit the macaques' [transmission](#) of this potentially fatal pathogen.

<http://bit.ly/2EGBY5U>

With these special bacteria, a broccoli a day can keep the cancer doctor away

Engineered probiotics can target and kill colorectal cancer cells in the presence of a substance found in some vegetables

Colorectal cancer is one of the most common cancers in the world, especially the developed world. Although the 5-year survival rates for

earlier stages of this cancer are relatively good, at later stages survival goes down and the risk of cancer recurrence goes up considerably.

To help address this problem, a team of researchers in the NUS Medicine lab of Associate Professor Matthew Chang have found a way to turn a humble cocktail of bacteria and vegetables into a targeted system that seeks out and kills colorectal cancer cells. The study, which was led by Dr Chun-Loong Ho, will be published online today and in the current issue of *Nature Biomedical Engineering*.

At the heart of this cancer-targeting system is an engineered form of *E. coli* Nissle, a harmless type of bacteria found in the gut. Using genetic techniques, the team engineered the bacteria into a probiotic that attached to the surface of colorectal cancer cells and secreted an enzyme to convert a substance found in cruciferous vegetables (like broccoli) into a potent anticancer agent. The idea was for the cancer cells in the vicinity to take up this anticancer agent and be killed. Normal cells cannot do this conversion, nor are they affected by the toxin, thus the system should be targeted only to colorectal cancer cells.

True enough, the mixture of engineered probiotics with a broccoli extract or water containing the dietary substance killed more than 95% of colorectal cancer cells in a dish. Moreover, the mixture had no effect on cells from other types of cancer such as breast and stomach cancer. Strikingly, the probiotics-veggie combination reduced tumour numbers by 75% in mice with colorectal cancer. Also, the tumours that were detected in these mice were 3 times smaller than those in control mice which were not fed with the mixture.

Dr Ho and Associate Professor Chang, along with colorectal cancer specialist Dr Yong Wei Peng at the National University Hospital, envision that these probiotics could be used in two ways: 1) as prevention, and 2) to clean up the cancer cells remaining after surgical removal of tumours. One day, colorectal cancer patients may be able to take the probiotics as a dietary supplement along with their broccoli to prevent colorectal cancer or to reduce recurrence after cancer surgery.

As Associate Professor Chang puts it, "One exciting aspect of our strategy is that it just capitalizes on our lifestyle, potentially transforming our normal diet into a sustainable, low-cost therapeutic regimen. We hope that our strategy can be a useful complement to current cancer therapies." Or, even more simply, in Dr Ho's words, "Mothers are right after all, eating vegetables is important."

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<http://bit.ly/2EDXl84>

Heart-muscle patches made with human cells improve heart attack recovery

This is the first large-animal study of muscle patches of a clinically relevant size.

BIRMINGHAM, Ala. - Large, human cardiac-muscle patches created in the lab have been tested, for the first time, on large animals in a heart attack model. This clinically relevant approach showed that the patches significantly improved recovery from heart attack injury.

The results are a step closer to the goal of treating human heart attacks by suturing cardiac-muscle patches over an area of dead heart muscle in order to reduce the pathology that often leads to heart failure.

The research was led by Jianyi "Jay" Zhang, M.D., Ph.D., the chair of University of Alabama at Birmingham Biomedical Engineering, a joint department of the UAB School of Medicine and the UAB School of Engineering.

Each patch is 1.57 by 0.79 inches in size and nearly as thick as a dime. Zhang and colleagues found that transplanting two of these patches onto the infarcted area of a pig heart significantly improved function of the heart's left ventricle, the major pumping chamber. The patches also significantly reduced infarct size, which is the area of dead muscle;

heart-muscle wall stress and heart-muscle enlargement; as well as significantly reducing apoptosis, or programmed cell death, in the scar boarder area around the dead heart muscle. Furthermore, the patches did not induce arrhythmia in the hearts, a serious complication observed in some past biomedical engineering approaches to treat heart attacks.

A key to success of the patches is how they are engineered.

Each patch is a mixture of three cell types -- 4 million cardiomyocytes, or heart-muscle cells; 2 million endothelial cells, which are well-known to help cardiomyocytes survive and function in a micro-environment; and 2 million smooth muscle cells, which line blood vessels. The three cell types were differentiated from cardiac-lineage, human induced pluripotent stem cells, or hiPSCs, rather than using hiPSCs created from skin cells or other cell types.

Each patch was grown in a three-dimensional fibrin matrix that was rocked back and forth for a week. The cells begin to beat synchronously after one day.

This mixture of three cell types and the dynamic rocking produced more heart muscle cells that were more mature, with superior heart-muscle physiological function and contractive force, as compared with patches made from a monolayer of cells that are not dynamically rocked. The patches resembled native heart-muscle tissue in their physiological and contractile properties.

Past attempts to use hiPSCs to treat animal models of heart attacks -- using an injection of cells or cells grown as a very thin film -- have shown very low rates of survival, or engraftment, by the hiPSCs. The present study had a relatively high rate of engraftment, 10.9 percent, four weeks after transplantation, and the transplantation led to improved heart recovery.

Part of the beneficial effects of the patches may occur through the release of tiny blebs called exosomes from cells in the patches. These exosomes, which carry proteins and RNA from one cell to another, are a common cell-to-cell signaling method that is incompletely understood. In tissue culture experiments, the researchers found that exosomes

released from the large heart-muscle patches appeared to protect the survival of heart-muscle cells.

Additionally, the patches appeared to prevent or reverse detrimental changes in protein phosphorylation in the sarcomeres of the heart-muscle tissue bordering the infarcted area of the heart. This result is the first to suggest that hiPSC-derived heart cells may improve contractile function after heart attacks by lessening maladaptive changes in phosphorylation states of sarcomeric proteins. The sarcomere is the contractile unit in a heart-muscle cell myofibril.

*Co-authors with Zhang of the paper, "[Large cardiac-muscle patches engineered from human induced-pluripotent stem-cell-derived cardiac cells improve recovery from myocardial infarction in swine](#)," published in the journal *Circulation*, are Ling Gao, Ph.D., Wuqiang Zhu, M.D., Ph.D., Saidulu Mattapally, Ph.D., Yasin Oduk, Ph.D., Xi Lou, Ramaswamy Kannappan, Ph.D., Anton V. Borovjagin, Ph.D., Gregory P. Walcott, Ph.D., Andrew E. Pollard, Ph.D., Vladimir G. Fast, Ph.D., and Steven G. Lloyd, M.D., Ph.D., all of the UAB Department of Biomedical Engineering; Zachery R. Gregorich, Ph.D., and Ying Ge, Ph.D., Department of Cell and Regenerative Biology, University of Wisconsin-Madison; and Xinyang Hu, M.D., Ph.D., Zhejiang University, Hangzhou, China.*

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At UAB, Zhang holds the T. Michael and Gillian Goodrich Endowed Chair of Engineering Leadership.

<http://bit.ly/2mxaqBb>

Babies stir up clouds of bio-gunk when they crawl

Infant and adult inhalation exposure research

WEST LAFAYETTE, Ind. - When babies crawl, their movement across floors, especially carpeted surfaces, kicks up high levels of dirt, skin cells, bacteria, pollen, and fungal spores, a new study has found. The infants inhale a dose of bio bits in their lungs that is four times (per kilogram of body mass) what an adult would breathe walking across the same floor.

As alarming as that sounds, lead researcher Brandon Boor of Purdue University is quick to add that this isn't necessarily a bad thing.

"We are interested in the biological material an infant inhales, especially during their first year of life when they are crawling. Many

studies have shown that inhalation exposure to microbes and allergen-carrying particles in that portion of life plays a significant role in both the development of, and protection from, asthma and allergic diseases," Boor says. "There are studies that have shown that being exposed to a high diversity and concentration of biological materials may reduce the prevalence of asthma and allergies later in life."

A YouTube is available at

<https://www.youtube.com/watch?v=QqTi9fK70t0&feature=youtu.be>.

Scientists have previously done studies to determine how much dirt and biological material is kicked up and resuspended into the air when an adult walks indoors, but this is the first study to look at what happens with infants and their unique forms of locomotion.

Human babies are the only mammals that can't get up and walk soon after being born. Elephants, giraffes, horses, all can take a few wobbly steps soon after they enter the world, but it's months before a human can claim the same accomplishment. (Anthropologist David Tracer of the University of Colorado has suggested that based on studies of indigenous cultures, crawling is not necessary for human development. In fact, he has suggested, it only became common once people began living in structures with wooden floors.)

As babies roll, slide and crawl on the floor, their movements stir up more particulates into the air, and their mouths and nostrils are much closer to the floor where the concentrations are greater. This is countered somewhat by the fact that babies tend to move in much shorter bursts of activity than do older children or adults.

To study just how much of the floor debris babies breathe, the research team built a robotic crawling baby (which is much less adorable than the real thing) and tested it crawling on actual carpet samples they had removed from homes. Then the researchers measured and analyzed the particulates in the breathing zone.

"We used state-of-the-art aerosol instrumentation to track the biological particles floating in the air around the infant in real-time, second by second. The instrument uses lasers to cause biological material to

fluoresce. Most bacterial cells, fungal spores, and pollen particles are fluorescent, so they can be reliably distinguished from non-biological material in the air," Boor says. "We also worked with a microbiology group at Finland's National Institute for Health and Welfare, which conducted DNA-based analysis of the microbes we collected onto filters."

The researchers found that a concentrated cloud of resuspended particles forms around the Pig-Pen wannabes, and that the concentrations around them can be as much as 20 times greater than the levels of material higher in the room. Moreover, infants' bodies aren't as good at blocking this dust storm, Boor says.

"For an adult, a significant portion of the biological particles are removed in the upper respiratory system, in the nostrils and throat. But for very young children, they more often breathe through their mouths, and a significant fraction is deposited in the lower airways--the tracheobronchial and pulmonary regions. The particles make it to the deepest regions of their lungs." Counterintuitively, perhaps, this may be just what nature intended.

In the late 1980s, British epidemiologist David Strachan was the first to propose the "hygiene hypothesis," which says that too clean of an environment may suppress the development of the immune system. Allergists also sometimes refer to this as "the farming effect."

"Exposure to certain bacterial and fungal species can result in the development of asthma, but numerous studies have shown that when an infant is exposed to a very high diversity of microbes, at a high concentration, they can have a lower rate of asthma later in life. Such exposures act to stimulate and challenge your immune system," Boor says.

In Western societies, infants spend nearly all of their time indoors, where indoor dust resuspension may contribute significantly to their respiratory encounters with biological material.

"While our research established new methods for infant microbial exposure assessment, much remains to be discovered," Boor says. "I

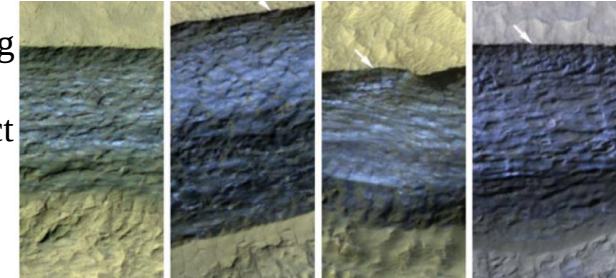
hope to continue to work with microbiologists and immunologists to better understand the role of indoor air microbes and allergens on early-childhood health."

<http://bit.ly/2r3zIns>

Large sheets of ice may have been spotted on Mars *Indications of layering suggest they may trap some of the planet's climate history.*

[John Timmer](#) - 1/12/2018, 5:20 AM

Mars clearly had a watery past, and it's expected that much of the water is still on the planet. Figuring out where the ice is hiding could tell us a lot about the planet's climate history and something about Mars' current water cycle. It could also help direct future landers to sample the planet's water and possibly use it to support human landings.



[Enlarge](#) / *Color enhanced images of the slopes, showing their distinctive blue tinge and layering.*

While we've found plenty of ice near the pole during the Phoenix Lander mission, that's not a very convenient location for future landings (in part because the site ended up frozen over with dry ice during that pole's Martian winter). In today's issue of *Science*, researchers are reporting the likely presence of ice sheets in more temperate regions. The sheets are at least 100 meters thick and appear to preserve layers that may help us reconstruct how the water ended up frozen there.

MRO data

As with many things Martian, the work relies on data from the Mars Reconnaissance Orbiter. It has a variety of instruments that can probe the chemical composition and subsurface structure of Mars, along with the [best camera we've ever sent to another planet](#). Over the years, MRO

has built up a comprehensive catalog of features on the Martian surface, many of them imaged from multiple angles.

Analyzing these features with a filter that accentuates colors, a team of researchers saw something notable for the Red Planet: a number of them had a distinctively blue color. They were found at mid-latitudes (roughly the Martian equivalent of Canada or the UK) and occupied poleward-facing slopes. The slopes appear to be the product of erosion along the edges of a broad, smooth elevated plain. Imaging with a spectrograph provided evidence of water at the Martian surface in the region, reinforcing the idea that this could be ice.

The bluish slopes were rather steep, having a slope that approached 55 degrees in some cases. Their lower reaches were covered in rubble, making it difficult to determine the total thickness of any ice deposits. Still, whatever it is is more than 100 meters thick and probably at least 130 meters. That's thick enough for the orbiting camera to resolve different colored bands within the material. That suggests the bands were deposited over time and trap different periods in Mars' history. A lack of craters indicates that some of that history could be quite recent. The authors favor the idea that what they've found is indeed ice, probably mixed with dust, and was deposited during a time when Mars experienced snow. "The presence of banding and color variations suggest layers," they argue, "possibly deposited with changes in the proportion of ice and dust under varying climate conditions." Thus, examining the layers could tell us about the history of how Mars' watery past came to a close.

Lots of ice

Currently, the ice sheets appear to be covered by a very shallow layer of dust that's frozen in place—the authors estimate that this is less than two meters thick. The slopes are probably being continuously exposed as the ice sublimates into the Martian atmosphere, likely to cycle up to the poles and end up frozen there. The researchers estimate that this is causing the loss of about a millimeter a year, which suggests that the ice sheets were once considerably larger than they are today.

These visible ice sheets are likely just a small representative of the total water ice on Mars. Radar studies of the subsurface have found features that have been interpreted as dust and rock covered glaciers and some indications of ice sheets in other areas of the Red Planet. But of course it's hard to confirm the identity of the layers seen in radar echoes, and the instrument doesn't have the resolution to figure out how close the ice might be to the surface beyond "less than 20 meters."

So, if these slopes still look like ice after more detailed examination, they seem like a great location to study the history of water on Mars. They could also make for accessible sites to extract water for human use, although that would obviously conflict with studying the ice's layers for clues to the past.

Science, 2017. DOI: [10.1126/science.aao1619](https://doi.org/10.1126/science.aao1619) ([About DOIs](#)).

<http://bit.ly/2Dcx8QK>

Soy can reverse breast cancer treatment, scientists warn
US research finds oestrogen-like compounds in food and fungus can reverse the effects of a widely used therapeutic combination.

Andrew Masterson reports.

Compounds found in food products such as soy can reverse the effects of a widely used breast cancer treatment, researchers have discovered. [In a paper in the journal *Cell Chemical Biology*](#), scientists from the Scripps Institute in California, US, warn that plant-derived oestrogen-mimicking compounds, found in several types of food and collectively called phyto-oestrogens, halt the effects of a combination therapy that involves two drugs, palbociclib and letrozole. They extended their warning to cover similar compounds found in some types of fungi (and called therefore myco-oestrogens), which sometimes enter the food chain via infected cereal crops. Collectively, oestrogen mimickers from all sources are called xeno-oestrogens.

The combination of palbociclib (PAL) and letrozole (LET) is used to treat postmenopausal women with oestrogen receptor positive, metastatic breast cancer. While neither drug used on its own produces strong results, the combination treatment (approved by the US Food and

Drug Administration in 2015) has been shown to significantly reduce cancer cell growth and increase survival periods for many patients.

In their research, however, the Scripps team, headed by Benedikt Warth, used laboratory populations of ER-positive breast cancer cell lines and exposed them to each of the target drugs, individually and in combination, and then to two oestrogen-mimics – zearalenone, derived from fungus, and genistein, found in soy.

The team used a metabolomics approach, using mass spectrometry to assess and measure small molecules known as metabolites. These are the end products of cellular activity. Metabolomics regards them as a reliable measure of the response of biological systems to genetic or environmental change.

The first part of the research reconfirmed that the two drugs worked much better in combination. Letrozole blocks the production of oestrogen, thus reducing the stimulation of oestrogen-receptors on cancer cells. Palbociclib works by disrupting a signalling pathway that left unchecked promotes cell division.

Adding zearalenone or genistein to cells lines treated with the two drugs produced remarkable and concerning results.

“Proliferation of both cell lines was markedly reduced after exposure to PAL+LET, when compared to untreated cells,” the researchers write. “Strikingly, co-administration of PAL+LET with either of the two xeno-oestrogens GEN or ZEN restored cell proliferation to levels that were comparable to non-treated cells.”

In other words, the fungus and soy derivatives stopped the drugs in their tracks. Warth and his colleagues, however, caution that much more research is needed to fully understand the results. There are epidemiological studies, they report, that find a correlation between high soy diets and reduced incidence of breast cancer.

The role of diet in relation to cancer risk and treatment is complex, they say, and clear causation difficult to establish. Asian women, they point out, generally consume much higher amounts of soy products than their

Western counterparts, raising the possibility that age of first exposure to phyto-oestrogens might be significant.

Nevertheless, says co-author Gary Siuzdak, a risk-averse approach to foods containing oestrogen mimics might be wise.

““Breast cancer patients taking palbociclib/letrozole should consider limiting their exposure to foods that contain xeno-oestrogens,” he says.

<http://wb.md/2AYySbh>

Hydrochlorothiazide and Skin Cancer: Should We Be Worried?

New data suggest hydrochlorothiazide is linked with an increased risk for skin cancer

Arefa Cassoobhoy, MD, MPH

Hello. I'm Dr Arefa Cassoobhoy, a practicing internist, Medscape advisor, and senior medical director for WebMD. Welcome to Morning Report, our 1-minute news story for primary care. Hydrochlorothiazide is a common blood pressure medicine. We've known for some time that it comes with an increased risk for sunburn. [New data suggest that it's also linked with an increased risk for skin cancer.](#)

Danish researchers analyzed prescription drug use in more than 80,000 patients with skin malignancies and compared them with controls.^[1] People who took hydrochlorothiazide daily for at least 6 years were 29% more likely to develop basal cell carcinoma. They were also almost four times more likely to get squamous cell cancer. And there was a dose-response relationship: The risk for skin cancer increased with more years of hydrochlorothiazide exposure.

This study doesn't explain why the drug is associated with skin cancer, but it does provide more proof that patients taking hydrochlorothiazide should protect their skin from UV light. And for patients at increased skin cancer risk, a change in blood pressure therapy might be warranted.

Follow Dr Cassoobhoy on Twitter at [@ArefaMD](#)

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