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Vegan sushi goes global with help of Japanese food wholesaler

Japanese company to pitch tuna and eel alternatives to health-conscious

TAKAYUKI YAO, Nikkei staff writer

TOKYO -- Nishimoto, Tokyo-based food wholesaler, plans to market "vegan fish" in the U.S., Europe, Southeast Asia and Japan.

The company will pitch Ahimi, a branded tuna alternative made from tomato, soy sauce, sugar, water and sesame oil. The product has a texture similar to tuna and can be used to make sushi.

Nishimoto plans to sell Ahimi, a tuna substitute made from tomato developed by a U.S. startup company, in the U.S., Europe and Asia.

Ahimi was developed by Ocean Hugger Foods, a U.S. startup founded in 2015. Nishimoto formed a capital and business tie-up with Ocean Hugger.

Nishimoto will use its 23 offices in North America and 14 offices in Europe and Asia to sell the product around the world.

According to a survey by Nielsen, a market research specialist, 39% of U.S. consumers say they are "actively trying to incorporate more plant-based food into their diets." That compares with 6% of Americans who are vegetarians and 3% who are vegans.

Nishimoto's Unami is an eel alternative made from eggplant.

Nishimoto believes many meat eaters are nonetheless interested in vegetarian foods. The company hopes to make vegan fish available in the U.S., where meat substitutes are already popular.

Ahimi is sold at Whole Foods Market and other supermarkets in the U.S., but Nishimoto wants to expand its sales to Europe and Southeast Asia, where there are many vegans. With the growing interest in sushi around the world, Nishimoto believes its vegan sushi ingredients will attract customers. The company is also considering selling the product in Japan, where consumers are becoming more health-conscious.

Nishimoto is developing new products. One, called Unami, is an eel alternative made from eggplant. In all, the company is aiming for 200 million yen ($1.82 million) in sales for the first fiscal year, rising to 1.5 billion yen within a few years.

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Sharp rise under-11s referred for mental health help

There has been a sharp rise in the number of children under 11 referred for mental health treatment by schools in the last four years, figures show.

By Hannah Richardson BBC News education reporter

Data obtained by children's charity the NSPCC shows that schools in England have made a total of 123,713 referrals for specialist help since 2014-15. But more than half of these came from primary schools. The youngest child referred for help was three years old.

The government says its reforms will transform services for children.

The figures were released under Freedom of Information laws to the NSPCC by 53 of the 66 health trusts known to provide mental health support to children.

Issues children were referred for included depression and anxiety, sometimes these were so severe that it can lead them to the brink of suicide, said Esther Rantzen founder and president of NSPCC's Childline.

In 2017-18, some 18,870 children aged under 11 were referred for specialist support. This was a rise of 5,183, or more than a third, on those referred in 2014-15.

The statistics also reveal that one-third of those referred to Child Adolescent Mental Health Services (Camhs) were declined help.

The NSPCC said increased demand for support was placing the system under real pressure, and jeopardising the well-being of thousands of children.

Its chief executive Peter Wanless said: "Our research shows schools are increasingly referring children for specialist mental health treatment, often when the child is at crisis point."

Sarah Hannafin, senior policy adviser at the National Association of Head Teachers, said: "More pupils are suffering from mental health issues and there is much more awareness in schools for spotting potential problems and intervening early to get support.

"However, more than a third of referrals are not accepted - schools have referred these pupils because they are concerned about their mental health and know that the child needs more specialist support than could (and should) be offered by school staff.

"However, many of these children are not meeting the thresholds set by Camhs - many are concerned about how high these thresholds are.

"The other concern is about what support those children can then get if they have been turned down by Camhs."

A government spokeswoman said they had pledged £1.7bn to young people's mental health and wellbeing.

"Making sure children and young people get the right support when they need it is imperative," she said. "That is why are allocating £300 million, over and above the additional £1.4bn being invested in specialist services, to provide more support linked to schools.

"This includes new mental health support teams to provide trained mental health workers to work closely with schools -including primary schools - to provide quicker support to children.

"We know we need to do more which is why we have extended our schools and NHS link pilot to deliver training in 20 more areas of the country this year. "This will improve links between up to 1,200 schools and their local specialist mental health service."

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Molecule that acts on human cells might provide hope for 'irresistible' cold cure

Researchers have lab-tested a molecule that can combat the common cold virus by preventing it from hijacking human cells.

Early lab-based tests with human cells have shown the molecule's ability to completely block multiple strains of cold virus, and the team hope to move to animal and then human trials. The results of initial tests are published today in the journal *Nature Chemistry*.

The common cold is caused by a family of viruses with hundreds of variants, making it nearly impossible to become immune to or vaccinate against all of them. On top of that, the viruses evolve rapidly, meaning they can quickly gain resistance to drugs. For these reasons, most cold remedies rely on treating the symptoms of the infection - such as runny nose, sore throat and fever - rather than tackling the virus itself.

However a new molecule, developed by researchers at Imperial College London, targets N-myristoyltransferase (NMT), a protein in human cells. Viruses 'hijack' NMT from human cells to construct the protein 'shell', or capsid, which protects the virus genome.

All strains of the virus need this same human protein to make new copies of themselves, so the molecule should work against all of them. Additionally, the molecule also works against viruses related to the cold virus, such as polio and foot and mouth disease viruses.

The molecule targets a human protein and not the virus itself, making emergence of resistant viruses highly unlikely.

Lead researcher Professor Ed Tate, from the Department of Chemistry at Imperial, said: "The common cold is an inconvenience for most of us, but can cause serious complications in people with conditions like asthma and COPD. A drug like this could be extremely beneficial if given early in infection, and we are working on making a version that could be inhaled, so that it gets to the lungs quickly."

There have been previous attempts to create drugs that target human cells rather than the viruses, but many have the side effect of being toxic.

The researchers showed that the new molecule completely blocked several strains of the virus without affecting human cells. Further study is needed to make sure it is not toxic in the body.

The research team included the labs of Professor Roberto Solari and Professor Seb Johnston at Imperial's National Heart & Lung Institute, Dr Aurelie Mousnier from Imperial and Queen's University Belfast, structural biologists at the University of York, and colleagues at the Pirbright Institute.

Professor Tate said: "The way the drug works means that we would need to be sure it was being used against the cold virus, and not similar conditions with different causes, to minimise the chance of toxic side effects."

The medicinal chemistry team in the Tate group at Imperial, led by Dr Andy Bell (who previously invented Viagra as a researcher at Pfizer), were originally looking for compounds that targeted the protein in malaria parasites. Screening large libraries of compounds, they found two hits and were surprised to discover that they worked best together. By inventing a novel way to combine the two, they created a molecule, codenamed IMP-1088, which is more than a hundred times more potent than previous molecules targeting the protein in humans.

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New tool predicts eye, hair and skin color from a DNA sample of an unidentified individual

New tool will be used when standard forensic profiling is not helpful

INDIANAPOLIS - An international team, led by scientists from the School of Science at IUPUI and Erasmus MC University Medical Center Rotterdam in the Netherlands, has developed a novel tool to accurately predict eye, hair and skin color from human biological material -- even a small DNA sample -- left, for example, at a crime scene or obtained from archeological remains. This all-in-one pigmentation profile tool provides a physical description of the person in a way that has not previously been possible by generating all three pigment traits together using a freely available webtool.

The tool is designed to be used when standard forensic DNA profiling is not helpful because no reference DNA exists against which to compare the evidence sample.

The HIrisPlex-S DNA test system is capable of simultaneously predicting eye, hair and skin color phenotypes from DNA. Users, such as law enforcement officials or anthropologists, can enter relevant data using a laboratory DNA analysis tool, and the webtool will predict the pigment profile of the DNA donor.

"We have previously provided law enforcement and anthropologists with DNA tools for eye color and for combined eye and hair color, but skin color has been more difficult," said forensic geneticist Susan Walsh from IUPUI, who co-directed the study. "Importantly, we are directly predicting actual skin color divided into five subtypes -- very pale, pale, intermediate, dark and dark to black -- using DNA markers from the genes that determine an individual's skin coloration. This is not the same as identifying genetic ancestry. You might say it's more similar to specifying a paint color in a hardware store rather than denoting race or ethnicity.

"If anyone asks an eyewitness what they saw, the majority of time they mention hair color and skin color. What we are doing is using genetics to take an objective look at what they saw," Walsh said.

The innovative high-probability and high-accuracy complete pigmentation profile webtool is available online without charge.

The study, "HIrisPlex-S System for Eye, Hair and Skin Colour Prediction from DNA: Introduction and Forensic Developmental Validation," is published in the peer-reviewed journal *Forensic Science International: Genetics*.

"With our new HIrisPlex-S system, for the first time, forensic geneticists and genetic anthropologists are able to simultaneously generate eye, hair and skin color information from a DNA sample, including DNA of the low quality and quantity often found in forensic casework and anthropological studies," said Manfred Kayser of Erasmus MC, co-leader of the study.

Walsh's forensic DNA phenotyping and predictive DNA analysis work was supported by the National Institute of Justice (grant 2014-DN-BX-K031) and IUPUI. She is an assistant professor of biology at IUPUI and a faculty member of the School of Science's highly respected Forensic and Investigative Sciences program.

She is currently working with the Indiana State Police to determine how this tool can help enhance victim identification and crime-solving.

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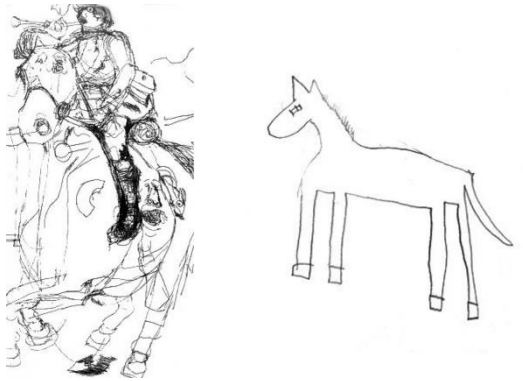
How our ancestors with autistic traits led a revolution in Ice Age art

The ability to focus on detail, a common trait among people with autism, allowed realism to flourish in Ice Age art, according to researchers at the University of York

The ability to focus on detail, a common trait among people with autism, allowed realism to flourish in Ice Age art, according to researchers at the University of York.

Around 30,000 years ago realistic art suddenly flourished in Europe. Extremely accurate depictions of bears, bison, horses and lions decorate the walls of Ice Age archaeological sites such as Chauvet Cave in southern France.



This is a drawing of a horse by Nadia, a gifted autistic child artist (left) and by a typically developing child of the same age (right). **Penny Spikins, University of York**

Why our ice age ancestors created exceptionally realistic art rather than the very simple or stylised art of earlier modern humans has long perplexed researchers.

Many have argued that psychotropic drugs were behind the detailed illustrations. The popular idea that drugs might make people better at art led to a number of ethically-dubious studies in the 60s where participants were given art materials and LSD.

The authors of the new study discount that theory, arguing instead that individuals with "detail focus", a trait linked to autism, kicked off an artistic movement that led to the proliferation of realistic cave drawings across Europe.

Lead author of the paper, Dr Penny Spikins from the Department of Archaeology at the University of York, said: "Detail focus is what determines whether you can draw realistically; you need it in order to be a talented realistic artist. This trait is found very commonly in people with autism and rarely occurs in people without it.

"We looked at the evidence from studies attempting to identify a link between artistic talent and drug use, and found that drugs can only serve to dis-inhibit individuals with a pre-existing ability. The idea that people with a high degree of detail focus, many of which may have had autism, set a trend for extreme realism in ice age art is a more convincing explanation."

The research adds to a growing body of evidence that people with autistic traits played an important role in human evolution.

Dr Spikins added: "Individuals with this trait - both those who would be diagnosed with autism in the modern day and those that wouldn't - likely played an important part in human evolution and survival as we colonised Europe.

"As well as contributing to early culture, people with the attention to detail needed to paint realistic art would also have had the focus to create complex tools from materials such as bone, rock and wood. These skills became increasingly important in enabling us to adapt to the harsh environments we encountered in Europe."

How do we explain 'autistic traits' in European Upper Palaeolithic art? is published in Open Archaeology.

http://bit.ly/2IhDh1i

Scientists Sucked a Memory Out of a Snail and Stuck It in Another Snail.

A new study strongly suggests that at least some memories are stored in genetic code, and that genetic code can act like memory soup.

By Rafi Letzter, Staff Writer | May 14, 2018 02:42pm ET

Suck it out of one animal and stick the code in a second animal, and that second animal can remember things that only the first animal knew.

That might sound like science fiction or remind some readers of debunked ideas from decades past. But it's serious science: In a new study, researchers at the University of California, Los Angeles (UCLA) extracted RNA, a genetic messenger molecule, from one snail and implanted it in another snail. Then, for good measure, they dribbled that same RNA over a bundle of loose neurons in a petri dish. In both experiments, the recipient — either the snail or the petri-neurons — remembered something the donor snail had experienced.

Aplysia californica, also known as the California sea hare **Genny Anderson/CC by 4.0**

The memory was simple, the kind of thing even a snail's reflex-based, brainless nervous system can hold onto: the shock of an electric zap in the butt.

When *Aplysia californica* sea snails get zapped in the tail, they send signals through their simple nervous systems: Retract the parapodia!

At that signal, the little fleshy flaps hanging from their little snail bellies retract.

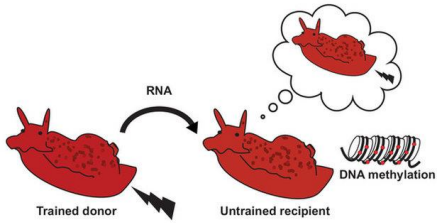
Shock a snail often enough, and it will remember that it's been getting zapped a lot lately, and its parapodia will retract for longer and longer periods of time. That's a simple behavior based on a simple memory. And in the new paper, published today (May 14) in the journal eNeuro, the UCLA scientists showed that they can suck that memory out of one snail in the form of RNA and stick it in another.

"All [that the recipients] were exposed to was RNA from a trained animal [a snail with the zap memory] or an untrained animal, or in some cases, just the chemical we used to deliver the RNA," said David Glanzman, said lead study author David Glanzman, a neuroscientist and integrative biologist at UCLA.

When the RNA came from a snail that hadn't been zapped, the memory recipients acted "naive," retracting their parapodia only briefly after a zap, as if no more zaps were coming. But when snails were exposed to the RNA from a snail that had been zapped, they retracted their parapodia for longer periods after zaps.

"This is important, because it says it's not just [any implanted RNA] that is producing widespread excitability in neurons," Glanzman told Live Science.

Instead, snails with RNA from other snails that had been shocked — and from only those snails — acted just like they had received those initial "teaching" tail shocks themselves.



An illustration from Glanzman's paper shows the transfer of RNA from one snail to another. **David Glanzman/UCLA**

Glanzman and his colleagues were able to see the effect on an even more basic level in their bundle of snail neurons in a petri dish. When the researchers bathed the neurons in RNA from a trained snail for 24 hours, then doused the cells in the chemical messenger that means "butt zap!" (in snails, that chemical is serotonin), the neural cells fired wildly, telling their nonexistent parapodia to retract.

When the neurons were bathed in RNA from untrained snails, the nerve cells' reactions were shorter and less intense.

A long-simmering debate

"This paper describes potentially transformative findings on whether memory could be transplanted through transcriptome [genetic] transfer," said Sathya Puthanveettil, a neuroscientist at the Scripps Research Institute in California who studies memory, but who was not involved in the study.

There's been a long-simmering debate in neuroscience about whether the essential units of memory are stored primarily in the

"transcriptome" (the long molecules inside cells also used to record genes) or the "connectome" (the network of links between nerve cells).

The transcriptome was more popular in the 20th century, when scientists tried and failed to hunt down "memory RNA" in cruder experiments that broadly resembled Glanzman's. Eventually, however, that idea fell into disfavor, and more and more research and funding turned toward the connectome. Today, there are several active attempts to map the connectome in humans, and certain researchers even suggest that the connectome could be used to preserve human memories after death — though this has yet to be proven.

But connectome studies — including the mapping of the entire connectome of the worm *Caenorhabditis elegans* have failed to produce conclusive, predictive evidence of the stuff of memory, and so some scientists have looked less favorably on that work as well.

Indeed, Glanzman is something of a partisan in that debate, and he said he sees his experiment as evidence for his side.

"In my opinion, we're spending way too much time and money studying synaptic connections, and way not enough money studying these RNA-based changes and epigenetics," or changes in how cells interact with their genetic code, he said.

This apparent demonstration of the stuff of memory in snails represents a powerful argument for that cause. Still, it's important to keep in mind that this is just one experiment.

"At the moment, we do not have much mechanistic insight about how this memory transfer is achieved," Puthanveettil told Live Science. "We would need more confirmatory experiments to validate these findings in other models."

In other words, scientists don't know at all how this transfer happened, and it's possible there's something going on in this experiment they don't understand.

Right now, there's a lot more work to be done before scientists can say they've found the stuff of memory. Importantly, the type of memory transferred here, the sensitization of a reflex, is among the most basic that exists.

Glanzman said the next step in this research is to attempt similar feats of memory transfer involving more-complex kinds of memories in more-complex animals, like mice.

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Researcher pinpoints optimal age of puppy cuteness

The popular meme proclaiming that all dogs are puppies assumes that humans' adoration of canines is not conditional on their age.

But a new study led by Clive Wynne, professor of psychology and director of Arizona State University's Canine Science Collaboratory, suggests otherwise.

In a paper published this month in *Anthrozoos: A Multidisciplinary Journal of the Interactions of People and Animals*, Wynne and colleagues describe the study, which found dogs' attractiveness to humans peaks at roughly eight weeks, the same point in time at which their mother weans them and leaves them to fend for themselves.

While spending time in the Bahamas, Wynne was able to observe the many street dogs there. According to him, there are around a billion dogs in the world, 80 percent of whom are feral. For those dogs, human intervention is crucial to their survival. Wynne wondered if there was a connection between pups' weaning age—when they are at their most vulnerable—and their level of attractiveness to humans. So he designed an experiment to test his query.

"It came out exactly as I'd hoped it would—that there is indeed an optimal age of maximum cuteness, and that age does line up pretty closely with the age at which mothers wean their pups," Wynne said.

"This could be a signal coming through to us of how dogs have evolved to rely on human care. This could be dogs showing us how the bond between human and dog is not just something that we find immensely satisfying in our lives. … But for them, it's the absolute bedrock of their existence. That being able to connect with us, to find an emotional hook with us is what actually makes their lives possible."

Sample images of three breeds at different ages. The top row of images depicts a cane corso, the middle row depicts a Jack Russell terrier and the bottom row depicts a white shepherd. The middle column shows each dog at it's "most attractive" age, as rated by participants: six weeks for Cane corsos; a little over seven weeks for Jack Russell terriers; and eight weeks for white shepherds.
Arizona State University

The study was carried out using a series of photographs of puppies at different ages, from the first weeks of life through young adulthood. Fifty-one participants were asked to rank the puppies' level of attractiveness in each photo. Three distinctive-looking breeds were ranked: Jack Russell terriers, cane corsos and white shepherds.

Results showed that the pups' attractiveness was lowest at birth and increased to a maximum before 10 weeks of age before declining and then leveling off.

Cane corsos showed a maximum attractiveness at 6.3 weeks of age; Jack Russell terriers showed a maximum attractiveness at 7.7 weeks of age; and white shepherds showed a maximum attractiveness at 8.3 weeks of age.

"Around seven or eight weeks of age, just as their mother is getting sick of them and is going to kick them out of the den and they're going to have to make their own way in life, at that age, that is exactly when they are most attractive to human beings," Wynne said.

The findings provide insight into the depth and origin of the relationship between humans and dogs, the oldest and most enduring of any human-animal relationship. And while some theories attribute the survival of the canine species to their intelligence, Wynne dissents.

"I think that the intelligence of dogs is not the fundamental issue," he said. "It's this tremendous capacity to form intimate, strong, affectionate bonds. And that starts at maybe eight weeks of life, when they're so compelling to us."

Though humans and other animals, such as cats and birds, have the capacity to form strong bonds, dogs in particular are especially suited to the task because of their gregarious nature. Even in hand-reared wolves, the species from which all dogs are descended, the willingness to engage humans does not match that of the domestic dog.

"It does seem to me that the dog has something rather special," Wynne said. "Dogs have a very open-ended social program. That they are ready and willing to make friends with anybody."

Wynne has thought of a couple of interesting ways to follow up on the cuteness study. One way is to show participants video of puppies at different ages, instead of still photos, to determine if perhaps there is something in the pups' movement that attracts people. Another is to

determine what the pups' mother thinks about their level of attractiveness at different ages, though that is obviously easier said than done.

The takeaway from the study for Wynne is that extra piece of the puzzle that makes up the human-dog connection.

"[The study] doesn't mean to say that we stop loving our dogs past [eight weeks]," he said. "The eight-week point is just the point where the hook is biggest, the ability of the animal to grab our interest is strongest. But, having grabbed our interest, we continue to love them all their lives."

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F.D.A. Moves to Stop Rogue Clinics From Using Unapproved Stem Cell Therapies

The Food and Drug Administration said on Wednesday that it was seeking court orders to stop two clinics from using unapproved stem cell treatments that in some cases have seriously harmed patients.

By Denise Grady and Sheila Kaplan

The clinics remove fat from patients' bellies by liposuction and then inject an extract of it into various parts of the body like knees or the spinal cord, on the theory that the extract contains stem cells that can provide replacement cells that will repair the damage from injury or illness.

The agency filed two complaints seeking permanent injunctions in federal court, one against U.S. Stem Cell Clinic L.L.C. of Sunrise, Fla.; its chief scientific officer, Kristin Comella; and its co-owner and managing officer, Theodore Gradel.

The second complaint was against the California Stem Cell Treatment Center, with locations in Rancho Mirage and Beverly Hills; the Cell Surgical Network Corporation of Rancho Mirage; and Dr. Elliot B. Lander and Dr. Mark Berman.

The U.S. Stem Cell Clinic marketed stem cell products to patients without F.D.A. approval and "while violating current good manufacturing practice requirements, including some that could impact the sterility of their products, putting patients at risk," the F.D.A. said in a statement.

The agency said it was acting because the U.S. Stem Cell Clinic did not address violations outlined in a warning letter from the F.D.A. last August.

Three patients lost their sight after the material extracted from fat by the U.S. Stem Cell Clinic was injected directly into their eyes in 2015 to treat macular degeneration. During an interview in 2017, Ms. Comella said the clinic did not need F.D.A. approval because it was treating patients with their own cells, which are not a drug.

In response to the F.D.A. injunction filings on Wednesday, Ms. Comella issued a statement that said, in part: "It is my life's work to pioneer regenerative medicine and educate the public about its healing potential. I remain steadfast that no government agency should deprive individuals of their right to harness the cells that exist in their body."

In the complaint against the California Stem Cell Treatment Center, the F.D.A. said it had acted in August to prevent the use of a "potentially dangerous and unproven treatment belonging to StemImmune Inc. in San Diego," and given to patients at the clinics in Rancho Mirage and Beverly Hills.

In August, United States marshals, acting on behalf of the F.D.A., seized vials of smallpox vaccine that was being used to create a stem cell product that was being given to cancer patients at the California clinics. The product posed a risk to those patients of inflammation of the heart and surrounding tissues, the agency said.

The California center trains other physicians in how to extract stem cells and has affiliates around the country. A Florida woman, Doris Tyler, lost her sight after being treated at an affiliate, the Ageless Wellness Center in Peachtree City, Ga. Cells from her fat were injected into both eyes.

Dr. Berman said that many people had been helped by his clinic and that he had tried to work out a compromise with the F.D.A. but was unable to do so. He also said he believed the cells that are harvested

from individuals do not constitute a drug and should not be regulated as such.

In its statement, the F.D.A. also said that both the U.S. Stem Cell Clinic and the California Stem Cell Treatment Center were using cell extracts to treat serious conditions — including Parkinson's disease, amyotrophic lateral sclerosis and chronic obstructive pulmonary disease — but that their products were not approved for any use.

The F.D.A. oversight of stem cell therapies and regenerative medicine is still in flux. In August, Dr. Scott Gottlieb, the agency's commissioner, called the field one of the most promising areas of science and medicine, holding great promise for some of the world's most intractable illnesses. He vowed that the F.D.A. would ease the path to approval for researchers and companies that were developing legitimate treatments — a program authorized by Congress in the 21st Century Cures Act.

At the same time, however, Dr. Gottlieb vowed to crack down on clinics making hollow claims and marketing unsafe treatments. He also announced the action against the California Stem Cell Treatment Centers in Rancho Mirage and Beverly Hills and against the U.S. Stem Cell Clinic.

In November, the F.D.A. continued work along both themes.

The agency acknowledged the difficulty in pursuing rogue clinics and suggested that consumers check up on stem cell clinics before receiving treatment.

Dr. Peter Marks, director of the F.D.A.'s center for biologics evaluation and research, said that the agency would continue to pursue unscrupulous clinics, but that those performing orthopedic procedures — injecting the fat-derived cells into joints — would take a back seat to clinics that inject or infuse cells into the central nervous system or bloodstream.

At the time, Dr. Marks said: "There are hundreds and hundreds of these clinics. We simply don't have the bandwidth to go after all of them at once."

http://bit.ly/2rVYjZk

Scientists' discovery in Yellowstone 'extremely relevant' to origin of life

The findings were published today in the scientific journal Nature Microbiology

BOZEMAN -- Montana State University scientists have found a new lineage of microbes living in Yellowstone National Park's thermal features that sheds light on the origin of life, the evolution of archaeal life and the importance of iron in early life.

Professor William Inskeep and his team of researchers published their findings May 14 in the scientific journal *Nature Microbiology*.

"The discovery of archaeal lineages is critical to our understanding of the universal tree of life and evolutionary history of the Earth," the group wrote. "Geochemically diverse thermal environments in Yellowstone National Park provide unprecedented opportunities for studying archaea in habitats that may represent analogues of early Earth."

Archaea is one of the three domains of life, the others being bacteria and eukaryotes. Like bacteria, archaea are single-cell organisms. The eukaryote domain contains more cellularly complex organisms, such as humans, other animals, plants and fungi.

The scientists called the new archaeal lineage Marsarchaeota after Mars, the red planet, because these organisms thrive in habitats containing iron oxides. Within Marsarchaeota, they discovered two main subgroups that live throughout Yellowstone and thrive in hot, acidic water where iron oxide is the main mineral. One subgroup lives in water above 122 degrees Fahrenheit, and the other lives in water above 140 to 176 degrees. The water is about as acidic as grapefruit juice. Their microbial mats are red because of the iron oxide.

"It's interesting that the habitat of these organisms contains (iron) minerals similar to those found on the surface of Mars," Inskeep said.

He added that microbes produce iron oxide, but the Marsarchaeota do not. They might be involved in reducing iron into a simpler form,

"which is important from an early Earth standpoint. Iron cycling has been implicated as being extremely important in early Earth conditions."

The Marsarchaeota live fairly deep in microbial mats, but they still require low levels of oxygen, Inskeep said. The subgroups are so abundant that, together, they can account for as much as half of the organisms living within a single microbial mat.

The scientists studied microbial mats throughout Yellowstone. Microorganisms in these "microbial beaver dams" produce iron oxide that creates terraces, which, in turn, block streams. As water (only a couple of millimeters deep) runs over the terraces, oxygen is captured from the atmosphere and supplied to the Marsarchaeota.

"Physics comes together with chemistry and microbiology," Inskeep said. "It's like a sweet spot of conditions that this group of organisms likes."

In addition to learning more about life on early Earth and the potential for life on Mars, Inskeep said the research can help scientists understand more about high-temperature biology.

"Knowing about this new group of archaea provides additional pieces of the puzzle for understanding high-temperature biology," he said. "That could be important in industry and molecular biology."

The work that resulted in the Nature Microbiology paper was the culmination of research that took place over the past decade, said Inskeep, who has studied the geochemistry and microbiology of Yellowstone's high-temperature environments for the last 20 years. Inskeep is a professor of geomicrobiology in MSU's Department of Land Resources and Environmental Sciences in the College of Agriculture and co-founder of MSU's Thermal Biology Institute.

The lead authors of the Nature Microbiology paper earned their doctorates at MSU and were part of NSF's Integrative Graduate Education and Research Traineeship (IGERT) program while at MSU. Zackary Jay is now a postdoctoral researcher in the Department of Chemical and Biological Engineering in the Norm Asbjornson College of Engineering and the Center for Biofilm Engineering at MSU. Jacob Beam is now a postdoctoral researcher at Bigelow Laboratory for Ocean Sciences at East Boothbay, Maine.

"In the end, after many years of work, it's exciting, and a relief, to have our team's work recognized and published, particularly in a high impact journal," Jay said.

Other co-authors were Mensur Dlakic from MSU's Department of Microbiology and Immunology in the College of Letters and Science and College of Agriculture; Douglas Rusch from the Center for Bioinformatics at Indiana University; and Mark Kozubal from the Thermal Biology Institute, MSU's Department of Land Resources and Environmental Sciences, and Sustainable Bioproducts in Bozeman.

The Yellowstone research was a collaboration involving the Thermal Biology Institute, the Montana Agriculture Experiment Station (MAES) and the Yellowstone Center for Resources (National Park Service). Funding came from IGERT, the Pacific Northwest National Laboratory and MAES. The U.S. Department of Energy Joint Genome Institute in Walnut Creek, California, sponsored the genetic sequencing.

http://bit.ly/2IzWU0J

For 'Flesh-Eating' Bacteria, Your Agonizing Pain Is Their Pleasure

Bacteria that "eat" your flesh are also hijacking your pain receptors for their own benefit.

By Mindy Weisberger, Senior Writer | May 15, 2018 06:57am ET

The microbe *Streptococcus pyogenes* causes strep throat, but it's also responsible for a deadly "flesh-eating" disease called necrotizing fasciitis. During the initial stages of the flesh-destroying infection, the bacteria emit a toxin that causes excruciating pain. And this awful side effect is very useful to *S. pyogenes*; the chemical that causes the intense pain also hampers the host's immune system and creates a more hospitable environment for the microbe to thrive and reproduce, scientists recently discovered.

But the chemical weapons that make *S. pyogenes* so formidable may also contain the means to defeat it. By investigating the bacteria's toxic arsenal, researchers may have also figured out how to turn that mechanism to a patient's own advantage, according to a new study, published online May 10 in the journal Cell.

Other types of bacteria can cause necrotizing fasciitis, including *Clostridium*, *Staphylococcus aureus* and *Escherichia coli*, but *S. pyogenes*, also known as Group A strep, is the most common culprit, the study authors reported. Infection usually sets in after the bacteria enter the body through a break in the skin, and the disease attacks fascia — the connective tissue surrounding nerves, muscles, blood vessels and fat — and spreads rapidly. In its earliest stages, it brings pain that is "out of proportion" to the infection. In later stages, the infection has a mortality rate as high as 32 percent, the researchers wrote.

Terrible pain signals to an infected host that something is wrong. But in the case of *S. pyogenes*, its method for inflicting pain also benefits the bacteria by shielding it against host defenses that would normally attack microscopic invaders, the researchers discovered.

A chemical disruption

In experiments using mice, the scientists found that *S. pyogenes* produced a toxin called streptolysin S (SLS), which activated certain pain-related neurons to trigger extreme pain. But the toxin also prodded the same neurons into emitting a peptide that disrupted communication with the immune system. In doing so, *S. pyogenes* effectively muted the body's call to action for disease-fighting cells, leaving the bacteria free to multiply and kill off even more tissue, according to the study.

The peptide also interfered with normal function in the immune cells that did manage to reach the infection site, preventing them from dispensing an enzyme that would kill the invasive bacteria, the scientists reported.

"This neuronal signal silences the alarm system that normally calls on the body's infection fighters to curb infection," the study's senior author Isaac Chiu, an assistant professor of microbiology and immunobiology at Harvard Medical School, said in a statement.

Based on this observation, the researchers suspected that they could sideline the bacteria's battle plan and treat necrotizing fasciitis with compounds that interacted with neurons — suppressing pain and muffling the release of the peptide that switched off the host's defense responses.

They injected mice with *S. pyogenes*, as well as another compound: botulinum neurotoxin A, a protein used to smooth facial wrinkles and treat muscle spasms. Botulinum toxin — also known as Botox — works by blocking nerve signals. In the infected mice, this prevented the bacteria from gaining the upper hand, regardless of whether the mice received the nerve-blocking agent before or after they were exposed to *S. pyogenes*.

In another experiment, the scientists introduced another compound, which blocked the release of the neurotransmitter that paused the host's immune system, also preventing the bacteria from going undetected.

Their work revealed not only that neurons play a pivotal role in the progression of necrotizing fasciitis, but also suggested that manipulating neurons might be a path to treating this terrible disease, the researchers concluded.

"Our findings provide a striking example of how closely intertwined the nervous and immune systems are and how intricate their interaction can be in the setting of infection," Chiu said in the statement.

"Our study also underscores the therapeutic potential of modulating one system to affect the other as a way to treat infection."

The study was done in mice, so more research is needed to confirm whether the same mechanisms apply in humans.

http://bit.ly/2Iy4Yza

Scientists crack how primordial life on Earth might have replicated itself

Scientists have created a new type of genetic replication system which demonstrates how the first life on Earth - in the form of RNA - could have replicated itself.

The scientists from the Medical Research Council (MRC) Laboratory of Molecular Biology say the new RNA utilises a system of genetic replication unlike any known to naturally occur on Earth today.

A popular theory for the earliest stages of life on Earth is that it was founded on strands of RNA, a chemical cousin of DNA. Like DNA, RNA strands can carry genetic information using a code of four molecular letters (bases), but RNA can be more than a simple 'string' of information. Some RNA strands can also fold up into three-dimensional shapes that can form enzymes, called ribozymes, and carry out chemical reactions.

If a ribozyme could replicate folded RNA, it might be able to copy itself and support a simple living system.

Previously, scientists had developed ribozymes that could replicate straight strands of RNA, but if the RNA was folded it blocked the ribozyme from copying it. Since ribozymes themselves are folded RNAs, their own replication is blocked.

Now, in a paper published today in the journal *eLife*, the scientists have resolved this paradox by engineering the first ribozyme that is able to replicate folded RNAs, including itself.

Normally when copying RNA, an enzyme would add single bases (C, G, A or U) one at a time, but the new ribozyme uses three bases joined together, as a 'triplet' (e.g. GAU). These triplet building blocks enable the ribozyme to copy folded RNA, because the triplets bind to the RNA much more strongly and cause it to unravel - so the new ribozyme can copy its own folded RNA strands.

The scientists say that the 'primordial soup' could have contained a mixture of bases in many lengths - one, two, three, four or more bases joined together - but they found that using strings of bases longer than a triplet made copying the RNA less accurate.

Dr Philipp Holliger, from the MRC Laboratory of Molecular Biology and senior author on the paper, said: "We found a solution to the RNA replication paradox by re-thinking how to approach the problem - we stopped trying to mimic existing biology and designed a completely new synthetic strategy. It is exciting that our RNA can now synthesise itself.

"These triplets of bases seem to represent a sweet spot, where we get a nice opening up of the folded RNA structures, but accuracy is still high. Notably, although triplets are not used in present-day biology for replication, protein synthesis by the ribosome - an ancient RNA machine thought to be a relic of early RNA-based life - proceeds using a triplet code.

"However, this is only a first step because our ribozyme still needs a lot of help from us to do replication. We provided a pure system, so the next step is to integrate this into the more complex substrate mixtures mimicking the primordial soup - this likely was a diverse chemical environment also containing a range of simple peptides and lipids that could have interacted with the RNA."

The experiments were conducted in ice at -7°C, because the researchers had previously discovered that freezing concentrates the RNA molecules in a liquid brine in tiny gaps between the ice crystals. This also is beneficial for the RNA enzymes, which are more stable and function better at cold temperatures.

Dr Holliger added: "This is completely new synthetic biology and there are many aspects of the system that we have not yet explored. We hope in future, it will also have some biotechnology applications, such as adding chemical modifications at specific positions to RNA polymers to study RNA epigenetics or augment the function of RNA."

Dr Nathan Richardson, Head of Molecular and Cellular Medicine at the MRC, said: "This is a really exciting example of blue skies research that has revealed important insights into how the very beginnings of life may have emerged from the 'primordial soup' some 3.7 billion years ago. Not only is this fascinating science, but understanding the minimal requirements for RNA replication and how these systems can be manipulated could offer exciting new strategies for treating human disease."

http://bit.ly/2GxYmz5

What we inherited from our bug-eating ancestors

Genes for digesting chitin found in most mammal genomes, betraying our insectivore heritage

People who advocate adding insects to the human diet may be channeling their distant ancestors.

Based on an analysis of the genomes of 107 different species of mammals, University of California, Berkeley, scientists conclude that our distant ancestors - the small, furry creatures that scurried around the feet of the dinosaurs 66 million years ago - were mostly insect eaters.

The scientists inferred this because the genes for the enzymes that allowed these early ancestors of all mammals to digest insects are still hanging around in nearly all mammal genomes today. Even animals like tigers and seals that would never touch an insect have non-functional pieces of these genes sitting in their chromosomes, betraying their ancient ancestors' diet.

A spectral tarsier (Tarsius tarsier) feeding on a grasshopper in Tangkoko National Park, Northern Sulawesi, Indonesia. Tarsiers have five chitinase genes to digest the high amount of chitin in their insectivorous diet, which likely represents the ancestral condition of all placental animals, including humans.
Quentin Martinez

"One of the coolest things is, if you look at humans, at Fido your dog, Whiskers your cat, your horse, your cow; pick any animal, generally speaking, they have remnants in their genomes of a time when mammals were small, probably insectivorous and running around when dinosaurs were still roaming Earth," said postdoctoral fellow Christopher Emerling. "It is a signature in your genome that says, once upon a time you were not the dominant group of organisms on Earth. By looking at our genomes, we are looking at this ancestral past and a lifestyle that we don't even live with anymore."

The genetic evidence independently corroborates the conclusions paleontologists reached years ago based on the shapes of fossils and teeth from early mammals.

"In essence, we are looking at genomes and they are telling the same story as the fossils: that we think these animals were insectivorous and then dinosaurs went extinct. After the demise of these large carnivorous and herbivorous reptiles, mammals started changing their diets," he said.

The finding could shed light on other roles played by these enzymes, called chitinases, which are found not only in the gut but the salivary glands, the pancreas and the lungs, where they may be involved in asthma.

Emerling and colleagues Michael Nachman, a professor of integrative biology and director of the UC Berkeley Museum of Vertebrate Zoology, and Frédéric Delsuc of the French National Center for Scientific Research (CNRS) and Université de Montpellier in France, will report their findings May 16 online in the journal *Science Advances*. Emerling currently is a PRESTIGE & Marie Curie postdoctoral fellow in Montpellier working on the ConvergeAnt project.

Breaking down insects' exoskeletons

Many bacteria have genes that produce an enzyme that breaks down insects' hard, outer shells, which are composed of a tough carbohydrate called chitin. It's not surprising that humans and mice have a chitinase gene, since many humans today include insects in their diets, as do mice. But humans actually have remnants of three other chitinase genes in their genome, though none of them are functional. Emerling showed that these gene remnants in humans aren't unique to humans or primates, but instead can be traced to the ancestral placental mammals.

In all, he and his colleagues found five different chitinase enzyme genes by looking through the genomes of the largest group of mammals, those that have placentas that allow longer development in the womb, which excludes marsupials like opossums and egg-laying monotremes like the platypus. These placental mammals ranged from shrews and mice to elephants and whales.

They found that the greater the percentage of insects in an animal's diet, the more genes for chitinase it has.

"The only species that have five chitinases today are highly insectivorous, that is, 80 to 100 percent of their diet consists of insects. Since the earliest placental mammals likely had five chitinases, we think that this makes for a strong argument that they were highly insectivorous," Emerling said.

As you would expect, ant and termite specialists such as aardvarks and certain armadillos have five functioning chitinase genes. But so do the insect-loving primates called tarsiers. They appear to be the only primates that have so many functional chitinase genes, Emerling said.

Dominated by dinosaurs

The story told by these chitinase genes is one of early mammals hunkering down eating insects while the big guys, the huge herbivorous dinosaurs like the brontosaurus and the big meat-eaters like T. rex gobbled up the most abundant food resources. Only 66 million years ago at the end of the Cretaceous Period, when all non-bird dinosaurs died out, were mammals able to expand into other niches, which they quickly did. The first carnivorous and herbivorous mammals, as indicated by their teeth, arose within 10 million years of the dinosaurs' demise.

Emerling, who compares genomes to see how mammals and humans evolved, was interested in what mammal genomes could tell us about that transition from insectivory to herbivory and carnivory since the last mass extinction.

He focuses primarily on weird animals that eat insects, including anteaters and armadillos, the unrelated aardvark and the distantly related pangolin. In exploring how these animals are able to digest insects, he decided to look at chitinases, whose roles in mammals are still poorly understood. It's not known, for example, whether the enzymes allow animals to break down chitin into its component sugars and use them for energy, or if chitinases' sole function is to break up the exoskeleton to allow access to the soft interiors of insects.

Using databases of animal genomes, plus newly sequenced genomes of armadillos and a lesser anteater (tamandua) obtained by colleagues at the Broad Institute at MIT and Harvard, he searched for genes similar to the known chitinase gene and dredged up four new varieties.

Based on what is known about chitinase genes in bacteria and other animals, he was able to deduce which genes are functional and which are not, and draw conclusions about the tissues in which the genes are expressed and the enzyme active.

Among the surprises was that the insect-eating-specialist pangolin has only one functional chitinase gene, in contrast to the five in the aardvark and four in the lesser anteater. All eat ants and termites exclusively, but pangolins may have possibly evolved from carnivores that lost their chitinase genes shortly after taking over the ecological niche opened up when meat-eating dinosaurs died out.

Bison, gibbons and the dromedary camel have only one functional chitinase. Tigers, rhinos and polar bears have none.

Emerling has many other questions he thinks chitinases can answer about mammal evolution and physiology.

"This is suggesting that there are a lot of these enzymes that might be helping organisms digest their food. This goes from being a simple curiosity - humans have a chitinase, how cool! - to being something that can help us understand how different animals are adapted to their specialized diets."

The research was supported by the National Science Foundation, France-Berkeley Fund, PRESTIGE Programme and European Research Council.

http://bit.ly/2Izh5fe

Traditional Chinese medicine is widely used for cardiovascular disease

A recently published article in the journal of Cardiovascular Innovations and Applications

In this Letter to the Editor, the authors comment on a review article by Hao et al. Traditional Chinese Medicine for Cardiovascular Disease: Evidence and Potential Mechanisms, J Am Coll Cardiol

2017;69(24):2952-66 which assesses the efficacy and safety of TCM for cardiovascular disease, as well as the pharmacological effects of active TCM ingredients on the cardiovascular system and potential mechanisms.

The authors provide a brief summary addressing nonpharmacotherapy in TCM, including acupuncture, moxibustion, Qigong, and Tai Chi. They also discuss traditional antiarrhythmic drug-related randomized controlled trials to make the coverage more comprehensive, before noting that they support the concept that research into, development of, and application of active ingredients is part of modern TCM.

Traditional Chinese Medicine Is Widely Used for Cardiovascular Disease

Yanwei Xing, MD, PhD1, Hector Barajas-Martinez, PhD2 and Dan Hu, MD, PhD3,4
1Guang' Anmen Hospital, Chinese Academy of Chinese Medical Sciences, Beijing 100053, China
2Global Genetics Corporation, Ventura, CA 93003, USA
3Department of Cardiology and Cardiovascular Research Institute, Renmin Hospital of Wuhan University, Wuhan 430060, China
4Hubei Key Laboratory of Cardiology, Wuhan 430060, China

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http://bit.ly/2rVFmpH

Microglia are key defenders against prion diseases

Helpful activity of microglia may have a role in slowing the progression of prion diseases

WHAT: Prion diseases are slow degenerative brain diseases that occur in people and various other mammals. No vaccines or treatments are available, and these diseases are almost always fatal. Scientists have found little evidence of a protective immune response to prion infections. Further, microglia--brain cells usually involved in the first level of host defense against infections of the brain--have been thought to worsen these diseases by secreting toxic molecules that can damage nerve cells.

Now, scientists have used an experimental drug, PLX5622, to test the role of microglia against scrapie, a prion disease of sheep. PLX5622 rapidly kills most of the microglia in the brain. When researchers gave the drug to mice infected with scrapie, microglia were eliminated and the mice died one month faster than did untreated mice. The results, published in the *Journal of Virology* by researchers from the National Institute of Allergy and Infectious Diseases at the National Institutes of Health, suggest that microglia can defend against a prion infection and thus slow the course of disease. The scientists hypothesize that microglia trap and destroy the aggregated prion proteins that cause brain damage.

The findings suggest that drugs that increase the helpful activity of microglia may have a role in slowing the progression of prion diseases. Researchers are now studying the details of how microglia may be able to destroy prions in the brain. The scientists note that microglia could have a similar beneficial effect on other neurodegenerative diseases associated with protein aggregation, such as Alzheimer's disease and Parkinson's disease.

ARTICLE: J Carroll, et al. Microglia are critical in host defense against prion disease. Journal of Virology DOI: 10.1128/JVI.00549-18 (2018).

WHO: Bruce Chesebro, M.D., chief of the NIAID Laboratory of Persistent Viral Diseases, is available to comment on this study.

http://bit.ly/2rWv9bK

Sex, viruses and cancer

Erectile dysfunction drugs and flu vaccine may work together to help immune system fight cancer after surgery

A new study suggests that a common treatment for erectile dysfunction combined with the flu vaccine may be able to help the immune system mop up cancer cells left behind after surgery. The study, published in OncoImmunology, shows that this unconventional strategy can reduce the spread of cancer by more than 90 percent in a mouse model. It is now being evaluated in a world-first clinical trial.

"Surgery is very effective in removing solid tumours," said senior author Dr. Rebecca Auer, surgical oncologist and head of cancer research at The Ottawa Hospital and associate professor at the University of Ottawa. "However, we're now realizing that, tragically, surgery can also suppress the immune system in a way that makes it easier for any remaining cancer cells to persist and spread to other organs. Our research suggests that combining erectile dysfunction drugs with the flu vaccine may be able to block this phenomenon and help prevent cancer from coming back after surgery."

The current study investigated sildenafil (Viagra), tadalafil (Cialis) and an inactivated influenza vaccine (Agriflu) in a mouse model that mimics the spread of cancer (metastasis) after surgery. The researchers

evaluated these treatments by counting the number of metastases in mouse lungs. They found an average of:

- ***37 metastases with cancer cells alone***
- ***129 metastases with cancer cells and surgery***
- ***24 metastases with cancer cells, surgery and one of the erectile dysfunction drugs***
- ***11 metastases with cancer cells, surgery, one of the erectile dysfunction drugs and the flu vaccine***

Dr. Auer is now leading the first clinical trial in the world of an erectile dysfunction drug (tadalafil) and the flu vaccine in people with cancer. It will involve 24 patients at The Ottawa Hospital undergoing abdominal cancer surgery. This trial is designed to evaluate safety and look for changes in the immune system. If successful, larger trials could look at possible benefits to patients.

"We're really excited about this research because it suggests that two safe and relatively inexpensive therapies may be able to solve a big problem in cancer," said Dr. Auer. "If confirmed in clinical trials, this could become the first therapy to address the immune problems caused by cancer surgery."

Using a variety of mouse and human models, Dr. Auer's team has also made progress in understanding how erectile dysfunction drugs and the flu vaccine affect cancer after surgery. Normally, immune cells called natural killer (NK) cells play a major role in killing metastatic cancer cells. But surgery causes another kind of immune cell, called a myeloid derived suppressor cell (MDSC), to block the NK cells. Dr. Auer's team has found that erectile dysfunction drugs block these MDSCs, which allows the NK cells to do their job fighting cancer. The flu vaccine further stimulates the NK cells.

"Cancer immunotherapy is a huge area of research right now, but we're still learning how best to use it in the time around surgery," said first author Dr. Lee-Hwa Tai, former postdoctoral fellow in Dr. Auer's lab and now assistant professor at the Université de Sherbrooke. "This research is an important step forward that opens up many possibilities."

Dr. Auer noted that although erectile dysfunction drugs and the flu vaccine are widely available, people with cancer should not self-medicate. Any changes in medication should be discussed with an oncologist.

Acknowledgements and additional information: Dr. Auer's research is supported by generous donations to cancer research at The Ottawa Hospital. She also holds a Scientist Award from the Canadian Institutes of Health Research and a Tier 2 Clinical Research Chair in Perioperative Cancer Therapeutics from the University of Ottawa. This study was also supported by the Canadian Cancer Society Research Institute and the Cancer Research Society. The trial is funded by Gateway for Cancer Research, a non-profit dedicated to funding innovative, patient-centric Phase I and Phase II clinical trials for cancers of all types. Dr. Auer is a member of BioCanRx, the Canadian Oncolytic Virus Consortium (funded by the Terry Fox Research Institute) and the Ontario Immuno-oncology Translational Research Initiative at the Ontario Institute for Cancer Research. The Ottawa Health Science Network Research Ethics Board has approved the trial, as well as this media release. The makers of tadalafil, sildenafil and the flu vaccine have no role in this research. People in Ottawa who are interested in participating in Dr. Auer's trial should speak with their surgeon or oncologist.

http://bit.ly/2IBbQMb

Doctors in US and Canada launch sweeping pharmaceutical reform proposal

Plan published today in the British Medical Journal outlines 7 steps to slash costs, improve access, and increase safety of prescription drugs

WASHINGTON, D.C. -- The skyrocketing cost of prescription drugs is one of the biggest concerns for American voters. However, in his proposal last Friday, President Donald Trump failed to offer any new policies that would expand access, reduce costs, or increase the safety and efficacy of prescriptions.

Today, a group of 21 prominent physicians published a comprehensive proposal to ensure universal access to safe, innovative, and affordable medications. "Healing an ailing pharmaceutical system: prescription for reform for the U.S. and Canada," identifies seven critical areas for reform, along with both short- and long-term solutions to improve the development, approval process, affordability, and marketing of medications:

1. Access: Even insured patients face high out-of-pocket costs, leaving them unable to fill prescriptions. To achieve universal access, the proposal calls on the U.S. and Canada to establish national formularies of the safest, most effective, and least expensive medications, and provide all residents with full coverage of formulary drugs without copays or deductibles.

2. Affordability: The industry's pricing strategy is to charge whatever the market will bear, regardless of the actual cost of development. As a result, the U.S. spends about twice as much per-capita on prescriptions than any other nation. Under this proposal, public agencies would negotiate with manufacturers to make branded medications more affordable, and if negotiations fail, issue a "compulsory license" to allow generic manufacturing. The U.S. and Canadian governments also would create a publicly owned manufacturing capacity to produce needed products, along with an increase in public funding for the development of non-patented medications.

3. Preclinical development and patent protection: The current patent system encourages the development of "me-too" products that offer only trivial modifications and higher costs. Under this proposal, patents would be limited to medications that provide real innovation. While current law allows publicly funded researchers to patent and sell their discoveries to private firms, this proposal would keep publicly funded research in the public domain. The plan also calls for health agencies to fund a new public research program to develop and test new treatments outside of the patent system, prioritizing medications with high clinical value, and for conditions deemed unprofitable and ignored by the industry. Such treatments could be sold cheaply as generics as soon as they are brought to market.

4: Clinical testing: Most clinical trials are conducted by private firms, often using unsound methods and selective reporting, calling into question the objectivity of research and the usefulness and safety of new therapies. Corporate ownership of trial data can hide safety problems and obstruct further research. The proposal calls on approval agencies to increase standards for clinical trials and increase transparency by making all trial data publicly available. Experts believe that most clinical trials should be funded and supervised by public health agencies to maintain safety standards and to facilitate innovation for needed treatments.

5. Approval reform: Regulatory agencies are funded primarily by industry fees, creating conflicts of interest. Too many unsafe products are approved, and the increased use of "expedited reviews" and weaker standards of evidence threatens to bring more unsafe or ineffective products to market. This proposal would strengthen regulators' independence by funding them exclusively with public funds. Approval agencies would strictly limit expedited reviews and the use of surrogate endpoints only to treatments likely to offer genuine clinical advances.

6. Postmarketing surveillance: Due to weakening of the approval process, postmarket studies are critical to confirm the efficacy and safety of medications already in use. However, regulators fail to penalize firms that don't complete them. The proposal would require that companies promptly perform and submit safety studies after their products are on the market, increase regulators' funding for postmarketing surveillance, and give regulators the power to order safety warnings and remove unsafe therapies from the market.

7. Promotion: : Pharmaceutical corporations spend more on marketing than on research and development, and their promotional materials often include inaccurate or misleading claims. This proposal would improve monitoring and stiffen sanctions for misleading or off-label promotions. Companies would be prohibited from funding continuing medical education programs for providers.

"Our pharmaceutical system prioritizes industry profits over public health, but it doesn't have to be this way," said Dr. Adam Gaffney, a critical care physician and faculty member at Harvard Medical School, and co-chair of the Pharmaceutical Reform Working Group. "Through a series of commonsense reforms, we can increase the affordability, safety, and effectiveness of medicine for our patients."

Dr. Gaffney warned that combating the power of major pharmaceutical firms won't be easy, noting that the industry spent a combined $171 million on lobbying last year. "Every year we wait for reform means another spike in drug prices," he said.

"The pharmaceutical industry directly funds the regulating arm of the FDA, and paid more than $800 million in user fees in 2017," said Dr. Sidney Wolfe, founder of Public Citizen's Health Research Group. "The

FDA's independence is too important to expose to the influence and money of the industry." Dr. Wolfe added that increasing affordability of lifesaving therapies should be a national priority. "Lack of access to medicines results in preventable deaths and serious illness to hundreds of thousands of patients a year," he said.

"Healing an ailing pharmaceutical system: prescription for reform for U.S. and Canada," by Adam Gaffney, M.D., and Joel Lexchin, M.S., M.D., British Medical Journal, went online today (May 17, 2018). The writing committee includes Marcia Angell, M.D., Michael Carome, M.D., Steffie Woolhandler, M.D., M.P.H., David U. Himmelstein, M.D., Gordon Schiff, M.D., and Sidney Wolfe, M.D.

The full proposal and supplemental materials can be found at http://www.pnhp.org/pharma.

http://bit.ly/2IxtAIh

Study: Cost Effective to Test for All Lung Cancer Mutations at Once

Testing lung cancer patients for all genetic mutations driving their cancer at once more cost effective than testing for a limited number of genes at a time

CHICAGO - Testing advanced lung cancer patients for all of the possible genetic mutations that could be driving their cancer at once is more cost effective than testing for one or a limited number of genes at a time, U.S. researchers reported Wednesday.

There are eight targeted therapies doctors can use to treat nonsmall-cell lung cancer (NSCLC) patients based on genetic defects, and more treatments are in clinical trials or awaiting approval.

Companies such as Foundation Medicine Inc. and Thermo Fisher Scientific Inc. offer genetic profiling tests using so-called next-generation sequencing that can identify hundreds of potential cancer-causing gene mutations from a small tissue sample at once. These tests are used to match patients to specific therapies targeting those genes or to clinical trials testing new drugs.

Insurance companies have been slow to pay for sequencing for all possible mutations at once, arguing such comprehensive testing amounts to funding research, not medical care. They often require doctors to test for individual genes sequentially or use a limited panel that looks for suspect genes associated with approved treatments.

“Our results showed there were substantial cost savings compared with all the other strategies,” Dr. Nathan Pennell of the Cleveland Clinic’s lung cancer program said in a telephone briefing Wednesday.

Last November, the U.S. Food and Drug Administration approved Foundation’s next-generation test, and the Centers for Medicare and Medicaid Services in March said it would pay for next-generation sequencing for Medicare-eligible patients with advanced cancer.

Often, tumor tissue from a biopsy is scarce, and sequential testing can sometimes require a second biopsy to gather more sections of the tumor.

In the study released ahead of the American Society of Clinical Oncology Meeting in Chicago next month, researchers at the Cleveland Clinic and colleagues modeled the cost of next-generation sequencing versus other types of testing to Medicare and to a commercial health plan with one million hypothetical members.

In the model, which was based on the number and age of NSCLC patients in the United States, next-generation sequencing saved as much as $2.1 million for Medicare, the government health plan for older Americans, and more than $250,000 for commercial providers.

The study did not factor in the cost of treatment. The study was funded by Swiss drugmaker Novartis, maker of Zykadia, a drug that targets ALK mutations found in about 4 percent of NSCLC cases.

http://bit.ly/2s1QUYD

Moon Dust Is Super Toxic to Human Cells

In space, they say, no one can hear you sneeze.

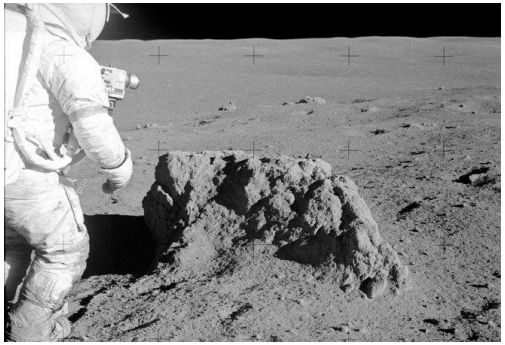
By Brandon Specktor, Senior Writer | May 17, 2018 07:02am ET

But Apollo 17 astronaut Harrison Schmitt was doing a lot of that inside the Challenger command module when he visited the moon in 1972.

One day, after a lunar walk, Schmitt accidentally breathed in some of the abundant moon dust that he and his commander had tracked back in to the Challenger living quarters. For a full day, Schmitt suffered from

what he described as "lunar hay fever." His eyes watered, his throat throbbed, and he broke into a sneezing fit.

No, Schmitt wasn't allergic to the moon. NASA scientists now understand that pieces of moon dust — especially the smallest, sharpest particles — pose clear health risks to astronauts. A recent study published in the April issue of the journal GeoHealth examined exactly how dangerous that dust can be on a cellular level — and the results are as ominous as the dark side of the moon. In several lab tests, a single scoop of replica moon dust proved toxic enough to kill up to 90 percent of the lung and brain cells exposed to it.



Moon dust clings to clothing and poses serious health risks to astronauts, a new study finds. **NASA**

A dusty dilemma

Dust on the moon behaves a little differently than dust on Earth. For starters, it's sharp. Because there's no wind on the moon, the dust never erodes. Instead, grains of moon dust — which are largely the products of micrometeorite impacts — remain sharp and abrasive and can easily slice into an astronaut's lung cells if breathed in too deeply.

On top of this, moon dust can float. With no atmosphere to protect the moon from constant bombardment by solar winds and the charged particles they carry, lunar soil can become electrostatically charged like clothing with static cling.

"This charge can be so strong that the soil particles actually levitate above the lunar surface," the authors wrote in the new study.

From there, it's easy enough for dust to cling in the nooks and crannies of an astronaut's spacesuit and follow him or her back inside living quarters. These loose particles can clog sensitive equipment, jam zippers, ruin clothing and — as Schmitt discovered — wreak havoc on the human body if accidentally ingested by astronauts.

Making moon dust

In their new study, a team of researchers from Stony Brook University in New York wanted to find out just how dangerous a lungful of moon dust could really be. Because actual lunar soil is hard to come by on Earth, the team used five Earth-sourced simulants to represent the dust found on various parts of the moon's terrain. The simulants included volcanic ash from Arizona, dust skimmed from a Colorado lava flow and a glassy, lab-made powder designed by the U.S. Geological Survey for use in lunar soil studies like these.

The team gauged the effects of moon dust on human organs by mixing their soil samples directly with human lung cells and mouse brain cells grown in their lab. The scientists ground each soil sample to three different degrees of graininess, the finest of which was just a few micrometers wide (smaller than the width of a human hair) and easily capable of being sucked up into human lungs.

When the team took stock of their cells 24 hours later, they found that every soil type had caused some degree of brain and lung cell death. The finest-grain samples proved most lethal, killing up to 90 percent of the cells that had been exposed to them. Cells that weren't decimated outright showed signs of DNA damage that could lead to cancer or neurodegenerative diseases if not repaired, the researchers wrote.

"Clearly, avoidance of lunar dust inhalation will be important for future explorers," the authors wrote.

But as humans explore the moon in future decades, chance exposures are likely, the researchers wrote.

Fortunately, NASA has taken this problem seriously for a long time and is developing several dust-mitigation methods. One promising strategy: Cover sensitive surfaces with an Electrodynamic Dust Shield — essentially, electrically charged panels that shoot currents through thin wires to zap dust away. Early lab tests have shown that the shields work well, and some sample panels are currently being tested on the International Space Station. Whether the panels could be incorporated into astronauts' spacesuits remain to be seen.

http://bit.ly/2LiRMQy

The secret of the green-blooded lizards

Analysis finds green blood, and resistance to jaundice, evolved independently four times.

Tanya Loos reports.

There are several lizard species in New Guinea with green blood, instead of the usual red. The lime green colour is due to high concentrations of bile pigments in their bloodstreams, and are toxic in other vertebrates. Now, a genomic analysis of the lizards reveals this remarkable physiology may have arisen in the group four separate times in their evolutionary history.

The green skink (Prasinohaema virens) has blood to match its skin colour.
Christopher Austin

The bile pigments, known as biliverdin and bilirubin, are toxic by-products of red blood cell catabolism – the process by which enzymes breakdown large molecules into smaller components. In humans, and, indeed, all other vertebrates, chronic accumulation of these pigments in the blood causes jaundice.

But this small group of lizards, in the genus *Prasinohaema*, have such high concentrations in their blood that their muscles, flesh and bones are bright green. Yet they suffer no ill effects. Understanding the evolution and mechanism of such an unusual physiology may provide insights into jaundice and related diseases in humans. In adults, the condition indicates serious underlying disease, usually related to the liver or gall bladder.

An earlier study from the University of Texas, US, found that *Prasinohaema* plasma contains a biliverdin concentration approximately 40 times greater than that found in jaundiced humans. How the lizards avoid developing the condition is unknown.

In the latest study, a team led by Zachary Rodriguez from Louisiana State University, US, has brought us a step closer to unpacking the mystery, with research revealing that green blood evolved independently in the *Prasinohaema* genus four times.

The lizards are skinks, members of the very diverse Scincadae family. In terms of body shape and habitat they bear little resemblance to each other – and are only classified as belonging to a single genus because of the colour of their blood. Until now, their evolutionary relationship has been unclear.

Rodriguez and colleagues analysed the genome data and conducted a phylogenetic and ancestral state character reconstruction in 24 individual lizards from six species in the genus, along with 95 related Australasian lizards with normal red blood.

The team's analyses indicate four independent origins of green blood from a single red-blooded ancestor. The researchers say that the discovery of multiple origins demonstrates the "surprising evolutionary dynamism of green blood".

Now that a thorough analysis of the data has been done, the stage is set, as it were, for further analysis into the role natural selection may have played in shaping this curious trait, as well as understanding the genetic and biochemical basis for the lizards' remarkable lack of jaundice.

The study is published in the journal *Science Advances*.

http://bit.ly/2IDoF8z

Alternative medicine: ineffectual, or a victim of colonial arrogance?

A journal argues that traditional therapies have been unfairly condemned by western medicine. Former medical doctor turned philosopher

Paul Biegler examines the evidence.

Much like politics, raising the subject of complementary medicine at a dinner party can pose a serious threat to congenial discussion. Dropping like a meteorite into that polarising fray comes a commentary on

regulation of Traditional and Chinese Medicine (TCM), published in the *Journal of Alternative and Complementary Medicine* (*JACM*).

Its authors, Nadine Ijaz, from the Arts and Science Program at McMaster University, and Heather Boon, from the Leslie Dan Faculty of Pharmacy, University of Toronto, both in Canada, argue that regulating TCM under a western "biomedical model" is not only wrong-headed, but extends the predatory nation-gobbling of European colonialism to the medical arena.

A traditional Chinese medicine pharmacy in Ho Chi Minh in Vietnam. **Godong/Getty Images**

The result, they contend, is that traditional health practices such as moxibustion (burning mugwort over acupuncture points), Ayurveda and Unani (medical systems tracing back to Indian and Hellenic cultures respectively) risk being absorbed by a dominant therapeutic culture that could, ultimately, wipe them out.

"[T]raditional medicine treatments and practices have long been subjugated, devalued, co-opted, and in some cases decimated across the globe within the context of European colonisation," they write. "Still today, many indigenous healthcare systems remain under threat due to colonisation's impacts."

There are plenty of reasons to see that as a problem.

For a start, the authors cite data suggesting up to a quarter of modern medicines are derived from natural products. It's worth recalling, also, that a 2015 Nobel Prize was awarded to Chinese researchers for extracting a malaria drug from the wormwood herb.

Then there's the glaring fact that, according to the World Health Organisation (WHO), nearly 100 million Europeans are current TCM users. In Australia, 30 to 40% of GPs use complementary medicine in their practice and 75% refer patients for it.

Moreover, as *JACM* Editor-in-Chief John Weeks notes in an accompanying editorial, Western medicine has notched up a litany of deaths from medical error, memorably detailed in the landmark US Institute of Medicine report "To Err is Human", published in 1999. Nor have things improved much.

A 2016 report in the *British Medical Journal* estimated medical error to be the third leading cause of death in the US, claiming more than 251,000 lives annually.

TCM emerges from all this as a precious, yet threatened, species upon which regulation must tread carefully – a task, the authors argue, facing a bevy of obstacles.

First and foremost, they write, are the "evidentiary tensions that surround traditional medicine's political subjugation to Western biomedical knowledge systems". Gold standard evidence in mainstream medicine is the clinical trial, which uses a control arm and randomised patient allocation to aim at a uniform, if aspirational, benchmark.

That format doesn't fit so well with traditional healing.

"Indigenous knowledges can never be standardised,'' write the authors, "due to their inherent internal diversity and living dynamic character."

But they also take issue with the very idea that the Western model could ever be an impartial arbiter.

"[B]iomedicine is widely and falsely universalised as 'culturally neutral'." they write.

"Far from being an 'unbiased' system of healthcare, biomedicine is itself a cultural artefact, rooted in the European scientific revolution and the linear reductionism of Rene Descartes and his contemporaries."

Descartes saw the workings of the body as something that could be explained, machine-like, by analysing its constituent bits and bobs. Likewise, modern healthcare often cops it for treating people as bags of symptoms, in contrast to the ethos of complementary therapy to treat the "person as a whole".

And it is precisely because of those cultural roots, the researchers say, that when biomedicine tries to bring traditional health knowledge under its regulatory umbrella, bad things happen.

One of those things has a longish name.

"Paradigm assimilation," write the authors, is a, "'predatory' strategy [that] 'reinterprets' a particular healthcare approach from an indigenous system, reframing the approach in biomedical terms."

The vision conjured is one of Western medicine ingesting, multinational-like, defenceless minnows in the world of healthcare. It is a threat for which the authors invoke high level support.

In its Traditional Medicine Strategy, the WHO stresses the need "to protect the intellectual property rights of indigenous peoples and local communities and their health care heritage."

Ijaz and Boon make much of this, casting TCM regulation as an intellectual property claim over bodies of indigenous knowledge. The looming threat is one, no less, of "cultural misappropriation — in other words, the abuse of indigenous medical intellectual property".

The authors call for wide-ranging discussions on how best to protect traditional knowledge and prevent "further misappropriation", while conceding that "additional work will be needed to elaborate upon how these principles may be operationalised."

What to make of it all?

At the very least, the commentary raises the gnarly issue of whether knowledge can ever be "relative". Many people tolerate the idea that cultural values – a tribal predilection to get about naked, for example – are fine for that group, even if we might not be so keen. "Relativism" about values isn't so hard to swallow.

A lot of those folk would, however, get jittery at the idea that facts – knowledge itself – could be relative. The molecular structure of water, from wherever you look at it, is H2O. Just as chemistry could never be a cultural artefact, the actual effects of a medicine, surely, are discernible irrespective of cultural belief.

On that score, it might also be argued that people tend to vote with their feet when things go down to the wire. A diagnosis of cancer or HIV, for example, can make people especially partial to treatments that have stood the tests of rigorous "biomedicine".

One wonders, then, if cultural imperialism might be something of a straw man in the argument of Ijaz and Boon.

Few dispute that traditional cultures should be protected and knowledge preserved. But that is a long way from saying that cultural longevity confers legitimacy on a health treatment. By turning the torch on colonialism are the authors sidestepping the awkward fact that the real threat to traditional medicine comes from science, a discipline that bridges the global North and South?

The back-story is that practitioners of traditional medicine (Ijaz is a medical herbalist and shiatsu therapist) have good reason to see the randomised clinical trial (RCT) as a threat. One criterion of the US Food and Drug Administration (FDA) for approving medicines is that they been shown superior to placebo on two RCTs. It's a standard that could ring the death knell on some TCM practices, should they be compelled to conform to it.

Which, of course, plays to the authors' point that the Western model threatens to extinguish many venerable and ancient therapies.

Remember, though, that plenty of Western medicines fall at the very same hurdle. An infamous recent example was researcher Irving Kirsch's use of Freedom of Information to unearth 47 failed antidepressant trials from the FDA, trials subsequently buried by the parent pharmaceutical companies.

If Western medicine is predatory, then, it also eats its own.

Ken Harvey AM, of the School of Public Health and Preventive Medicine at Monash University in Melbourne, Australia, points out the debate has special relevance in his country just now.

The Australian Therapeutic Goods Administration recently issued a determination that means, says Harvey, 86% of over 1000

complementary product claims can be supported by appeal to "traditional" evidence.

That's a problem because, as Harvey writes in a letter he (and colleagues from lobby group Friends of Science in Medicine) will send to federal senators objecting to the determination, traditional evidence doesn't rate on the National Health and Medical Research Council's levels of evidence. Worse, consumers are apt to confuse it with scientific evidence.

"Ultimately, it's all about ensuring consumers can make informed decisions about conventional, complementary and alternative medical practice and products considering cultural needs, quality, safety and efficacy," says Harvey. This, he adds, needs "creative regulation and a lot of education."

Complicating things further is the fact that many complementary, and indeed Western medicines may work via the placebo effect, a mind-body healing mechanism with ever deepening scientific roots.

All of which leaves consumers in something of a quandary. The regulatory morass, varying standards of evidence, and competing claims, can make an answer to their most pressing question seem like a receding dream.

What, when all is said and done, actually works?

http://bit.ly/2KCc0Ub

FDA has named names of pharma companies blocking cheaper generics [Updated]

Commissioner Gottlieb hopes the list will discourage bad behavior.

Beth Mole - 5/18/2018, 3:05 AM

Update 5/17/2018*: The FDA has now launched the website listing the names of brand name drugs and their makers who have stood in the way of generic drug companies trying to make more affordable alternatives. You can view the list here. It includes notable medications, such as Accutane (for acne), Methadone (used for opioid dependency), and Tracleer (to treat high blood pressure in the lungs). The brand name drug makers to be shamed includes big hitters such as Celgene Corp, GlaxoSmithKline, Pfizer, Valeant Pharmaceuticals International, Gilead Sciences Inc, and Actelion Pharmaceuticals Ltd, now a Johnson & Johnson company. Our original story, published May 16, is unedited below.*

The Food and Drug Administration plans this week to effectively begin publicly shaming brand-name drug companies that stand in the way of competitors trying to develop cheaper generic drugs.

FDA Commissioner Scott Gottlieb told reporters on Monday and Tuesday that the agency will unveil a website on Thursday, May 17 that names names of such companies. More specifically, the website will publicly reveal the identity of 50 branded drugs and their makers that have blocked generic development. The website will also be updated "on a continuous basis" to list additional names.

In fielding questions from reporters, Gottlieb denied that the effort was a form of public shaming. "I don't think this is publicly shaming," Gottlieb said, according to S&P Global Market Intelligence. "I think this is providing transparency in situations where we see certain obstacles to timely generic entry."

But as S&P points out, Gottlieb had a different take on such tactics in a May 25, 2017 congressional hearing, in which he said he was "happy to work" on "a shaming initiative." The comment was in response to Rep. David Young, R-Iowa, who noted that: "There is a power in shaming. Sunlight is the best disinfectant to put people in place and to try to get to a better behavior."

Shaming or not, getting better behavior is certainly the FDA's goal for the upcoming website. Gottlieb said he hoped that it would deter companies from abusive practices that are "antithetical to the spirit, if not the letter" of the law behind the generic drug industry—aka the Hatch-Waxman Act.

The key abusive practice that the FDA's website spotlights is the tactic of brand-name drug makers to withhold samples of their drugs from generic drug makers. Without those samples, generic drug makers cannot perform bio-equivalency testing necessary for regulatory approval. The brand-name drug makers seem to withhold samples in at least one of two ways.

Disinfecting light

The first is that they can effectively hide behind FDA drug safety programs, called risk evaluation and mitigation strategies or REMS. These are programs to ensure that drugs with serious side effects are used safely, which can sometimes limit when, where, and how a drug is delivered. With a REMS in place, the brand-name drug maker may claim that the safety program hampers their ability to provide samples to generic developers.

In this case, generic drug makers often turn to the FDA to ask—in written letters—if such a REMS is in place for a drug and if it indeed prohibits the maker from providing samples. It is these inquiry letters that reveal to the FDA which brand name drugs are being withheld. The 50 names to be released on the website Thursday will in fact be revealed via more than 150 such inquiry letters that the agency has received.

In response, the FDA sometimes writes letters to brand-name drug makers—at the behest of the generic company—that essentially give the brand-name company the green light to release the drug. But Gottlieb noted this week that the FDA plans to begin simply offering generic drug makers waivers that override any REMS restrictions that branded drug makers claim inhibit access to drug samples.

The second method branded drug companies use to withhold samples is to add contract provisions with drug distributors that prevent them from delivering samples to generic competition.

In speaking with reporters, Gottlieb said he hoped the website and the agency's other efforts would dig up the "root cause" of the issue—whether it be REMS or distribution—and squash bad behavior. "And if it does, I think that's a useful public health outcome," Gottlieb said.

https://bbc.in/2GyxlLK

Growing resistance to antifungal drugs 'a global issue'

Scientists are warning that levels of resistance to treatments for fungal infections are growing, which could lead to more outbreaks of disease.

Intensive-care and transplant patients and those with cancer are most at risk because their immune systems cannot fight off the infections.

Writing in Science, researchers said new treatments were urgently needed.

Fungal infections had some of the highest mortality rates of infectious diseases, an expert said.

An international team, led by researchers from Imperial College London and the University of Exeter, found a huge increase in resistance to antifungal drugs worldwide over the past 30-40 years.

Everywhere in the air

Prof Matthew Fisher, professor of epidemiology at Imperial College London, said this was probably down to farmers spraying their affected crops with the same drugs used to treat fungal infections in patients.

The "unintentional by-product of this 'dual use' of drugs in the field and the clinic" was that drugs were no longer working in patients who were unwell, he said.

"There are fungi in the air all the time, in every lung-full of air we breathe," Prof Fisher said.

"Bodies with a fully functioning immune system do an amazing job of curing the infection - but it can become an invasive fungal infection in others and [this] needs a drug."

He said the number of people at risk from fungal infections was rising rapidly as a result of increased numbers:

- ***people with HIV***
- ***the elderly***
- ***patients in hospital***

The review said improvements were needed in how existing drugs were used, as well as an increased focus on the discovery of new treatments, in order to avoid a "global collapse" in the fight against fungal infections.

'Under the radar'

Prof Sarah Gurr, from the University of Exeter, said: "Emerging resistance to antifungal drugs has largely gone under the radar, but

without intervention, fungal conditions affecting humans, animals and plants will become increasingly difficult to counteract."

Prof Gordon Brown, director of the Medical Research Council Centre for Medical Mycology, said some fungal infections had mortality rates of more than 50%.

He said: "Given the high rates of mortality of these infections, these disturbing trends suggest that even our limited ability to treat these diseases is being severely compromised."

Prof Brown said we were also seeing the rise of new multidrug-resistant fungi such as *Candida auris*.

Candida auris is responsible for increasing rates of invasive fungal infections in hospitals around the world - but there are very few treatments for it.

The review said it was resistant to all antifungal drugs and "presents a threat to intensive-care units" because it could survive normal efforts at decontamination.

http://bit.ly/2rYPhtN

Study finds more than 40 percent of prostate biopsies could be avoided with new blood test

Cleveland Clinic to present findings during 2018 Annual Meeting of the American Urological Association

San Francisco: A multi-center study that validates the clinical performance of IsoPSA - a new blood test that has proven to be more accurate in predicting overall risk of prostate cancer than standard prostate-specific antigen (PSA) - will be presented during a special press conference at the 13th Annual Meeting of the American Urological Association (AUA) on May 18 in San Francisco.

Results showed that more than 40 percent of biopsies could have been avoided in both the preliminary study (45.1 percent) and validation study (47 percent), suggesting that use of IsoPSA may substantially reduce the need for biopsy, and may thus lower the likelihood of overdetection and overtreatment of nonlethal prostate cancer.

The study, Prospective Validation of the IsoPSA Assay for Detection of High Grade Prostate Cancer, was conducted as a follow-up to early studies which demonstrated that IsoPSA, a structure-focused protein biomarker, may be an effective means of discriminating between high-grade prostate cancer (Gleason≥7) and low-grade/benign disease (Gleason=6).

The research team, led by Cleveland Clinic's Eric Klein, M.D., conducted a multicenter validation trial and evaluated performance data with a new cohort, including cutoff parameters derived from a preliminary study, using the detection of cancer by biopsy as the endpoint.

"To be clinically useful, a biomarker must be both tissue-specific and cancer-specific. While PSA is prostate-specific, it is not specific for prostate cancer, leading to diagnostic inaccuracy and too many unneeded biopsies," said Dr. Klein, chair of Cleveland Clinic's Glickman Urological & Kidney Institute. "IsoPSA fulfills both the tissue- and cancer-specificity needed for a useful biomarker, and this validation study shows that it can more accurately detect high-grade cancer and reduce the rate of unneeded biopsies in patients at low risk of this disease."

The IsoPSA test was developed by Cleveland Diagnostics, a company co-founded by Cleveland Clinic, in which it has financial interest. Dr. Klein has no personal financial interest in the company. Mark Stovsky. M.D., a Cleveland Clinic urologist and co-author on the study, has a leadership position (Chief Medical Officer) and investment interest in Cleveland Diagnostics. In late 2017, Cleveland Diagnostics and Genomic Health announced an exclusive licensing agreement to develop and commercialize the IsoPSA test.

http://bit.ly/2kck7eY

Biotin supplements caused misleading test results, almost led to unnecessary procedure

FDA issued warning about biotin interference with lab tests in November 2017

A new case report in the *Journal of the Endocrine Society* documents how a patient's use of a common biotin supplement, also known as vitamin B7, caused her to have clinically misleading test results, which

prompted numerous consultations and unnecessary radiographic and laboratory testing.

The patient in the case report took a 5000 mcg dose of biotin daily. Biotin supplements in that dosage are commonly sold over-the-counter, without a prescription, in many grocery and drug stores for about $8-$20 a bottle. They are marketed as being good for healthy hair, skin and nails, but there is no scientific evidence to support this claim.

In this patient's case, "The negative clinical impact included weeks of psychological distress concerning the possibilities of hypercortisolemia or a testosterone-producing tumor. Most significantly, these abnormal test results nearly resulted in an unnecessary invasive procedure for a complex patient with a hypercoagulable state," the case report says. Hypercortisolemia is a condition involving a prolonged excess of cortisol -- a steroid hormone -- in blood.

Maya Styner, MD, associate professor of endocrinology and metabolism in the department of medicine, is the case report's corresponding author.

"The literature is lacking with regard to biotin interference with serum cortisol and testosterone immunoassays, as in our case-report," Styner said. "Patients are ingesting supplements in a higher frequency, and higher doses, and therefore this case is timely and relevant from both a clinical and basic-science perspective."

She added, "Our manuscript is a product of a collaboration between endocrinology, reproductive endocrinology/gynecology and clinical chemistry at UNC and at the Mayo Clinic. This collaboration enabled us to ascertain the underlying diagnosis and perform relevant research-based biotin quantification in our patient's sample."

Co-authors of the case report are Heather M. Stieglitz, PhD, Nichole Korpi-Steiner, PhD, Brooke Katzman, PhD and Jennifer E. Mersereau, MD. All are at UNC except for Katzman, who is co-director of the Hospital Clinical Laboratory and Point of Care, at the Mayo Clinic in Rochester, Minnesota.

In November 2017, the U.S. Food & Drug Administration issued a warning "alerting the public, health care providers, lab personnel, and lab test developers that biotin can significantly interfere with certain lab tests and cause incorrect test results which may go undetected."

http://bit.ly/2kcPSoj

Natural antioxidant bilirubin may improve cardiovascular health

Not only a sign of liver problems or a bruise

Bilirubin, a yellow-orange pigment, is formed after the breakdown of red blood cells and is eliminated by the liver. It's not only a sign of a bruise, it may provide cardiovascular benefits, according to a large-scale epidemiology study.

A recent analysis of health data from almost 100,000 veterans, both with and without HIV infection, found that within normal ranges, higher levels of bilirubin in the blood were associated with lower rates of heart failure, heart attack and stroke.

The results are published in the *Journal of the American Heart Association*.

Several studies have suggested that bilirubin may have beneficial effects, by acting as an antioxidant or interfering with atherosclerosis. The data from the veterans adds to this evidence, and specifically looks at people living with HIV and at an anti-HIV drug, atazanavir, known to elevate bilirubin.

The researchers did not see an independent effect of atazanavir on cardiovascular risk.

Even if well-controlled by antiretroviral drugs, HIV infection has negative effects on cardiovascular health, says lead author Vincent Marconi, MD.

"We initially wanted to see if bilirubin and cardiovascular disease had a different relationship in people who were HIV positive, compared to HIV negative," says Marconi, professor of medicine and global health at Emory University School of Medicine and Rollins School of Public Health. He is also director of infectious disease research at the Atlanta Veterans Affairs Medical Center.

Study authors include VACS principal investigator Amy Justice, MD, PhD from Yale, Matt Freiberg, MD and others from Vanderbilt, Jeff

Lennox, MD from Emory and additional investigators from Vanderbilt, Boston University, Penn, Pitt, UCLA and Baylor.

Marconi and his colleagues examined data from the Veterans Aging Cohort Study, a nationwide look at HIV infection, supported by the National Institutes of Health. VACS data included 31,418 HIV-positive and 66,987 HIV-negative veterans, almost all men and 48 percent African American. Their age was an average of 48 years.

The researchers divided study participants into four groups according to their bilirubin levels.

Higher levels of bilirubin meant lower risk of heart attack, heart failure or stroke.

The group with the highest level of bilirubin had 76 percent of the risk for combined cardiovascular events as the group with the lowest level, with effects seen even in people without liver disease.

"Large increases in bilirubin were not required to see an effect on CVD risk reduction," Marconi says. "Most of the change happened well within the normal physiologic range and specifically from the first to the second quartile."

Atazanavir is a HIV protease inhibitor, and is designed to stop HIV from processing itself. It has a side effect on an enzyme in human cells that is necessary for the recycling of bilirubin. There are some indications that the drug itself has negative effects, balancing out the benefits of bilirubin, Marconi adds.

The authors conclude:

This work provides epidemiologic rationale for future studies to investigate how the antioxidant effect of bilirubin could be harnessed to reduce chronic disease morbidity risk.

Future studies should explore the use of bilirubin as a biomarker for other inflammation?mediated conditions and all-cause mortality.

The VACS study was supported by the National Institute of Alcohol Abuse and Alcoholism and the National Heart, Lung, and Blood Institute. Marconi is supported by the Emory Center for AIDS Research (P30AI050409).

https://wb.md/2wUUTeo

Can Obesity Ever Be Healthy?

New study questions concept of metabolically healthy obesity

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.

The controversial concept of "metabolically healthy obesity" has been around for a while. It's the idea that people can carry extra weight without having high blood pressure, glucose intolerance, or high cholesterol—the signs of metabolic syndrome.

A new study of more than 6800 individuals questions that assumption. It found that metabolically healthy obesity at baseline did not predict a person's future risk for cardiovascular morbidity or mortality. Almost half of the metabolically healthy obese patients eventually developed metabolic syndrome, raising their cardiovascular risk. And the longer a person was metabolically unhealthy, the higher the risk.

What can we take from this? Early identification of this group is an opportunity for primary prevention. The research is a reminder that we can't assume that our metabolically healthy obese patients will remain that way. Obesity is a risk factor for developing metabolic syndrome.

http://bit.ly/2rWyaJ9

Could intermittent fasting diets increase diabetes risk?

Fasting every other day to lose weight impairs the action of sugar-regulating hormone, insulin, which may increase diabetes risk, according to data presented in Barcelona at the European Society of Endocrinology annual meeting, ECE 2018

Fasting every other day to lose weight impairs the action of sugar-regulating hormone, insulin, which may increase diabetes risk, according to data presented in Barcelona at the European Society of Endocrinology annual meeting, ECE 2018. These findings suggest that fasting-based diets may be associated with long-term health risks and

careful consideration should be made before starting such weight loss programmes.

Type-2 diabetes is a growing global epidemic that is often attributed to poor diet and a sedentary lifestyle, so is closely linked to obesity. Blood sugar is partially regulated by the hormone insulin, which is produced by the pancreas, if insulin levels are too low, or the body becomes resistant to its effects, type-2 diabetes results and high blood sugar levels can cause serious health issues, including heart, kidney and eye damage. In addition to medical strategies used to treat type-2 diabetes, patients are also advised to make lifestyle and dietary changes to lose weight. Recently, intermittent fasting diets have gained general popularity for weight loss, however, evidence on their success has been contradictory and there is a lack of knowledge and some debate on their potentially harmful long-term health effects. Previous research has also shown that short-term fasting can produce molecules called free radicals, which are highly reactive chemicals that can cause damage to the body at a cellular and may be associated with impaired organ function, cancer risk and accelerated aging.

In order to investigate whether an intermittent fasting diet could also generate damaging free radicals, Ana Bonassa and colleagues, from the University of Sao Paulo in Brazil, examined the effects of fasting every other day on the body weight, free radical levels and insulin function of normal, adult rats, over a 3-month period. Although the rats' body weight and food intake decreased as expected over the study period, the amount of fat tissue in their abdomen actually increased. Furthermore, the cells of the pancreas that release insulin showed damage, with the presence of increased levels of free radicals and markers of insulin resistance were also detected.

Ana Bonassa comments, "This is the first study to show that, despite weight loss, intermittent fasting diets may actually damage the pancreas and affect insulin function in normal healthy individuals, which could lead to diabetes and serious health issues."

The researchers now plan to investigate how this diet impairs pancreas and insulin function. There are many conflicting reports on the benefits and disadvantages, and many different types of intermittent fasting diets. Although these data were obtained in normal weight rats with positive effects on weight gain and food intake, the results suggest that in the long-term harm may be caused and that more investigation is needed to assess how people may be affected, particularly those with existing metabolic issues.

Ana cautions, "We should consider that overweight or obese people who opt for intermittent fasting diets may already have insulin resistance, so although this diet may lead to early, rapid weight loss, in the long-term there could be potentially serious damaging effects to their health, such as the development of type-2 diabetes."

Abstract 605

Intermittent fasting for three months decreases pancreatic islet mass and increases insulin resistance in Wistar rats.

Ana Cláudia Munhoz Bonassa, Angelo Rafael Carpinelli
University of São Paulo, São Paulo, Brazil.

Introduction: *It is known that fasting causes several physiological changes in the endocrine pancreas, such as insulin secretion, pancreatic islet metabolism and beta cells redox state. However, there is still no consensus about the effects of intermittent fasting (IF), a fad diet widespread by the media and adopted by individuals seeking rapid weight loss. In the present study, we sought to study the effects of the IF diet for three months in an animal model.*

Methods: *Thirty-day-old female Wistar rats were submitted to IF for three months. During this time body weight and food intake were recorded. After the treatment the animals were killed, and pancreatic islets, perigonadal white adipose tissue, extensor digitorum longus muscle tissue and liver were collected for different analyses.*

Results: *IF decreased body weight and food intake. The stomach was greatly increased in size. There was an increase in adipose tissue and a decrease in muscle tissue. IF caused elevation of plasmatic insulin levels, both baseline and after glucose administration. In vitro, IF pancreatic islets had increased insulin secretion, glucose metabolism and net reactive oxygen species*

production, while decreased their mass. In addition, impairment in AKT phosphorylation was observed in peripheral tissues indicating insulin resistance.

Discussion: *Previous studies showed an increase in orexigenic neurotransmitters production in IF, inducing hunger and hyperphagia in the ad libitum feeding days. Our experiments demonstrate that, despite the weight loss, IF treatment induces undesirable effects on tissue homeostasis. Therefore, the hyperinsulinemia registered in vivo and in vitro, associated with the impairment of glucose tolerance and the decrease in AKT phosphorylation, make clear the occurrence of peripheral insulin resistance. The increased metabolism of pancreatic islets dispersed cells, after IF treatment, indorses the higher insulin secretion. Furthermore, the decrease in the pancreatic islet mass indicates that three months of IF treatment cause severe impairment in glucose homeostasis. In conclusion, intermittent fasting diet may not be healthy to be adopted by individuals seeking rapid weight loss.*

https://theatln.tc/2LjmyIT

The Coming Wave of Murders Solved by Genealogy

The same DNA analysis used to find the alleged Golden State Killer has led to the arrest of a second alleged murderer. It'll likely lead to more.

Sarah Zhang

Just three weeks ago, law enforcement in California announced the arrest of the Golden State Killer using DNA. The press conference was vague, but the details of the novel method soon trickled out: Joseph James DeAngelo was found by matching DNA from a crime scene with that of his distant relative on the genealogy site GEDmatch.

Tanya Van Cuylenborg, 18, and Jay Cook, 21, who were found murdered in 1987 in Washington State **Snohomish County Sheriff's Office**

On Friday, police in Washington State announced the arrest of William Earl Talbott II for a double murder in 1987, and this time, they proudly announced the use of the same method of tracing distant relatives through DNA—a field known as genetic genealogy. Steven Armentrout, the president of Parabon NanoLabs, the forensics company that did the DNA analysis, spoke at the press conference. So did CeCe Moore, a genetic genealogist who now works with the company.

Parabon has jumped headlong into this technology. On May 8, it announced the creation of a new genetic-genealogy unit led by Moore. The company recently told *BuzzFeed* it had uploaded DNA from about 100 crime scenes to GEDmatch.com, with about 20 of them generating matches of a third cousin or closer. "I think there is going to be press around this very soon," the company's director of bioinformatics had said to *BuzzFeed*.

Moore and other genetic genealogists have been using a similar technique to find the families of adoptees for years. The raw data from 23andMe, AncestryDNA, and other DNA-testing services can be uploaded on a volunteer-run site called GEDmatch, which allows genealogists to compare segments of DNA. These tests are more sophisticated than the DNA tests police typically run, and they generate more data than is stored in the FBI's CODIS database. These DNA segments can then be crossmatched with family trees and public records to find an adoptee's birth family—or a criminal.

In the double murder in Washington State, the suspect's DNA matched two relatives, both fairly close by the standards of this research: a second cousin and a half–first cousin once removed. The former relative was on the mother's side, the latter the father's side, so the suspect was not hard to identify. "No cases are easy, but when they are straightforward, it really falls into place very quickly," says Moore.

She says she had been talking to Parabon for about a year and a half. She had initially hesitated to work on criminal cases because she was unsure of legal and ethical issues, especially if people uploading their DNA to GEDmatch were unaware police were trawling through the

database. But the positive feedback since the Golden State Killer case convinced her to make the plunge. Plus the publicity of that case has made it well-known that police can search genealogy databases. Moore is not the only genetic genealogist doing this kind of work for police departments.

Now, the floodgates are open. The strangest part of this story may be that a small, volunteer-run website, GEDmatch.com, has become, as the genealogist Debbie Kennet has similarly observed, the de facto DNA and genealogy database for all of law enforcement.

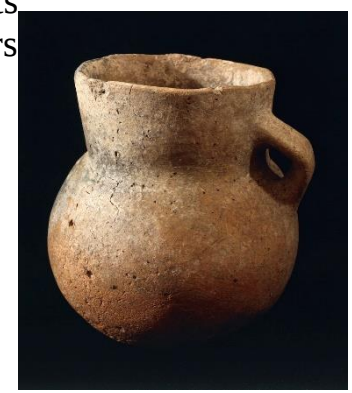
http://bit.ly/2KFDc4q

Going to pot: how a single artefact reveals life in the Bronze Age

Exploring the "micro-history" of a broken container yields surprising insight into life thousands of years ago.

Andrew Masterson reports.

Perhaps it became a treasured family heirloom, or perhaps it was simply cheaper to repair than replace, but chemical analysis of a banged-up Bronze Age pot is providing remarkable insights into community life in Sicily thousands of years ago.



A Bronze Age pot from Sicily, from the same period as the one studied. **DEA / A. DAGLI ORTI / Getty Images**

In a paper published in the *Journal or Archaeological Science: Reports* a team led by Roberta Mentesana of Italy's Università del Salento uses a combination of techniques to reconstruct the history of a single artefact, and, through it, throws light on how commodities were shared over long distances.

The research focusses on fragments of a repaired clay pot unearthed several years ago by Mentesana and colleagues at the site of a long-disappeared village known as Coste di Santa Febronia, which was occupied between 2200 and 1450 BCE. It stood 500 metres above sea level, looking down on a plain called Piana di Catania and near a tributary of the Gornalunga river.

A crack in the pot had been repaired using a tar-like substance – and it was this fact that prompted the researchers to spend subsequent years investigating the source of the pot itself, and that of the tar, to try to determine its history.

The pot was too fragmented to permit a complete reconstruction, but two things were obvious: it was large, and it wasn't unusual for the period. Discovering why and how it had been repaired, therefore, meant it could serve as an object of "micro-history", an item that could throw light on the broader cultural history of the region.

To do this, the researchers conducted chemical analyses of the clay, the tar, and the charred ground in which it was found, identifying mineral and botanical elements in each.

The pot was found to comprise bits of micrite, microfossils, quartz, feldspar and volcanic rock fragments. Size and distribution of the components suggested that all were present in the raw clay, with none added by the potter during manufacture.

The mixture matched that of material available around the ancient village, leading Mentesana's team to conclude that it had been made locally.

The black resin used for repair, however, was a different matter. Analysis using gas chromatography revealed that it contained biomarkers diagnostic for tar made from birch bark.

Although birch bark tar was widely used from prehistoric to Roman times – for everything from securing flint tools to handles, waterproofing ships and even as chewing gum – earlier reconstructions of the climate and plant life around the village indicated that there were no birch trees anywhere near.

The closest suitable trees grew on the slopes of Mt Etna, some 70 kilometres distant, and at least 1500 metres above sea level. The discovery threw up some immediate questions, which, while still unresolved, illuminate possible scenarios for Bronze Age society.

Did villagers from Coste di Santa Febronia make the long trek to the volcano to harvest the bark? Did Mt Etna residents make an equivalent journey to trade it? Or was it acquired through a series of transactions between villages along the way, coming ever closer?

The bark itself had to be heated and converted into resin: was that done at the village, or elsewhere?

Analysis of charcoal recovered from the site revealed that no trace of birch – only the oak trees known to have been common in the area.

For Mentesana and colleagues these findings throw up still more questions. Other pot fragments recovered from the site showed evidence of repair, but by using a different method – holes were drilled and the cracked pieces stitched back together. This pot was clearly different, or, at least, repaired for a different purpose.

The use of birch bark tar to seal the breakage suggests that it was used to hold a liquid or some kind. The researchers note that birch bark tar has been associated with brewing in ancient times, because of its waterproof nature and disinfectant properties. However, they concede, there is no other evidence to suggest this particular pot held booze.

Nevertheless, it was definitely repaired instead of being discarded. This must have been done consciously, for a reason.

It may have been a banal one, of course. "It may be that repairing the jar had an economic significance: the manufacture of a new jar would have involved more resources and energy than repairing one," the researchers write.

On the other hand, perhaps the pot was – or became over its life – special. The researchers suggest that it may have been handed down over many generations. "Its significance for people using it could have changed over time from being a simple container to 'belonging to the history of a place' in the same way as people do," they note.

Also, they speculate, the very act of repair might have had a cultural purpose and meaning. It might indicate a practise roughly analogous the Japanese concept of kintsugi – repairing something, but repositioning its significance by highlighting its cracks and imperfections.

"Whatever the reasons for restoring the vessel might have been, the mending process could have had a powerful meaning for the persons performing it," they conclude.

The real reason for the repair of a single not-very-special pot many thousands of years ago will never be known, of course. But, by looking deeply at the processes involved, Mentesana and her collaborators have firmly established that the people of Bronze Age Sicily were very aware of their landscape, and their neighbours. They knew how to gather or acquire raw materials – and the notion of "giving a new life" to something broken was important.

http://bit.ly/2kfLrZX

Nanoparticles derived from tea leaves destroy lung cancer cells: Quantum dots have great potential

Nanoparticles derived from tea leaves destroy up to 80% of lung cancer cells

Nanoparticles derived from tea leaves inhibit the growth of lung cancer cells, destroying up to 80% of them, new research by a joint Swansea University and Indian team has shown.

The team made the discovery while they were testing out a new method of producing a type of nanoparticle called quantum dots. These are tiny particles which measure less than 10 nanometres. A human hair is 40,000 nanometres thick.

Although nanoparticles are already used in healthcare, quantum dots have only recently attracted researchers' attention. Already they are showing promise for use in different applications, from computers and solar cells to tumour imaging and treating cancer.

Quantum dots can be made chemically, but this is complicated and expensive and has toxic side effects. The Swansea-led research team were therefore exploring a non-toxic plant-based alternative method of producing the dots, using tea leaf extract.

Tea leaves contain a wide variety of compounds, including polyphenols, amino acids, vitamins and antioxidants. The researchers mixed tea leaf extract with cadmium sulphate (CdSO4) and sodium sulphide (Na2S)

and allowed the solution to incubate, a process which causes quantum dots to form. They then applied the dots to lung cancer cells.

They found:

Tea leaves are a simpler, cheaper and less toxic method of producing quantum dots, compared with using chemicals, confirming the results of other research in the field.

Quantum dots produced from tea leaves inhibit the growth of lung cancer cells. They penetrated into the nanopores of the cancer cells and destroyed up to 80% of them. This was a brand new finding, and came as a surprise to the team.

The research, published in Applied Nano Materials, is a collaborative venture between Swansea University experts and colleagues from two Indian universities.

Dr Sudhagar Pitchaimuthu of Swansea University, lead researcher on the project, and a Ser Cymru-II Rising Star Fellow, said:

"Our research confirmed previous evidence that tea leaf extract can be a non-toxic alternative to making quantum dots using chemicals.

The real surprise, however, was that the dots actively inhibited the growth of the lung cancer cells. We hadn't been expecting this.

The CdS quantum dots derived from tea leaf extract showed exceptional fluorescence emission in cancer cell bioimaging compared to conventional CdS nanoparticles.

Quantum dots are therefore a very promising avenue to explore for developing new cancer treatments.

They also have other possible applications, for example in anti-microbial paint used in operating theatres, or in sun creams."

Dr Pitchaimuthu outlined the next steps for research:

"Building on this exciting discovery, the next step is to scale up our operation, hopefully with the help of other collaborators. We want to investigate the role of tea leaf extract in cancer cell imaging, and the interface between quantum dots and the cancer cell.

We would like to set up a "quantum dot factory" which will allow us to explore more fully the ways in which they can be used."

Notes to editors:

The research: the paper is called "Green-Synthesis-Derived CdS Quantum Dots Using Tea Leaf Extract:Antimicrobial, BioImaging and Therapeutic Applications in Lung Cancer Cells". Published in Applied Nano Materials, April 2018

The authors: Kavitha Shivaji, Suganya Mani, Mythili Gnanamangai Balasubramanian (K. S. Rangasamy College of Technology, Tamil Nadu, India); Ponnosamy Ponmurugan (Bharathiar University, Coimbatore, India); Catherine Suenne De Castro, Matthew Lloyd Davies, Sudhagar Pitchaimuthu (SPECIFIC, Materials Research Centre, Swansea University).

Lung cancer mortality: survival rates for lung cancer are generally lower than for other cancers. Cancer Research reports that the 5 year survival rate is less than 10%.