http://www.eurekalert.org/pub_releases/2015-05/uoe-afr052115.php

## Special fats proven essential for brain growth

***Research led by a Duke-NUS Graduate Medical School Singapore (Duke-NUS) scientist has proved that certain special fats found in blood are essential for human brain growth and function.***

Duke-NUS Associate Professor David Silver co-led two Nature Genetics published studies which showed that mutations in the protein Mfsd2a cause impaired brain development in humans. Mfsd2a is the transporter in the brain for a special type of fat called lysophosphatidylcholines (LPCs) - composed of essential fatty acids like omega-3. These studies show, for the first time, the crucial role of these fats in human brain growth and function.

In the first study, two families in Libya and Egypt with Mfsd2a mutations were identified with severely reduced brain size, or microcephaly. Their mutations eliminated Mfsd2a's ability to transport LPCs, which meant not enough LPCs were absorbed by the brain. In these families, children affected by these mutations died between one and six years of age. The study not only establishes a link between the transport of LPCs by Mfsd2a and human brain growth and function, it is also the first time a genetic disease has been related to LPC transport in humans. The research was co-led by senior author Professor Joseph Gleeson from Rockefeller University.

In a second, separate study, a family in North Pakistan was found to have another type of mutation in the Mfsd2a gene which reduced its transport activity. The individuals with this mutation also had microcephaly, but in this case it was not lethal. However, they did have intellectual disabilities, impaired control of their limbs, and absent speech. Like the first study, findings are proof of the importance of LPCs in brain development and function. The research was co-led by senior author Professor Andrew H. Crosby from Exeter University.

In 2014, Dr. Silver published a landmark study in Nature which served as a basis for these two studies. He and his team discovered that Mfsd2a is the transporter for LPCs. Prior to this breakthrough, LPCs were known to be found at high concentrations in our blood but their function was a mystery. Dr. Silver's team showed that mice genetically engineered without Mfsd2a failed to transport LPCs into their brains - which resulted in microcephaly. Since DHA deficiency in animals does not result in microcephaly, this meant that LPCs are critical factors in brain growth and function. Also, while it was previously believed the brain made all the fat it needed, Dr. Silver's research showed that LPCs are transported there from the blood past the blood-brain barrier. His work with Rockefeller and Exeter prove this in humans.

"Our work confirms the essential role of LPCs in brain development and function in humans, and indicates that brain uptake of LPCs during foetal development and in adult life is important," said Dr. Silver, co-lead on both studies, based in the Cardiovascular and Metabolic Disorders Programme at Duke-NUS. "Now we are studying the functions of LPCs in the brain, and the implications for application are very exciting. We might be able to develop therapeutics in the future that could prevent and treat neurological disorders, and improve brain growth and function. We may even be able to target better brain nutrition for babies, mothers, and the aged."

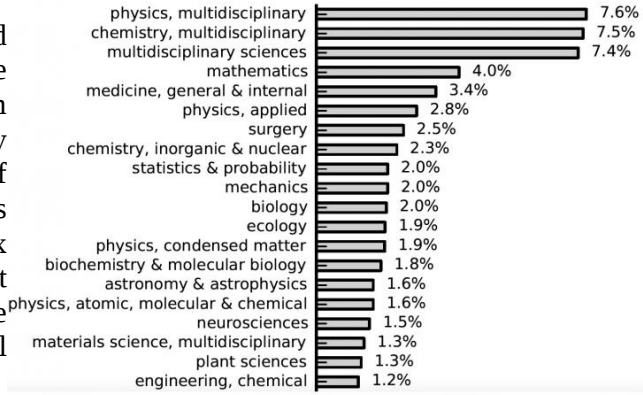
http://www.eurekalert.org/pub_releases/2015-05/iu-lsb052215.php

## Like Sleeping Beauty, some research lies dormant for decades, IU study finds

***Why do some discoveries fade into obscurity while others blaze a new trail the moment they are published?***

BLOOMINGTON, Ind. - More mysteriously, why do some research papers remain dormant for years and then suddenly explode with great impact upon the scientific community?

The last group, dubbed "sleeping beauties," is the subject of a new study from the Indiana University Bloomington School of Informatics and Computing's Center for Complex Networks and Systems. It was released today in the Proceedings of the National Academy of Sciences.




***This list shows the top 20 disciplines producing sleeping beauties in science.*** **Indiana University**

"This study provides empirical evidence that a paper can truly be 'ahead of its time,'" said Alessandro Flammini, an associate professor of informatics and corresponding author on the study. "A 'premature' topic may fail to attract attention even when it is introduced by authors who have already established a strong scientific reputation."

A prime example is a seminal paper by Albert Einstein, Boris Podolsky and Nathan Rosen that laid out the "EPR Paradox," a major puzzle in quantum entanglement theory in which particles with past interaction remain linked in their

behavior no matter their distance, including across a galaxy. The IU study found that the paper, published in 1935, didn't receive widespread citation until 1994.

The drowsiest sleeping beauty in the study came from the influential statistician Karl Pearson. His paper that was published in 1901 in the journal Philosophical Magazine did not "awaken" until 2002.

Among the top 15 sleeping beauties, four were published over 100 years ago.

"The potential application of some studies are simply unforeseen at the time," Flammini said. "The second-ranked sleeping beauty in our study, published in 1958, concerns the preparation of graphic oxide, which much later became a compound used to produce graphene, a material hundreds of time more resistant than steel and therefore of great interest to industry."

The disciplines with the highest rate of delayed recognition were physics, chemistry, multidisciplinary science, mathematics, and general and internal medicine, with several papers experiencing hibernation periods upwards of 70 years. The top journals for the publication of sleeping beauties were PNAS, Nature and Science.

To conduct the study, Flammini and collaborators drew upon a massive dataset of tens of millions of publications across multiple disciplines over more than a century. The trove of data came from the archives of the American Physical Society, a major publication outlet in physics, and the Web of Science, which includes papers in both the sciences and social sciences.

The scientists drew upon over 380,000 publications from the American Physical Society and 22.4 million from Web of Science.

To calculate a paper's "beauty coefficient," the IU scientists compared a paper's citation history against a line of reference based upon publication year, the maximum number of citations received in a year (within a multi-year observation period) and the year when maximum citation was achieved. They also calculated the "awakening time," the year in which an abrupt change occurred compared to past citations.

Using a massive dataset and open parameters, Flammini found delayed recognition is not as rare a phenomenon as suggested in previous work on the topic, including a 2004 study from the Dutch statistician Anthony F.J. van Raan, who coined the term "sleeping beauties."

The IU study also revealed that statistics, a discipline that had not been previously seen as rich in sleeping beauties, was among the top five fields to experience delayed citations, possibly due to the recent explosion in the availability of extremely large datasets. In addition to the study by Pearson, Flammini's top 15 list included a paper from Edin Bidell Wilson, dormant for 70 years, that introduced an important formula for analyzing small datasets or calculating extreme probability.

Other disciplines named for the first time among those experiencing delayed recognition were probability, surgery and the social sciences.

Broadly, Flammini said the greatest proportion of delayed recognition occurred in papers whose citations made the jump to a new discipline, with different scholars finding new resonances in their own fields.

But sleeping beauties are also fickle, and defy easy definition. The study found no clear demarcation value separating them from "normal" papers, or a method to predict the timing or nature of renewed interest in their topics.

"We found the delayed recognition occurs on a wide and continuous range, in sharp contrast with previous results claiming that long dormant studies are extraordinary cases," Flammini said. "But more work is needed to uncover the 'trigger mechanisms' for awakening these sleeping beauties."

*In addition to Flammini, IU scientists contributing to this study were Qing Ke, research assistant; Emilio Ferrara, research assistant professor; and Filippo Radicchi, assistant professor, all of the School of Informatics and Computing. Flammini is also an affiliated faculty member at the IU Network Science Institute. This study was support in part by the National Science Foundation (Grant SMA-1446078). This article will be available online at 9 a.m. Tuesday, May 26, at http://news.indiana.edu/releases/iu/2015/05/sleeping-beauties.shtml.*

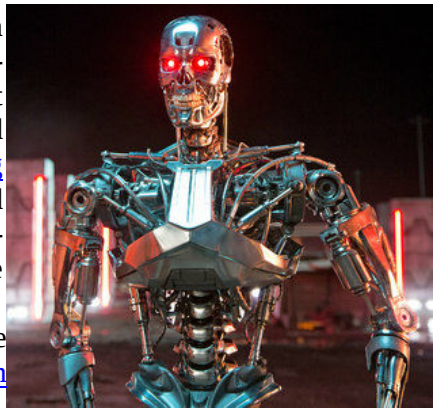
***http://nyti.ms/1Ay1Gq6***

## Relax, the Terminator Is Far Away

***Review o recent work suggests that nobody needs to worry about a Terminator creating havoc anytime soon***

**By JOHN MARKOFF MAY 25, 2015**

In glossy sci-fi movies like "Ex Machina" and "Chappie," robots move with impressive - and frequently malevolent - dexterity. They appear to confirm the worst fears of prominent technologists and scientists like Elon Musk, Stephen Hawking and Bill Gates, who have all recently voiced alarm over the possible emergence of self-aware machines out to do harm to the human race.



"I don't understand why some people are not concerned," Mr. Gates said in an interview on Reddit.

***A robotics contest aims to provide a reality check on the rise of machines like this one from "Terminator Genisys."*** **Paramount Pictures and Skydance Productions**

"I think we should be very careful about artificial intelligence," Mr. Musk said during an interview at M.I.T. "If I had to guess at what our biggest existential threat is, it's probably that," he added. He has also said that artificial intelligence would "summon the demon."

And Mr. Hawking told the BBC that "the development of full artificial intelligence could spell the end of the human race."

Not so fast. Next month, the Defense Advanced Research Projects Agency, a Pentagon research arm, will hold the final competition in its Robotics Challenge in Pomona, Calif. With $2 million in prize money for the robot that performs best in a series of rescue-oriented tasks in under an hour, the event will offer what engineers refer to as the "ground truth" - a reality check on the state of the art in the field of mobile robotics.

A preview of their work suggests that nobody needs to worry about a Terminator creating havoc anytime soon. Given a year and a half to improve their machines, the roboticists, who shared details about their work in interviews before the contest in June, appear to have made limited progress.

In the previous contest in Florida in December 2013, the robots, which were protected from falling by tethers, were glacially slow in accomplishing tasks such as opening doors and entering rooms, clearing debris, climbing ladders and driving through an obstacle course. (The robots had to be placed in the vehicles by human minders.) Reporters who covered the event resorted to such analogies as "watching paint dry" and "watching grass grow."

This year, the robots will have an hour to complete a set of eight tasks that would probably take a human less than 10 minutes. And the robots are likely to fail at many. This time they will compete without belays, so some falls may be inevitable. And they will still need help climbing into the driver's seat of a rescue vehicle.

None of the robots will be autonomous. Human operators will guide the machines via wireless networks that will occasionally slow to just a trickle of data, to simulate intermittent communications during a crisis. This will give an edge to machines that can act semi-autonomously, for example, automatically walking on uneven terrain or grabbing and turning a door handle to open a door. But the machines will remain largely helpless without human supervisors.

"The extraordinary thing that has happened in the last five years is that we have seemed to make extradorinary progress in machine perception," said Gill Pratt, the Darpa program manager in charge of the Robotics Challenge.

Pattern recognition hardware and software has made it possible for computers to make dramatic progress in computer vision and speech understanding. In contrast, Dr. Pratt said, little headway has been made in "cognition," the higher-level humanlike processes required for robot planning and true autonomy. As a result, both in the Darpa contest and in the field of robotics more broadly, there has been a re-emphasis on the idea of human-machine partnerships.

"It is extremely important to remember that the Darpa Robotics Challenge is about a team of humans and machines working together," he said. "Without the person, these machines could hardly do anything at all."

In fact, the steep challenge in making progress toward mobile robots that can mimic human capabilities is causing robotics researchers worldwide to rethink their goals. Now, instead of trying to build completely autonomous robots, many researchers have begun to think instead of creating ensembles of humans and robots, an approach they describe as co-robots or "cloud robotics."

Ken Goldberg, a University of California, Berkeley, roboticist, has called on the computing world to drop its obsession with singularity, the much-ballyhooed time when computers are predicted to surpass their human designers. Rather, he has proposed a concept he calls "multiplicity," with diverse groups of humans and machines solving problems through collaboration.

For decades, artificial-intelligence researchers have noted that the simplest tasks for humans, such as reaching into a pocket to retrieve a quarter, are the most challenging for machines.

"The intuitive idea is that the more money you spend on a robot, the more autonomy you will be able to design into it," said Rodney Brooks, an M.I.T. roboticist and co-founder two early companies, iRobot and Rethink Robotics. "The fact is actually the opposite is true: The cheaper the robot, the more autonomy it has."

For example, iRobot's Roomba robot is autonomous, but the vacuuming task it performs by wandering around rooms is extremely simple. By contrast, the company's Packbot is more expensive, designed for defusing bombs, and must be teleoperated or controlled wirelessly by people. The first Darpa challenge more than a decade ago had a big effect on the perception of robots. It also helped spark greater interest in the artificial intelligence and robotics industries.

During the initial Darpa challenge in 2004, none of the robotic vehicles was able to complete more than seven of the 150 miles that the course covered. However, during the 2005 challenge, a $2 million prize was claimed by a group of artificial-intelligence researchers from Stanford University whose vehicle defeated a Carnegie Mellon entrant in a tight race.

The contest led to Google's decision to begin a self-driving-car project, which in turn spurred the automotive industry to invest heavily in autonomous vehicle technology.

Developing a car to drive on an unobstructed road was a far simpler task than the current Darpa Robotics Challenge, which requires robots to drive and, while they're walking, navigate around obstacles, remove debris, use vision and grasp with dexterity, and perform tasks with tools.

"We had a relatively easy task," said Sebastian Thrun, a roboticist who led the Stanford team in 2005 and later started the Google self-driving-car project. "Today they're doing the hard stuff."

His view about the relationship between humans and robots has been shaped by the two contests. "I'm a big believer that technology progresses by complementing people rather than replacing them," he said.

Most of the Robotics Challenge teams receive university and corporate financing, and in some cases use a Darpa-funded, 6-foot-2 Atlas robot that weighs 380 pounds. (All of the competitors must design their own software and controls.)

But one team of hobbyists will bring a homegrown robot financed with credit cards and the help of family members.

"We're not a big company," said Karl Castleton, an assistant professor of computer science at Colorado Mesa University and the leader of Grit Robotics, which has constructed a robot that rolls slowly on four wheels. "We're just some guys who have a lot of love for what we're doing."

***http://www.eurekalert.org/pub_releases/2015-05/bidm-sip052215.php***

## Study identifies possible role for carbon monoxide in treating hemorrhagic stroke

***Potent effects in a mouse model of subarachnoid hemorrhage show that administration of gas can protect the brain, reduce neuronal injury and improve memory***

BOSTON - Carbon monoxide is known by many as a poisonous gas that causes brain injury and other neurological symptoms, including memory loss and confusion. But a new study led by investigators at Beth Israel Deaconess Medical Center (BIDMC) suggests the opposite may be true: When administered in small, carefully controlled amounts, carbon monoxide may actually protect the brain from damage following subarachnoid hemorrhage, a devastating stroke that results from bleeding in the brain.

Published online today in The Journal of Clinical Investigation (JCI), the new findings show that carbon monoxide can help accelerate a natural process that minimizes cognitive damage by speeding the clearance of heme, a highly toxic component of red blood cells that can accumulate and cause brain inflammation following hemorrhagic stroke.

"Aneurysmal subarachnoid hemorrhage [SAH] affects about 40,000 individuals in the U.S. each year," explained co-senior and corresponding author Khalid A. Hanafy, MD, PhD, Neurological Director of the Neurointensive Care Unit at BIDMC and Assistant Professor of Neurology at Harvard Medical School (HMS). "SAH is a terrible condition that begins with a catastrophic headache, which patients describe as being like a bomb exploding in their heads."

SAH is a type of stroke that develops as the result of an aneurysmal rupture that coats the exterior of the brain in blood. It predominantly affects women between the ages of 45 and 55 and has a 50 percent mortality rate within 12 months of onset. Thirty to 40 percent of surviving SAH patients suffer long-term cognitive damage.

In this new work, Hanafy teamed with co-senior author Leo E. Otterbein, PhD, an investigator in the Transplant Institute at BIDMC and Associate Professor of Surgery at HMS who has investigated the therapeutic applications of carbon monoxide for more than 15 years. Otterbein's novel studies have revealed a number of promising therapeutic applications for the gas, including treatment of pulmonary hypertension, prevention of organ rejection following transplantation, reduction of vascular restonsis, shrinkage of cancerous tumors and infection-fighting abilities.

"My laboratory has been studying the properties of carbon monoxide for years, but we've never investigated a possible therapeutic role for CO in the brain," said Otterbein. "As a neurologist specializing in intensive care medicine, Dr. Hanafy was very interested in subarachnoid hemorrhage and was already investigating mechanisms by which heme caused inflammation in the brain following stroke. It was this natural multidisciplinary collaboration between our laboratories that helped lead to this exciting paradoxical discovery."

The findings hinge on a group of brain cells called microglia. "Microglia can have many different functions, but in this work, we found that they were acting as something of a 'trash collector' for the brain," explained Hanafy.

One of the principal components in the "trash" that piles up following SAH is a pigment called heme, which is found in the hemoglobin protein within red blood cells. When red blood cells become damaged, as is the case in hemorrhagic stroke, the heme pigment is released from the protein and ventures outside the confines of the red blood cell where it becomes highly injurious, causing inflammation and death to surrounding brain tissue.

"In their trash-collecting capacity, microglia remove the heme using an enzyme called heme oxygenase-1 [HO-1]," said Hanafy, adding that this critical function is accomplished, in large part, through the generation of carbon monoxide.

"What appears to be happening is that HO-1 in the microglia removes the heme burden from the extracellular space and rapidly transforms it into iron, bile pigments and carbon monoxide," added Otterbein.

After determining that CO was the protective element observed with HO-1, the researchers went on to test whether safe, modest levels of inhaled CO could help mitigate brain damage following SAH. They created a mouse model of SAH and exposed one group of mice to normal air and a second group to one hour of inhaled CO gas per day for seven days following the onset of subarachnoid hemorrhage.

The mice then underwent a series of maze experiments to test cognitive abilities. "The mice that were exposed to CO performed substantially better," said lead author Nils Shallner, PhD, a research fellow in the Otterbein lab and investigator at the University Medical Center Freiburg, Germany. "This told us that CO could improve functional outcome following a hemorrhagic stroke."

"Both neuronal injury and cognitive function were restored when we treated the mice with safe, low amounts of carbon monoxide," added Hanafy. "Moreover, this occurred even when HO-1 was missing. In other words, CO therapy effectively substituted for the lack of endogenous CO generated by HO-1."

The new findings offer an important avenue for future clinical research and development of CO-based therapies for the treatment of patients with ruptured cerebral aneurysms and provide compelling data that - in carefully controlled amounts - CO can protect the brain.

"Much of the CO toxicity that has been described over the years focuses on adverse neurological effects such as confusion, nausea and headache that likely result from exposure to very high levels of CO as well as to hundreds of other toxic molecules that are found in combustion products, such as auto exhaust," said Hanafy. "Our investigations lay the groundwork for future clinical trials to test CO in patients with SAH. In the future, we could potentially provide a therapeutic option for a devastating disease that primarily strikes women in their 40s and 50s."

"We have been asking the same question for years: Why would the body naturally produce CO if it was inherently toxic to cells?" added Otterbein. "In this collaborative work, our teams were able to show that a small dose of CO can offer neurological protection and that it is the production of CO by HO-1 that helps to prevent brain damage following hemorrhagic stroke."

*In addition to Hanafy, Otterbein and Schallner, coauthors include BIDMC investigators Rambhau Pandit , Robert LeBlanc III Ajith J. Thomas, Christopher Ogilvy and David Gallo; and Brian Zuckerbraun of the University of Pittsburgh Medical Center.*

*This study was supported, in part, by grants from the National Institutes of Health (K08 NS078048, HL-071797; HL-076167) and grants from the German Research Foundation, as well as support from the Julie Henry Fund at the Transplant Center of BIDMC.*

***http://www.eurekalert.org/pub_releases/2015-05/b-pds052215.php***

## Psychedelic drugs should be legally reclassified as they may benefit patients

***Psychedelic drugs such as LSD are much less harmful than claimed and should be legally reclassified to allow further research on their medical use, says expert***

James Rucker, a psychiatrist and honorary lecturer at the Institute of Psychiatry, Psychology and Neuroscience, King's College London, describes how these drugs "were extensively used and researched in clinical psychiatry" before their prohibition in 1967.

He explains that many trials of psychedelics published before prohibition, in the 1950s and 1960s, suggested "beneficial change in many psychiatric disorders".

However, research ended after 1967. In the UK psychedelic drugs were legally classified as schedule 1 class A drugs - that is, as having "no accepted medical use and the greatest potential for harm, despite the research evidence to the contrary," he writes.

Rucker points out that psychedelics remain more legally restricted than heroin and cocaine. "But no evidence indicates that psychedelic drugs are habit forming; little evidence indicates that they are harmful in controlled settings; and much historical evidence shows that they could have use in common psychiatric disorders."

In fact, recent studies indicate that psychedelics have "clinical efficacy in anxiety associated with advanced cancer, obsessive compulsive disorder, tobacco and alcohol addiction, and cluster headaches," he writes.

And he explains that, at present, larger clinical studies on psychedelics are made "almost impossible by the practical, financial and bureaucratic obstacles" imposed by their schedule 1 classification. Currently, only one manufacturer in the world produces psilocybin for trial purposes, he says, at a "prohibitive" cost of £100,000 for 1 g (50 doses).

In the UK, to hold a schedule 1 drug, institutions require a license, which costs about £5,000, he adds. Only four hospitals currently hold such licenses, which come with regular police or home office inspections and onerous rules on storage and transport.

This, he argues, "means that clinical research using psychedelics costs 5-10 times that of research into less restricted (but more harmful) drugs such as heroin."

As a result, "almost all grant funders are uncomfortable funding research into psychedelics," writes Rucker, while prohibition as a condition of UN membership is "arguably causing more harm than it prevents."

He concludes that psychedelics are neither harmful nor addictive compared with other controlled substances, and he calls on the UK Advisory Council on the Misuse of Drugs and the 2016 UN General Assembly Special Session on Drugs, "to recommend that psychedelics be reclassified as schedule 2 compounds to enable a comprehensive, evidence based assessment of their therapeutic potential."

***http://www.eurekalert.org/pub_releases/2015-05/b-dtt052215.php***

## Drug treatment to prevent hip fracture is neither viable nor cost effective

***Current strategy is inefficient and associated with considerable harms, say experts***

Professor Teppo Järvinen and colleagues say drug treatment "can achieve at best a marginal reduction in hip fractures at the cost of unnecessary harms and considerable waste of monetary resources."

The article is part of The BMJ's Too Much Medicine campaign - to highlight the threat to human health and the waste of resources caused by unnecessary care. Worldwide, about 1.5 million hip fractures occur each year. They impose an enormous burden on healthcare resources and, with a growing elderly population, their incidence is predicted to rise.

Before the late 1980's, osteoporosis was diagnosed after a bone fracture. But in 1994, a new definition - based on low bone mineral density - was introduced to identify people at increased fracture risk who were likely to benefit from bone building drugs.

Fracture risk calculators now classify 72% of US white women aged over 65 years and 93% of those aged over 75 years as candidates for long term drug treatment. Yet rates of hip fracture have fallen steadily in most Western countries, regardless of access to drugs, say the authors. Most hip fractures, they say, have little to do with osteoporosis, but rather are caused by falls in frail older adults.

Evidence on cost effectiveness of drug treatment is completely lacking, they add, while the focus on drug treatment means that feasible alternative strategies, such as physical activity, are overlooked.

They also point to the harms from overdiagnosis and treatment, including the psychological burden associated with a disease label, and adverse effects of drug treatment such as nausea, vomiting, and serious bone complications (osteonecrosis of the jaw and drug-induced pathological fractures of the thigh bone). Recent evidence also challenges the justification for the general use of calcium and vitamin D supplements to prevent fractures, they write.

The dominant approach to hip fracture prevention "is neither viable as a public health strategy nor cost effective," conclude the authors.

"Pharmacotherapy can achieve at best a marginal reduction in hip fractures at the cost of unnecessary psychological harms, serious medical adverse events, and forgone opportunities to have greater impacts on the health of older people," they add. "As such, it is an intellectual fallacy we will live to regret."

***http://www.eurekalert.org/pub_releases/2015-05/tjnj-sfa052115.php***

## Study finds association between exposure to aflatoxin and gallbladder cancer

***Exposure to a toxin produced by mold was associated with an increased risk of gallbladder cancer***

In a small study in Chile that included patients with gallbladder cancer, exposure to aflatoxin (a toxin produced by mold) was associated with an increased risk of gallbladder cancer, according to a study in the May 26 issue of JAMA.

In Chile, gallbladder cancer is a leading cause of cancer death in women. Exposure to aflatoxin, a liver carcinogen, is associated with gallbladder cancer in primates. Aflatoxin contamination has been identified in Chile, including in aji rojo (red chili peppers). Aji rojo is associated with gallbladder cancer; however, the association of aflatoxin with gallbladder cancer in humans has not been directly evaluated, according to background information in the article.

Catterina Ferreccio, M.D., M.P.H., of the Pontificia Universidad Catolica de Chile, Santiago, Chile, and colleagues evaluated plasma aflatoxin-albumin adducts (a compound) and gallbladder cancer in a pilot study conducted from April 2012 through August 2013. Aflatoxin forms adducts with albumin in peripheral blood that accumulate up to 30-fold higher with chronic vs single exposure. The researchers assessed aflatoxin B1-lysine adduct (AFB1 adduct) in participants. Aji rojo consumption was determined via questionnaire.

The final analysis included 36 patients (cases) with gallbladder cancer, 29 controls with gallstones, and 47 community controls. Cases and controls had similar characteristics except for aji rojo consumption (greater percentage of case patients had weekly consumption). AFB1-adducts were detected in 23 cases (64 percent), 7 controls with gallstones (18 percent), and 9 community controls (23 percent). AFB1-adduct levels were highest in cases.

"Despite the small number of participants, the associations between aflatoxin exposure and gallbladder cancer were statistically significant. Recall bias may affect self-reported variables, but not exposure measurement. We cannot rule out reverse causation (i.e., cancer may affect AFB1-adduct detection) using cross-sectional data. Larger and longitudinal efforts are needed to substantiate these

preliminary findings, obtain more precise effect estimates, and identify sources of aflatoxin. These findings, if confirmed, may have implications for cancer prevention," the authors write.

*(doi:10.1001/jama.2015.4559; Available pre-embargo to the media at http://media.jamanetwork.com)*

***http://bit.ly/1LNBuJ7***

## Ancient Carnivores Had a Taste for Neanderthal Meat

***Researchers link bite marks on a Neanderthal skull to the fangs of an ancient big cat***

**By Helen Thompson**

Neanderthal hunters may themselves have been prey for big cats and other carnivores. According to a recent study, some punctures on Neanderthal fossils are likely bite marks from large carnivore attacks.

Scientists know what the average Neanderthal ate, how they hunted, who they mated with, how they divvied up chores and to some degree where they crossed paths with large carnivores.

***Unearthed at the Cova Negra site in Spain, skull fragments from a Neanderthal child have telltale punctures in the right parietal region.* (IPHES)**

Evidence from archaeological and paleontological sites indicates that Neanderthals scavenged the leftovers of big carnivores, hunted them and even competed with them for cave shelters.

Recently, a team of Spanish researchers used modern cases of carnivore attacks on humans to see if bite marks on Neanderthal bones bore similarities. Looking at 124 recent case of attacks by lions, tigers, bears, leopards and other carnivores on modern humans, they found similarities to marked bones in the fossil record during the Pleistocene between 40,000 and 200,000 years ago. The group posits that bite marks could have been the result of a carnivore attack. However, it's unclear how often these attacks might have occurred.

In one case, they pinpointed the carnivorous perpetrator. Puncture marks in the skull of a young Neanderthal child unearthed in a cave in Valencia, Spain, resemble those from modern big cat attacks. Their results appear in this month's issue of *Archaeological and Anthropological Sciences*.

Understanding how Neanderthals interacted with big cats and other contemporary predators could perhaps inform how we share our own environment with large wildlife. "The conflict between humans and large carnivores has been present and constant throughout human evolution, enduring even to modern times," the researchers write. Though modern humans outcompeted Neanderthals for resources, it's possible that carnivore threats exacerbated their demise, they argue. Given that Neanderthals lived amid these predators, perhaps it's not too surprising that some of the hominids met their end at the jaws of a ferocious animal.

***http://www.eurekalert.org/pub_releases/2015-05/p-lwo052115.php***

## Lethal wounds on skull may indicate 430,000-year-old murder

***Human remains in Spanish cave site provides further evidence for early funerary practices***

Lethal wounds identified on a human skull in the Sima de los Huesos, Spain, may indicate one of the first cases of murder in human history, some 430,000 years ago, according to a study published May 27 2015 in the open-access journal PLOS ONE by Nohemi Sala from Centro Mixto UCM-ISCIII de Evolución y Comportamiento Humanos, Spain, and colleagues.

The archeological site, Sima de los Huesos in northern Spain, is located deep within an underground cave system and contains the skeletal remains of at least 28 individuals that date to around 430,000 years ago, during the Middle Pleistocene. The only access to the site is through a 13-meter deep vertical shaft, and how the human bodies arrived there remains a mystery.

***This is a frontal view of Cranium 17 showing the position of the traumatic events T1 (inferior) and T2 (superior).* Credit: Javier Trueba / Madrid Scientific Films**

A nearly complete skull, Cranium 17 from the Sima de los Huesos, is comprised of 52 cranial fragments recovered during excavations at the site over the last 20 years. This skull shows two penetrating lesions on the frontal bone, above the left eye. Relying on modern forensic techniques, such as contour and trajectory analysis of the traumas, the authors of the study showed that both fractures were likely produced by two separate impacts by the same object, with slightly different trajectories around the time of the individual's death. According to the authors, the injuries are unlikely to be the result of an accidental fall down the vertical shaft. Rather, the type of fracture, their location, and that they appear to have been produced by two blows with the same object lead the authors to

interpret them as the result of an act of lethal interpersonal aggression - or what may constitute the earliest case of murder in human history.

Furthermore, if this individual was already dead, the authors found that they were likely carried to the top of the vertical shaft by other humans. The authors suggest that humans were likely responsible for the accumulation of bodies in the Sima de los Huesos, which supports the idea that this site represents early evidence of funerary behavior.

*Adapted by PLOS ONE from release provided by the author* *http://dx.plos.org/10.1371/journal.pone.0126589*

***http://bit.ly/1HWxMvs***

## Mission to Europa will test Jupiter moon's friendliness to life

***Is Europa habitable? That's the big question that NASA hopes to answer in a future mission to the icy moon, slated to launch sometime in the 2020s.***

- **20:17 26 May 2015 by Aviva Rutkin and Lisa Grossman**

New details emerged on Tuesday when NASA revealed the nine scientific instruments chosen to chip away at Europa's mysteries.

Europa is thought to be the best candidate for hosting extraterrestrial life in the solar system, thanks to its suspected ocean beneath a crust of ice that could be up to several kilometres thick. Earlier this year, NASA announced plans to send a solar-powered spacecraft out to Jupiter, where it will spend three years in orbit around Jupiter and perform 45 fly-bys of Europa.

"We're trying to answer the big questions," said NASA science administrator John Grunsfeld in a press conference. "Where did we come from? Where are we going? And are we alone?"

The answers will start with a better understanding of what Europa looks like. Currently, our best pictures were taken by the Galileo spacecraft, which orbited Jupiter from 1995 to 2003 and photographed about 10 per cent of the moon's surface at high resolution.

**Beneath the ice**

The new mission will bring a camera developed at the Johns Hopkins Applied Physics Laboratory in Laurel, Maryland, which will shoot pictures of up to 90 per cent of the surface at 50-metre resolution, far higher than Galileo's.

"It will really be a revolution to have a global surface map at sufficient resolution to see details," says Cynthia Phillips of the SETI Institute in California, who worked on the Galileo mission.

Two instruments will map the moon's salty oceans: a magnetometer, built by the Jet Propulsion Laboratory, and ice penetrating radar, built by the University of Texas at Austin. The first machine will "essentially take an MRI of the interior structure of Europa", explained project scientist Curt Niebur, determining how deep and how salty the ocean really is. The second will scan the ice shell itself to determine its internal structure, perhaps revealing hidden lakes like those seen in Antarctica.

The spacecraft will carry an infrared spectrometer to determine what materials sit on the surface of the ice. Mysterious reddish-brown gunk seen in older images of the moon will be first for examination. Some scientists have proposed that they might be irradiated sea salt or even frozen chunks of bacteria.

**Water spout**

NASA is also searching for evidence of water plumes. In 2013, the Hubble Space Telescope spotted a geyser spurting from the moon's south pole, but nothing like it has been seen since. An ultraviolet spectrograph from the Southwest Research Institute in Colorado will hunt down data about the plumes, if they exist: where they are, how active they are and what kinds of materials they contain.

In addition, a thermal imaging system from Arizona State University will search for "hot spots" on the ice up to 100 °C warmer than the average temperature, a sign that plumes are erupting nearby.

"The instrument suite they picked looks fabulous," says Phillips. "It has everything you would want."

One thing the mission lacks is an instrument specifically designed to look for life – like, for example, a mass spectrometer that could detect the left-handed molecules favoured by living things on Earth. Niebur cautions that the search for life will be difficult: it's unlikely that we will run across the kind of clear evidence common here on Earth, such as chlorophyll or fossilised bones. "Mother Nature is not going to be that kind to us," he says.

***http://www.bbc.com/news/health-32881552***

## Cold sore virus 'treats skin cancer'

***A genetically engineered version of a virus that normally causes cold sores shows real promise for treating skin cancer, say researchers.***

**By Michelle Roberts Health editor, BBC News online**

The modified herpes virus is harmless to normal cells but when injected into tumours it replicates and releases substances to help fight the cancer.

Trial results published in the Journal of Clinical Oncology show the therapy could lengthen survival by years - but only for some melanoma patients. The treatment is not yet licensed.

Similar "immunotherapy" treatments for melanoma are already available in the US and in Europe, but researchers believe T-Vec would be a welcome addition to these. It would also be the first melanoma treatment that uses a virus.

The latest study is the largest ever randomised trial of an anti-cancer virus and involved 436 patients from 64 centres in the US, the UK, Canada and South Africa who had inoperable malignant melanoma.

UK trial leader Prof Kevin Harrington, from the Institute of Cancer Research, London, said: "There is increasing excitement over the use of viral treatments like T-Vec for cancer, because they can launch a two-pronged attack on tumours - both killing cancer cells directly and marshalling the immune system against them. "And because viral treatment can target cancer cells specifically, it tends to have fewer side effects than traditional chemotherapy or some of the other new immunotherapies."

**More research**

Dr Hayley Frend, science information manager at Cancer Research UK, said: "Previous studies have shown T-Vec could benefit some people with advanced skin cancer, but this is the first study to prove an increase in survival.

"The next step will be to understand why only some patients respond to T-Vec, in order to help better identify which patients might benefit from it."

**Analysis**

Although it has not yet been licensed, doctors are excited about the very real prospect of a brand new type of treatment for advanced melanoma - and, in the future, possibly other cancers too.

The idea of using viruses to enter and kill cancerous cells has been gathering scientific pace and kudos.

This latest study in the Journal of Clinical Oncology is the largest ever randomised trial of an anti-cancer virus and provides tantalising evidence that the treatment concept could soon be moved into the clinic, after decades of work in the lab.

Researchers now want to do more studies to identify which patients might benefit from the treatment and whether it should be used alongside other melanoma drugs that are already approved. Drug regulators will be watching closely and will soon make a final decision about T-Vec.

Earlier this year an immunotherapy drug, pembrolizumab, became the first treatment "fast-tracked" for NHS patients in England with advanced melanoma, under a new government scheme.

Drugs approved through the Early Access to Medicines scheme, launched in England in April 2014, have been scrutinised by regulators weighing up the risks and benefits.

Melanoma is the sixth most common cancer in the UK and kills more than 2,000 people in Britain each year. Damage to the skin by the sun's harmful UV rays increases your risk of developing this cancer.

***http://www.eurekalert.org/pub_releases/2015-05/acs-nes052715.php***

## New electronic stent could provide feedback and therapy - then dissolve

***New kind of multi-tasking stent could minimize risks***

Every year, an estimated half-million Americans undergo surgery to have a stent prop open a coronary artery narrowed by plaque. But sometimes the mesh tubes get clogged. Scientists report in the journal ACS Nano a new kind of multi-tasking stent that could minimize the risks associated with the procedure. It can sense blood flow and temperature, store and transmit the information for analysis and can be absorbed by the body after it finishes its job.

Doctors have been implanting stents to unblock coronary arteries for 30 years. During that time, the devices have evolved from bare metal, mesh tubes to coated stents that can release drugs to prevent reclogging. But even these are associated with health risks. So researchers have been working on versions that the body can absorb to minimize the risk that a blood clot will form. And now Dae-Hyeong Kim, Seung Hong Choi, Taeghwan Hyeon and colleagues are taking that idea a step further.

The researchers developed and tested in animals a drug-releasing electronic stent that can provide diagnostic feedback by measuring blood flow, which slows when an artery starts narrowing. The device can also heat up on command to speed up drug delivery, and it can dissolve once it's no longer needed.

***http://bit.ly/1FkfSPX***

## Why Your Immune System Doesn't Eat You Alive

***Contrary to conventional wisdom, T cells that cause autoimmune disease actually abound in the body but are held in check***

**By Esther Landhuis | May 21, 2015**

For a long time researchers figured the body had a tidy way of dealing with immune cells that might trigger diabetes, lupus or other autoimmune diseases - it must kill off these rogue cells early in life, before the immune system matures. New research published on May 19 in Immunity challenges this age-old thinking. Instead, the body seems to keep these so-called self-reactive T cells in benign form to fight potential invaders later.

That conclusion comes from a comprehensive set of immune analyses in mice and people, in which a team at Stanford University has found surprisingly large numbers of self-reactive T cells lurking in the bloodstream through adulthood. The cells are not easily activated, though, suggesting the presence of “a built-in brake,” says immunologist Mark Davis, the paper’s senior author. The findings

renew debate about how the immune system manages to marshal its forces against myriad foreign invaders all the while leaving our own tissues alone.

The controversy emerged decades ago when researchers learned the secret to the immune system's incredible versatility. They discovered that a special gene-shuffling process makes millions of antibodies and receptors. Their sheer number and variety allow our immune cells to recognize any conceivable pathogen, in principle. But the explanation also posed a puzzle: Those random gene rearrangements also produce T cells that could attack the body's own tissues. As a solution, some scientists proposed that the body wipes out those self-reactive cells while the immune system is developing.

Subsequent experiments by several labs supported this proposal. In one study published in 1988 researchers in Switzerland genetically engineered a mouse so that most of the animal's T cells recognized the same antigen - a snippet of protein called H-Y that is found only in males. In female mice, which lack this protein, H-Y–specific T cells developed normally, just like T cells that recognize flu viruses or other foreign material. But in male mice H-Y–specific T cells hardly made it into circulation. The results appeared consistent with the longstanding theory about the elimination of self-reactive cells during development.

Still, some scientists were not convinced. The mice in the 1988 study were an artificial system. The female animals' T cells were predominantly specific for a single protein, H-Y, whereas the 200 billion T cells in a typical human adult recognize millions of different substances. And therein lay the challenge: how to fish out of that huge mix the few cells of interest.

Davis and his colleagues overcame this hurdle in the 1990s when they figured out how to place a fluorescent label on specific, individual T cells. That enabled the researchers to take batches of immune cells and use conventional sorting procedures to isolate the rare cells they wanted to study. With later refinements by Marc Jenkins's lab at the University of Minnesota Medical School, the method became sensitive enough to examine specific naturally occurring T cells in the context of a normal immune system.

In the current study Davis's group used this approach to determine the frequency of H-Y–specific T cells in a group of blood donors. In the women about one in 68,000 killer T cells were specific for H-Y. (About a third of our T cells are "killer" T cells, which fight cancer cells and other invaders. The other two thirds are "helper" T cells that help initiate the fight.) In the men the frequency of H-Y–specific cells was only a little lower (one in 200,000). That meant a sizeable number of their H-Y-specific killer T cells had escaped deletion.

A bigger surprise came when the scientists surveyed the blood samples for killer T cells specific to other foreign peptides. The number of foreign-specific T cells was essentially the same as T cells recognizing various "self" peptides. They did not behave the same, though. Cultured in petri dishes, foreign-specific cells grew easily whereas self-specific cells languished. Plus, foreign-specific T cells turned on a set of proliferation-related genes that were expressed at much lower levels in self-specific T cells. "There was something funky about the self-specific cells," Davis says. "More was required to get them going."

Considering that infectious diseases are historically the number-one killer, the results arguably make sense. "You still want [self-reactive cells] to be there in case a pathogen comes along with that specificity," Davis says. In support of that idea his team modified a pivotal section of a hepatitis C viral peptide by substituting in each of 20 possible amino acids. They found that human blood samples contained T cells specific for all 20 versions of the virus.

Some researchers think the new findings could shift the field's view on how the body handles self-reactive T cells. Instead of killing them wholesale, Jenkins says, it's more like the system "stuns them so they're present but don't function."

Others see things differently. Philippa Marrack of National Jewish Health, Denver, says the immune system "has got to let self-reactive cells through anyway" because some become specialized regulatory T cells that help the body by suppressing other immune cells.

Whatever their fate, self-reactive cells could also hold clues to cancer immunotherapy, Davis says. This therapeutic approach uses the body's own T cells to attack tumors - but often the therapy is unreliable. T cells may be inhibited "because they think the cancer cell is a self antigen," Davis says. Figuring out how to lessen that inhibition could motivate them to attack the cancer.

***http://nyti.ms/1GJixHs***

## The Human Family Tree Bristles With New Branches

***For scientists who study human evolution, the last few months have been a whirlwind.***

**Carl Zimmer**

Every couple of weeks, it seems, another team pulls back the curtain on newly discovered bones or stone tools, prompting researchers to rethink what we know about early human history. On Wednesday, it happened again. Yohannes Haile-Selassie of the Cleveland Museum of Natural History and his colleagues reported finding a jaw in Ethiopia that belonged to an ancient human relative that lived sometime between 3.3 and 3.5 million years ago. They argue that the jaw belongs to an entirely new species, which they named Australopithecus deyiremeda.

While some experts agree, skeptics argue that the jaw belongs to a familiar hominid species, known as Australopithecus afarensis, that existed about 3.9 to 3 million years ago.

Studies like this one are adding fresh fuel to the debate over the pace of human evolution. Some researchers now believe the human family tree bore exuberant branches early on. "I'm so excited about these discoveries I'm driving my friends crazy," said Carol V. Ward, a paleoanthropologist at the University of Missouri. "It makes us stop and rethink everything."

***Researchers who discovered this jaw fossil say it belongs to a new species, Australopithecus deyiremeda.*** **Yohannes Haile-Selassie/Cleveland Museum of Natural History**

In the 1990s, the broad outlines of human evolution seemed fairly clear. Early human ancestors, known as hominids, evolved from an ancestor shared with chimpanzees about six or seven million years ago. These hominids were short, bipedal apes with small brains and arms and legs still adapted for climbing trees. Until about three million years ago, experts thought, there weren't a lot of hominid species. In fact, some researchers argued that most hominid fossils represented just a single species.

In 1974, the paleoanthropologist Donald Johanson and his colleagues found a fairly complete, 3.4-million-year-old skeleton in Ethiopia, which they nicknamed Lucy. The species was named Australopithecus afarensis, and many more examples have come to light, dating from about 3.9 to 3 million years ago.

***The find suggests that hominids, like the one this jaw came from, may have been much more diverse much earlier than previously thought.*** **Yohannes Haile-Selassie Cleveland Museum of Natural History**

Scientists had thought that hominid evolution became more complex just 2.4 million years ago. New species split apart from Australopithecus afarensis, at least a few of them coexisting in Africa.

One lineage, called Paranthropus, evolved powerful jaws it probably used to grind tough plant matter. Other hominids developed nimble hands, which they used to make stone tools for butchering meat. Eventually they evolved into tall, long-distance walkers. These hominids belonged to the genus Homo, which produced our own species about 200,000 years ago.

But with new discoveries like Australopithecus deyiremeda, this eons-long story may need to change. Hominids may have become much more diverse much earlier than previously thought. Australopithecus afarensis may have had a lot of company.

In 1995, Ronald J. Clarke of the University of the Witwatersrand in Johannesburg and his colleagues discovered Australopithecus fossils in a South African cave. While the fossils have yet to be formally named, Dr. Clarke and his colleagues have started referring to the putative new species as Australopithecus prometheus. Geologists initially estimated that the rock layer atop the bones was 2.2 million years old. But that research did not tell them exactly how much older the fossils might be. More recently, Dr. Clarke and his colleagues have used new methods to date the rock layer in which the fossils were embedded. In April, they reported that Australopithecus prometheus was 3.67 million years old.

Yet another possible contemporary of Australopithecus afarensis lived in Kenya. In 2001, researchers reported the discovery of a flat-faced hominid skull dating back 3.5 million years. They called it Kenyanthropus platyops.

And even before Wednesday's announcement, Dr. Haile-Selassie had been adding to the debate about early hominid evolution. In 2012, he and his colleagues reported finding 3.4-million-year-old foot bones in Ethiopia from a previously unknown hominid.

The long, grasping toes appear to have been better suited for tree climbing than those of Australopithecus afarensis, suggesting it belonged to a species of its own. Until scientists can describe more bones from its skeleton, it remains without a species name.

These early hominids may have been more mentally sophisticated than previously thought, scientists also have found. Until now, the oldest stone tools ever found dated back 2.6 million years - about 400,000 years after Australopithecus afarensis became extinct.

But last week, Sonia Harmand of Stony Brook University and her colleagues reported discovering tools in Kenya that they estimate to have been made 3.3 million years ago. The researchers suggested that the tools were made by Kenyanthropus, because its fossils come from rocks about the same age and in the same region of Kenya where the tools were found.

Dr. Ward, of the University of Missouri, said the evidence gathered so far pointed to a much earlier explosion of hominid diversity. "It changes our view of human evolution in a fundamental way," she said.

Four or more species may have coexisted with Australopithecus afarensis. Some may have specialized in different ways of getting food, perhaps with newly developed stone tools, for example. Or they may have competed with one another.

The tools also hint that at least some of these early hominids were capable of more complex thinking than previously believed. “The stone tools represent a sophistication in how they use and manipulate objects,” Dr. Ward said.

Scientists have also shed new light on the transition from Australopithecus to Homo. In March, Kaye E. Reed of Arizona State University and her colleagues reported finding the oldest Homo fossil, dating back 2.8 million years. It has some anatomical features found only in Homo, such as narrow molars. But it has other traits, like a rounded chin, that make it look more like Australopithecus afarensis.

Dr. Ward said scientists now must trace Homo’s origins to one of the several hominid species that may have lived between three million and four million years ago - and figure out why the other species became extinct.

But some hominid experts remain unconvinced that the road to Homo took so many turns. Tim D. White, a paleoanthropologist at the University of California, Berkeley, argues that most of the new studies have been rushed into publication without careful peer review.

The 3.3-million-year date for the ancient stone tools, for example, “seemed quite sketchy to me,” Dr. White said. The tools could have been made hundreds of thousands of years later, he said.

Dr. White is also skeptical that the new fossils represent a wealth of new species. He suspects that most of them, including Australopithecus deyiremeda, are just Australopithecus afarensis.

“Lucy’s species just got a few more new fossils,” he said of Wednesday’s announcement.

The peculiar anatomical quirks described by other scientists are no more unusual than the variations found within living ape species, he said. When scientists discover a fossil, Dr. White warned, it can be easy to blow minor variations out of proportion.

“A piece of a mandible doesn’t tell you much,” he said. “Whenever you have small samples, you run a very real risk of mischaracterization.”

Dr. White said it would be wiser to assume that new fossils belonged to documented species, like Australopithecus afarensis, instead of hypothesizing a new species with every new fossil. As he sees it, human evolution isn’t the bushy tree that Dr. Ward describes.

“A saguaro cactus would be the metaphor,” said Dr. White.

Even Dr. Ward expects that scientists will eventually decide some of the new “species” really aren’t species. Even so, she predicted that early hominids would remain more diverse than traditionally thought.

“There were at a bare minimum two hominins around at that time, and perhaps three or more, which is exciting and important however it falls out,” she said.

***http://www.eurekalert.org/pub_releases/2015-05/uow-rcr052015.php***

## Robots can recover from damage in minutes

***Robots will one day provide tremendous benefits to society, such as in search and rescue missions and putting out forest fires - but not until they can learn to keep working if they become damaged.***

A new paper in the journal Nature, called "Robots That Can Adapt Like Animals," shows how to make robots automatically recover from injury in less than two minutes.

A video of the work shows a six-legged robot that adapts to keep walking even if two of its legs are broken. It also shows a robotic arm that learned how to correctly place an object even with several broken motors.

Antoine Cully and Jean-Baptiste Mouret, from the Pierre and Marie Curie University in France, led the work in collaboration with Jeff Clune (University of Wyoming) and Danesh Tarapore (Pierre and Marie Curie University).

In contrast to today's robots, animals exhibit an amazing ability to adapt to injury. There are many three-legged dogs that can catch Frisbees, for example, and if your ankle is sprained, you quickly figure out a way to walk despite the injury. The scientists took inspiration from these biological strategies.

"When injured, animals do not start learning from scratch," senior author Jean-Baptiste Mouret said. "Instead, they have intuitions about different ways to behave. These intuitions allow them to intelligently select a few, different behaviors to try out and, after these tests, they choose one that works in spite of the injury. We made robots that can do the same."

Before it is deployed, the robot uses a computer simulation of itself to create a detailed map of the space of high-performing behaviors. This map represents the robot's "intuitions" about different behaviors it can perform and their predicted value. If the robot is damaged, it uses these intuitions to guide a learning algorithm that conducts experiments to rapidly discover a compensatory behavior that works despite the damage. The new algorithm is called "Intelligent Trial and Error."

"Once damaged, the robot becomes like a scientist," explains lead author Antoine Cully. "It has prior expectations about different behaviors that might work, and begins testing them. However, these predictions come from the simulated, undamaged robot. It has to find out which of them work, not only in reality, but given the damage.

"Each behavior it tries is like an experiment and, if one behavior doesn't work, the robot is smart enough to rule out that entire type of behavior and try a new type," Cully continues. "For example, if walking, mostly on its hind legs, does not work well, it will next try walking mostly on its front legs. What's surprising is how

quickly it can learn a new way to walk. It's amazing to watch a robot go from crippled and flailing around to efficiently limping away in about two minutes."

The same Intelligent Trial and Error algorithm allows robots to adapt to unforeseen situations, including adapting to new environments and inventing new behaviors.

Jeff Clune explains that "technically, Intelligent Trial and Error involves two steps: (1) creating the behavior-performance map, and (2) adapting to an unforeseen situation."

The map in the first step is created with a new type of evolutionary algorithm called MAP-Elites. Evolutionary algorithms simulate Darwinian evolution by hosting "survival of the fittest" competitions in computer simulations to evolve artificially intelligent robots. The adaptation in the second step involves a "Bayesian optimization" algorithm that takes advantage of the prior knowledge provided by the map to efficiently search for a behavior that works despite the damage.

"We performed experiments that show that the most important component of Intelligent Trial and Error is creating and harnessing the prior knowledge contained in the map," Clune says.

This new technique will help develop more robust, effective, autonomous robots. Danesh Tarapore provides some examples.

"It could enable the creation of robots that can help rescuers without requiring their continuous attention," he says. "It also makes easier the creation of personal robotic assistants that can continue to be helpful even when a part is broken."

*This work was funded by the Agence Nationale pour la Recherche (Creadapt, ANR-12-JS03-0009), the European Research Commission (ResiBots, grant agreement No. 637972) and a Direction Générale de l'Armement scholarship to A. Cully.*

***http://nyti.ms/1Ffie1z***

## A Robot That Can Perform Brain Surgery on a Fruit Fly

***Even performing micro-brain surgery*** can now be assigned to a robot

**By JOHN MARKOFF MAY 27, 2015**

STANFORD, Calif. - On a small darkened platform a handful of fruit flies wander aimlessly. There is a brief flash of light and a robotic arm darts downward, precisely targeting a fly's thorax, a moving target roughly the size of a pinhead.

The fly seems unfazed, appearing not to notice that it has been snatched by a high-speed laboratory robot.

The system, which has been prototyped by a team of biologists and roboticists at Stanford, makes it possible automate many aspects of research on Drosophila, one of the most popular experimental animals. Tasks such as determining gender, measuring the size of body parts and even performing micro-brain surgery - long performed by graduate students armed with tweezers - can now be assigned to a robot.

In one experiment, the robot exposed a fly running on a tiny trackball to different odors as the researchers recorded its changing path. The robot arm is extremely precise and uses the fly's legs as shock absorbers, to avoid crushing or impaling the insects.

The robot is also far more efficient than the previous grad student-powered methods. As described Monday in the journal Nature Methods, one $5,000 robot was able to study as many as 1,000 flies in a 10 hour period.

***http://bit.ly/1GKuWeb***

## A Museum Keeps The Fake Noses That Once Replaced Those Missing on Ancient Sculptures

***The exhibit is a testament to art restoration's changing values***

**By Marissa Fessenden smithsonian.com**

Sometimes the best intentions in art preservation can go awry (even stupendously awry). Most professional restorations are careful, but people still debate how far they should go. There's a museum exhibit in Copenhagen that showcases the results of this ever-evolving discussion, reports Joshua Foer for *Atlas Obscura*. It's a collection of noses.

The Ny Carslberg Glyptotek in Copenhagen contains thousands of works of art, including many statues from ancient Greek, Roman, Etruscan and Egyptian civilizations. However, the white marble often used by ancient sculptors breaks easily and by the time their work makes it to modern days, noses and even arms are missing.

In the 19th century, it was common practice to fashion new noses to replace those missing, but in the 20th century museums began to favor the "more authentic" display of noseless artwork as time has rendered them. The result was a lot of leftover noses, writes Foer.

***Like many ancient statues, this Medusa is missing a nose*** **(Franz-Marc Frei/CORBIS)**

Hands literally full of noses that once graced some of history's most prized countenances, curators were to decide what to do with the physical evidence of their ancestors' art crimes.

Rather than bury them, the Nasothek was born, which takes its name from the Latin for "nose" and Greek for "container."

Not all body parts are lost by the ravages of time, of course. Noses and other body parts on sculptures have long attracted the ire of those seeking to deface the art for one reason or another. Now the Nasothek gives a home to pieces of art history while simultaneously offering a kind of memorial to the bits that were lost.

***http://nyti.ms/1AFsuVd***

## Scientists Warn to Expect More Weather Extremes

***Climatologists warn unpredictable and heavy rains are a big part of what many Texans can expect in years to come***

**By JOHN SCHWARTZ MAY 27, 2015**

Torrential rains and widespread flooding in Texas have brought relief from a yearslong drought to many parts of the state. Such unpredictable and heavy rains are a big part of what climate scientists say that many Texans can expect in years to come.

The relief has come at a great cost. The death toll from storms across the state and Oklahoma has reached at least 19, by some estimates, and the property damage is so extensive that Gov. Greg Abbott of Texas has declared some 40 counties disaster areas.

It was not long ago that the state was dealing with a searing drought. In 2011, the drought was so pronounced that the governor then, Rick Perry, proclaimed three days in April "days of prayer for rain in Texas." Parts of the state began to see the drought ease by 2012, but much of it has remained parched.

Now, Texans are more likely to be asking for divine intervention to provide a little sunshine. Reservoirs that had reached historically low levels are brimming, or at least rising fast. The water level at Lake Travis near Austin rose nearly 24 feet in the last week. It was just 34.2 percent full a year ago; today it is 65.5 percent full. Across the state, reservoirs have collected about eight million acre feet of water, rising to 82 percent full from 73 percent full in a month, according to the Texas Water Development Board.

Texans are no strangers to extreme weather, said Katharine Hayhoe, a climate change researcher at Texas Tech University and an author of the 2014 United States National Climate Assessment. "It's famous for floods and drought, hurricanes and tornadoes, dust storms and ice storms," she said. "Climate change is not causing these events — they've always happened naturally. But climate change is exacerbating these events."

She noted that the enormous building boom that Texas has enjoyed in recent decades has led to greater problems with water runoff and higher costs of storm damage. "The choices we're making today are actually increasing our risk," she added.

Trying to link individual weather events to climate change can invite criticism. Bill Nye, a popularizer of science and a climate activist, came under attack this week for talking about the rains as a climate-change event; some pointed out that in 2012, he suggested that the Western drought "is absolutely consistent with the mathematical models and predictions associated with climate change."

Yet different parts of the country, and different parts of the country-size state of Texas, can expect different kinds of weather extremes. Severe rainstorms are consistent with the physics of a warming world, with plenty of moisture evaporating off the oceans, Professor Hayhoe noted — especially in the eastern part of the state near the Gulf of Mexico, where things tend to be wet and getting wetter. But the western part of the state is more like the American Southwest, and drier.

John W. Nielsen-Gammon, Texas' state climatologist and a professor at Texas A & M University, said that Texas weather was heavily influenced by long-term weather phenomena, including El Niño and natural variations of temperatures in both the Atlantic and Pacific oceans.

For now, he said, the slight rise in sea surface temperatures may have added 4 or 5 percent to the recent rainfall, but the longer-term trends for much of the state call for "a decrease of a few percent" in rainfall. It could take many decades, he said, before the effects of warming become a more important factor in the state's weather than the natural variability.

Andrew E. Dessler, a climate researcher at Texas A & M, compared the question of climate change and weather to trying to figure out which of Barry Bonds's home runs were caused by his steroid use.

"You know statistically some of them were, but you don't know which ones," he said. "Almost certainly, it would have rained a lot even without climate change — but it's possible climate change juiced it, added a little bit."

***http://www.eurekalert.org/pub_releases/2015-05/w-lbu052715.php***

## Large but unexplained variations in paracetamol-induced liver failure among European countries

***Six-times higher risk in Ireland and a 2-fold higher risk in the UK highlighted in study***

A fifty-fold between-country difference in rates of paracetamol-induced acute liver failure that leads to liver transplant (ALFT) has been revealed by a study that compared patient data from seven countries at the request of the European Medicines Agency: France, Greece, Ireland, Italy, Netherlands, Portugal and the UK. Researchers discovered that this variation was even more pronounced on a per-capita basis, with a 200-fold difference in ALFT cases. Publishing these

findings in the British Journal of Clinical Pharmacology, the authors call for further research to identify the underlying causes.

Paracetamol is used extensively to combat pain, but when taken above the recommended dose it can cause severe liver damage. On occasions the damage is so severe that it leads to complete liver failure and, when this occurs, patients are recommended to have a transplant. A Study of Acute Liver Transplantation (SALT) identified patients with paracetamol-linked liver failure between 2005-2007, and compared the rate of these events per person and also per tonne of paracetamol sold in the country.

Although the average event rate of ALFT in the seven participating European countries over three years was one case per 6 million inhabitants per year, the rate was the highest in Ireland (one case for every 286,000 inhabitants) and the lowest in Italy (one case for every 180 million people in Italy), with a 200-fold difference between these two countries. A similar variation was seen when looking at the frequency of events for each tonne of paracetamol sold: while there was one ALFT event in Ireland for every 20.7 tonnes of paracetamol sold, the value was only one for every 1,074 tonnes sold in Italy.

Furthermore, paracetamol overdose represented 20% of all causes of this type of ALFT across Europe, but rose to 52% in Ireland and 28% in the UK, but dropped to only 1% in Italy. There were no cases at all recorded in Greece. Intriguingly while France had the highest per-person use of paracetamol, it had the third-lowest ALFT rate.

"Overall, we found a six-times higher risk in Ireland and a two-fold higher risk in the UK compared to the average of the countries participating in the study," says lead researcher Sinem Ezgi Gulmez, the associate Professor of Pharmacology at the University of Bordeaux, France.

Gulmez also points out that the highest rates of overdose ALFT per metric ton of paracetamol sold or per inhabitant were found in the two English-speaking countries (Ireland and the UK) in the study: "Since we do not have event rates for overdoses not leading to liver failure, we cannot conclude anything about the rates of non-ALFT overdoses in the different countries, but indicators point to more common use of paracetamol for self-poisoning in these countries".

"The differences in the figures for harm caused by paracetamol within different countries in Europe are not marginal, and suggest that there are some underlying causes. Paracetamol overdose is a serious public health issue and we should start looking into hepatotoxicity associated with paracetamol at normal doses," says Gulmez.

http://bit.ly/1EK4OtP

## Spacecraft built from graphene could run on nothing but sunlight

***Graphene to the stars. The material with amazing properties has just had another added to the list.***

**28 May 2015 by Jacob Aron**

It seems these sheets of carbon one atom thick can turn light into action, maybe forming the basis of a fuel-free spacecraft.

Graphene was discovered accidentally by researchers playing with pencils and sticky tape. Its flat structure is very strong and conducts electricity and heat extremely well. Yongsheng Chen of Nankai University in Tianjin, China, and his colleagues have been investigating whether larger arrangements of carbon can retain some of these properties. Earlier this year they published details of a "graphene sponge", a squidgy material made by fusing crumpled sheets of graphene oxide.

While cutting graphene sponge with a laser, they noticed the light propelled the material forwards. That was odd, because while lasers have been used to shove single molecules around, the sponge was a few centimetres across so should be too large to move.

The team placed pieces of graphene sponge in a vacuum and shot them with lasers of different wavelength and intensity. They were able to push sponge pieces upwards by as much as 40 centimetres. They even got the graphene to move by focusing ordinary sunlight on it with a lens.

But how was this movement happening? One explanation is that the material acts like a solar sail. Photons can transfer momentum to an object and propel it forwards, and in the vacuum of space this tiny effect can build up enough thrust to move a spacecraft. Just last week, the Planetary Society in Pasadena, California, launched a small solar sail to test the technology. But the forces the team saw were too large to come from photons alone. The team also ruled out the idea that the laser vaporises some of the graphene and makes it spit out carbon atoms.

Instead, they think the graphene absorbs laser energy and builds up a charge of electrons. Eventually it can't hold any more, and extra electrons are released, pushing the sponge in the opposite direction. Although it's not clear why the electrons don't fly off randomly, the team was able to confirm a current flowing away from the graphene as it was exposed to a laser, suggesting this hypothesis is correct (arxiv.org/abs/1505.04254).

Graphene sponge could be used to make a light-powered propulsion system for spacecraft that would beat solar sails. "While the propulsion force is still smaller than conventional chemical rockets, it is already several orders larger than that from light pressure," they write.

"The best possible rocket is one that doesn't need any fuel," says Paulo Lozano of the Massachusetts Institute of Technology. He thinks a graphene-powered spacecraft is an interesting idea, but losing electrons would mean the craft builds up a positive charge that would need to be neutralised, or it could cause damage.

***http://www.bbc.com/news/health-32913659***

## Sleeping cancer cells can 'wake up' decades later

***Scientists say they have found evidence that cancer cells can go to 'sleep', avoiding the effects of chemotherapy, and then 'reawaken' years later.***

Researchers at the Institute of Cancer Research say this may explain why some cancers return, many years after they appear to have been cured. They analysed a patient whose leukaemia returned after 20 years in remission. The findings may help scientists to root out these dormant cancer cells, wake them up and kill them.

The study, published in the journal Leukemia, found that the cancer cells which 'woke up' in the patient after a period of two decades were similar to a group of cancer cells that pre-dated the original bout of the disease.

Blood and bone marrow samples were taken from the patient when he was diagnosed with a rare form of leukaemia at four years old and compared to samples taken when he relapsed aged 25.

Researchers identified a specific DNA mutation in cancer cells from both blood samples, in which two genes called BCR and ABL1 fuse together. They said this showed a common link between the original and the relapsing leukaemia.

But they also found many new genetic changes had occurred in the cancer cells when the patient relapsed. This implies that cancer cells had become dormant, resisted chemotherapy and then 'woke up' after many years of rest.

The cells may have survived because they were growing much more slowly than other cancer cells - and chemotherapy attacks rapidly dividing cells.

Study leader Professor Mel Greaves, director of the Centre for Evolution and Cancer at The Institute of Cancer Research in London, said the research showed that cancer cells are cunning. "It provides striking evidence of cancer evolution in action, with cancer cells able to lie dormant to avoid treatment, and then to accumulate new mutations capable of driving a new bout of disease. "Blood stem cells regularly fluctuate between being dormant or 'asleep' and dividing very quickly, so it seems cancer cells are just borrowing this trick to avoid being killed by chemotherapy."

Prof Greaves added: "In future it might be possible to speed up the growth of these pre-cancerous dormant cells so that they can be targeted and killed using chemotherapy, to reduce the risk of relapse even further."

Dr Matt Kaiser, head of research at Leukaemia and Lymphoma Research, said there were still too many children whose cancer returns.

"If we can build up a picture of what causes rare cases of late relapse and how we can detect and prevent it, we may be able to deliver more true cures for this terrible disease."

***http://bit.ly/1JbemGj***

## Giant International Trade Treaties Center on Science

***The proposed deals have the potential to boost research but could also weaken health and environmental protections***

**By Daniel Cressey and Nature magazine | May 28, 2015**

TTIP is between the United States and the European Union (EU) and the TPP is between a variety of North American and Asian nations whose economies together account for around 60% of the world's gross domestic product.

Two treaties that would govern most of the world's trade—and change how nations across the globe use scientific evidence to craft regulations—inched closer to fruition this week. On May 22, the US Senate approved legislation that could speed up approval of the Transatlantic Trade and Investment Partnership (TTIP) and the Trans-Pacific Partnership (TPP).

Public attention has focused on the economic impact of the treaties: TTIP is between the United States and the European Union (EU) and the TPP is between a variety of North American and Asian nations (including the United States, Mexico, Japan, Australia and Malaysia, but not China or India) whose economies together account for around 60% of the world's gross domestic product. But researchers, industry groups and non-governmental organizations (NGOs) are urging scrutiny of the treaties' impact on science.

Supporters point to the agreements' potential to boost research in pharmaceuticals. Critics say that the treaties could undermine countries' abilities to protect the health of their citizens, as well as to cleave to nation-specific comfort levels with genetically modified (GM) organisms.

"TTIP really falls squarely within the domain of science and technology policy," says Sebastian Pfotenhauer, a science-policy researcher at the Massachusetts Institute of Technology in Cambridge. "What is at stake is the sovereignty of countries to interpret scientific data and regulate risks in the way they choose."

In the case of TTIP, tariffs between the EU and United States are already so low that the benefits to business are expected to come mainly from harmonization of regulations, which differ significantly between the two blocs. The EU is sceptical of GM crops, limit-ing what can be grown and imported there. In the United States, by contrast, the crops are widespread and are generally accepted by the public. However, the United States has tougher standards in other areas of trade: for example, it heavily restricts beef purchases from the EU because of fears over BSE (bovine spongiform encephalitis), also known as mad cow disease.

## Race to the bottom

Some groups fear that agreements such as TTIP could be used to force all nations to adopt the rules of the country with the least regulation in each field. “It sets up a series of regulatory steps that will undoubtedly create a race to the bottom,” says David Azoulay, an attorney with the Center for International Environmental Law (CIEL) in Geneva, Switzerland. “We believe that there are basically no benefits that will come from TTIP for people or the environment,” adds Fabian Flues, a campaigner for Friends of the Earth Europe in Geneva. CIEL notes that the agrochemical industry is already considering using TTIP to increase the acceptable level of pesticide residues on food by pushing for the higher US threshold to be adopted in the EU.

Others dismiss the idea of a ‘race to the bottom.’ The European Commission says that harmonization need not lower regulatory protection. And Alberto Alemanno, a lawyer at the business school HEC Paris who has done consultancy work for the EU’s TTIP negotiating team, says that TTIP aims to create a system that allows regulators to discuss when their standards are equivalent, which does not necessarily mean making all regulations identical, as many people assume. If regulations are harmonized in some instances, he points out, citizens would be able to push for the higher standard—not the lower—to be adopted.

Greater clarity on how medicines will be treated by regulators would be a boon for pharmaceutical research, says Richard Bergström, director-general of the European Federation of Pharmaceutical Industries and Associations in Brussels. It could also mean that drugs reach patients earlier, because companies would no longer have to apply separately to US and EU regulators, a process that can involve costly and time-consuming tests, especially for paediatric medicines. “I’m both surprised and quite frustrated by the debate around TTIP,” he says.

Another fear surrounding the trade agreements is that if they are ratified they will include a legal framework known as an investor-to-state dispute resolution mechanism, which would allow companies to take governments to court and overturn legislation. A company could thus limit a government’s ability to regulate a certain chemical on health grounds if that were seen as an unreasonable restriction of the company’s trade as laid out in the treaty. Objectors to the treaties fear that a dispute provision would also discourage governments from passing strict legislation in the first place.

The history of the North American Free Trade Agreement (NAFTA) and other such agreements is littered with such cases, says Pfotenhauer. The pharmaceutical firm Eli Lilly is currently suing Canada under NAFTA after the government invalidated patents on two of the company’s drugs in an argument over interpretation of clinical-trial data. Companies have also tried to use NAFTA to force Canada to allow toxic-waste exports and to include an additive in petrol that the nation’s regulators claimed was dangerous.

These cases revolved around the interpretation of scientific knowledge, notes Pfotenhauer. Indeed, one thing that NGOs, lawyers and governments agree on is that scientists should care about the trade deals. “TTIP is set to change the way in which scientific cooperation is set to take place across the Atlantic,” says Alemanno.

And there may be little point in fighting the deals. Against a background of gloom and pro-free-trade governments, says Alemanno, even if this particular trade negotiation breaks down, as a philosophy, “TTIP is here to stay.”

***http://www.eurekalert.org/pub_releases/2015-05/wtsi-ooa052715.php***

## Out of Africa via Egypt

***Humans migrated north, rather than south, in the main successful migration from Cradle of Humankind***

New research suggests that European and Asian (Eurasian) peoples originated when early Africans moved north - through the region that is now Egypt - to expand into the rest of the world. The findings, published in the American Journal of Human Genetics, answer a long-standing question as to whether early humans emerged from Africa by a route via Egypt, or via Ethiopia.

The extensive public catalogue of the genetic diversity in Ethiopian and Egyptian populations developed for the project also now provides a valuable, freely available, reference panel for future medical and anthropological studies in these areas.


Two geographically plausible routes have been proposed for humans to emerge from Africa: through the current Egypt and Sinai (Northern Route), or through Ethiopia, the Bab el Mandeb strait and the Arabian Peninsula (Southern Route). Some lines of evidence have previously favoured one, some the other.

***225 human genome sequences from Ethiopians and Egyptians point to a Northern exit out of Africa as the most likely route by the ancestors of all Eurasians.*** **Luca Pagani**

"The most exciting consequence of our results is that we draw back the veil that has been hiding an episode in the history of all Eurasians, improving the understanding of billions of people of their evolutionary history," says Dr Luca

Pagani, first author from the Wellcome Trust Sanger Institute and University of Cambridge. "It is exciting that, in our genomic era, the DNA of living people allows us to explore and understand events as ancient as 60,000 years ago."

The team produced whole-genome sequences from 225 people from modern Egypt and Ethiopia. In previous studies, they and others have shown that these modern populations have been subject to gene flow from West Asian populations, so they excluded the Eurasian contribution to the genomes of the modern African people.

The remaining masked genomic regions from Egyptian samples were more similar to non-African samples and present in higher frequencies outside Africa than the masked Ethiopian genomic regions, pointing to Egypt as the more likely gateway in the exodus to the rest of the world.

The team also used high-quality genomes to estimate the time that the populations split from one another: people outside Africa split from the Egyptian genomes more recently than from the Ethiopians (55,000 as opposed to 65, 000 years ago), supporting the idea that Egypt was last stop on the route out of Africa.

"While our results do not address controversies about the timing and possible complexities of the expansion out of Africa, they paint a clear picture in which the main migration out of Africa followed a Northern, rather than a Southern route," says Dr Toomas Kivisild, a senior author from the Department of Archaeology and Anthropology, University of Cambridge.

The Northern Route as the preferential direction taken out of Africa is in better agreement with the known genetic mixture of all non-Africans with Neanderthals, who were present in the Levant at the time, and with the recent discovery of early modern human fossils in Israel (close to the Northern Route) dating to around 55,000 years ago.

"This important study still leaves questions to answer," says Dr Chris Tyler-Smith, a senior author from the Wellcome Trust Sanger Institute. "For example, did other migrations also leave Africa around this time, but leave no trace in present-day genomes? To answer this, we need ancient genomes from populations along the possible routes. Similarly, by adding present-day genomes from Oceania, we can discover whether or not there was a separate, perhaps Southern, migration to these regions.

"Our approach shows how it is possible to use the latest genomic data and tools to answer these intriguing questions of our human origins and migrations."

*Pagani L et al. (2015) Tracing the route of modern humans out of Africa using 225 human genome sequences from Ethiopians and Egyptians. American Journal of Human Genetics. http://dx.doi.org/10.1016/j.ajhg.2015.04.019*

*This research was funded by the Wellcome Trust (Grant No. 098051), by an ERC Starting Investigator grant (Grant No. FP7 - 261213) and by an ERC Advanced grant (Grant No. FP7-295733).*

***http://www.eurekalert.org/pub_releases/2015-05/ifhm-ncc052715.php***

## New cancer cases rise globally, but death rates are declining in many countries

***Prostate cancer and breast cancer have increased significantly since 1990, and cancer poses a special challenge in developing countries where access to screening and costly treatment is rare***

SEATTLE -- New cases of virtually all types of cancer are rising in countries globally - regardless of income - but the death rates from cancer are falling in many countries, according to a new analysis of 28 cancer groups in 188 countries.

Thanks to prevention and treatment, progress has been made in fighting certain cancers, such as childhood leukemia. But researchers found that of all the cancers studied, there was just one - Hodgkin lymphoma - where the number of new cases dropped between 1990 and 2013. Over the same period, age-standardized death rates for all cancers fell in 126 out of 188 countries.

Published in *JAMA Oncology* on May 28, the study, "The Global Burden of Cancer 2013," was conducted by an international consortium of researchers led by the Institute for Health Metrics and Evaluation (IHME) at the University of Washington.

In 2013, there were 14.9 million new cancer cases and 8.2 million cancer deaths worldwide. The leading cause of cancer incidence for men was prostate cancer, which caused 1.4 million new cases and 293,000 deaths. Prostate cancer cases have increased more than threefold during this period due in part to population growth and aging.

For women, similar factors contributed to the rise in breast cancer incidence. In 2013 there were 1.8 million new cases of breast cancer and 464,000 deaths. Breast cancer has remained the leading cause of incident cancer cases for women between 1990 and 2013, but the number of new cases doubled during this period.

Other leading causes of incident cases globally include colon and rectum cancers, which have increased 92%, stomach cancer, up 23% since 1990, and liver cancer, with a 70% increase.

"Cancer remains a major threat to people's health around the world," said oncologist Dr. Christina Fitzmaurice, a Visiting Fellow at IHME and lead author of the study. "Cancer prevention, screening, and treatment programs are costly, and it is very important for countries to know which cancers cause the highest disease burden in order to allocate scarce resources appropriately."

The death toll from cancer is also changing as new cases increase. Cancer was the second-leading cause of death globally after cardiovascular disease, and the proportion of deaths around the world due to cancer has increased from 12% in 1990 to 15% in 2013. Lung, stomach, and liver cancer have remained the three leading causes of cancer deaths for both sexes combined during this time period. Lung cancer deaths have increased by 56%, stomach cancer deaths by 10%, and liver cancer deaths by 60%.

Cancer is often seen as a problem primarily in more affluent nations, but the disease is an issue in developing countries as well as developed countries. Even though breast cancer remains the leading cause of incident cancer cases for women globally, in developed countries incidence rates have been stable or declining since the early 2000s. The reverse is true in developing countries, where incidence rates are lower but rising faster than in developed countries.

The rankings for developed and developing countries are largely the same when it comes to cancer deaths for both sexes, though there are some notable differences. Cervical cancer ranks eighth in developing countries, compared to 18th in developed countries, and prostate cancer ranks 13th in developing countries but sixth in developed countries. Cervical cancer has a particularly significant impact in sub-Saharan Africa, where it's the most commonly diagnosed cancer in almost two dozen countries in the region, including Ghana, Nigeria, and Zambia, and the most common cause of cancer death for women in 40 countries, such as Ethiopia, Kenya, and Tanzania.

"With better screening and treatment sub-Saharan Africa can lead the way in the fight against cervical cancer," said Mr. Yohannes Adama Melaku, of Mekelle University in Ethiopia and a co-author of the study. "Prevention will be a critical part of the effort to save lives."

Although cancer is a global phenomenon, countries around the world show important variations. In China, stomach cancer, not breast cancer, is the second-most common cause of cancer death for women. Non-Hodgkin lymphoma is the most commonly diagnosed cancer for men in United Arab Emirates and Qatar rather than prostate cancer. Mouth cancer, which is not prominent globally, is the second-most diagnosed cancer in India. Japan, Norway, Portugal, Spain, and Sweden are the only countries in the world where colon and rectum cancer was the most deadly form of cancer for women.

"The most effective strategies to address cancer will be tailored to local needs," said IHME Director Dr. Christopher Murray. "Country-specific data can drive policies aimed to reduce the impact of cancer now and in the future."

**Leading causes of cancer deaths globally for both sexes in 2013, with the number of deaths**

| | | |
|---|---|---|
| *1* | *Lung cancer* | *1,639,645* |
| *2* | *Stomach cancer* | *840,953* |
| *3* | *Liver cancer* | *817,969* |
| *4* | *Colorectal cancer* | *771,100* |
| *5* | *Breast cancer* | *471,011* |
| *6* | *Esophageal cancer* | *440,202* |
| *7* | *Other neoplasms* | *369,605* |
| *8* | *Pancreatic cancer* | *352,435* |
| *9* | *Prostate cancer* | *292,729* |
| *10* | *Leukemia* | *265,125* |

**Leading causes of cancer deaths globally for men in 2013, with the number of deaths**

| | | |
|---|---|---|
| *1* | *Lung cancer* | *1,154,629* |
| *2* | *Liver cancer* | *564,201* |
| *3* | *Stomach cancer* | *530,318* |
| *4* | *Colorectal cancer* | *413,986* |
| *5* | *Esophageal cancer* | *307,886* |
| *6* | *Prostate cancer* | *292,729* |
| *7* | *Other neoplasms* | *194,544* |
| *8* | *Pancreatic cancer* | *185,133* |
| *9* | *Leukemia* | *148,931* |
| *10* | *Lymphoma* | *133,129* |

**Leading causes of cancer deaths globally for women in 2013, with the number of deaths**

| | | |
|---|---|---|
| *1* | *Lung cancer* | *485,017* |
| *2* | *Breast cancer* | *463,990* |
| *3* | *Colorectal cancer* | *357,114* |
| *4* | *Stomach cancer* | *310,635* |
| *5* | *Liver cancer* | *253,768* |
| *6* | *Cervical cancer* | *235,732* |
| *7* | *Other neoplasms* | *175,061* |
| *8* | *Pancreatic cancer* | *167,302* |
| *9* | *Ovarian cancer* | *157,754* |
| *10* | *Esophageal cancer* | *132,315* |

*Download the study at [http://www.healthdata.org/research-article/global-burden-cancer-2013](http://www.healthdata.org/research-article/global-burden-cancer-2013).*

http://www.eurekalert.org/pub_releases/2015-05/miot-san052815.php

# Spinning a new version of silk

***Simulations and experiments aim to improve on spiders in creating strong, resilient fibers***

CAMBRIDGE, Mass--After years of research decoding the complex structure and production of spider silk, researchers have now succeeded in producing samples of this exceptionally strong and resilient material in the laboratory. The new development could lead to a variety of biomedical materials -- from sutures to scaffolding for organ replacements -- made from synthesized silk with properties specifically tuned for their intended uses.

The findings are published this week in the journal Nature Communications by MIT professor of civil and environmental engineering (CEE) Markus Buehler, postdocs Shangchao Lin and Seunghwa Ryu, and others at MIT, Tufts University, Boston University, and in Germany, Italy, and the U.K.

The research, which involved a combination of simulations and experiments, paves the way for "creating new fibers with improved characteristics" beyond those of natural silk, says Buehler, who is also the department head in CEE. The work, he says, should make it possible to design fibers with specific characteristics of strength, elasticity, and toughness.

The new synthetic fibers' proteins -- the basic building blocks of the material -- were created by genetically modifying bacteria to make the proteins normally produced by spiders. These proteins were then extruded through microfluidic channels designed to mimic the effect of an organ, called a spinneret, that spiders use to produce natural silk fibers.

**No spiders needed**

While spider silk has long been recognized as among the strongest known materials, spiders cannot practically be bred to produce harvestable fibers -- so this new approach to producing a synthetic, yet spider-like, silk could make such strong and flexible fibers available for biomedical applications. By their nature, spider silks are fully biocompatible and can be used in the body without risk of adverse reactions; they are ultimately simply absorbed by the body.

The researchers' "spinning" process, in which the constituent proteins dissolved in water are extruded through a tiny opening at a controlled rate, causes the molecules to line up in a way that produces strong fibers. The molecules themselves are a mixture of hydrophobic and hydrophilic compounds, blended so as to naturally align to form fibers much stronger than their constituent parts. "When you spin it, you create very strong bonds in one direction," Buehler says.

The team found that getting the blend of proteins right was crucial. "We found out that when there was a high proportion of hydrophobic proteins, it would not spin any fibers, it would just make an ugly mass," says Ryu, who worked on the project as a postdoc at MIT and is now an assistant professor at the Korea Advanced Institute of Science and Technology. "We had to find the right mix" in order to produce strong fibers, he says.

**Closing the loop**

This project represents the first use of simulations to understand silk production at the molecular level. "Simulation is critical," Buehler explains: Actually synthesizing a protein can take several months; if that protein doesn't turn out to have exactly the right properties, the process would have to start all over.

Using simulations makes it possible to "scan through a large range of proteins until we see changes in the fiber stiffness," and then home in on those compounds, says Lin, who worked on the project as a postdoc at MIT and is now an assistant professor at Florida State University.

Controlling the properties directly could ultimately make it possible to create fibers that are even stronger than natural ones, because engineers can choose characteristics for a particular use. For example, while spiders may need elasticity so their webs can capture insects without breaking, those designing fibers for use as surgical sutures would need more strength and less stretchiness. "Silk doesn't give us that choice," Buehler says.

The processing of the material can be done at room temperature using water-based solutions, so scaling up manufacturing should be relatively easy, team members say. So far, the fibers they have made in the lab are not as strong as natural spider silk, but now that the basic process has been established, it should be possible to fine-tune the materials and improve its strength, they say.

"Our goal is to improve the strength, elasticity, and toughness of artificially spun fibers by borrowing bright ideas from nature," Lin says. This study could inspire the development of new synthetic fibers -- or any materials requiring enhanced properties, such as in electrical and thermal transport, in a certain direction.

*The research was supported by the National Institutes of Health, the National Science Foundation, the Office of Naval Research, the National Research Foundation of Korea, and the European Research Council.*

http://www.eurekalert.org/pub_releases/2015-05/nu-pwf052815.php

# Protecting women from multiple sclerosis

***Step closer to understanding why men are better protected from MS than women***

CHICAGO - An innocent mistake made by a graduate student in a Northwestern Medicine lab (she accidentally used male mice instead of female mice during an experiment) has led scientists to a novel discovery that offers new insight into why women are more likely than men to develop autoimmune diseases such as

multiple sclerosis (MS). The finding, detailed in a paper published in The Journal of Immunology, focuses on a type of white blood cell, the innate lymphoid cell, that exhibits different immune activities in males versus females.

MS is a disease that affects the brain and spinal cord and is the result of a dysregulated immune response. Using a mouse model of MS in which only females get disease, this study showed that innate lymphoid cells are activated and protect male mice from the disease. Although female mice have these same cells, they remain inactive and do not protect them.

The research opens up new avenues for investigation into sex-determined disease susceptibility and could one day lead to better therapies for both men and women with MS and other autoimmune diseases. "Women are three to four times more likely than men to develop MS, and much of the current research focuses on the question, 'Why do females get worse disease?'" said Melissa Brown, lead author of the study and professor of microbiology-immunology at Northwestern University Feinberg School of Medicine.

"Now, thanks to a serendipitous moment in the laboratory, we are approaching this research from the opposite way, asking, 'Why are males protected from disease?'" Brown said. "Understanding the mechanisms that limit disease in men can provide information that could be used in future therapy to block disease progression in women."

Like most laboratories that study the mouse model of MS, female mice were used in almost all of Brown's experiments. "When we induce the disease in this strain of female mice, virtually 100 percent of them get very sick," Brown said. "Male mice either get no disease or very little, so MS researchers typically use females in their studies."

A few years ago, a new graduate student in Brown's laboratory was asked to run an experiment using two groups of female mice. One group was normal; the other had a genetic mutation in a growth factor receptor (c-kit) that prevented the development of a subset of immune cells.

Previous experiments in Brown's lab showed that female mice with the mutation didn't get as sick as normal mice, and Brown was looking into reasons why. However, instead of using females, the graduate student chose male littermates from each group. "It was an honest mistake, but the results were striking; the male mice with the mutation got very, very sick," Brown said. "Because this strain of male mice never get very sick, I thought there was some sort of mistake, so I asked the student to repeat the experiment."

The results were the same. Brown and colleagues realized that the mutation was behaving differently in males and females. Brown asked Abigail Russi, a Feinberg MD/PhD student working in her lab, to investigate further.

Russi found that mice with the c-kit mutation lacked type 2 innate lymphoid cells. These cells are normally present in bone marrow, lymph nodes and the thymus of both males and females. The researchers think that in males these cells produce a protein that may help to protect from the disease by interfering with the damaging immune response.

"In the paper we show that when these cells are missing in the males with the mutation, that changes the whole immune response of the male animals and causes this lack of protection," Russi said. "We are now looking at what activates these cells preferentially in males and not in females. The next question is can we activate the innate lymphoid cells in females to decrease disease susceptibility?"

This isn't the first sex difference study in the field of MS research. In the 1990s, scientists found that testosterone was a protective hormone for women with MS, but long-term treatment of women with MS with testosterone is not a viable option because of undesirable side effects.

Type 2 innate lymphoid cells have been well studied in allergy, where they are thought to promote allergic inflammation. But this is the first study to show these cells exhibit sex differences in their activity and actually can protect in autoimmune disease. Early trials are underway, and the scientists are hoping they will find clues to explain potential activators of these cells and whether those activators can be used in therapy.

The findings could lead to a new approach to designing drug therapy that modulates instead of completely suppresses the immune system of MS patients, shifting the response to one that is not so damaging.

"The hope is to target these cells in a sex-specific way and provide a therapy with fewer side effects," Brown said. "This early research may have implications for understanding other diseases such as lupus and rheumatoid arthritis, which also show a female bias."

*Other authors of this study are Margaret E. Walker-Caulfield of the Mayo Clinic and Mark E. Ebel of Northwestern.*

***http://www.eurekalert.org/pub_releases/2015-05/nu-hst052615.php***

## HIV's sweet tooth is its downfall

### *New strategy to halt HIV growth: Block its sugar and nutrient pipeline*

CHICAGO - HIV has a voracious sweet tooth, which turns out to be its Achilles' heel, reports a new study from Northwestern Medicine and Vanderbilt University.

After the virus invades an activated immune cell, it craves sugar and nutrients from the cell to replicate and fuel its wild growth throughout the body.

Scientists discovered the switch that turns on the immune cell's abundant sugar and nutrient pipeline. Then they blocked the switch with an experimental

compound, shutting down the pipeline, and, thereby, starving HIV to death. The virus was unable to replicate in human cells in vitro.

The discovery may have applications in treating cancer, which also has an immense appetite for sugar and other nutrients in the cell, which it needs to grow and spread. The study will be published May 28 in PLOS Pathogens.

"This compound can be the precursor for something that can be used in the future as part of a cocktail to treat HIV that improves on the effective medicines we have today," said corresponding study author, Harry Taylor, research assistant professor in medicine at Northwestern University Feinberg School of Medicine.

"It's essential to find new ways to block HIV growth, because the virus is constantly mutating," said Taylor, also a scientist at Northwestern Medicine's HIV Translational Research Center. "A drug targeting HIV that works today may be less effective a few years down the road, because HIV can mutate itself to evade the drug."

HIV needs to grow in a type of immune cell (CD4+ T cell) that is active, meaning it is already responding to pathogens in the blood. Activation increases the T cell's supplies of sugar and other critical nutrients needed for both cell and virus growth. Until now, no one knew the first step that signaled a newly activated T cell to stock up on sugar and other nutrients. Those nutrients become the building blocks of genetic material the cell and the virus need to grow.

Northwestern and Vanderbilt scientists figured out that first step in stocking the T cell's pantry involved turning on a cell component called phospholipase D1 (PLD1). Then they used an experimental compound to block PLD1 and shut down the pipeline.

This is believed to be the first time scientists have targeted the virus's ability to pilfer the cell's pantry to stop its growth. A related approach was attempted in the 1990s but the drugs used sometimes killed healthy cells and had serious side effects in HIV patients. The Northwestern team's new approach is a gentler, non-toxic way to block HIV access to the cell's "pantry."

**New strategy could reduce organ damage**

The approach has additional benefits beyond the initial goal of preventing HIV from reproducing. The compound also slowed the proliferation of the abnormally activated immune cells, the study found. Current HIV medications stop HIV growth but do not affect the abnormal excess activation and growth of immune cells triggered by HIV.

The excess immune cell growth is believed to contribute to the life-long persistence of HIV and leads to excess inflammation that causes premature organ damage in HIV patients -- even when the virus is suppressed by current medicines.

"Perhaps this new approach, which slows the growth of the immune cells, could reduce the dangerous inflammation and thwart the life-long persistence of HIV," Taylor said.

**HIV's hunt for sugar and world domination**

When HIV enters the bloodstream, it searches out active CD4+ T cells, the commanders-in-chief of the immune system. These active cells are already responding to other pathogens or allergens in the blood and are guzzling glucose and amino acids from the blood, which they need to churn out the building blocks of DNA. The cells' factories are at full throttle, making these building blocks to produce an army of soldiers to fight that cold that has just started to give you a sore throat or the chills.

When HIV finds an active CD4+ T cell, it hijacks the cell's glucose supply and factory to build millions of copies of itself and invade other cells.

"It's a monster that invades the cell and says 'feed me!' " Taylor said. "It usurps the entire production line."

**Cancer cells crave sugar, too**

The idea to test this compound for HIV evolved from Taylor's relationship with chemists at Vanderbilt University, where he was on faculty before he joined Northwestern in 2012.

Taylor knew his Vanderbilt colleagues had identified a compound in their massive screening for potential drugs that block the growth of breast cancer cells. The compound stopped breast cancer cells from spreading by blocking PLD1. Taylor and his Vanderbilt colleagues wondered if blocking this same enzyme in the CD4+ T cell would cut off HIV's use of the cell's nutrient supply and slow the invading HIV.

That's exactly what their study shows. In vitro, the compound shut off the glucose and other nutrients and prevented HIV from having enough building blocks of DNA to make the genetic material it needed to reproduce.

Now, Taylor wants to identify even more compounds for development into future medicines that will limit re-stocking of the cell's pantry to starve HIV -- without harming cells.

"This discovery opens new avenues for further research to solve today's persisting problems in treating HIV infection: avoiding virus resistance to medicines, decreasing the inflammation that leads to premature aging, and maybe even one day being able to cure HIV infection," said Dr. Richard D'Aquila, director of Northwestern's HIV Translational Research Center. He also is the Howard Taylor Ricketts Professor of Medicine at Feinberg and a physician at Northwestern Memorial Hospital.

*Key Vanderbilt collaborators are Craig W. Lindsley and H. Alex Brown.*

*This research was supported in part by Northwestern Medicine's HIV Translational Research Center, the National Institute of Mental Health grant U54-MH084659, National Institute of Diabetes and Digestive and Kidney Diseases grant 5R21DK094735, the National Center for Research Resources grant 5KL2RR024977 and the National Cancer Institute grant CA060553, of the National Institutes of Health.*

***http://www.eurekalert.org/pub_releases/2015-05/hlmc-aci052815.php***

## ASCO: Component in green tea may help reduce prostate cancer in men at high risk

***Polyphenon E reduced combined rates of prostate cancer and atypical small acinar proliferation rates, as well as decreased levels of prostate-specific antigen in men who have premalignant prostate lesions or high-grade intraepithelial neoplasia***

TAMPA, Fla. - Prostate cancer is the second most common type of cancer in men and is predicted to result in an estimated 220,00 cases in the United States in 2015. In recent years, an emphasis has been placed on chemoprevention - the use of agents to prevent the development or progression of prostate cancer. A team of researchers led by Nagi B. Kumar, Ph.D., R.D., F.A.D.A. at Moffitt Cancer Center recently published results of a randomized trial that assessed the safety and effectiveness of the active components in green tea to prevent prostate cancer development in men who have premalignant lesions. The results will be presented at the 2015 American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago.

Twenty percent of green tea is consumed in Asian countries where prostate cancer death rates are among the lowest in the world and the risk of prostate cancer appears to be increased among Asian men who abandon their original dietary habits upon migrating to the U.S.

Laboratory studies have shown that substances in green tea called, "catechins" inhibit cancer cell growth, motility and invasion, and stimulate cancer cell death. Green tea catechins also prevent and reduce tumor growth in animal models. Epigallocatechin-3-gallate (EGCG) is the most abundant and potent catechin found in green tea responsible for these cancer prevention effects.

The goal of this trial was to evaluate if a one-year intervention with green tea catechins could suppress prostate cancer development in men who had high-grade intraepithelial neoplasia (HGPIN) or atypical small acinar proliferation (ASAP). The researchers used decaffeinated green tea capsules called Polyphenon E that contained a mixture of catechins that predominantly contained EGCG at a dose of 200 mgs twice a day.

The researchers compared Polyphenon E in 49 men to placebo tablets in 48 men over a 1 year treatment period. Overall, the difference in the number of prostate cancer cases at the end of 1 year between the two treatment groups was not statistically significant. However, in men who only had HGPIN at the beginning of the trial, they observed a lower combined rate of ASAP and prostate cancer development with Polyophenon E. ASAP is an entity that reflects a broad group of lesions in the prostate with insufficient changes in the cells to be definitively diagnosed as prostate cancer. Additionally, men on Polyphenon E had a significant decrease in prostate-specific antigen (PSA) levels. PSA is a biomarker that in combination with other risk factors is used to screen patients for prostate cancer, and high levels signify a higher risk of prostate cancer.

The Moffitt researchers observed a significant increase in the levels of EGCG in the blood plasma of men on Polyphenon E, and the capsules at this dose were tolerated in this group of men.

*The ASCO poster session will take place Monday, June 1, 1:15-4:45 p.m. in S Hall A. The study was published in the April 14 issue of the journal Cancer Prevention Research. Funding support was received from the National Institutes of Health/National Cancer Institute (R01 CA12060-01A1).*

***http://bit.ly/1PW7RLi***

## Alzheimer's Origins Tied to Rise of Human Intelligence

***Factors that drove the evolution of our intellectual capacity are also implicated in the memory disorder***

**By Nala Rogers and Nature magazine**

Alzheimer’s disease may have evolved alongside human intelligence, researchers report in a paper posted this month on BioRxiv.

The study finds evidence that 50,000 to 200,000 years ago, natural selection drove changes in six genes involved in brain development. This may have helped to increase the connectivity of neurons, making modern humans smarter as they evolved from their hominin ancestors. But that new intellectual capacity was not without cost: the same genes are implicated in Alzheimer's disease.

Kun Tang, a population geneticist at the Shanghai Institutes for Biological Sciences in China who led the research, speculates that the memory disorder developed as ageing brains struggled with new metabolic demands imposed by increasing intelligence.Humans are the only species known to develop Alzheimer's; the disease is absent even in closely related primate species such as chimpanzees.

Tang and his colleagues searched modern human DNA for evidence of this ancient evolution. They examined the genomes of 90 people with African, Asian or European ancestry, looking for patterns of variation driven by changes in population size and natural selection.

**Marked by selection**

The analysis was tricky, because the two effects can mimic each other. To control for the effects of population changes—thereby isolating the signatures of natural selection—the researchers estimated how population sizes changed over time. Then they identified genome segments that did not match up with the population history, revealing the DNA stretches that were most likely shaped by selection.

In this way, the researchers looked back at selection events that occurred up to 500,000 years ago, revealing the evolutionary forces that shaped the dawn of modern humans, thought to be around 200,000 years ago. Most previous methods for uncovering such changes reach back only about 30,000 years, says Stephen Schaffner, a computational biologist at the Broad Institute in Cambridge, Massachusetts.

The analytical approach that Tang's team used is promising, he adds. “It's treating all kinds of selection in a uniform framework, and it's also treating different eras of selection in a more or less uniform way.” But Schaffner says that further research is needed to confirm that the method is broadly applicable.

Still, even the most powerful genomic-analysis methods can be limited by the vagaries of history. Asian and European people descended from a small number of people who left Africa around 60,000 years ago, and that population bottleneck erased earlier patterns of genetic variation in Europeans. The genomes of African people allow researchers to look much further back in time, offering more information about the evolutionary changes that shaped humanity.

***http://www.bbc.com/news/health-32914227***

## Pocket optician 'good as eye charts'

***A smartphone app is as effective at testing eyesight as an optician's clinic, a trial suggests.***

**By James Gallagher Health editor, BBC News website**

The team, at the London School of Hygiene and Tropical Medicine, hopes it can transform eye care for millions of people in remote parts of the world. Trials on 233 people in Kenya, published in JAMA Ophthalmology, showed the phone produced the same results as eye charts. More than 285 million people around the world are blind or visually impaired. It is often easy to treat with something as simple as a pair of glasses or cataract surgery. But too often people are beyond the reach of even a basic eye exam.

The team in London, with colleagues in Scotland, modified a smartphone to develop a series of eye tests that could be used with little training and were easily portable. The Portable Eye Examination Kit (Peek) uses the phone's camera to scan the lens of the eye for cataracts.

Its "Acuity App" uses a shrinking letter which appears on screen and is used as a basic vision test. It uses the camera's flash to illuminate the back of the eye to check for disease. The first clinical data from tests in Kenya show the vision test gives the same results as the rows of letters pinned to an optician's wall. Their eyes were examined both in their homes and at an eye clinic. Further results on scanning the retina are about to be published and are described as 'compelling'.

Dr Andrew Bastawrous, who led the project, told the BBC: "The main reason for most people not getting eye treatment is simply that they don't access the services and that's usually because the services are so far away from them or are unaffordable. "If we can detect people with visual impairment much earlier on then we have a much greater chance of increasing awareness and ensuring they have appropriate treatment. "So something as simple as a vision test can be part of that journey."

The phone is relatively cheap, costing around £300 rather than using bulky eye examination equipment costing in excess of £100,000.

The International Agency for the Prevention of Blindness believes the app could be a "game changer". It has previously said: "We simply don't have the trained eye health staff to bring eye care services to the poorest communities. This tool will enable us to do that with relatively untrained people."

But even if everyone could be tested it would leave the massive problem of who is going to pay for millions of people to be treated?

***http://www.bbc.com/news/world-asia-32919416***

## Mers virus: Concern growing in South Korea

***Concern is growing in South Korea over the spread of the Mers virus after a man defied quarantine to travel to China.***

Seven people have been infected with the disease so far in South Korea, said the country's health ministry. Chinese officials said they had traced the son of a patient who had refused voluntary quarantine. Cases of the virus, for which there is no known cure, have been confirmed in more than 20 countries.

Two new cases of Mers (Middle East Respiratory Syndrome) in South Korea were confirmed on Thursday. The health ministry said that all of them had been linked to a man who returned from the Middle East - where Mers is more common.

Dozens of people are now in quarantine.

**'Deeply sorry'**

Meanwhile, Chinese officials said they had identified and isolated a South Korean man who had ignored quarantine restrictions to fly to China through Hong Kong.

Local media said that health workers had contacted 35 people who came into close contact with him. His father was diagnosed with the virus earlier in May.

"We should have checked more actively and broadly on family-related issues. We are deeply sorry about that," said Yang Byung-kook, director of the Korea Centers for Disease Control and Prevention.

http://www.bbc.com/news/world-asia-china-32926170

## Mers virus: China tracking nearly 200 for possible infections

***China is trying to track down at least 193 people who may have come in contact with a man with Mers, the country's first confirmed case of the virus.***

The alert came as South Korea announced it had two more Mers cases, bringing the total within the country to nine. The outbreak has been traced to a South Korean who visited the Middle East.

China's first case was another South Korean who had ignored quarantine restrictions and flew to Hong Kong, before travelling south by bus. It confirmed the case on Thursday night, two days after the 44-year-old made the trip.

The World Health Organization says there has so far been no sustained human-to-human spread of the Mers (Middle East respiratory syndrome) virus, which has no known cure.

**'High possibility'**

Chinese media reported on Friday that the unnamed 68-year-old man had flown into Hong Kong's Chep Lap Kok airport on Asiana Airlines Flight OZ 723, then took a bus through the busy Shenzhen crossing to Huizhou in the southern Guangdong province. He also stayed in a hotel. He later went to a Huizhou hospital and tested positive for Mers. Guangdong health authorities warned that it was likely the disease would spread as he had been in busy or crowded places.

He Jianfeng, director for the Guangdong Provincial Center for Disease Control, told reporters that the possibility of Mers transferring to others in the area was "very high".

So far 38 people who came into close contact with the man have been tested and have not showed any signs of illness. But a Hong Kong woman who was on the same flight was rushed to hospital on Friday after showing symptoms, said The South China Morning Post.

Mers comes from the same family of viruses as Sars (Severe acute respiratory syndrome) which originated in China in 2002 and infected thousands worldwide.

http://bit.ly/1SJKq6U

## A New Strain of Canine Flu Is on the Rise

***Possible cases of dog flu pop up in 13 states***

**By Helen Thompson**

Your dog can get the flu, and just not from you. Since April, a strain of canine specific influenza is popping up in various states. In April, an outbreak in Chicago infected close to 1,000 dogs. Since then, Cornell's Animal Health Diagnostic Center says that cases have emerged in 11 additional states: Alabama, California, Texas, Massachusetts, New York, Wisconsin, Michigan, New Jersey, Iowa, Indiana and Georgia. USA Today's Lori Grisham reports a case in Ohio, as well, putting other states and pet owners on alert.

Before fearing for Fido's life, there are a few key things to know about this strain and dog flu in general. The virus spreads from nose to nose between dogs, and symptoms look much like the flu in humans: Fever, lots of snot, coughing and fatigue. The way dog flu spreads is not unlike "how respiratory disease spreads at a daycare or airport - people sneezing and coughing on each other," Keith Poulsen, a veterinarian at the University of Wisconsin at Madison, told USA Today.

They share the same name, but this viral strain is different from the seasonal H3N2 flu virus that infects humans. Researchers do sometimes worry about flu strains spreading from humans to pets and vice versa, as Smithsonian's Joey Stromberg reported in 2012, but that's not what's going on here. In fact, this version of H3N2 has shown no ability to infect humans, as the Centers for Disease Control said back in April.

H3N2 is actually a strain of bird flu that can pass between dogs and cats, perhaps guinea pigs and ferrets, as well. Scientists suspect the strain emerged in Asian bird markets before adapting and making the jump between species. In 2007, the viral strain first showed up in dogs in South Korea, but has also infected dogs in China and Thailand.

However, H3N2 isn't the first strain of dog flu to emerge stateside. A strain called H3N8 has been infecting canines here since 2009. The virus had been prevalent for 40 years in horses before spreading to dogs. There is a vaccine for the H3N8 strain, but some key genetic differences between the strains suggest it will not be incredibly effective against H3N2.

Just like with people, very young dogs and very old dogs are most susceptible, but most recover. Though the numbers point to the virus spreading, don't panic. Vets suspect that the fatality rate for dog flu is very low - possibly as low as two or three percent of cases.

http://www.eurekalert.org/pub_releases/2015-05/uocm-psr052815.php

## Pembrolizumab shows real promise against head and neck cancer

***Biomarker reliably predicts which patients will not benefit***

Immunotherapy with the anti-PD-1 antibody pembrolizumab (Keytruda®) was effective in one out of four patients with recurrent or metastatic head and neck cancer, according to results presented at the 2015 meeting of the American Society for Clinical Oncology (ASCO).

Pembrolizumab decreased the size of tumors by 30 percent or more in 24.8 percent of 132 patients, making it nearly twice as effective as the current preferred treatment using platinum-based chemotherapy plus cetuximab, an epidermal growth factor inhibitor.

The results suggest that pembrolizumab, a checkpoint blocker, may soon begin to fill a large, unmet need for better treatments of this common form of cancer.

"The efficacy was remarkable," said Tanguy Seiwert, MD, assistant professor of medicine and associate program leader for head and neck cancer at the University of Chicago, "roughly twice as good as any drug combination in our arsenal."

"In this study," he said, "pembrolizumab was active across a wide range of patient subgroups including HPV-associated and HPV-negative tumors. Overall, 56 percent of patients experienced a measurable decrease in the size of their tumors."

Unlike epidermal growth factor receptor inhibitors, which appear to be less effective in HPV-positive tumors, pembrolizumab showed similar levels of activity in both HPV-associated and HPV-negative tumors.

"This may have the potential to prolong survival for a large proportion of our patients," Seiwert said. "Immunotherapy has been very well tolerated by our patients and serious side effects have been quite uncommon. We hope this approach will change the way we treat head and neck cancer."

In a related study (abstract #6017), also presented at ASCO, Seiwert and colleagues report that an experimental test--applied to an earlier cohort of head and neck cancer patients treated with pembrolizumab--could predict which patients were not likely to benefit from PD-1/PD-L1 agents, with a negative predictive value of 95 percent.

"This assay is quick and reproducible," Seiwert said. "The high negative predictive value may help us select out patients who may not benefit from immunotherapy."

Head and neck cancer is the sixth most common cancer in the United States and worldwide. Recurrent/metastatic head and neck cancer is currently considered incurable, with a poor prognosis and median overall survival of approximately 10 to 12 months. Standard treatment involves platinum-based doublet chemotherapy with or without cetuximab, the only approved targeted therapy.

Second-line options include methotrexate, docetaxel and cetuximab. Only 10 to 13 percent of patients respond to cetuximab as a single agent, and recent data suggest that efficacy in HPV-positive tumors may differ from HPV-negative tumors. While chemotherapy can be effective, it also causes significant side effects such as hair loss, nausea and vomiting, and increased risk of infection due to low immune function.

In the study presented at ASCO, 132 patients with recurrent or metastatic squamous cell carcinoma of the head and neck received a 200-mg infusion of pembrolizumab every 3 weeks. The objective response rate was 24.8 percent (26.3 percent in HPV-negative patients and 20.6 percent in HPV-positive patients). Fifty-six percent of patients saw their target lesions shrink.

Pembrolizumab was well tolerated. Fewer than 10 percent of patients had serious side effects. The most common were fatigue, rash, and pruritus. More serious immune-related side effects such as grade 3 pneumonitis and colitis were observed in a three patients.

Unlike a prior report presented at last year's ASCO Annual Meeting, the current cohort was not selected for PD-L1 expression (a candidate predictive biomarker). Fifty-nine percent of the patients enrolled had already received two or more lines of prior therapy.

"Our 25 percent response rate may underestimate the benefit in patients," Seiwert said. "We know from other disease entities such as lung cancer--where the experience with immunotherapy is broader--that patients who have disease stabilization or even pseudo-progression may benefit in ways that translate into longer survival."

Two ongoing phase III studies are evaluating pembrolizumab vs. standard treatment in patients with recurrent/metastatic head and neck cancer. Additional phase III studies with nivolumab (another anti-PD-1 antibody) and MEDI4736 (an anti-PD-L1 antibody) are underway for head and neck cancer.

*This study was funded by Merck Sharp & Dohme Corp., the makers of pembrolizumab.*

***http://bit.ly/1FX5uBE***

## Warmer Waters Are Making Pacific Typhoons Stronger

***Decades of storm data show that tropical cyclones in the Pacific are getting more intense as ocean temperatures rise***

**By Sarah Zielinski**

Tropical cyclones in the northwestern Pacific have strengthened about 10 percent since the 1970s because of warming ocean temperatures, researchers report this week in Science Advances. According to an extensive analysis of historical cyclone data, nearly 65 percent of typhoons now reach category 3 or higher on the Saffir-Simpson scale, compared with around 45 percent just decades ago.

The northwestern Pacific produces some of the world's most intense and most devastating tropical cyclones, called typhoons in the Pacific and hurricanes in the Atlantic. The category 5 super typhoon Haiyan, for instance, had record winds that reached nearly 200 miles per hour, and the 2013 storm killed at least 6,300 people in the Philippines.

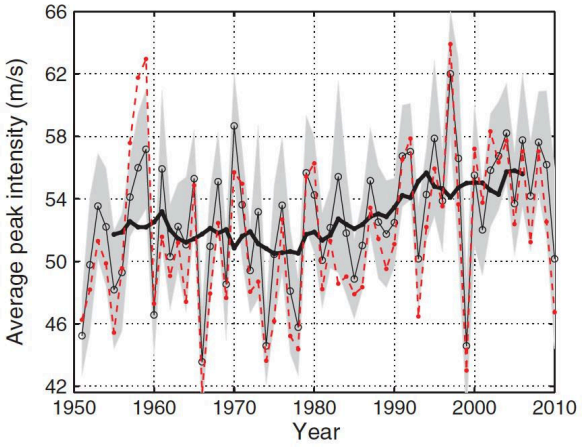
"It is important to understand what controls typhoon intensity and to predict how it will change," says lead study author Wei Mei of the Scripps Institute of Oceanography.

For years scientists have been working to determine how climate change is affecting these storms. Warmer waters should make for more intense storms in theory, but plenty of other factors can affect tropical cyclone development. This

year's Atlantic hurricane season, for instance, should be below normal in part because of El Niño, according to the most recent forecast from the National Oceanic and Atmospheric Administration. Such variability has made finding a signal from climate change difficult.

In the new study, Mei's team looked at the average intensity of tropical cyclones that occurred in the northwestern Pacific between 1951 and 2010. They focused on storms that reached at least category 1 on the Saffir-Simpson scale and examined season-to-season variability, of which there was quite a bit. Some seasons saw much stronger storms on average than others, others much weaker. Plotted out over the years, though, the average intensity could be seen starting to rise in the 1970s.

But what is causing that rise? The team considered several factors that influence tropical cyclones, such as air pressure, sea surface temperatures and localized differences in wind speed and direction, known as wind shear. They were surprised to find that the variability in ocean temperatures, rather than atmospheric conditions, were dominant in controlling the observed changes in typhoon intensity, Mei says.




***While cyclone intensity shows a lot of seasonal variability, it has been on the rise since the 1970s, the team found.*** **(Mei et al. Sci. Adv. 2015;1:e1500014)**

"How strongly and quickly a cyclone can grow depends on two oceanic factors: pre-storm sea surface temperature and the difference in temperature between the surface and subsurface," Mei explains. "A warmer sea surface generally provides more energy for storm development and thus favors more intense typhoons. A large change in temperature from the surface to subsurface, however, can disrupt this flow of energy, because strong winds drive turbulence in the upper ocean, bringing cold water up from below and thereby cooling the sea surface."

Since the mid-1970s, sea-surface temperatures in the tropical northwestern Pacific have risen by about 1 degree Fahrenheit, while temperatures at 250 feet below the surface have gone up by about 1.4 degrees. This reduction in the vertical temperature difference favors more intense typhoons, Mei says.

The researchers project that even under a scenario of moderate warming—one in which there are cutbacks in greenhouse gas emissions—the average typhoon intensity will still increase by another 14 percent by 2100. If emissions continue apace, "we anticipate that the typhoons will intensify even more," Mei says.

There appears to be a trade-off between typhoon number and intensity. A recent study published in Nature Climate Change found that as ocean waters have warmed over the last 30 years, tropical cyclones globally have slightly decreased in number but increased in intensity. And earlier this year, a team led by Mei reported in the Journal of Climate that the number of storms in the northwestern Pacific has declined since the mid-1990s due to rising sea surface temperatures.

But the decline in storm number should not put anyone at ease, Mei notes: "It is the most intense typhoons that cause the most damage."

***http://www.bbc.com/news/health-32936877***

## Lung cancer therapy is 'milestone'

***A lung cancer therapy can more than double life expectancy in some patients, a "milestone" trial shows.***

**By James Gallagher Health editor, BBC News website**

Nivolumab stops cancerous cells hiding from the body's own defences, leaving the cancer vulnerable to attack. The results from 582 people, presented at the American Society of Clinical Oncology, were described as "giving real hope to patients". Lung cancer is the most deadly type of cancer, killing nearly 1.6 million people every year. It is hard to treat as it is often diagnosed late and many people with smoking-related diseases are unsuitable for surgery.

**Natural defences**

Your immune system is trained to fight infection, but it also attacks parts of the body if they malfunction - such as in cancers. However, tumours have a few tricks up their sleeve in order to survive. They can produce a protein called PD-L1 which switches off any part of the immune system that tries to attack them.

Nivolumab is one of a suite of drugs called "checkpoint inhibitors" being developed by pharmaceutical companies. They stop cancers turning off the immune system so the body can keep on attacking the tumour.

The trial, conducted in Europe and the US, was on patients who had advanced lung cancer and who had already tried other treatments. People on standard therapy lived for another 9.4 months at this stage, but those taking Nivolumab lived for 12.2 months on average.

However, some patients did spectacularly well. Those whose tumours were producing high levels of PD-L1 lived for another 19.4 months.

**'Milestone'**

The data was presented by the pharmaceutical company Bristol-Myers Squibb.

Lead researcher Dr Luis Paz-Ares, from the Hospital Universitario Doce de Octubre in Madrid, Spain, said: "[The results] mark a milestone in the development of new treatment options for lung cancer."

"Nivolumab is the first PD-1 inhibitor to show a significant improvement in overall survival in a phase III trial in non-squamous non-small cell lung cancer."

Many other companies are assessing similar drugs.

Dr Martin Forster, from the University College London Cancer Institute, is trialling some of them. He told the BBC News website: "It's really exciting, I think these drugs will be a paradigm shift in how we treat lung cancer." He said that after chemotherapy failed, current survival rates were "dire". "But in those that respond [to immunotherapy] there seems to be very prolonged disease control, I think it's a huge shift in lung cancer and for patients it's going to be dramatic," he said.

**'Real hope'**

Cancer Research UK said harnessing the immune system would be an "essential part" of cancer treatment. Dr Alan Worsley, the charity's senior science information officer, told the BBC: "This trial shows that blocking lung cancer's ability to hide from immune cells may be better than current chemotherapy treatments." "Advances like these are giving real hope for lung cancer patients, who have until now had very few options."

It is hoped these drugs will work in a range of cancers. Nivolumab has already been approved in the US for melanoma. But there are still big questions to be answered. The long-term consequences of modifying the immune system are still unknown and the best way of figuring out who will respond to therapy is uncertain. And these therapies are also likely to be very expensive and so will pose a challenge for health services trying to offer them.

***http://www.bbc.com/news/uk-wales-32917141***

## Acelarin cancer drug impact hope 'remarkable'

**By Steffan Messenger BBC News**

***The potential impact of a new cancer drug invented in Cardiff has been praised at the world's biggest gathering of oncologists in Chicago.***

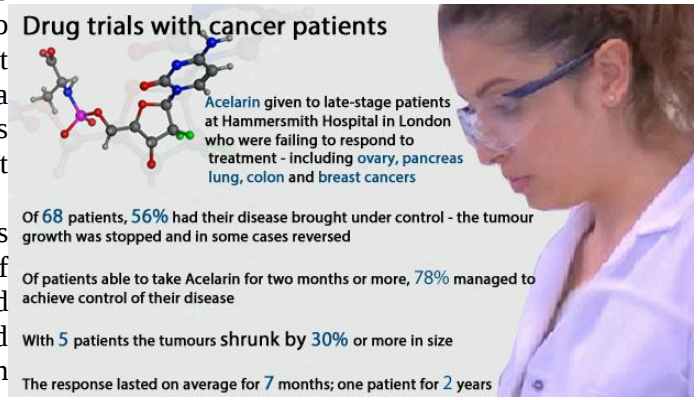
Acelarin is designed to stop patients becoming resistant to common therapies in treating cancer of the lung, ovary, breast, colon and pancreas.

Two phases of clinical trials show half of 78 patients responded to treatment.

The treatment was invented at Cardiff University and Prof Chris McGuigan said the drug's success was "remarkable". It was tested on patients who had exhausted all other forms of treatment at London's Hammersmith Hospital.

"These were terminal cancer patients, all of whom had solid tumours that were growing," explained Prof Chris McGuigan from Cardiff University. "Seventy-eight patients were given Acelarin - and remarkably half had their disease brought under control; the tumour growth was stopped, and in some cases reversed."

Dr Ian Lewis, director of research and policy for Tenovus Cancer Care said: "The great thing about this treatment is that it appears not only to be effective for patients who have become resistant to common therapies but also for patients with a range of different types of cancer. That makes it particularly exciting."




***The drug was given weekly for three weeks over a month cycle***

"The fact that it has come from Cardiff showcases a wider trend for some really world class cancer research here in Wales."

**'Bolt-on'**

The drug was particularly effective against gynaecological tumours. In 13 out of 14 patients, the drug achieved disease control - the greatest success rate ever seen at Hammersmith Hospital. The third and final round of clinical trials are now being planned and the drug has been licensed to Edinburgh-based pharmaceutical company Nucana for further development. The results are being presented to 30,000 cancer specialists attending the Asco conference in Chicago.

Prof McGuigan believes the method his team invented to design the drug could be used more generally in medicinal research.

It works by adding new compounds to conventional therapies as a 'bolt-on', which helps the drug cut through any resistance the body has built up. "Many companies have started to adopt this technology, to bolt it on to various drugs and improve them," Prof McGuigan said. "I believe that this will change therapies for cancer and viruses forever - and it originated here in the labs in Cardiff."

***http://www.eurekalert.org/pub_releases/2015-05/mskc-ici052815.php***

## Immunotherapy combo increases progression-free survival in advanced melanoma patients

***Phase III trial findings shed light on who will benefit most from combination***

CHICAGO, IL - Treating advanced melanoma patients with either a combination of the immunotherapy drugs nivolumab (Opdivo™) and ipilimumab (Yervoy™) or

nivolumab alone significantly increases progression-free survival (PFS) over using ipilimumab alone, according to new findings from researchers at Memorial Sloan Kettering Cancer Center (MSK) simultaneously presented today at the American Society of Clinical Oncology (ASCO) annual meeting and published online in the New England Journal of Medicine (NEJM). Examining specific characteristics of each patient's tumor has also given researchers clearer understanding of which patients should receive the combination.

These initial findings from the phase III clinical trial confirm the results of the phase II trial, presented just weeks ago at the American Association of Cancer Research annual meeting in Philadelphia and published by MSK researchers online in NEJM.

Jedd Wolchok, Chief of MSK's Melanoma and Immunotherapeutics Service, designed and led the phase III randomized, double-blind trial, in which 945 patients with untreated advanced melanoma were randomized to receive ipilimumab alone, nivolumab alone, or a combination of the two.

While this study was not designed for a formal statistical comparison between the nivolumab group and the combination group, exploratory analyses revealed more frequent responses and longer PFS in the combination group when compared with nivolumab alone. Patients receiving the combination experienced a median PFS of 11.5 months, while median PFS for patients receiving nivolumab alone was 6.9 months and ipilimumab alone was 2.9 months.

Of the 314 patients receiving the combination, 57.6 percent had an objective response, measured as a significant reduction in tumor size, versus 43.7 percent of the 316 receiving nivolumab alone and 19 percent of the 315 receiving ipilimumab alone.

"All the early preclinical and clinical work supported the idea that combining these two immunotherapy drugs could result in better outcomes for patients," said Dr. Wolchok. "We're encouraged by the progression-free survival data we're currently reporting. It is a testament to how drastically immunotherapy has altered the prognostic landscape for some advanced melanoma patients. Just five years ago, many of these patients would have been expected to live for only seven months following diagnosis -- but it's important to remember that overall survival data for this group is not yet available."

Adverse side effects such as diarrhea and increased lipase occurred in 55 percent of patients receiving the combination -- leading about one-third of these patients to stop the regimen. About 16 percent of patients receiving nivolumab alone and 27 percent of patients receiving ipilimumab alone experienced side effects, with nearly 8 percent and 15 percent of patients discontinuing, respectively.

Ipilimumab and nivolumab are part of a class of drugs called immune checkpoint inhibitors, which unleash patients' immune system to attack their cancer. The immune system has several checkpoints in place to avoid an overreaction. Ipilimumab works by blocking the CTLA-4 checkpoint, a molecular brake that stops T cells from becoming fully and persistently activated. Similarly, nivolumab prevents the molecule PD-L1, expressed by tumors, from binding to T cells and deactivating them.

Notably in this trial, patients whose tumors expressed PD-L1 experienced a median PFS of 14 months regardless of whether they received the combination or nivolumab alone, but for patients whose tumors did not express PD-L1, the median PFS was longer on the combination (11.2 months) than on nivolumab alone (5.3 months).

"One of the biggest questions in the field of immunotherapy has been how to determine which patients will respond to immune-modulating drugs. Now we have another piece of data," said Dr. Wolchok. "A simple pathology test can identify patients whose tumors express PD-L1, and this information will help the patient and physician decide whether to use the combination or nivolumab alone, knowing the toxicity risks and the difference in PFS. However, if a patient's tumor does not express PD-L1, the data suggests it makes more sense to offer the combination. This understanding gets us closer to 'precision immunotherapy.'"

Dr. Wolchok, who is also the Associate Director of the Ludwig Center for Cancer Immunotherapy at MSK, designed this clinical trial on a napkin at the 2012 ASCO annual meeting ¬before the data from the phase I trial were even presented. "Even then, we knew the potential that immunotherapy could have for the lives of patients diagnosed with advanced melanoma and other cancers," he said. "As we present this exciting and hopeful data to the international oncology community, we pause and thank the patients who enrolled in this -- and all -- clinical trials. These individuals are blazing the trails of cancer research, and we are indebted to them for helping to better the care of patients for generations to come."

***http://sen.com/news/rosetta-team-propose-ending-mission-by-landing-on-comet***

## Rosetta team propose ending mission by landing on comet

***Rosetta space scientists put forward a daring proposal this week to end the probe's mission by sending it to land on the comet it has been accompanying through the Solar System since August 2014.***

**Paul Sutherland, News Editor**

Sen - The European Space Agency (ESA) spacecraft is still weeks away from the exciting climax of its mission as Comet 67P/Churyumov-Gerasimenko grows ever more active on its journey closer to the Sun. But the Rosetta team are busy planning ahead.

Comet 67P reaches perihelion—its closest approach to the Sun—on Aug. 13, 2015, at a distance from it of 186 million km (116 million miles) after which it will start to head further out into the Solar System again on its 6.5-year orbit.

The mission is currently set to end in December 2015, after which Rosetta could simply be switched off as it continues to orbit the comet, and the mission team disperse to work on new projects. But for several months now a plan has been quietly hatched to see the craft go out with a bang by being brought down to a collision with 67P.

The dramatic grand finale was officially put forward to ESA this week by project scientist Matt Taylor. It is expected that the ESA science committees that decide such things will have an answer by the end of next month. An extension to the mission would require extra funding to keep the Rosetta operations team together, but supporters of the move believe the extra science gained would be invaluable.

It would see the spacecraft brought gradually closer to the comet in a slowly spiralling orbit that would allow its cameras and instruments to gain ever more detailed views and measurements of the twin-lobed icy body. Then eventually—probably in September 2016—it would collide with the comet, bringing the mission to an end.

Of course, Rosetta has already attempted one landing on Comet 67P when it despatched its companion probe Philae, which bounced twice before settling in a shaded spot where it swiftly lost power—though only after achieving its full range of initial experiments. The ESA team are still attempting to resurrect the tiny lander, hoping that the comet's changing orientation and proximity to the Sun will give it enough sunlight to recharge its batteries.

Matt told Sen: "Our mission was due to end at the end of this year. We have simply asked to extend to September next year, by which time the energy from the Sun to the solar panels starts to drop again. Plus we will have a solar conjunction (when the Sun lies between Earth and Rosetta), so data rates will be reduced. Also, we have limited fuel, which is sufficient to take us comfortably up to the point, but not much further."

He added: "If we just left Rosetta as is, we would need to put it into hibernation again, for longer, as it is now in the same orbit as the comet. We would then have to go through the difficult process of 1) putting it into hibernation and then 2) getting it out of hibernation again. Then we have the issues of minimal fuel etc. The spacecraft would remain in a similar orbit as the comet for years, dependent on whether the comet breaks up, etc."

Matt told Sen that landing Rosetta would produce some great science. He told us: "The proposal to put the probe on the comet's surface provides us with unique, close comet observations that we could not have if we don't do this. Also, I feel from a 'personal' perspective, there is something rather fitting in putting Rosetta down on the surface, re-uniting it with Philae."

He added: "We have a few more hurdles to jump through—higher level science committees—but we will know whether we have it (the go-ahead) by end of June. What happens then is that we can start planning into that period. We will have a science meeting in June in Rome, and will likely discuss such plans in the case that we do get extended."

The cost of extending the mission is not clear at present. Matt said: "Costs are not my department, but we simply want to carry on at the level we have now."

Meanwhile, mission scientists are about to begin their fourth series of attempts to re-establish contact with Philae, following earlier unsuccessful efforts in March, April and earlier in May. From tomorrow, May 30, Rosetta will again try to pick up a signal from its companion probe.

The efforts are being managed by the French national centre for space studies, CNES, in Toulouse. CNES' Science Operation and Navigation Centre (SONC) is busy working out the best times when Philae's solar panels might get sufficient sunlight to produce energy to wake it up.

Éric Jurdo, of SONC, said on the CNES website on Thursday that, thanks to data from various instruments on Rosetta and the lander before it lost power, "we know with an accuracy of less than 50 metres the final landing point of Philae. We also know how the undercarriage is oriented relative to the surface."

The SONC team has also been planning for the moment that contact is made again with Philae, so that command sequences can be sent at once to put it to work again while it has power.