http://www.bbc.com/news/health-35650171

Major insight into killer pancreatic cancer

Pancreatic cancer is at least four separate diseases each with a different cause and needing a different treatment, scientists have discovered.

By James Gallagher Health editor, BBC News website

The researchers say the knowledge will lead to new drugs targeting the Achilles' heel of each patient's cancer and that they have already seen some "exceptional" results. Cancer charities said the findings were "incredibly exciting".

The analysis, published in the journal Nature, looked at 456 patients' cancer.

Tumours are caused by mutations in DNA that make healthy tissue turn cancerous - but there is more than one way to make a cancer. While all the pancreatic cancers looked similar, there were four classes of genetic error that led to tumour formation.

And these four cancers have been labelled:

- ***squamous-type***
- ***pancreatic progenitor***
- ***immunogenic***
- ***aberrantly differentiated endocrine exocrine***

New treatments

One example of how different the cancers are is the average survival time from diagnosis with squamous-type cancers was just four months - roughly half that of the other types. But crucially, the knowledge could lead to new treatments.

Dr Andrew Biankin, one of the researchers at the University of Glasgow, told the BBC News website: "This is the most comprehensive analysis of the blueprint of pancreatic cancer. "So this knowledge reveals what makes these cancers tick and which ones may be vulnerable to particular treatments by defining the Achilles' heel of every cancer."

It would be a much needed breakthrough for a type of cancer stubbornly difficult to treat. Most people diagnosed with pancreatic cancer are told they have less than a year to live. And just 1% of them are alive 10 years after being diagnosed - a survival rate unchanged for four decades.

Meanwhile, dramatic improvements in breast, prostate and colon cancer care mean pancreatic tumours are predicted to kill more people than any other cancer, apart from lung, in some countries. "It's just a really tough cancer," Dr Biankin said. But he hopes matching drugs to specific errors in tumours will help patients.

He said: "The fact that we see, through chance, that some patients respond exceptionally to a particular therapy allows us to expand these insights so we can treat more patients with similar cancers at a genetic level."

It is thought the "immunogenic" pancreatic cancers may be vulnerable to a new wave of immunotherapies already transforming cancer, and clinical trials are already under way.

'Incredibly exciting'

Leanne Reynolds, the head of research at Pancreatic Cancer UK, said: "The findings of this research are incredibly exciting for anyone affected by pancreatic cancer, as they should mean that in the future the right patients can be given the right treatment at the right time.

"If we can predict more accurately which treatment would be most effective for each patient, we can ensure patients have the best chance of living for as long as possible, as well as possible."

Dr Emma Smith, from Cancer Research UK, said: "Identifying different types of pancreatic cancer and revealing the disease's complexity is an important step towards finding more effective treatments. "This will help to ensure patients are given the therapies that are most likely to help."

http://www.eurekalert.org/pub_releases/2016-02/uok-uok022616.php

University of Kentucky physicist discovers new 2-D material that could upstage graphene

One atom-thick, truly 2D material has properties that can be fine-tuned to suit various applications beyond what is possible with graphene

LEXINGTON, Ky. - A new one atom-thick flat material that could upstage the wonder material graphene and advance digital technology has been discovered by a physicist at the University of Kentucky working in collaboration with scientists from Daimler in Germany and the Institute for Electronic Structure and Laser (IESL) in Greece.

Reported in Physical Review B, Rapid Communication, the new material is made up of silicon, boron and nitrogen - all light, inexpensive and earth abundant elements - and is extremely stable, a property many other graphene alternatives lack.

"We used simulations to see if the bonds would break or disintegrate - it didn't happen," said Madhu Menon, a physicist in the UK Center for Computational Sciences. "We heated the material up to 1,000 degree Celsius and it still didn't break."

Using state-of-the-art theoretical computations, Menon and his collaborators Ernst Richter from Daimler and a former UK Department of Physics and Astronomy post-doctoral research associate, and Antonis Andriotis from IESL, have demonstrated that by combining the three elements, it is possible to obtain a one

atom-thick, truly 2D material with properties that can be fine-tuned to suit various applications beyond what is possible with graphene.

While graphene is touted as being the world's strongest material with many unique properties, it has one downside: it isn't a semiconductor and therefore disappoints in the digital technology industry. Subsequent search for new 2D semiconducting materials led researchers to a new class of three-layer materials called transition-metal dichalcogenides (TMDCs). TMDCs are mostly semiconductors and can be made into digital processors with greater efficiency than anything possible with silicon. However, these are much bulkier than graphene and made of materials that are not necessarily earth abundant and inexpensive.

Searching for a better option that is light, earth abundant, inexpensive and a semiconductor, the team led by Menon studied different combinations of elements from the first and second row of the Periodic Table.

Although there are many ways to combine silicon, boron and nitrogen to form planar structures, only one specific arrangement of these elements resulted in a stable structure. The atoms in the new structure are arranged in a hexagonal pattern as in graphene, but that is where the similarity ends.

The three elements forming the new material all have different sizes; the bonds connecting the atoms are also different. As a result, the sides of the hexagons formed by these atoms are unequal, unlike in graphene. The new material is metallic, but can be made semiconducting easily by attaching other elements on top of the silicon atoms.

The presence of silicon also offers the exciting possibility of seamless integration with the current silicon-based technology, allowing the industry to slowly move away from silicon instead of eliminating it completely, all at once.

"We know that silicon-based technology is reaching its limit because we are putting more and more components together and making electronic processors more and more compact," Menon said. "But we know that this cannot go on indefinitely; we need smarter materials."

Furthermore, in addition to creating an electronic band gap, attachment of other elements can also be used to selectively change the band gap values - a key advantage over graphene for solar energy conversion and electronics applications.

Other graphene-like materials have been proposed but lack the strengths of the material discovered by Menon and his team. Silicene, for example, does not have a flat surface and eventually forms a 3D surface. Other materials are highly unstable, some only for a few hours at most.

The bulk of the theoretical calculations required were performed on the computers at the UK Center for Computational Sciences with collaborators Richter and Andriotis directly accessing them through fast networks. Now the team is working in close collaboration with a team led by Mahendra Sunkara of the Conn Center for Renewable Energy Research at University of Louisville to create the material in the lab.

The Conn Center team has had close collaborations with Menon on a number of new materials systems where they were able to test his theory with experiments for a number of several new solar materials.

"We are very anxious for this to be made in the lab," Menon said. "The ultimate test of any theory is experimental verification, so the sooner the better!"

Some of the properties, such as the ability to form various types of nanotubes, are discussed in the paper but Menon expects more to emerge with further study.

"This discovery opens a new chapter in material science by offering new opportunities for researchers to explore functional flexibility and new properties for new applications," he said. "We can expect some surprises."

http://bit.ly/1QoOZSH

People will follow a robot in an emergency – even if it's wrong

Would you follow?

A university student is holed up in a small office with a robot, completing an academic survey. Suddenly, an alarm rings and smoke fills the hall outside the door. The student is forced to make a quick choice: escape via the clearly marked exit that they entered through, or head in the direction the robot is pointing, along an unknown path and through an obscure door.

That was the real choice posed to 30 subjects in a recent experiment at the Georgia Institute of Technology in Atlanta. The results surprised researchers: almost everyone elected to follow the robot – even though it was taking them away from the real exit.

“We were surprised,” says Paul Robinette, the graduate student who led the study. “We thought that there wouldn’t be enough trust, and that we’d have to do something to prove the robot was trustworthy.”

The unexpected result is another piece of a puzzle that roboticists are struggling to solve. If people don’t trust robots enough, then the bots probably won’t be successful in helping us escape disasters or otherwise navigate the real world. But we also don’t want people to follow the instructions of a malicious or buggy machine. To researchers, the nature of that human-robot relationship is still elusive.

In the emergency study, Robinette’s team used a modified Pioneer P3-AT, a robot that looks like a small bin with wheels and has lit-up foam arms to point. Each participant would individually follow the robot along a hallway until it pointed to

the room they were to enter. They would then fill in a survey to rate the robot's navigation skills and read a magazine article. The emergency was simulated with artificial smoke and a First Alert smoke detector.

A total of 26 of the 30 participants chose to follow the robot during the emergency. Of the remaining four, two were thrown out of the study for unrelated reasons, and the other two never left the room.

Misplaced trust?

The results suggest that if people are told the robot is designed to do a particular task – as was the case in this experiment – they will probably automatically trust it to do it, say the researchers. Indeed, in a survey given after the fake emergency was over, many of the participants explained that they followed the robot specifically because it was wearing a sign that read "EMERGENCY GUIDE ROBOT."

The work will be presented in March at the ACM/IEEE International Conference on Human-Robot Interaction in Christchurch, New Zealand.

Robinette likens the relationship to the way in which drivers sometimes follow the odd routes mapped by their GPS devices. "As long as a robot can communicate its intentions in some way, people will probably trust it in most situations," he says.

"It amazes me that everyone followed that robot," says Holly Yanco, who studies human-robot interaction at the University of Massachusetts Lowell. She wonders whether the fact that it was an emergency situation rather than an ordinary laboratory task pushed people to trust the robot in that split second.

"It might just be that they thought the robot had more information than they did," she says.

How far would that blind trust go? In a series of follow-up experiments, Robinette and his colleagues put small groups of people through the same experience, but with added twists. Sometimes the robot would "break down" or freeze in place during the initial walk along the hallway, prompting a researcher to come out and apologise for its poor performance. Even so, almost everyone still followed the robot during the emergency.

In another follow-up test, the robot would point to a darkened room, with the doorway partially blocked by a piece of furniture. Two of six participants tried to squeeze past the obstruction rather than taking the clear path out.

Too much trust in a robot can be a serious problem, says Kerstin Dautenhahn at the University of Hertfordshire, UK. "Any piece of software will always have some bugs in it," she says. "It is certainly a very important point to consider what that actually means for designers of robots, and how we can maybe design robots in a way where the limitations are clear."

http://bit.ly/1QoOZSH

Seventh new dinosaur discovery confirmed in Japan

A new kind of dinosaur has been confirmed in Katsuyama, Fukui Prefecture, researchers said Friday, bringing the number of species discovered in Japan to seven.

According to fossil analysis, the new creature was a small theropod that had both primitive and derived features, according to the Fukui Prefectural Dinosaur Museum and Fukui Prefectural University. It has been named Fukuivenator paradoxus, or "paradoxical hunter of Fukui."

Fukuivenator is a species that existed when theropods began to evolve into birds, according to Yoichi Azuma, a professor at the university. Fukuivenator "failed to become a bird."

Fukuivenator was about 2½ meters long and weighed about 25 kg, Azuma said.

The discovery emerged from a study of some 160 fossil fragments from an animal found in August 2007 in a stratum from the Lower Cretaceous period, some 120 million years ago. Some 70 percent of its body parts were left in very good condition.

Fukuivenator, which was covered with feathers, had two-forked cervical vertebrae, which are not found in any other theropod. Its hearing was equivalent to that of birds, and the shapes of its scapula and thighbones are similar to those of the primitive Coelurosaur, from which flying animals originated.

http://bit.ly/21LQRdi

Human Teeth Likely Shrank Due to Tool Use

Finding could lead to a new way of figuring out how closely related fossil species are to modern humans

By Charles Q. Choi, LiveScience

Wisdom teeth may have shrunk during human evolution as part of changes that started with human tool use, according to a new study.

The research behind this finding could lead to a new way of figuring out how closely related fossil species are to modern humans, scientists added.

Cast of the skull of Lucy, the australopith Australopithecus afarensis from Ethiopia, included in the study. **David Hocking**

Although modern humans are the only surviving members of the human family tree, other species once lived on Earth. However, deducing the relationships between modern humans and these extinct hominins—humans and related species dating back to the split from the chimpanzee lineage—is difficult because fossils of ancient hominins are rare. [Image Gallery: Our Closest Human Ancestor]

Teeth are the hominin fossils most often found because they are the hardest parts of the human body. "Teeth are central to how a fossil ancestor lived, and can tell us about which species they belonged to, how they are related to other species, what they ate, and how quickly or slowly they developed during childhood," said lead study author Alistair Evans, an evolutionary biologist at Monash University in Melbourne, Australia.

Hominin teeth have shrunk in size throughout evolution, a trend perhaps most clearly seen with the wisdom teeth located at the back of the mouth, the researchers said. In modern humans, wisdom teeth are often very small or do not even develop, while in many other hominin species they were huge, with chewing surfaces two to four times larger than those of their modern human counterparts.

Previous research suggested this profound shrinking in modern human wisdom tooth size was due to the advent of cooking or other changes in diet unique to modern humans. However, Evans and his colleagues now suggest this shift may have begun much earlier in human evolution.

The scientists analyzed tooth size in modern humans and fossil hominins. They found that hominin teeth fell into two major groups. One group was composed of the genus *Homo*, which includes both modern humans and extinct human relatives. The other group was made up of early hominins preceding *Homo*, such as the australopiths, the first primates to walk on two feet.

In australopiths and other early hominins, the scientists found that teeth tended to get bigger toward the back of the mouth, with proportions that stayed constant regardless of the overall size of the teeth. However, in the genus *Homo*, the smaller all the teeth were, the smaller the teeth were toward the back of the mouth. "There seems to be a key difference between the two groups of hominins—perhaps one of the things that defines our genus *Homo*," Evans said in a statement. This change in how teeth developed between genus *Homo* and earlier hominins may have occurred due to the advent of advanced tool use in the genus *Homo*, Evans said.

"It's always been presumed that sometime in early *Homo*, we started using more advanced tools," Evans told Live Science. "Tool use meant we didn't need as big teeth and jaws as earlier hominins. This may then have increased evolutionary pressure to spend less energy developing teeth, making our teeth smaller."

In modern humans, tooth-size reduction has reached the point where wisdom teeth are increasingly failing to develop, Evans said. "The advent of cooking made food easier to eat, meaning we didn't need big teeth as much," Evans said.

Prior work suggested there was a lot of variation in how teeth evolved in hominins. "Now we're seeing some very simple, clear patterns in hominin tooth evolution instead," Evans said. [Infographic: Human Origins – How Hominids Evolved]

These patterns could help researchers decide whether ancient hominins were members of genus *Homo* or not, Evans said.

"It's been suggested a number of times over the past 20 years that maybe *Homo habilis*, often considered the earliest member of *Homo*, should be considered an australopith instead," Evans said. "We found *Homo habilis* tooth proportions followed the australopith rule and not the *Homo* rule, which supports the argument that *Homo habilis* should be reclassified to something like *Australopithecus habilis*."

This new work builds on previous experiments with mice that suggested teeth could influence each other during development. In this "inhibitory cascade model," teeth that develop early can inhibit the size of teeth that develop later. These new findings suggest this mechanism underlying tooth size in mice and most mammals is seen in hominins as well, Evans said.

These findings suggest that by knowing the size of a single hominin tooth and the group to which it belongs, scientists could infer the size of the hominin's remaining teeth with considerable accuracy. "Sometimes we find only a few teeth in a fossil," Evans said. "With our new insight, we can reliably estimate how big the missing teeth were."

Future research could analyze controversial hominin discoveries such as *Homo naledi*, recently unearthed in South Africa, Evans said. "It's got an interesting mix of traits, some that look like *Homo*, some that look australopith," Evans said. "It'd be interesting to examine its teeth and see which pattern it fits best."

The scientists detailed their findings in the Feb. 25 issue of the journal Nature.

http://bit.ly/1Qv9yya

Mysterious chimpanzee behaviour may be evidence of 'sacred' rituals

Marked trees and piles of rocks reminiscent of those archaeologists have uncovered in human history

Laura Kehoe PhD researcher in wildlife conservation and land use, Humboldt University of Berlin

I trampled clumsily through the dense undergrowth, attempting in vain to go a full five minutes without getting snarled in the thorns that threatened my every move. It was my first field mission in the savannahs of the Republic of Guinea. The aim

was to record and understand a group of wild chimpanzees who had never been studied before. These chimps are not lucky enough to enjoy the comforts of a protected area, but instead carve out their existence in the patches of forests between farms and villages. We paused at a clearing in the bush. I let out a sigh of relief that no thorns appeared to be within reach, but why had we stopped?

I made my way to the front of the group to ask the chief of the village and our legendary guide, Mamadou Alioh Bah. He told me he had found something interesting – some innocuous markings on a tree trunk. Something that most of us wouldn't have even noticed in the complex and messy environment of a savannah had stopped him in his tracks. Some in our group of six suggested that wild pigs had made these marks, while scratching up against the tree trunk, others suggested it was teenagers messing around.

But Alioh had a hunch – and when a man that can find a single fallen chimp hair on the forest floor and can spot chimps kilometres away with his naked eye better than you can (with expensive binoculars) as a hunch, you listen to that hunch. We set up a camera trap in the hope that whatever made these marks would come back and do it again, but this time we would catch it all on film.

A world first

Camera traps automatically start recording when any movement occurs in front of them. For this reason they are an ideal tool for recording wildlife doing its own thing without any disturbance. I made notes to return to the same spot in two weeks (as that's roughly how long the batteries last) and we moved on, back into the wilderness.

Whenever you return to a camera trap there is always a sense of excitement in the air of the mysteries that it could hold – despite the fact that most of our videos consisted of branches swaying in strong winds or wandering farmers' cows enthusiastically licking the camera lens, there is an uncontrollable anticipation that maybe something amazing has been captured.

***Selection of stone throwing behaviour*, from carefully placing stones inside hollow trunks to full-on hurling. Video credit: Kühl et al (2016)**

What we saw on this camera was exhilarating – a large male chimp approaches our mystery tree and pauses for a second. He then quickly glances around, grabs a huge rock and flings it full force at the tree trunk.

Nothing like this had been seen before and it gave me goose bumps. Jane Goodall first discovered wild chimps using tools in the 1960s. Chimps use twigs, leaves, sticks and some groups even use spears in order to get food. Stones have also been used by chimps to crack open nuts and cut open large fruit. Occasionally, chimps throw rocks in displays of strength to establish their position in a community.

But what we discovered during our now-published study wasn't a random, one-off event, it was a repeated activity with no clear link to gaining food or status – it could be a ritual. We searched the area and found many more sites where trees had similar markings and in many places piles of rocks had accumulated inside hollow tree trunks – reminiscent of the piles of rocks archaeologists have uncovered in human history.

Videos poured in. Other groups working in our project began searching for trees with tell-tale markings. We found the same mysterious behaviour in small pockets of Guinea Bissau, Liberia and Côte d'Ivoire but nothing east of this, despite searching across the entire chimp range from the western coasts of Guinea all the way to Tanzania.

Sacred trees

I spent many months in the field, along with many other researchers, trying to figure out what these chimps are up to. So far we have two main theories. The behaviour could be part of a male display, where the loud bang made when a rock hits a hollow tree adds to the impressive nature of a display.

This could be especially likely in areas where there are not many trees with large roots that chimps would normally drum on with their powerful hands and feet. If some trees produce an impressive bang, this could accompany or replace feet drumming in a display and trees with particularly good acoustics could become popular spots for revisits.

On the other hand, it could be more symbolic than that – and more reminiscent of our own past. Marking pathways and territories with signposts such as piles of rocks is an important step in human history. Figuring out where chimps' territories are in relation to rock throwing sites could give us insights into whether this is the case here.

Even more intriguing than this, maybe we found the first evidence of chimpanzees creating a kind of shrine that could indicate sacred trees. Indigenous West African people have stone collections at "sacred" trees and such man-made stone collections are commonly observed across the world and look eerily similar to what we have discovered here.

A vanishing world

To unravel the mysteries of our closest living relatives, we must make space for them in the wild. In the Ivory Coast alone, chimpanzee populations have decreased by more than 90% in the past 17 years.

Stone throwing - in action and on site. Top line: Adult male tossing, hurling and banging a stone. Bottom line: Stones accumulated in a hollow tree; typical stone throwing site; and stones in between large roots. **Kühl et al (2016), Author provided**

A devastating combination of increasing human numbers, habitat destruction, poaching and infectious disease severely endangers chimpanzees. Leading scientists warn us that, if nothing changes, chimps and other great apes will have only 30 years left in the wild. In the unprotected forests of Guinea, where we first discovered this enigmatic behaviour, rapid deforestation is rendering the area close to uninhabitable for the chimps that once lived and thrived there. Allowing chimpanzees in the wild to continue spiralling towards extinction will not only be a critical loss to biodiversity, but a tragic loss to our own heritage, too.

You can support chimps with your time, by instantly becoming a citizen scientist and spying on them at www.chimpandsee.org, and with your wallet by donating to the Wild Chimpanzee Foundation. Who knows what we might find next that could forever change our understanding of our closest relatives.

Disclosure statement

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http://bit.ly/1OUY69x

Scientists Breed Pigs Resistant to a Devastating Infection Using CRISPR

And the race to develop commercial applications for the revolutionary gene-editing tool is off and running

By Monique Brouillette on March 1, 2016

One of the worst things that can happen to a pig farmer is a pen infected with porcine reproductive and respiratory syndrome virus (PRRSV).

It emerged in the 1980s, and the syndrome now afflicts these hoofed animals worldwide, causing illness, death and miscarriage. In fact, it has been designated the most economically significant disease for swine, costing livestock producers in North America $600 million annually from deaths and medical treatments. Vaccinations have mostly failed to prevent the syndrome's spread, but a new approach by biologists at the University of Missouri may mark a turning point. They are one of the first teams to develop a commercial agricultural application for the revolutionary CRISPR/Cas9 gene-editing method—to breed pigs resistant to infection.

CRISPR/Cas9 is a gene-manipulation tool that allows scientists to make changes to DNA with razor-sharp accuracy. The tool has generated excitement in the research community because it allows rapid modification of gene function, replacing older and less efficient methods.

For porcine reproductive and respiratory syndrome, Missouri's Randall Prather, Kristen Whitworth and Kevin Wells turned to the technique to breed three piglets that lacked a protein on cells that acts as a doorway for the virus. The edited piglets were grouped together in a pen with seven normal piglets, and then they all were inoculated with PRRSV.

About five days later the normal pigs grew feverish and ill, but the genetically edited pigs did not. Despite sharing close quarters with their sick pen mates, they remained in top health throughout the 35-day study period. Blood testing also revealed that the edited animals did not produce antibodies against the virus—further evidence that they evaded infection entirely.

“I expected the pigs would get the virus but not get as sick,” Prather says. “But it is just night and day. The pigs are running around with the other pigs coughing on them, but they are just fine.” The study's results were published in the journal Nature Biotechnology.

This work and other recent experiments demonstrate the promise of CRISPR/Cas9 for the care of domestic animals. Late last year geneticists at the University of California, Davis, employed the new technique to breed dairy cows that do not grow horns. The outcome is a boon: cows are routinely dehorned to protect farmers and other cattle from being injured, but the process can be brutally painful and dangerous for the bovines.

More livestock will likely be produced in such a way, says Alison Van Eenennaam, a geneticist who worked on the development of the hornless cows. “This is analogous to breeding,” she notes. “It's just precision breeding.”

http://www.eurekalert.org/pub_releases/2016-03/asfm-sci022916.php

Study calls into question current MERS vaccine strategy

MERS develops mutations that make the virus less virulent during an outbreak rather than more virulent.

Washington, DC - A new study suggests that the Middle East Respiratory Syndrome coronavirus (MERS-CoV) develops mutations that make the virus less virulent during an outbreak rather than more virulent. The study, published this week in mBio, an online open-access journal of the American Society for Microbiology, has implications for vaccine development.

MERS-CoV causes severe respiratory infection and has a worldwide mortality rate of approximately 35%. Similar to other coronaviruses, MERS-CoV utilizes a large surface spike glycoprotein to enter human CD26 cells and cause infection.

From May to July 2015, a large outbreak of MERS initiated by an infected traveler from the Arabian Peninsula swept South Korea and resulted in 186 confirmed cases and 38 deaths. "The unexpected outbreak raised strong concerns about the possible generation of mutant viruses and prompted us to investigate the MERS viruses infecting Korean patients," said Nam Hyuk Cho, PhD, principal investigator of the new study and a faculty member at the Seoul National University College of Medicine in Korea.

In the new study, investigators isolated 13 new viral genomes from 14 infected patients with MERS treated during the outbreak. They found that 12 of the genomes had two specific point mutations (I529T and D510G mutations) in the receptor-binding domain (RBD) of the viral spike protein. Further analysis showed that the acquired mutations impaired viral fitness and virulence, rather than making the virus more virulent.

"Strikingly, both mutations resulted in reduced affinity of RBD to human CD26 compared to wild-type RBD," explained Dr. Cho. "This is an interesting strategy of coronavirus evolution to survive in nature and live together with the new host. The virus may tune down its power to attack for the sake of longer survival in the new host. The unexpected findings suggest that MERS-CoV adaptation during human-to-human spread may be driven by host immunological pressure such as neutralizing antibodies, resulting in reduced affinity to the host receptor."

Currently, most vaccine trials for MERS prevention are using the spike antigen to generate effective neutralizing antibodies against it. "Strategies for vaccine development also need to consider the chance of emergence of neutralizing antibody-escape mutants," said Dr. Cho. "Vaccines for MERS need to target the more stable and conserved region of the spike."

http://www.eurekalert.org/pub_releases/2016-03/uog-dim030116.php

Depression is more than a mental disorder: It affects the whole organism

Depression associated with important alterations of oxidative stress and so should be considered a systemic disease

An international team of researchers lead by the University of Granada has scientifically proven, for the first time, that depression is associated with important alterations of the oxidative stress, so it should be considered a systemic disease.

An international team of researchers lead by the University of Granada (UGR) has scientifically proven, for the first time, that depression is more than a mental disorder: it causes important alterations of the oxidative stress, so it should be considered a systemic disease, since it affects the whole organism.

The results of this work, published in the renowned Journal of Clinical Psychiatry magazine (one of the most important magazines in the field of Psychiatry), could explain the significant association that depression has with cardiovascular diseases and cancer, and why people suffering from depression die younger. At the same time, this research may help finding new therapeutic targets for the prevention and treatment of depression.

The lead author of this work is Sara Jiménez Fernández, PhD student at the UGR and psychiatrist at the Child and Adolescent Mental Health Unit at Jaén Medical Center (Jaén, Spain). The co-authors are the UGR Psychiatry professors Manuel Gurpegui Fernández de Legaria and Francisco Díaz Atienza, in collaboration, among others, with Christoph Correll from the Zucker Hillside Hospital (New York, USA).

A study with 3961 people

This research is a meta analysis of 29 previous studies which comprise 3961 people, and it's the first detailed work of its kind about what happens in the organism of people suffering from depression. It studies the imbalance between the individual increase of various oxidative stress parameters (especially malondialdehyde, a biomarker to measure the oxidative deterioration of the cell

membrane) and the decrease in antioxidant substances (such as uric acid, zinc, and the superoxide dismutase enzyme).

The researchers have managed to prove that, after receiving the usual treatment against depression, the patients' malondialdehyde levels are significantly reduced, to the point that they are indistinguishable from healthy individuals. At the same time, zinc and uric acid levels increase until reaching normal levels (something that does not occur in the case of the superoxide dismutase enzyme).

http://www.eurekalert.org/pub_releases/2016-03/asoa-san030116.php

Surgery, anesthesia not linked to long-term cognitive impairment in older adults

Large twin study suggests pre-op mental functioning, underlying diseases have stronger influence on post-op cognitive abilities

Chicago - New research suggests older patients should not feel reluctant to have quality of life enhancing surgeries due to concerns that undergoing anesthesia may boost their risk of developing cognitive issues.

In a study of more than 8,500 middle-aged and elderly Danish twins published in Anesthesiology, the official medical journal of the American Society of Anesthesiologists (ASA), researchers found no clinically significant association between major surgery and general anesthesia with long-term cognitive decline.

"Our use of twins in the study provides a powerful approach to detect subtle effects of surgery and anesthesia on cognitive functioning by minimizing the risk that the true effects of surgery and anesthesia are mixed up with other environmental and genetic factors," said study lead author Unni Dokkedal, M.P.H., Unit of Epidemiology, Biostatistics, and Biodemography, University of Southern Denmark.

"We found no significant cognitive effects related to surgery and anesthesia in these patients, suggesting that other factors, such as preoperative cognitive levels and underlying diseases, are more important to cognitive functioning in aging patients following surgery."

More than one in 10 people who have surgery are 65 or older and advanced age can affect the potential for surgical risks. Postoperative cognitive dysfunction for a few weeks after surgery is one of these potential risks, but the effects of surgery, anesthesia, pre-existing health conditions, and other factors have been unclear. Whether this short-term postoperative cognitive dysfunction leads to long-term memory loss and lessened ability to learn, concentrate and think is uncertain, but the current study suggests it is unlikely.

In the study, researchers examined the association between exposure to surgery and level of cognitive functioning in a sample of 4,299 middle-aged twins younger than 70 and 4,204 elderly twins who were aged 70 or older. Results from cognitive tests of twins who had either major, minor, hip and knee replacement or other surgery within 18 to 24 years before cognitive examination were compared to the cognitive results of a reference group, comprised of twins who had no surgical procedures.

Test results were also compared in an intrapair analysis of twins, one of whom was exposed to surgery while the other was not, to assess genetic and shared environmental confounding.

Twins who had undergone major surgery had slightly lower cognitive scores, compared to the reference group, but when compared to their twin, when genetic and shared environmental factors were adjusted, no association was observed. Interestingly, twins who had undergone hip and knee replacement surgery had slightly higher cognitive scores, but the difference was not statistically significant. No differences were found in the minor or other surgery group when compared to the reference group.

The authors also analyzed data for patients who had undergone surgery from three months to two years before cognitive examination and found no effect of the short time interval between surgery and cognitive examination on cognitive function. The results suggest preoperative cognitive functioning and underlying diseases are more important for cognitive functioning in mid- and late life than surgery and anesthesia, the authors report.

"It is important to know whether surgery and anesthesia have any negative effects, especially with regard to preoperative counselling of the patient," said Dokkedal. "This research has the potential to become a key piece of this very complex research puzzle."

An accompanying editorial commented favorably on the study:

"On the basis of a growing body of evidence, of which the study by Dokkedal et al. is symbolic, older patients should today be reassured that surgery and anesthesia are unlikely to be implicated in causing persistent cognitive decline or incident dementia," said editorial authors Michael S. Avidan, M.B., B.Ch. and Alex S. Evers, M.D., Washington University School of Medicine in St. Louis. "The large number of patients and the use of rigorous longitudinal cognitive testing in the study increased the reliability of the findings."

In 2016, ASA will launch a patient safety initiative on improving brain health, fostering understanding, developing best practices and increasing awareness of postoperative cognitive dysfunction and delirium with the goal of laying the groundwork for research into minimizing its effects.

http://www.eurekalert.org/pub_releases/2016-03/uomh-twf022516.php

They work for stores and airlines -- could customer loyalty programs work in health care too?

U-M team predicts perks could make patients happier and improve their care, while saving health care dollars

ANN ARBOR, Mich. -- When you buy a cup of coffee, a load of groceries, an airline ticket or a tank of gas these days, you probably pull out a customer loyalty card without even thinking about it. It might even be linked to how you pay.

You may be thinking mostly about the perks you're earning. But the place you're buying from is focused on keeping your business, getting your positive word of mouth to family and friends -- and even making you more tolerant of problems for the sake of rewards.

Now, a team from the University of Michigan Medical School has proposed that healthcare providers should offer the same kinds of programs -- for reasons that go far beyond what other businesses use them for.

In a new viewpoint piece in the journal JAMA, a trio of U-M healthcare researchers affiliated with the U-M Institute for Healthcare Policy and Innovation lays out the case for customer loyalty programs in healthcare.

The main driver, they say, should be the need for hospitals, clinics and other providers to keep patients coming back to them so they can succeed as Accountable Care Organizations.

ACOs give healthcare providers a chance to earn extra payments if they provide high-quality care and keep healthcare cost growth down for a defined population of patients, in part by keeping patients healthy so they need less medical care.

Trouble is, those populations keep shifting. About 38 percent of those who saw doctors in a Medicare ACO's network in a given year, according to one study, were seeing patients outside the ACO by the next year.

The federal rules for ACOs ensure that patients have freedom of choice for which doctors they see -- but ACO-participating hospitals, clinics and doctors only get rewarded when they can coordinate patients' care in a continuous way.

For instance, by encouraging patients to get screenings and preventive care, and reducing inappropriate use of care, ACOs can try to hold down the growth of costs while delivering high-quality care. Plus, hospitals and clinics, even outside of ACOs, can earn bonuses based on how satisfied their patients say they are.

"Loyalty programs have the potential to enhance both health and financial benefits to patients and health system," says Laurence McMahon, M.D., MPH, lead author of the piece and chief of general medicine at U-M.

However, he and his colleagues note, healthcare loyalty programs should differ from coffee shop and gas station programs in a key way: they should never base their rewards solely on the basis of how often patients visit or receive care.

But offering perks to patients based on how long they've stayed with the same doctors, or how often they've chosen to receive the care they need from sites within the network, could work. So could expanding the concept of the "network" that the patients can visit to earn perks -- for instance, urgent care centers and pharmacies, or even restaurants and grocery stores offering healthy food programs.

Unlike hospital programs designed to cultivate wealthy patients by offering them different levels of hospital accommodations, food and clinic access, broad-based loyalty programs could be open to all patients.

While the new piece only lays out the concept of healthcare loyalty programs for others to consider, the authors point to the potential effects.

"Loyalty programs could empower patients to manage their health in new and innovative ways while enhancing the business model for health systems," they write. "If successful, such programs may help improve both customer care and clinical care. That's one membership card worth having."

In addition to McMahon, the piece's authors are corresponding author Vineet Chopra, M.D., M.Sc., and Renuka Tipirneni, M.D., M.Sc., both in the Division of General Medicine.

Reference: JAMA, March 1, 2015, DOI://jvp150210

http://www.eurekalert.org/pub_releases/2016-03/nu-lvd030116.php

Low vitamin D predicts aggressive prostate cancer

Low level of vitamin D at time of surgery is linked to potentially lethal cancer in men

CHICAGO --- A new study provides a major link between low levels of vitamin D and aggressive prostate cancer. Northwestern Medicine research showed deficient vitamin D blood levels in men can predict aggressive prostate cancer identified at the time of surgery. The finding is important because it can offer guidance to men and their doctors who may be considering active surveillance, in which they monitor the cancer rather than remove the prostate.

"Vitamin D deficiency may predict aggressive prostate cancer as a biomarker," said lead investigator Dr. Adam Murphy, an assistant professor of urology at Northwestern University Feinberg School of Medicine and a Northwestern Medicine urologist. "Men with dark skin, low vitamin D intake or low sun exposure should be tested for vitamin D deficiency when they are diagnosed with an elevated PSA or prostate cancer. Then a deficiency should be corrected with supplements."

Previous studies showing an association between vitamin D levels and aggressive prostate cancer were based on blood drawn well before treatment. The new

Northwestern study provides a more direct correlation because it measured D levels within a couple of months before the tumor was visually identified as aggressive during surgery to remove the prostate (radical prostatectomy).

The relationship between vitamin D and prostate cancer may explain some disparities seen in prostate cancer, especially among African American men. Prior research by Murphy and colleagues showed African American men who live in low sunlight locations are up to 1½ times more likely to have vitamin D deficiency than Caucasian men.

But because vitamin D is a biomarker for bone health and aggressiveness of other diseases, all men should check their levels, Murphy said. "All men should be replenishing their vitamin D to normal levels," Murphy said. "It's smart preventive health care."

Aggressive prostate cancer is defined by whether the cancer has migrated outside of the prostate and by a high Gleason score. A low Gleason score means the cancer tissue is similar to normal prostate tissue and less likely to spread; a high one means the cancer tissue is very different from normal and more likely to spread.

The study was published in the Journal of Clinical Oncology Feb. 22. Murphy collaborated on the study with Rick Kittles, associate director of cancer disparities at the University of Arizona Cancer Center.The study was part of a larger ongoing study of 1,760 men in the Chicago area examining vitamin D and prostate cancer. The current study included 190 men, average age of 64, who underwent a radical prostatectomy to remove their prostate from 2009 to 2014.

Of that group, 87 men had aggressive prostate cancer. Those with aggressive cancer had a median level of 22.7 nanograms per milliliter of vitamin D, significantly below the normal level of more than 30 nanograms/milliliter. The average D level in Chicago during the winter is about 25 nanograms/milliliter, Murphy noted.

Most people in Chicago should be on D supplements, particularly during winter months, Murphy said. "It's very hard to have normal levels when you work in an office every day and because of our long winter," he said. The Institute of Medicine recommends 600 international units of D per day, but Murphy recommends Chicago residents get 1,000 to 2,000 international units per day.

The paper is titled: "Associations Between Serum Vitamin D and Adverse Pathology in Men Undergoing Radical Prostatectomy."

This work was supported by the following grants: 1R01MD007105-01, National Institute of Minority Health and Health Disparities of the National Institutes of Health (NIH); IK2CX000926-01, the Veterans Health Administration), W81XWH-10-1-0532 pd22E, the U.S. Department of Defense; and P50 CA090386-10S from the National Cancer Institute of the NIH.

http://bit.ly/1Qxp9dc

How to Tell if Fluffy Is in Pain, According to the Experts

A new study identifies 25 ways to tell if your kitty isn't feeling well

By Danny Lewis

Cats may be adorable little murderbeasts with ninja-like agility and swords for fingers, but they're not immune to pain. But judging pain in cats, is often near impossible.

Cats can behave erratically at the best of times, making it tough for their owners to detect injuries, sickness, or other pain. Thankfully for cat lovers, a panel of 19 cat experts from around the world recently gathered to assemble a set of telltale signs that Fluffy is hurting.

The panel compiled 25 behaviors which were published recently in the journal *PLOS One* that could help you figure out whether your cat is just being weird or if the erratic behaviors might be a sign of something more serious.

The behaviors, which include a lack of grooming, not wanting to move, and hiding are each seemingly small things on their own, but together could indicate that your cat needs a checkup, Daniel Oberhaus writes for *Motherboard*.

"Both owners and veterinarians are clearly able to recognize many behavioral changes in cats which relate to pain," Daniel Mills, study co-author and professor of veterinary behavioral medicine at the United Kingdom's University of Lincoln, said in a statement. "However, owners may not always recognize the clinical relevance of what they see. We hope that having an agreed list of more objective criteria, which relates to specific signs of pain, could improve the ability of both owners and vets to recognize it."

According to Mills, this paper is the first time that behavioral experts have been able to nail down these behaviors. Funded by the British cat charity Feline Friends, the study analyzed an initial list of 91 different behaviors, narrowing it down to 25 through a process of categorization to judge how often the behaviors were exhibited by sick or injured cats, Rebecca Flood writes for *The Independent*.

"Cats are notorious for not showing that they are in pain, and the more that we can find out what the signals are, then the sooner we can get them to the vets for diagnosis and treatment," Feline Friends' chairman, Caroline Fawcett, said in a statement.

There is still some variation on how much pain a cat can be in before it shows these symptoms. Some of the indicators, like a decrease in appetite, being grumpier than usual, and not grooming, can show that your cat is in some amount of pain. Meanwhile, avoiding bright lights and groaning or growling indicate that Fluffy is hurting pretty badly. Others, like hissing or trying to scratch you could show some pain, but the researchers determined that those behaviors depend too

much on a cat's personality to tell whether it is a universal sign of pain, Flood writes.

Keeping an eye out for these behaviors can help cat owners know when it's time to take a trip to the vet, but for Mills the list is just a start. He hopes that this list will be a foundations for future studies into how cats express pain, especially in their faces, Oberhaus writes.

Behaviour sufficient for pain	Presence in low level pain	Presence in high level pain	Participant comments
Lameness	Frequent	Frequent	
Difficulty to jump	Frequent	Frequent	
Abnormal gait	Frequent	Frequent	Can be provoked by other conditions: e.g. cerebellar hypoplasia
Reluctant to move	Frequent	Frequent	
Reaction to palpation	Frequent	Frequent	
Withdraw/hiding	Frequent	Frequent	
Absence of grooming	Frequent	Frequent	
Playing less	Frequent	Frequent	
Appetite decrease	Frequent	Frequent	
Overall activity decrease	Frequent	Frequent	
Less rubbing toward people	Frequent	Frequent	
General mood [1]	Frequent	Frequent	
Temperament [2]	Frequent	Frequent	
Hunched up posture	Frequent	Frequent	
Shifting of weight	Frequent	Frequent	It is relatively subjective
Licking a particular body region	Frequent	Frequent	
Lower head posture	Frequent	Frequent	
Blepharospasm*	Frequent	Frequent	Caused by any chronic eye disease
Change in form of feeding behaviour	Rare	Frequent	Require extensive knowledge of prior feeding behaviour. Not reliable to pain
Avoiding bright areas	Rare	Frequent	Any disease of the eyes can cause it
Growling	Rare	Frequent	More useful if it is a new behaviour, related to mood
Groaning	Rare	Frequent	Not reliable sign of pain
Eyes closed	Rare	Frequent	Other possible causes for it (not specified)

* this behaviour was considered reliable for an acute condition.

[1] Mood states: i.e., enduring episodic changes in underlying affective predisposition arising as a result of a series of emotional events of congruent emotional valence, for example a tendency to be irritable from time to time as a result of pain[25]

[2] Temperament, i.e., a general disposition or trait that is consistent across time and contexts. This indicates that the pain is persistent, or relief is only temporary, and that a state of pain has become an integral part of the animal's constitution and its behavioural predispositions shifted accordingly to adapt to the impact of this. For example, a cat in chronic pain might be described as jumpy or irritable the whole time[25].

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(Isabella Merola, Daniel S. Mills)

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What Clinicians Should Know About the New Lyme Species

Two recent borrelial species deserve some attention for anyone who treats patients who might have acquired a tickborne infection

Paul G. Auwaerter, MD

Hello. This is Paul Auwaerter with Medscape Infectious Diseases, from the Division of Infectious Diseases at Johns Hopkins. Tickborne infections continue to surprise us. Lyme disease historically has been the top vector-borne illness in North America, with 20,000-36,000 reported cases annually, although estimates suggest that the actual number of cases occurring in the United States annually might be upwards of 300,000.[1]

Other members of the *Borrelia* genus cause disease in the United States. Perhaps the oldest, known for many decades, have been the agents of relapsing fever—either louse-borne (which is fairly rare in this country) or, more commonly, tickborne. Tickborne relapsing fever is spread by soft ticks that like to bite at night, especially campers in sleeping bags, and often in elevated climates of 2000-7000 feet above sea level in the western United States.[2]

But two more recent borrelial species deserve some attention for anyone who treats patients who might have acquired a tickborne infection. The first is *B miyamotoi*.[3] This was first described in Russia a few years ago and was initially thought to cause a relapsing fever-like illness, but in the United States it was first described as causing a meningoencephalitis. *B miyamotoi* seems to be transmitted by the same deer tick that transmits Lyme disease, and commercial assays for testing for it aren't yet widely available. However, this infection can be severe enough to cause hospitalization with a sepsis-like presentation. More commonly, it is associated with a febrile illness and can be confused with atypical Lyme disease (without a rash), ehrlichiosis, or anaplasmosis.

However, the newest kid on the block was just described by groups at the Mayo Clinic and the Centers for Disease Control and Prevention.[4] The Mayo Clinic has been a reference lab for many tests throughout the United States. They have drawn samples from around the country and found six samples using polymerase chain reaction (PCR) testing for suspected Lyme disease that had atypical melting curves. Upon further genetic analysis, they found that this was a new species, which they have given the candidate name of *B mayonii* in recognition of where the work was done.

Of interest, the six patients were all from the upper Midwest—Minnesota or Wisconsin. All were ill with fever and rash. One was described as having an erythema migrans rash, others had diffuse maculopapular rashes. There is a suggestion of neurologic syndromes. One patient had arthritis and two others were ill enough to be admitted to the hospital.

Somewhat different from Lyme disease, however, is that some of these patients had very high spirochete loads in their blood. This skews more to what you might find in traditional relapsing fever.

Now, what does this mean? The authors suggest that this is a newly emerging borrelial infection because it hadn't been described in more than 90,000 samples from different regions that they had analyzed earlier, so they think it could just be found in the upper Midwest. Obviously, however, this is very much in the earliest stages.

This situation seems very similar to that in Europe, where *B burgdorferi* sensu stricto (what we have had here in the United States) accounts only for a small proportion of Lyme borreliosis. *B garinii* and *B afzelii* account for far more cases. Several borrelial species account for infections there. We are no longer limited to only one now that *B mayonii* is a separate entity.

There are no specific diagnostic tests yet. It is uncertain whether a *B burgdorferi* PCR would pick this up routinely. The Lyme C6 antibody, which is US Food and Drug Administration approved, at least detected the infection in all four patients. Less successful was the traditional two-tier immunoblot testing, although the IgM Western blot was positive in three out of three people tested. The IgG assay was far less successful.

Whether these patients need different treatment is unclear. They were treated the way that we would treat any tickborne infection. That is the right response at the current time.

Stay tuned, because we might uncover more tickborne infections with advanced molecular technologies. Clinicians should pay attention to what they think might be Lyme disease, ehrlichiosis, or anaplasmosis, which may indeed represent some of these alternative infections. Thanks for listening.

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http://www.bbc.com/news/health-35699161

Rise in hip replacements for under 60s

The number of hip replacement operations on people aged under 60 has risen 76% in the last decade, NHS figures for England reveal.

By Michelle Roberts Health editor, BBC News online

In 2004-05 there were 10,145 hip replacements for people aged 59 and below, with 17,883 in 2014-15. The Royal College of Surgeons says this is partly because doctors are now more confident that replacement joints will be more durable than in the past. Patients are also said to be less willing to wait.

As a proportion of all hip replacements carried out, the rise among under 60s is small, but the Royal College of Surgeons says it is still noteworthy.

Demand for new hips across all ages has risen - there were 89,919 of the operations in 2004-05 and 122,154 in 2014-15.

Stephen Cannon, vice-president of the RCS, says as hip replacement techniques and prosthetics have improved, so have the numbers of younger patients undergoing this type of surgery. "It's no longer seen as a last resort.

"As surgeons, we now have more confidence about the wear rate of these prosthetics which allows us to be less restrictive on an age basis."

'Less arduous'

He said surgeons used to advise patients with hip pain to wait until they were 60 or 65 to have a replacement because the old-fashioned replacements had a shelf-life of about 15 years, meaning the operation might need redoing once in a lifetime - when the patient had turned 80.

"If you look at newer prosthetics, you could do the first operation at 55 and it is going to last for 20 years or more, so you would still only need one revision in a lifetime."

He said another factor might be patient demand. "Certainly, in my experience, patients do not get fobbed off. They don't want to wait for an operation. They say, 'I can't play a round of golf or tennis and I want to.'"

Mr Cannon said concerns over the safety of a particular type of hip replacement (metal-on-metal) in 2010 did not appear to have affected demand.

He said hip operations had become less arduous. Patients can be back on their feet with crutches on the same day or the day after surgery, and out of hospital within three days post-op. "They're off crutches altogether by six weeks."

'Perfect storm'

Most hip replacements are done if the joint becomes damaged from arthritis or an injury. Many of the conditions treated with a hip replacement are age-related so hip replacements are usually carried out in older adults.

Mr Cannon says it's not clear if conditions such as osteoarthritis are becoming more common and affecting people at younger ages, but it is worth exploring.

And with an ageing population, he says demand for hip operations could soon outstrip supply. "The ageing population is a perfect storm. We are not there quite yet, but we might be in 10 years from now. It's a continuing trend."

A spokesman for the National Joint Registry for England, Wales, Northern Ireland and the Isle of Man said: "The increase in numbers of under-60s undergoing primary hip surgery is entirely in line with the overall increase in provision of the operation.

"The orthopaedic sector must continue to work to get the first time surgery as right for the patient as possible - especially where younger patients are concerned as they are most likely to need at least one revision surgery in their lifetime.

"It is, of course, heartening and very encouraging that hip and knee implants are lasting ten years or more, with risk of revision lower than 5%.

"Joint replacement surgery offers significant benefits - getting patients back to their chosen lifestyle sooner, free from pain and with improved mobility."

http://www.eurekalert.org/pub_releases/2016-03/hfss-shr030116.php

Study: Hip replacement too soon after a steroid injection increases infection risk

Researchers recommend patients wait three months after steroid injection to avoid increased infection risk

Patients considering hip replacement surgery would do well to wait three months if they've had a steroid injection to relieve hip pain, according to a study by Hospital for Special Surgery (HSS) researchers.

"The risk of developing an infection after surgery increased significantly in patients who had a hip replacement within three months of receiving a steroid injection," said William Schairer, MD, lead study author. "However, in patients who had a steroid injection and then waited three months or longer to have the surgery, there was no increased risk at all."

Researchers reviewed thousands of patient records in California and Florida databases for their study, which was presented at the annual meeting of the American Academy of Orthopaedic Surgeons (AAOS) on March 2, in Orlando, Florida.

An injection of a steroid into the hip joint is a common treatment to relieve pain and inflammation in patients with arthritis. This the first large population study to provide strong evidence of an increased risk of surgical site infection in patients who have hip replacement 12 weeks or sooner after the injection, according to the researchers. They note that the immune system is weakened by corticosteroids, and this may contribute to the higher infection risk.

"Hip replacement is a common and safe procedure that relieves pain and improves quality of life, and overall, the risk of developing a joint infection is low," said Seth Jerabek, MD, an orthopedic surgeon at Hospital for Special Surgery and senior study author. "Although the risk is low, an infection is one of the most dreaded complications of joint replacement. Patients often need to undergo additional surgery, receive intravenous antibiotic treatment, and are off their feet during a lengthy recovery. "

For their study, investigators looked at the Statewide Ambulatory Surgery and Inpatient Databases for Florida and California from 2005-2012, which included more than 177,000 patients who had hip replacement surgery for osteoarthritis. Researchers narrowed down the list to those who had received steroid injections prior to surgery and reviewed follow-up records to determine which of those patients developed a surgical-site infection within one year of hip replacement.

Patients were grouped into those who received NO injection; those who had hip replacement within 6-12 months of an injection; those who had the surgery within 3-6 months; and those who had hip replacement within 0-3 months of receiving an injection.

The infection rate was 2.06% in non-injection patients and jumped to 2.81% in those who had the surgery from 0-3 months after an injection, representing an increased risk of 40 percent. There was no statistically significant increase in infection risk in patients who had hip replacement from 3 - 12 months after the injection.

"Based on study findings, we recommend that elective hip replacement surgery be deferred for at least three months from an injection to avoid the elevated risk of infection," said Dr. Jerabek. "However, in some cases, such as patients who are still in a great deal of pain after the injection, it may not be feasible to wait. This is something the patient and doctor should discuss to determine what will provide the most benefit and least risk to the patient."

http://www.eurekalert.org/pub_releases/2016-03/aaft-csd022916.php

Compound stems damage from brain bleeding

A compound that blocks iron-containing enzymes in the brain improves recovery following brain hemorrhage, a new study in rodents shows, and it works in an unexpected way.

Instead of binding all free iron released from burst blood vessels, it targets a small family of iron-containing enzymes without affecting total iron - an element required for various physiological processes such as mitochondrial function, cell signaling, and cell division.

Brain hemorrhage, bleeding inside the brain caused by a ruptured blood vessel that can lead to death or disability, is growing in prevalence.

Common causes include stroke, blunt trauma, brain tumors, and use of blood-thinners.

Blood cells that have leaked from burst vessels can break down, releasing toxic products like iron that damage surrounding tissues.

Compounds that bind to iron and remove it from the body, known as iron chelators, have been shown to protect the brain during bleeding.

However, these compounds can have wide-ranging side effects since they can also bind to iron in other parts of the brain where healthy cells need it to survive.

A challenge in developing iron chelators for use in human therapy is to reduce iron accumulation without disrupting iron-dependent cellular functions.

Here, Saravanan Karuppagounder and colleagues identified a more selective iron chelator compound that they named adaptaquin.

In a series of cell-based studies, they showed that it both blocked a family of iron-containing, oxygen-sensing enzymes called hypoxia-inducible factor prolyl-hydroxylases (HIF-PHD) and, critically, protected neurons by activating genes that protect them from oxidative stress.

The researchers used a series of molecular and pharmacological tools to show that, both in vitro and in vivo, inhibiting HIF-PHD with adaptaquin may be neuroprotective after a brain hemorrhage event.

Closer inspection revealed that the drug had little effect on either iron in the brain or, unexpectedly, the target of the oxygen-sensing enzymes.

Instead, adaptaquin seemed to work by blocking a protein called ATF4 that drove cell death in neurons.

Altogether, the findings support further development of adaptaquin as a potential treatment for brain bleeding.

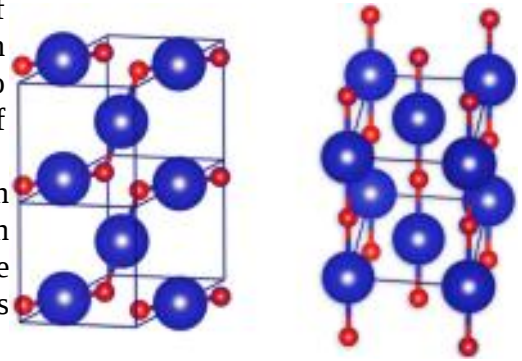
http://www.eurekalert.org/pub_releases/2016-03/iopc-scs030216.php

Superman can start worrying -- we've got the formula for (almost) kryptonite!

Synthesis of the first binary compound of krypton and oxygen: a krypton oxide

Theoretical chemists from the Institute of Physical Chemistry of the Polish Academy of Sciences have found how to synthesize the first binary compound of krypton and oxygen: a krypton oxide

It turns out that this exotic substance can be produced under extremely high pressure, and its production is quite within the capabilities of today's laboratories.



This image shows the crystal structures of krypton monoxide KrO: more stable on the left, less stable on the right. Krypton atoms coloured blue, oxygen atoms coloured red.
IPC PAS

Crystals of kryptonite, a material deadly to Superman and his race, were supposed to have been created within the planet Krypton, and therefore most likely under very high pressure. The progenitor of the name, real krypton, is an element with an atomic number of 36, a noble gas considered to be incapable of forming stable chemical compounds. However, a publication in the journal Scientific Reports by a two-man team of theoretical chemists from the Institute of Physical Chemistry of the Polish Academy of Sciences (IPC PAS) in Warsaw, Poland, presents the possibility of synthesizing a new crystalline material in which atoms of krypton would be chemically bonded to another element.

"The substance we are predicting is a compound of krypton with not nitrogen, but oxygen. In the convention of the comic book it should, therefore, be called not so much kryptonite as kryptoxide. So if Superman's reading this, he can stay calm - at the moment there's no cause for panic!" laughs Dr. Patrick Zaleski-Ejgierd (IPC PAS) and adds: "Our krypton monoxide, KrO, probably does not exist in nature. According to current knowledge, deep in the interiors of planets, that is, the only place where there is sufficient pressure for its synthesis, oxygen does not exist, nor even more so, does krypton."

Compounds of krypton have been produced before, in the laboratory under cryogenic conditions. They were, however, only single, linear and small molecules of the hydrogen-carbon-krypton-carbon-hydrogen type. The Polish chemists wondered if there were conditions in which krypton would not only bond chemically with another element, but also in which it would be capable of forming an extensive and stable crystal lattice. Their search, funded by an OPUS grant from the Polish National Science Centre, involved the researchers using genetic algorithms and models built on the so-called density functional theory. In the field of solid state physics, this theory has for years been a basic tool for the description and study of the world of chemical molecules.

"Our computer simulations suggest that crystals of krypton monoxide will be formed at a pressure in the range of 3 to 5 million atmospheres. This is a huge pressure, but it can be achieved even in today's laboratories, by skillfully squeezing samples in diamond anvils," says PhD student Paweł Lata (IPC PAS).

Crystal lattices are built from atoms or molecules arranged in space in an orderly manner. The smallest repetitive fragment of such structures - the basic 'building block' - is called a unit cell. In crystals of table salt the unit cell has the shape of a cube, the sodium and chlorine atoms, arranged alternately, are mounted on each corner, close enough to each other that they are bound by covalent (chemical) bonds.

The unit cell of krypton monoxide is cuboid with a diamond base, with krypton atoms at the corners. In addition, in the middle of the two opposite side walls, there is one atom of krypton.

"Where is the oxygen? On the side walls of the unit cell, where there are five atoms of krypton, they are arranged like the dots on a dice showing the number five. Single atoms of oxygen are located between the krypton atoms, but only along the diagonal - and only along one! Thus, on each wall with five krypton atoms there are only two atoms of oxygen. Not only that, the oxygen is not

exactly on the diagonal: one of the atoms is slightly offset from it in one direction and the other atom in the other direction," describes Lata.

In such an idiosyncratic unit cell, each atom of oxygen is chemically bound to the two nearest adjacent atoms of krypton. Zigzag chains of Kr/O\Kr\O/Kr will therefore pass through the crystal of krypton monoxide, forming long polymer structures. Calculations indicate that crystals of this type of krypton monoxide should have the characteristics of a semiconductor. One can assume that they will be dark, and their transparency will not be great.

Theorists from the IPC PAS have also found a second, slightly less stable compound of krypton: the tetroxide KrO_4. This material, which probably has properties typical of a metal, has a simpler crystalline structure and could be formed at a pressure exceeding 3.4 million atmospheres.

After formation, the two kinds of krypton oxide crystals could probably exist at a somewhat lower pressure than that required for their formation. The pressure on earth, however, is so low that on our planet these crystals would undergo degradation immediately.

"Reactions occurring at extremely high pressure are almost unknown, very, very exotic chemistry. We call it 'Chemistry on the Edge'". Often the pressures needed to perform syntheses are so gigantic that at present there is no point in trying to produce them in laboratories. In those cases even methods of theoretic description fail! But what is most interesting here is the non-intuitiveness. From the very first to the last step of synthesis you never know what's going to happen," says Dr. Zaleski-Ejgierd - and he returns to his computer where simulations of subsequent syntheses are nearing their end.

http://www.scientificamerican.com/article/fire-neandertal-chemistry/

Fire! Neandertal Chemistry

Archaic humans used manganese dioxide to start fires, not—as thought—just for body paint

By Emma Stoye, ChemistryWorld on March 2, 2016

Chunks of black manganese oxides have been recovered at Neanderthal sites for many years, and until now it was thought to have been used as a source of body paint, as it is often found alongside other coloured minerals. However, some have pointed out that there would have been more readily available sources of black pigment, including ash and charcoal.

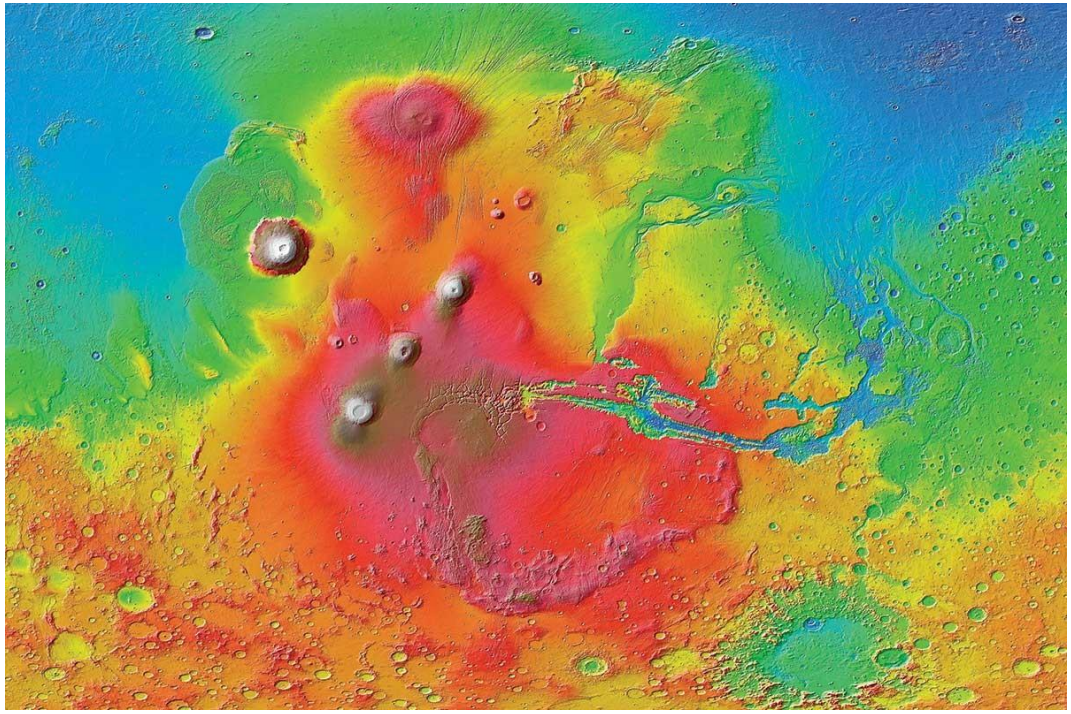
Now, a group led by Marie Soressi at Leiden University in the Netherlands has put forward the idea that these compounds were instead used as firelighters. When they analysed the composition of manganese oxide blocks recovered from the Pech-de-l'Azé Neanderthal site in southern France, they found that they mainly contained manganese dioxide, which is similar in colour but more flammable than other manganese oxides. They also noticed scratch marks on blocks, suggesting they may have been scraped or ground to produce a powder. They found that when ground-up samples of the blocks were sprinkled over wood it lowered the ignition temperature by more than 100°C. These findings support the view that that rather than just exploiting naturally occurring wildfires, Neanderthals were able to start their own.

http://bit.ly/1R11d7F

Volcanic mount spun Mars around and rearranged its rivers

Young Mars had its world turned upside-down by some hot stuff.

The emergence of a titanic mount of molten rock jostled the Red Planet's early tropics out of position, and may have helped usher in the cold, dry and dead version of the planet we know today.



The bringer of deformation **NASA/JPL-Caltech/Arizona State University**

That massive bulge of volcanic rock is called the Tharsis region. At 5000 kilometres across and more than 10 kilometres thick, it is the largest known volcanic complex in the solar system. When huge outpourings of lava between 4.1 and 3.7 billion years ago created it, it deformed the entire planet.

It was thought that Tharsis bent the planet's crust and dictated the direction of Martian rivers, which formed later.

But now, Sylvain Bouley of University of Paris-South and his colleagues suggest that the rivers and their valley networks formed first, and were concentrated along the equator. The formation of Tharsis tilted the planet around so much that, if it happened on Earth, Paris would sit atop the magnetic north pole – a rearrangement that would have wild, catastrophic effects on the climate and water.

"This may make it easier to explain the climate associated with the valley networks," says Robert Craddock, a geologist at the Smithsonian Institution in Washington DC. "It's actually pretty obvious, but no one saw it before."

Wandering poles

While writing his dissertation 8 years ago, Bouley noticed that valley networks that formed between 4 and 3 billion years ago were arranged almost as if they were in a circle, but tilted a bit from the equator.

Bouley and his colleagues calculated where Mars's poles would have been before Tharsis, and worked out that the circle would have followed the equator. They also looked for evidence of a polar-like climate at what would have been the poles. The "paleo" north pole is in a region with a large amount of ice, possibly corresponding to an ancient polar ice cap, and there is evidence of water at the ancient south pole as well. They conclude that the placement of the rivers makes the most sense if they were in place before the Tharsis region formed, or if they were forming concurrently – maybe even by rainfall or snowfall happening as the enormous volcanic structure was active.

Bouley says his next goal is studying how this crustal shifting might have contributed to Mars's loss of water and air. As a young planet, Mars may have had warm, wet, and humid tropics at its equator just like Earth does now. But at some point, it lost is thick protective atmosphere, and much of the water went with it. "What is certain is that the true polar wander occurred when the water and atmosphere disappeared or was disappearing," he says. "Is the polar wander the cause? I cannot tell now."

Journal reference: Nature, DOI: 10.1038/nature17171

http://www.eurekalert.org/pub_releases/2016-03/esoc-hcb022916.php

Happiness can break your heart too

Happy events can trigger a heart condition known as takotsubo syndrome, according to research published today (Thursday) in the European Heart Journal [1].

Takotsubo syndrome (TTS) is known as "broken heart syndrome" and is characterised by a sudden temporary weakening of the heart muscles that causes the left ventricle of the heart to balloon out at the bottom while the neck remains narrow, creating a shape resembling a Japanese octopus trap, from which it gets its name. Since this relatively rare condition was first described in 1990, evidence has suggested that it is typically triggered by episodes of severe emotional distress, such as grief, anger or fear, with patients developing chest pains and breathlessness. It can lead to heart attacks and death.

Now, for the first time, researchers have systematically analysed data from the largest group of patients diagnosed with TTS worldwide, and found that some patients have developed the condition after a happy or joyful event; they have named it "happy heart syndrome".

In 2011, Dr Christian Templin, principle investigator and consultant cardiologist, together with Dr Jelena Ghadri, resident cardiologist, established the first International Takotsubo Registry at the University Hospital Zurich in Switzerland. For this study they have analysed data from the first 1750 patients registered from the 25 collaborating centres in nine different countries [2].

They found 485 patients where there was a definite emotional trigger. Of these, 20 (4%) had TTS that had been precipitated by happy and joyful events, such as a birthday party, wedding, surprise farewell celebration, a favourite rugby team winning a game, or the birth of a grandchild; 465 (96%) had occurred after sad and stressful events, such as death of a spouse, child or parent, attending a funeral, an accident, worry about illness, or relationship problems; one occurred after an obese patient got stuck in the bath.

Ninety-five percent of the patients were women in both the "broken hearts" and "happy hearts" groups, and the average age of patients was 65 among the "broken hearts" and 71 among the "happy hearts", confirming that the majority of TTS cases occur in post-menopausal women.

Dr Ghadri said the new findings should lead to a paradigm shift in clinical practice. "We have shown that the triggers for TTS can be more varied than previously thought. A TTS patient is no longer the classic "broken hearted" patient, and the disease can be preceded by positive emotions too. Clinicians should be aware of this and also consider that patients who arrive in the emergency department with signs of heart attacks, such as chest pain and breathlessness, but after a happy event or emotion, could be suffering from TTS just as much as a similar patient presenting after a negative emotional event. Our findings broaden the clinical spectrum of TTS. They also suggest that happy and sad life events may share similar emotional pathways that can ultimately cause TTS."

The researchers found that "happy heart" patients were more likely to have hearts that had ballooned in the mid-ventricle than "broken heart" patients (35% versus 16%). Although this is a new and interesting finding, the small number of patients

in this group means that more research needs to be conducted in order to discover whether or not it sheds any light on the mechanisms involved in TTS.

Dr Templin said further research was needed to understand the exact mechanisms underlying both the "broken" and "happy" heart variants of TTS. "We believe that TTS is a classic example of an intertwined feedback mechanism, involving the psychological and/or physical stimuli, the brain and the cardiovascular system. Perhaps both happy and sad life events, while inherently distinct, share final common pathways in the central nervous system output, which ultimately lead to TCS."

The researchers are working to understand further the relationship between the heart and the brain; they are using functional MRI to look at the workings of parts of the brain known to be involved in the processing of emotions, reactions, behaviour, decision-making and memory, such as the amygdala and the prefrontal cortex.

[1] *"Happy heart syndrome: role of positive emotional stress in takotsubo syndrome", by Jelena R. Ghadri et al. European Heart Journal. doi:10.1093/eurheartj/ehv757*

[2] *The nine countries are Austria, Finland, France, Germany, Italy, Poland, Switzerland, UK and USA.*

http://www.eurekalert.org/pub_releases/2016-03/uobc-wag030216.php

Without ancestral gene life on Earth might not have evolved beyond slime

Researchers at the University of British Columbia have identified a common ancestral gene that enabled the evolution of advanced life over a billion years ago.

The gene, found in all complex organisms, including plants and animals, encodes for a large group of enzymes known as protein kinases that enabled cells to be larger and to rapidly transfer information from one part to another.

"If the duplications and subsequent mutations of this gene during evolution didn't happen, then life would be completely different today," said Steven Pelech, a professor in Division of Neurology in the UBC Faculty of Medicine. "The most advanced life on our planet would probably still be bacterial slime."

Plants, animals, mushrooms and more all exist because they are made up of eukaryotic cells that are larger and far more complex than bacteria. Inside of these eukaryotic cells are hundreds of organelles that perform diverse functions to keep them living, just as different organs do for the human body.

The new research, published this week in the Journal of Biological Chemistry, identifies the gene that gave rise to protein kinases. On a cellular scale, these highly interactive signaling proteins play a role similar to the neurons in the brain by transferring information throughout the cell by a process known as protein phosphorylation.

This ability to transmit signals from one part of the cell to another not only enabled cells to become more complex internally, but also allowed cells to come together to form systems, paving the way for the evolution of intelligent life.

Research into these enzymes has become very important to medicine. More than 400 human diseases like cancer and diabetes are linked to problems with cell signaling. Disease occurs when a cell gets misinformed or confused. Today about one-third of all pharmaceutical drug development is targeted at protein kinases.

For more than 30 years, researchers have known that most protein kinases came from a common ancestor because their genes are so similar.

"From sequencing the genomes of humans, we knew that about 500 genes for different protein kinases all had similar blueprints," said Pelech, also a researcher at Vancouver Coastal Health Research Institute. "Our new research revealed that the gene probably originated from bacteria for facilitating the synthesis of proteins and then mutated to acquire completely new functions."

The same gene that gave rise to protein kinases also led to the formation of a group of enzymes know as choline and ethanolamine kinases. The choline kinase enzyme is critical for the production of phosphatidylcholine, a major component of the membranes that wrap around eukaryotic cells and their organelles, but is missing from bacteria.

Pelech says that the approach they used to study the evolution of this gene could be adapted to study other important protein families and could eventually lead to the creation of a protein version of the evolutionary tree of life.

http://www.eurekalert.org/pub_releases/2016-03/uouh-avi022616.php

Ancient viral invaders in our DNA help fight today's infections

About eight percent of our DNA is viral in origin: remnants of ancient battles between infectious viruses and our ancestors.

Salt Lake City - These so-called endogenous viruses are often perceived as a mere oddity with no clear biological significance. But a new study by scientists at the University of Utah School of Medicine shows that evolution has repurposed some of these viral remains into weapons against its own kind.

Published in *Science* on March 4, the scientists report that bits of viral DNA embedded in our genome are regulating genes that are integral components of our innate immune system, the first line of defense against pathogens, including viruses. When some of these bits of foreign code are removed experimentally, the defense system becomes crippled.

"We show that some of these endogenous viruses have shaped our biology," says Cédric Feschotte, Ph.D., co-senior author and associate professor of human

genetics. "Within mammalian genomes are reservoirs of viral DNA that have fueled innovation of the innate immune system."

The human innate immune system's ability to defeat foreign invaders depends on a well-coordinated response. Upon infection, cells dispatch a silent alarm by releasing interferons, a molecular signal that triggers nearby cells to activate an arsenal of hundreds of genes that fight off intruders. By analyzing publicly available genomic datasets from human cells, the authors discovered thousands of endogenous retroviruses that appeared to be activated by interferons. However, because these retroviruses crash-landed into our genomes many millions of years ago, they have long lost the ability to produce infectious particles. One clue to a potential modern-day function of some of these interferon-inducible elements came from their location in the genome. Instead of being distributed randomly, they were enriched near genes with known functions in immunity.

"These were the first signs to us that some of these elements may be truly involved in switching on immunity genes," says Feschotte who collaborated on the project with assistant professor of human genetics and co-senior author Nels Elde, Ph.D., and lead author Edward Chuong, Ph.D., a Jane Coffin Childs postdoctoral fellow.

To test whether the pieces of viral DNA were indeed important for immunity, the scientists used the gene-editing tool CRISPR/Cas9 in cell culture to remove one by one several of these viral sequences, each located near known immune genes. In mutant cells lacking the foreign code the adjacent immune genes could not turn on properly in response to interferon, demonstrating that they act as virus-derived switches. Further, when cells lacking the viral DNA element near the AIM2 immune defense gene were infected with virus, their ability to execute an effective immune response was greatly reduced. Taken together, the results indicate that ancient viral DNA has become important for mounting a proper defense against today's viral infections.

Because similar virus-derived switches are embedded close to many immune genes, the implication is that together they help coordinate our cellular defenses. "The interferon response is like the alarm system of the cell. We found that some of the most important switches in this system are actually derived from ancient viruses," explains Chuong. The report also finds clues that other endogenous retroviruses may have independently "wired" the interferon responses of other mammals, potentially pointing to a widespread mechanism underlying species-specific immune responses.

"It's likely no accident that innate immune systems reclaimed some of these viral remnants", says Elde. Immune defenses are continually challenged by pathogens that rapidly evolve and change invasion tactics. In order to keep up, evolution simply retooled the genetic material that was previously supplied by viruses.

"Many viruses originally entered our genomes as part of the process of viral replication," says Elde. "The evolutionary process turned the tables to our benefit."

The research by Edward Chuong, Nels Elde, and Cédric Feschotte will be published as a report titled, "Regulatory evolution of innate immunity through co-option of endogenous retroviruses" in Science *on March 4, 2016*

The research was supported by the National Institutes of Health (GM082545, GM114514, GM112972, GM059290), the Jane Coffin Childs Memorial Fund, and the Pew Charitable Trusts.

http://www.eurekalert.org/pub_releases/2016-03/mgh-rau030116.php

Regular aspirin use found to protect against overall cancer risk

Preventive effect most apparent against colorectal, other gastrointestinal tumors

An analysis of data from two major, long-term epidemiologic studies finds that the regular use of aspirin significantly reduces the overall risk of cancer, a reduction that primarily reflects a lower risk of colorectal cancer and other tumors of the gastrointestinal tract. The findings published Online First in JAMA Oncology suggest that the use of aspirin may complement, but not replace, the preventive benefits of colonoscopy and other methods of cancer screening.

"We now can recommend that many individuals consider taking aspirin to reduce their risk of colorectal cancer - particularly those with other reasons for regular use, such as heart disease prevention - but we are not at a point where we can make a general recommendation for overall cancer prevention," says Andrew Chan, MD, MPH, chief of the Clinical and Translational Epidemiology Unit in the Massachusetts General Hospital (MGH) Division of Gastroenterology, the senior and corresponding author of the report.

"Our findings imply that aspirin use would be expected to prevent a significant number of colorectal cancers above and beyond those that would be prevented by screening and may have even greater benefit in settings in which the resources to devote to cancer screening are lacking."

A large number of studies have supported the ability of regular aspirin use to prevent colorectal cancer, but aspirin's effects on overall cancer risk has not been clear.

To investigate that question, the research team analyzed 32 years worth of data from almost 136,000 participants in the Nurses' Health Study and the Health Professionals Follow-up Study.

They found that participants who reported regular aspirin use - defined as taking either a standard or a low-dose aspirin tablet at least twice a week - had a 3

percent absolute lower risk of any type of cancer than did those not reporting regular aspirin use. Regular aspirin use reduced the risk of colorectal cancer by 19 percent and the risk of any gastrointestinal cancer by 15 percent. No reduction was seen in the risk of breast, prostate or lung cancer.

Aspirin's protective benefit appeared after five years of continuous use at dosages ranging from 0.5 to 1.5 standard tablets a week or one low-dose tablet a day. The researchers estimate that regular aspirin use could prevent close to 30,000 gastrointestinal tract tumors in the U.S. each year and could prevent an additional 7,500 colorectal tumors among U.S. adults over 50 who have endoscopic screening and 9,800 among the almost 30 million who are not screened.

The benefit related to other gastrointestinal tumors appeared after six years and at the same dosage level - equivalent to a daily low-dose tablet - used to prevent cardiovascular disease.

"At this point, it would be very reasonable for individuals to discuss with their physicians the advisability of taking aspirin to prevent gastrointestinal cancer, particularly if they have risk factors such as a family history," says Chan, an associate professor of Medicine at Harvard Medical School. "But this should be done with the caveat that patients be well informed about the potential side effects of regular aspirin treatment and continue their regular screening tests. Furthermore, aspirin should not be viewed as a substitute for colonoscopy or other cancer screening tests."

Yin Cao, MPH, ScD, Clinical and Translational Epidemiology Unit, MGH Gastroenterology, is the lead author of the JAMA Oncology paper. Additional co-authors are Reiko Nishihara, PhD, Shuji Ogino, MD, PhD, and Charles Fuchs, MD, MPH, Dana-Farber Cancer Institute; and Kana Wu, MD, PhD, Molin Wang, PhD, Walter Willett, MD, DrPH, Donna Spiegelman, ScD, and Edward Giovannucci, MD, ScD, Harvard T.H. Chan School of Public Health. The study was supported by a large number of National Institutes of Health grants.

http://www.eurekalert.org/pub_releases/2016-03/aaon-uac022216.php

Using a computer, social activities tied to reduced risk of memory decline

Keeping the brain active with social activities and using a computer may help older adults reduce their risk of developing memory and thinking problems

MINNEAPOLIS - Keeping the brain active with social activities and using a computer may help older adults reduce their risk of developing memory and thinking problems, according to a study released today that will be presented at the American Academy of Neurology's 68th Annual Meeting in Vancouver, Canada, April 15 to 21, 2016.

"The results show the importance of keeping the mind active as we age," said study author Janina Krell-Roesch, PhD, with the Mayo Clinic in Scottsdale, Ariz., and member of the American Academy of Neurology.

"While this study only shows association, not cause and effect, as people age, they may want to consider participating in activities like these because they may keep a mind healthier, longer."

For the study, researchers followed 1,929 people, age 70 and older, who were part of the larger Mayo Clinic Study of Aging in Rochester, Minn.

The participants had normal memory and thinking abilities at recruitment to the study. They were then followed for an average of four years until they developed mild cognitive impairment or remained impairment-free.

Participants were asked about their engagement in mentally stimulating activities such as computer use, reading, crafting and social activities within 12 months before participation in the study using a questionnaire.

The investigators then wanted to know if participants who engaged in mental activities at least once per week had a lower risk for new onset of mild cognitive impairment as compared to those participants who did not engage in these activities.

The study found that people who used a computer once per week or more were 42 percent less likely to develop memory and thinking problems than those who did not.

A total of 193 out of 1,077 people (17.9 percent) in the computer use group developed mild cognitive impairment, compared to 263 out of 852 (30.9 percent) people in the group that did not report computer use.

People who engaged in social activities were 23 percent less likely to develop memory problems than those who did not engage in social activities.

A total of 154 out of 767 (20.1 percent) people in the social activities group developed problems, compared to 302 out of 1,162 (26.0 percent) people who did not participate in social activities.

People who reported reading magazines were 30 percent less likely to develop memory problems.

Those who engaged in craft activities such as knitting were 16 percent less likely to develop memory problems.

Similarly, those who played games were 14 percent less likely to develop memory problems.

The study was supported by the National Institute on Aging, National Institute of Mental Health, the Robert Wood Johnson Foundation, the Robert H. and Clarice Smith and Abigail Van Buren Alzheimer's Disease Research Program, the European Regional Development Fund and the Arizona Alzheimer's Consortium.

http://www.eurekalert.org/pub_releases/2016-03/uamr-nsa030316.php

Novel small-molecule antiviral compound protects monkeys from deadly Ebola virus

Rhesus monkeys were completely protected from Ebola virus when treated three days after infection with a compound that blocks the virus's ability to replicate.

These encouraging preclinical results suggest the compound, known as GS-5734, should be further developed as a potential treatment, according to research findings published online this week in the journal Nature.

Ebola virus causes severe hemorrhagic fever in humans and nonhuman primates with high mortality rates and continues to emerge in new geographic locations, including Western Africa, the site of the largest outbreak to date. Since December 2013, over 28,600 cases have been reported in Guinea, Liberia and Sierra Leone, with over 11,300 deaths, according to the World Health Organization. Although several clinical trials have been conducted or are currently underway, there are no licensed vaccines or therapies against Ebola virus.

Travis Warren, Ph.D., a principal investigator at the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID) and first author of the paper, said the work published today is the result of continuing collaborations between USAMRIID and Gilead Sciences of Foster City, Calif. Scientists at the Centers for Disease Control and Prevention (CDC) also contributed by performing initial screening of the Gilead Sciences compound library to find molecules with promising antiviral activity.

That initial work identified the precursor to GS-5734, a small-molecule antiviral agent, which led to the effort by Gilead and USAMRIID to further refine, develop and profile the compound. Led by USAMRIID Science Director Sina Bavari, Ph.D., the paper's senior author, the research team used cell culture and animal models to demonstrate the compound's antiviral activity against several pathogens, including Ebola virus.

In animal studies, treatment initiated on day 3 post-infection with Ebola virus resulted in 100 percent survival of the monkeys. The animals also exhibited a substantial reduction in viral load and a marked decrease in the physical signs of disease.

"GS-5734 is a novel nucleotide analog prodrug. It inhibits Ebola virus by blocking the virus's ability to replicate its own genetic material," said Warren. "With this process inhibited, the virus can't make copies of itself. Additionally, we saw no evidence from genetic sequence analyses that the virus was able to generate resistance to GS-5734."

In cell culture studies, led at USAMRIID by Veronica Soloveva, Ph.D., GS-5734 was active against a broad spectrum of viral pathogens. These included Middle East Respiratory Syndrome (MERS) virus, Marburg virus, and multiple variants of Ebola virus, including the Makona strain causing the most recent outbreak in Western Africa.

"GS-5734 has several favorable characteristics for potential treatment of Ebola virus disease in humans. It is made using well-controlled chemical synthesis procedures, is stable, and can be made on a large scale," Bavari commented. "It shows substantive post-exposure protection against Ebola virus in nonhuman primates, even when treatments were started after virus had spread to the blood in some animals."

Taken together, the robust therapeutic efficacy observed in primates, the favorable drug-like properties, and the potential for broad-spectrum antiviral activity suggest that further development of GS-5734 for the treatment of Ebola virus and other viral infections is warranted, Bavari said.

According to Tomas Cihlar, Ph.D., of Gilead Sciences, the company is currently conducting a series of phase I clinical studies in healthy human volunteers to establish the safety and pharmacokinetic profile of GS-5734. The compound also has been provided for compassionate use to treat two patients with Ebola virus infection, both of whom were discharged from the hospital. One of them was the Scottish nurse with recrudescent disease and the other was an acutely infected newborn, thus far the last identified case of Ebola virus infection in Guinea.

"With the hope that the West African outbreak will remain under control, we are exploring alternative options for the development path of GS-5734, including potential use of the animal efficacy rule," Cihlar said. The animal rule is a regulatory mechanism under which the U.S. Food and Drug Administration may consider efficacy findings from adequate and well-controlled animal studies of a drug in cases where it is not feasible or ethical to conduct human trials.

Research on Ebola virus is conducted in Biosafety Level 4 (maximum containment) laboratories, where investigators wear positive-pressure "space suits" and breathe filtered air as they work. USAMRIID is the only organization in the Department of Defense with Biosafety Level 4 capabilities, and its research benefits both military personnel and civilians.

USAMRIID's mission is to provide leading-edge medical capabilities to deter and defend against current and emerging biological threat agents. The Institute plays a key role as the lead military medical research laboratory for the Defense Threat Reduction Agency's Joint Science and Technology Office for Chemical and Biological Defense. USAMRIID is a subordinate element of the U.S. Army Medical Research and Materiel Command. For more information, visit http://www.usamriid.army.mil.

Reference:

T Warren et al. Therapeutic efficacy of the small molecule GS-5734 against Ebola virus in rhesus monkeys. Nature DOI: 10.1038/nature17180 (2016)

Funding:

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http://www.eurekalert.org/pub_releases/2016-03/jhm-lbl022916.php

Likely biological link found between Zika virus, microcephaly

Discovery with lab-grown stem cells could be used to identify potential therapies

Working with lab-grown human stem cells, a team of researchers suspect they have discovered how the Zika virus probably causes microcephaly in fetuses. The virus selectively infects cells that form the brain's cortex, or outer layer, making them more likely to die and less likely to divide normally and make new brain cells.

The researchers say their experiments also suggest these highly-susceptible lab-grown cells could be used to screen for drugs that protect the cells or ease existing infections.

"Studies of fetuses and babies with the telltale small brains and heads of microcephaly in Zika-affected areas have found abnormalities in the cortex, and Zika virus has been found in the fetal tissue," says Guo-li Ming, M.D., Ph.D., a professor of neurology, neuroscience, and psychiatry and behavioral science at Johns Hopkins' Institute for Cell Engineering. "While this study doesn't definitely prove that Zika virus causes microcephaly, it's very telling that the cells that form the cortex are potentially susceptible to the virus, and their growth could be disrupted by the virus." Ming led the research team along with Hongjun Song, Ph.D., a professor of neurology and neuroscience in the Institute for Cell Engineering, and Hengli Tang, Ph.D., a virologist at Florida State University.

Results of the experiments, conducted by researchers at the Johns Hopkins University School of Medicine, Florida State University, and Emory University, are described online March 4 in the journal Cell Stem Cell.

In a quickly executed study that reflects the global public health threat posed by Zika, the researchers compared Zika's effect on cells known as cortical neural progenitor cells to two other cell types: induced pluripotent stem cells and immature neurons. Induced pluripotent stem cells are made by reprogramming mature cells, and can give rise to any cell type in the body, including cortical neural progenitor cells. Cortical neural progenitor cells in turn give rise to immature neurons.

The experiments, conducted in less than a month, began when Tang reached out to Ming and Song, who use stem cells to study early brain development. The Johns Hopkins labs sent team members and cells to Tang's lab, where the cells were exposed to Zika virus. Then the cells' genetic expression - evidence of which genes were being used by the cells and which weren't - were analyzed in Peng Jin's laboratory at Emory University.

According to Tang, three days after exposure to the virus, 90 percent of the cortical neural progenitor cells were infected, and had been hijacked to churn out new copies of the virus. Furthermore, the genes needed to fight viruses had still not been switched on, which is highly unusual, he adds. Many of the infected cells died, and others showed disrupted expression of genes that control cell division, indicating that new cells could not be made effectively.

Using specific, known types of cells allowed the researchers to see where the developing brain is most vulnerable, Song says. He and Ming are now using the cells to find out more about the effects of Zika infection on the developing cortex. "Now that we know cortical neural progenitor cells are the vulnerable cells, they can likely also be used to quickly screen potential new therapies for effectiveness," Song adds.

Zika virus has recently emerged as a public health concern, but it was first discovered in Uganda in the 1940s. Since then, small outbreaks have appeared in Asia and Africa, but symptoms were generally mild and did not appear to have any long-term effects. Carried by infected Aedes aegypti mosquitos, Zika is largely transmitted through bites, but can also occur through intrauterine infection or sexual transmission.

In 2015, the Zika virus began spreading throughout the Americas and a potential link was seen between the virus and a significant increase in cases of fetal microcephaly, as well as other neurologic abnormalities. This connection and the proliferation in cases led to the World Health Organization declaring Zika virus an international public health emergency.

Other authors of the study are Christy Hammack, Sarah Ogden, Emily Lee and Ruth Didier of Florida State University; Zhexing Wen, Xuyu Qian, Jaehoon Shin and Kimberly Christian of Johns Hopkins University; and Yujing Li, Bing Yao and Feiran Zhang of Emory University.

http://www.eurekalert.org/pub_releases/2016-03/uob-rrd030416.php

Rare respiratory disease gene carriers actually have increased lung function

Rare respiratory disease gene carriers actually have increased lung function

New research has revealed the healthy carriers of a gene that causes a rare respiratory disease are taller and larger than average, with greater respiratory capacity.

The disease, alpha1-antitrypsin deficiency (AATD) can result in severely reduced lung capacity due to emphysema. It is found in about 1 in 2,000 people, and occurs when an individual inherits a defective gene copy from both parents.

The findings from the University of Bristol study, published in the Journal of Medical Genetics, may have important implications for physical fitness training, and for the treatment of lung function disorders and short stature.

The researchers studied the AATD gene in relation to human health conditions in around 20,000 participants. They found carriers of the defective gene copy of the AATD gene have important enhanced respiratory capacity of about 10%. Additionally, on average, carriers display a significantly greater height (1.5cm) and size.

Professor Ian Day from the School of Social and Community Medicine was one of the study's senior authors. He said: "Over the past several thousands of years, the deficiency gene seems to have been positively selected, and is mainly found in north Europe, as have gene variants for larger height and size generally. These observations in carriers identify pathway effects that may be of relevance in the fields of physical fitness, and in therapeutic approaches to modify lung function or short stature.

"Our study suggests some treatment involving the alpha1-antitrypsin pathway might be able to make important modification of height in growth disorders. Hundreds of different common genetic combinations that influence height have been identified, which is itself a highly heritable trait. The most notable of these common genetic variant is HMGA2, which exerts about a 0.3cm effect on height. The AATD variant, which is present in about 4% of the population, exerts a height effect of 1.5cm. A drug treatment targeting this pathway might be able to get a much greater effect."

Alpha1-antitrypsin is already a therapeutic agent used for replacement therapy in deficient individuals suffering from respiratory disease. There is an opposite effect of the deficiency gene in carriers (i.e. enhanced respiratory capacity) compared with full deficiency (i.e. severely diminished respiratory capacity). This opposite effect may potentially be used to enhance respiratory capacity in selected disease contexts through therapeutic mimicry of the carrier status.

Paper: 'A study of common Mendelian disease carriers across ageing British cohorts: meta-analyses reveal heterozygosity for alpha 1-antitrypsin deficiency increases respiratory capacity and height' by T.L North et al in The Journal of Medical Genetics (Open access)

http://www.bbc.com/news/health-35718491

Scientists 'find cancer's Achilles heel'

Scientists believe they have discovered a way to "steer" the immune system to kill cancers.

By James Gallagher Health editor, BBC News website

Researchers at University College, London have developed a way of finding unique markings within a tumour - its "Achilles heel" - allowing the body to target the disease. But the personalised method, reported in Science journal, would be expensive and has not yet been tried in patients.

Experts said the idea made sense but could be more complicated in reality.

However, the researchers, whose work was funded by Cancer Research UK, believe their discovery could form the backbone of new treatments and hope to test it in patients within two years.

They believe by analysing the DNA, they'll be able to develop bespoke treatment.

People have tried to steer the immune system to kill tumours before, but cancer vaccines have largely flopped. One explanation is that they are training the body's own defences to go after the wrong target.

The problem is cancers are not made up of identical cells - they are a heavily mutated, genetic mess and samples at different sites within a tumour can look and behave very differently.

'Exciting'

They grow a bit like a tree with core "trunk" mutations, but then mutations that branch off in all directions. It is known as cancer heterogeneity.

The international study developed a way of discovering the "trunk" mutations that change antigens - the proteins that stick out from the surface of cancer cells.

Professor Charles Swanton, from the UCL Cancer Institute, added: "This is exciting. Now we can prioritise and target tumour antigens that are present in every cell - the Achilles heel of these highly complex cancers.

"This is really fascinating and takes personalised medicine to its absolute limit, where each patient would have a unique, bespoke treatment."

There are two approaches being suggested for targeting the trunk mutations.

The first is to develop cancer vaccines for each patient that train the immune system to spot them.

The second is to "fish" for immune cells that already target those mutations and swell their numbers in the lab, and then put them back into the body.

'Early days'

Dr Marco Gerlinger, from the Institute of Cancer Research, said: "This is a very important step and makes us think about heterogeneity as a problem and why this gives cancer this big advantage. "Targeting trunk mutations makes sense from many points of view, but it is early days and whether it's that simple, I'm not entirely sure.

"Many cancers are not standing still but they keep evolving constantly. These are moving targets which makes it difficult to get them under control.

"Cancers that can change and evolve could lose the initial antigen or maybe come up with smokescreens of other good antigens so that the immune system gets confused."

Analysis

James Gallagher, health editor, BBC News website

Harnessing the power of the immune system - what's known as immunotherapy - is the most exciting field in cancer and probably in all of medicine right now. But while that excitement is justified, claims that a cure for cancer is around the corner are not.

Medical research is littered with the graves of hyped treatments that just never worked. Two decades ago, gene therapy was "hype-central" and we're still waiting for it to transform medicine. This study demonstrates some spectacular science that furthers understanding of how the immune system and cancer interact.

But this new knowledge has not been used to treat a single patient. There have not even been animal studies. So there is a real risk it will not work. Even if it does, this is an hugely expensive approach that would need to be customised to every patient in a process that takes more than a year from start to finish.

Some immunotherapy treatments work spectacularly with some patients' cancer disappearing entirely.

They take the brakes off the immune system, freeing it up to fight cancer.

The researchers hope the combination of removing the immune system's brakes and then taking over the steering wheel, will save lives.

Professor Peter Johnson, from Cancer Research UK, said the research had shown "impressive results in the clinic" and although "the technology is complicated and quite recent... once you start doing it the cost will come down".

'Elegant study'

Dr Stefan Symeonides, clinician scientist in experimental cancer medicine at the University of Edinburgh, said designing a personalised vaccine was currently impractical, especially when a patient needed treatment straight away.

But he added that the "very elegant" study did provide a ground-breaking insight into current immunotherapy drugs, which do not yet work for most people.

"It's not just the number of antigens, it's how many of the cancer cells have them," he said.

"This data will be quoted in discussions for years, as we try to understand which patients benefit from immunotherapy drugs, which ones don't, and why, so we can improve those therapies."

http://www.bbc.com/news/health-35660621

The paralysed man who can ride a bike

Darek learns to cycle again

Fergus Walsh Medical correspondent

A man who was paralysed from the chest down after a knife attack in 2010 can now ride an adapted tricycle. In 2014, surgeons in Poland announced they had reversed Darek Fidyka's paralysis using cells taken from his nose to repair his spinal cord. The former fireman says he has noticed a gradual return of feeling and muscle control below his injury.

The surgical team are now launching a search for two more paralysed patients who they will try to help walk again. Mr Fidyka told me: "I can tell that sensation is coming back and I am getting stronger. A year ago I would not have been able to ride a tricycle. Now I can feel each muscle and each press of the foot on the pedals."

The BBC's Panorama told the remarkable story of Darek Fidyka and the 40-year research programme involving scientists in Britain and Poland.

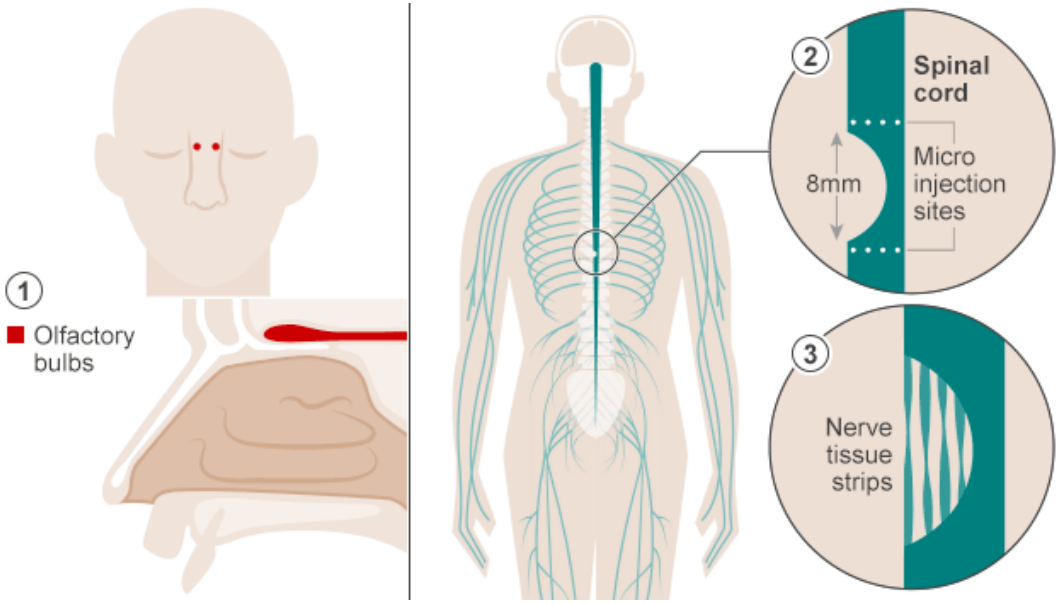
The medical team are now launching the worldwide search as they are looking for patients with an uncommon type of injury, where the spinal cord has been completely severed, which can happen after a knife injury.

The head of the project, surgeon Dr Pawel Tabakow said: "If we can bridge the gap between two spinal cord stumps then there will be no doubt that our technique works and this will be historic - if we succeed we will have found a cure for paralysis. "Then we will be able to help other patients with the most common type of injury, caused by a crush or compression."

The Wroclaw Walk Again Project will be conducted in Poland, but patients anywhere in the world aged 16-65 will be able to apply via the team's website, which will be officially launched on 8th March in Wroclaw.

All the treatment will be free, but to be eligible patients must have no feeling or voluntary muscle function below the injury and they must be prepared to spend around three years in Poland. They will undergo extensive physiotherapy before and especially after the transplant surgery.

The medical team are expecting to be inundated with applications in the months ahead. They will make an initial shortlist based on patient scans and medical notes and then invite a few potential volunteers for assessment in Poland. Those selected will undergo the same pioneering surgery that was performed on Darek Fidyka which was published in Cell Transplantation.



How Darek Fidyka's spinal injury was repaired

Analysis

Scientists have spent decades searching for a means of enabling the paralysed to walk again. Motorised exoskeletons, which are strapped on the body, bypassing the injury, are now available commercially.

Electrical stimulation techniques use implants to enable patients to flex their lower limbs. But neither method involves repairing the damaged spinal cord.

The approach in Poland aims to reconnect the brain with the lower limbs along the neural superhighway that is the spinal cord, enabling both motor control commands to travel down the body and sensation to travel up.

Darek Fidyka's spinal cord had been almost completely severed as a result of a knife attack, apart from a thin thread of external connective tissue and prior to the transplant, he had no feeling or control below his injury.

Now he has had to re-learn how to control his muscles and interpret sensations. He said: "I realise how important the brain is while cycling, and that thinking is more tiring than the exercise itself."

But the results from one patient, however impressive, would never be sufficient evidence on which to base a new approach to spinal cord injury. The forthcoming trial in Poland will be crucial if the wider scientific community is to be convinced that a patient's own cells can be used to regenerate their spinal cord.

It is also worth stressing that the patients selected will have to show enormous determination if they are to see the full benefits of the treatment.

In the first of two operations, surgeons will remove one of the patient's olfactory bulbs, which sit above the nasal cavity at the base of the brain, and process the sense of smell. The bulb contains specialist cells known as olfactory ensheathing cells (OECs) which act as a pathway that enables nerve fibres in the olfactory system to continually renew.

In a second operation the patient's OECs will be injected above and below the injury and strips of tissue laid across the gap in the cord. The team believe the OECs will enable nerve fibres to regenerate across the cord and so repair the damage.

An independent team of assessors led by neurophysiologists from Imperial College London will also be closely involved in monitoring the research.

Peter Ellaway, emeritus professor of physiology, at Imperial said: "I'm excited because this is a novel treatment with a lot of promise."

But he cautioned that even if it works it would take some years to refine and so would not be immediately available for patients.

The treatment in Poland will cost £250,000 per patient and is being funded by a small British charity, the Nicholls Spinal Injury Foundation (NSIF).

It was founded by chef David Nicholls after his 18-year-old son Daniel was paralysed from the neck down in a swimming accident.

Mr Nicholls said: "I know how important progress is to people living with spinal cord injury and am optimistic that success with the next two patients will result in an announcement that paralysis is curable."

NSIF and the UK Stem Cell Foundation both support the research of Prof Geoff Raisman, chair of neural regeneration at University College London (UCL), who has pioneered the use of OECs to repair the damaged spinal cord and leads the British side of the Walk Again project.

Prof Raisman said: "Darek's latest progress demonstrates the extraordinary power of (neuro) plasticity. But it depends on the patient's own efforts. It is like a baby learning to walk. We cannot teach it how. The progress comes from inside."

Darek underwent his transplant in April 2012, and he still spends five hours a day undergoing physiotherapy. He can now walk slowly using crutches or a small walking frame, but usually relies on a wheelchair as it is simply quicker and less

tiring.The return of sensation below his injury has brought other benefits like bladder control and the return of sexual function.

Darek was happy to discuss sex and explained that the reawakening of the erogenous zones was a crucial part of his recovery.

He said: "The return of sexual satisfaction - which travels along the spinal cord to the brain - is very important psychologically and is another part of my growing sense of independence."

http://bit.ly/1R1eLQw

Pint-Sized Lizards Trapped in Amber Give Clues to Life 100 Million Years Ago

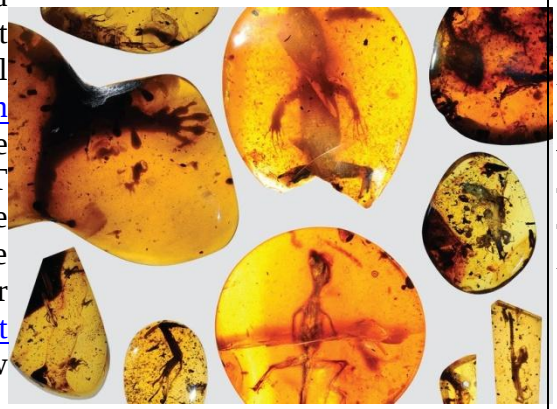
The trove of Cretaceous reptiles includes an early relative of the chameleon—the oldest yet discovered

By Maya Wei-Haas smithsonian.com

Nearly 100 million years ago, the tropical forests of the mid-Cretaceous period were hopping—winged beasts commanded the skies, large reptiles swaggered on land and insects buzzed around flowering plants that were just starting to flourish. Yet until now, little was known about small tropical lizards, whose fragile bones quickly disappeared when buried in the damp forest floors.

Now, scientists sifting through museum collections have described a dozen of these pint-sized reptiles all entombed in amber. The hapless lizards were caught in the sticky resin of ancient coniferous trees and remained suspended until the present day—several in exquisite condition with claws, bones, teeth, toe pads and even scales intact. These spectacular fossils give scientists a peek into life of the diminutive denizens of the mid-Cretaceous.

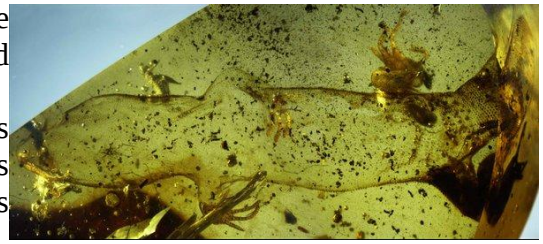
The fossils were actually discovered decades ago in a Burmese mine but remained in private collections until their recent donation to the American Museum of Natural History, which gave scientists access for study. Using CT scanners to image the fossils, the researchers could "digitally dissect" the lizards without harming the amber droplets, says postdoctoral student Edward Stanley, co-author of the new paper.



These ancient amber fossils from Burma in Southeast Asia help complete the patchy record of lizard evolution. **David Grimaldi**

What did they find? "A nice smattering of diversity," he says.

The set includes creatures similar to modern-day geckos and chameleons, as well as a range of species that sport a mash-up of features from both ancient and modern reptile relatives, according to the study published Friday in *Science Advances*. These animals help fill in the patchy evolutionary history of pint-sized lizards.



"This diverse lizard assemblage shows that back in the day, the tropics were as lizard-friendly as they are today," says Stanley.

Amber often has bizarre patterns of preservation, says de Queiroz. This lizard is just a shadow of the original creature with no skeleton or other innards remaining. **David Grimaldi**

Such wide variation is not necessarily unexpected, says Kevin de Queiroz, curator of the reptile and amphibian collection at the Smithsonian's National Museum of Natural History. "There's a fair amount of diversity in the tropics now," he says. "So it's not too surprising that they've been diverse in the past."

Even so, capturing this diversity in the fossil record is less common, says de Queiroz. The fossil record is strongly biased to large animals living in particular environments that can preserve creatures after their death, like deserts or riverbeds. The damp, hot climate in the tropics rarely preserves small and delicate fossils—unless the unfortunate creatures become trapped in tree resin. This ancient group therefore paints a much more complete picture of minute mid-Cretaceous reptiles than scientists have seen before.

One of the reptiles, a dime-sized baby relative of the chameleon, is the oldest discovered representative of that lineage, beating out the previous title-holder by nearly 80 million years. Chameleons' closest relative is the *agamidae*—a group that includes the bearded dragon lizards. Based on genetic evidence, chameleons were thought to have split from these relatives around the mid-Cretaceous period, but fossil evidence from this time had been lacking until now.

The fossils also help sort out when many of the modern reptile traits appeared. The tiny chameleon-like fossil shows early development of the lizards' ballistic tongues—evidenced by the presence of a large bone that supports the modern chameleon's sticky weapon, says Stanley. But the fossil did not have the specialized claw-like fused toes modern chameleons use to hang onto branches. Similarly, one of the gecko relatives has preserved toe pads with the modern designs already present.

"We actually have a really good representation of what we have today," says Stanley, "[just] 100 million years ago."

http://www.eurekalert.org/pub_releases/2016-03/osu-ttr030416.php

Time to rethink your vegetable oil?

Leaner bodies, less heart disease and diabetes risk found in people with higher levels of linoleic acid

COLUMBUS, Ohio - Risk of heart disease and diabetes may be lowered by a diet higher in a lipid found in grapeseed and other oils, but not in olive oil, a new study suggests.

Researchers at The Ohio State University found that men and women with higher linoleic acid levels tended to have less heart-threatening fat nestled between their vital organs, more lean body mass and less inflammation.

And higher linoleic acid levels also meant lower likelihood of insulin resistance, a precursor to diabetes.

This finding could have obvious implications in preventing heart disease and diabetes, but also could be important for older adults because higher lean body mass can contribute to a longer life with more independence, said Ohio State's Martha Belury, a professor of human nutrition who led the research.

But there's a catch. Low-cost cooking oils rich in linoleic acid have been disappearing from grocery shelves, fueled by industry's push for plants that have been modified to produce oils higher in oleic acid.

"Vegetable oils have changed. They're no longer high in linoleic acid," said Belury, an expert in dietary fats and part of Ohio State's Food Innovation Center.

The research appears online in the journal Molecular Nutrition & Food Research.

The research team also looked at the health effects of oleic acid, found in olive oil and some other vegetable oils, as well as long-chain omega-3 fatty acids, found in fatty fish including salmon and tuna.

Though inflammation decreased as blood levels of those fatty acids rose, higher levels of oleic acid or long-chain omega-3s did not appear to have any relationship to body composition or signs of decreased diabetes risk despite longstanding recommendations that people eat more of these "healthy" fats.

"It really kind of popped out and surprised us," Belury said.

Previous research found that taking linoleic acid supplements increased lean body mass and lowered fat in the midsection. As little as a teaspoon and a half was all it took, Belury said. The current study is the first study to examine linoleic acid alongside body composition and other health markers in people who hadn't been given supplements or prescriptive diets, she said.

Because of previous research showing cardiovascular benefits of linoleic acid, the American Heart Association in 2009 recommended people take in at least 5 to 10 percent of their energy in the form of omega-6 fatty acids, which includes linoleic acid.

But U.S. consumption of linoleic acid is declining because of genetic modification of plants for food manufacturers seeking oils higher in oleic acid, Belury said.

There's been a pronounced shift in the last five years, she said, and it is linked to the push against trans fats. When linoleic acid is made solid (hydrogenated) for processed foods, it is more likely to convert to trans fat than its oleic cousin.

So oils, notably safflower, sunflower and soybean, now routinely contain less linoleic acid - it often makes up less than 20 percent of the fatty acids in commonly purchased oils, based on food labels and confirmed by testing in her lab, Belury said.

Grapeseed oil for now remains an excellent source of linoleic acid, which constitutes about 80 percent of its fatty acids, she said. Corn oil also remains a decent source, she said.

The team used data from two previous studies that focused on stress and included 139 people. In those studies, researchers assessed body composition using DXA scanning, an advanced way of measuring fat and muscle mass.

They tested blood drawn after the men and women fasted for 12 hours, calculating the amount of linoleic acid (and other fatty acids) in red blood cells. All of the linoleic acid in our bodies comes from food sources.

They also evaluated the blood for insulin resistance and two markers of inflammation that are connected with disease.

Then they plotted results for each health category against the group's results for each of the three fat categories: linoleic acid, oleic acid and long-chain omega-3 fatty acids.

Belury said the study doesn't explain the apparent interplay between linoleic acid and measures of risk for heart disease and diabetes. It shows an association between those things, but not a cause and effect. And its power is limited because it relied on looking back on two previous research efforts and those involved middle-aged men and women who were slightly healthier on average than the general population.

The study participants lived in and around Columbus, Ohio. It's possible that the results would have been different in a population with diets that tend to be higher in omega-3 rich fatty fish, Belury said.

Financial support for the study came from the National Institutes of Health.

Belury's collaborators, all from Ohio State, were Rachel Cole and Jia-Yu Ke of the College of Education and Human Ecology, Brittney Bailey and Rebecca Andridge of the College of Public Health and Janice Kiecolt-Glaser, director of the Institute for Behavioral Medicine Research.

 Name _____ Student number _____