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New drug hope for mesothelioma

A new drug is showing promise as a treatment for mesothelioma - one of the most lethal cancers of all.

The drug, known as HRX9, works by preventing the cancer cells from avoiding apoptosis - the natural process by which unhealthy and damaged cells close themselves down and die.

"Both the immune system and nearby healthy cells send signals instructing damaged and unhealthy cells to undergo apoptosis, which is like programmed 'cell suicide'. But cancer cells have developed a wide range of strategies to ignore these instructions," says Professor Richard Morgan, from the University of Bradford's Institute of Cancer Therapeutics, who developed the drug and who led the research. "There's a range of drugs which try to force apoptosis in different cancers, but this is the first one to work in mesothelioma."

Mesothelioma is a cancer of the lining of the lung. It's almost invariably caused by exposure to asbestos and is resistant to all current chemotherapies. Its prognosis is dismal, with those diagnosed usually given a year to live at most.

A study by the universities of Bradford and Surrey found that after three weeks' treatment with HXR9, human mesothelioma tumours in mice stopped growing, with a complete loss of tumour blood vessels and widespread cancer cell death. The results are published in BMC Cancer journal.

HXR9 targets the HOX gene family, which includes 39 fairly similar genes that help enable the remarkably rapid cell division in growing embryos. Many of these genes are usually switched off in adults, but previous research has shown that in many cancers - including prostate, ovarian, and brain cancer, melanoma, and leukaemia - HOX genes are switched back on, helping the cancer cells to proliferate and survive. "We've effectively knocked out a key defence mechanism in this cancer through targeting the HOX genes," says Professor Morgan.

A further key finding reported in the study, funded by the British Lung Foundation, was that mesothelioma has a very strong association with one of the HOX genes in particular - known as HOXB4.

"We examined the amount of HOXB4 protein in tumours of 21 mesothelioma patients and compared it with their length of survival. There was a clear link: the more HOXB4 we found, the shorter time the patient survived, so we may also have found a way to predict which patients have the most aggressive form of this cancer," says Professor Morgan.

Because of greater awareness of the danger of asbestos in the West, the future incidence of mesothelioma is expected to decline. However, in Africa and some parts of Asia, asbestos is still commonly used in industries such as construction and ship building, and few precautions are taken when demolishing buildings that contain asbestos.

"Mesothelioma may become much less of a problem in the West, but it's still going to be a significant public health problem in many parts of the world. We already know that it's resistant to available drugs, which is why we need entirely new treatments," says Professor Morgan.

Ian Jarrold, Head of Research at British Lung Foundation said: "Although still early days, this study is a significant step forward in that it is the first time a drug has been observed causing so-called 'cell suicide' in mesothelioma.

"People living with mesothelioma often tell us that among their first reactions to diagnosis is despair at the lack of treatment available. We hope that the progress being made in research we fund will soon provide new treatments and new hope for patients."

http://www.eurekalert.org/pub_releases/2016-03/uouh-hip030916.php

Hidden in plain sight: Well-known drug could yield new treatment for herpes viruses

Heart failure drug shown to also inhibit Epstein Barr virus by targeting a pathway common to all herpesviruses

Today, there is only one class of antiviral medicines against herpesviruses -- a family of viruses that cause mononucleosis, herpes, and shingles, among other illnesses - meaning options for treating these infections are limited. If viruses become resistant to these frontline treatments, a growing problem particularly in clinical settings, there are no alternative drugs to serve as backup.

In a search for new drugs to treat viral infections, scientists from the University of Utah School of Medicine found that a medicine routinely used to treat heart failure, spironolactone, has an unexpected ability to block infection by Epstein Barr virus (EBV), a herpesvirus that causes mono and is associated with several human cancers. They find that the drug's antiviral properties stem from its ability to block a key step in viral infection that is common to all herpesviruses. Spironolactone's target is distinct from that of existing drugs, revealing that it could be developed into a new class of anti-herpesvirus drug.

"It's remarkable that a drug we have used safely in the clinic for over 50 years is also an effective EBV inhibitor," says senior author Sankar Swaminathan, M.D., chief of infections disease at University of Utah Health Care and professor of internal medicine. "It goes to show how basic research can reveal things we would never have found otherwise." In collaboration with research assistant professor of internal medicine Dinesh Virma, Ph.D., and Jacob Thompson, he published the study in the Proceedings of the National Academy of Sciences.

Swaminathan's team uncovered spironolactone's antiviral properties in a screen to identify drugs that work through a mechanism that is different from that of existing anti-herpesvirus drugs. Currently available drugs block a middle step of the viral infection cycle by inhibiting virus' ability to replicate DNA. They found that like these drugs, spironolactone can block EBV replication in cells, but it does so by targeting the so-called SM protein, required for a late step in the infection cycle.

Importantly, spironolactone's ability to block viral infection appears to be independent from its ability to treat heart failure. Previous studies showed that the drug treats heart failure through a different, metabolic mechanism. This study demonstrates that a drug similar to spironolactone shares its ability to treat heart failure but not its antiviral properties. Together the results suggest the two mechanisms are separable.

"We think there is great potential to modify this molecule so that it can work as an antiviral without having undesired side effects," explains Swaminathan. Spironolactone could be developed as a new medicine against EBV, a common and dangerous infection among transplant and other immunocompromised patients. But because all herpesviruses depend on SM-like proteins to spread infection, the work also has broader implications. Spironolactone could be a template for a new class of drug directed against all herpesviruses.

"We have found a new therapeutic target for herpesviruses," says Swaminathan. "We think it can be developed it into a new class of antiviral drugs to help overcome the problem of drug resistant infections."

"Spironolactone blocks Epstein Barr virus production by inhibiting EBV SM protein function" by Dinesh Verma, Jacob Thompson and Sankar Swaminathan will be published online in PNAS

http://bit.ly/1nQptvn

From Brains to Brawn: How T. Rex Became King of the Dinosaurs

The skull of a horse-size dinosaur, a distant relative of the colossal* Tyrannosaurus rex*, suggests that braininess was behind the beast's rise to dominance millions of years ago.

by Laura Geggel, Staff Writer | March 14, 2016 03:01pm ET

The dinosaur fossils, discovered in the desert of Uzbekistan, suggest that although early tyrannosaurs were small animals, they had advanced brains, said study lead researcher Steve Brusatte, a paleontologist at the University of Edinburgh in the United Kingdom. These keen brains likely helped tyrannosaurs become apex predators when they evolved into bigger beasts during the last 20 million years of the dinosaur age.

"Tyrannosaurs got smart before they got big, and they got big quickly right at the end of the time of the dinosaurs," Brusatte told Live Science.

T. rex may be famous, but little is known about its family tree. Tyrannosaurs originated about 170 million years ago in the mid-Jurassic, but they were mostly small, human- to horse-size dinosaurs at that time. Because of a 20-million-year gap in the fossil record, it's long been a mystery how these relatively small tyrannosaurs transitioned from marginal hunters to top predators, the researchers said in the study.

***This illustration shows* T. euotica *prowling around Central Asia about 90 million years. Back then, the Central Asian climate was less like a desert, and more forested with rivers and lakes.* Todd Marshall**

The new specimen fills that important gap. Paleontologists and study co-authors Alexander Averianov and Hans Sues discovered the tyrannosaur fossils in the Kyzylkum Desert of northern Uzbekistan. They dated the newfound species, named *Timurlengia euotica*, to the mid-Cretaceous, about 90 million years ago. During that time, Uzbekistan would have been hot and desertlike, but it also had forests, rivers and lakes, the researchers said.

"The middle Cretaceous is a mysterious time in evolution because fossils of land-living animals from this time are known from very few places," Averianov, of Saint Petersburg State University in Russia, said in a statement. "Uzbekistan is one of these places. The early evolution of many groups like tyrannosaurs took place in the coastal plains of central Asia in the mid-Cretaceous."

The paleontologists uncovered a number of fossils, including vertebrae, claws and teeth. But the tyrannosaur's braincase — the part of the skull that holds the brain — was, by far, the most significant finding, they said. In fact, the researchers teamed up with Brusatte because of his experience with studying the braincases of theropods (bipedal, mostly meat-eating dinosaurs).

Using a computer tomography (CT) scan, the researchers found that *T. euotica* might have been only about the size of a horse and likely weighed up to 550 lbs. (about 250 kilograms) — a pip-squeak compared to the 9-ton (8 metric tons) *T. rex* — but its brain and senses were highly developed.

"It has a really advanced brain, really advanced senses," Brusatte said.

The CT scan revealed that *T. euotica* had a long cochlea in its inner ear, which would have enabled it to hear low-frequency sounds.

"Low-frequency sounds allow you to hear potential prey, maybe from a longer distance, but just better in general," Brusatte said. "Tyrannosaurs were better at hearing low-frequency sounds than almost any other type of dinosaur."

The scan also allowed the scientists to digitally reconstruct the dinosaur's sinuses, nerves and blood vessels within its skull. "It turns out that it basically has the same type of brain as *T. rex*, just smaller, Brusatte said.

The rest of the skeleton also provided clues about *T. euotica*.

"*Timurlengia* was a nimble pursuit hunter with slender, bladelike teeth suitable for slicing through meat," Sues, a curator of vertebrate paleontology at the Smithsonian Museum of Natural History in Washington, D.C., said in the statement. "It probably preyed on the various large plant eaters, especially early duck-billed dinosaurs, which shared its world."

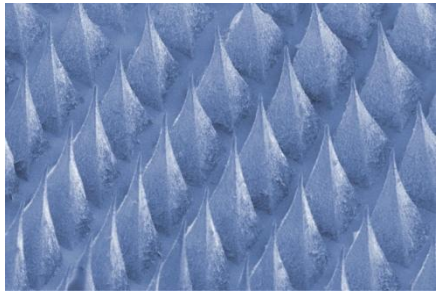
The study was published online today (March 14) in the journal Proceedings of the National Academy of Sciences.

http://www.eurekalert.org/pub_releases/2016-03/uonc-scp031416.php

Scientists create painless patch of insulin-producing beta cells to control diabetes

This new 'smart cell patch' developed at UNC and NC State is a proof of principle to treat millions of people with type-1 and advanced type-2 diabetes

CHAPEL HILL, NC - For decades, researchers have tried to duplicate the function of beta cells, the tiny insulin-producing entities that don't work properly in patients with diabetes. Insulin injections provide painful and often imperfect substitutes. Transplants of normal beta cells carry the risk of rejection or side effects from immunosuppressive therapies.



This is a scanning electron microscopic (SEM) image of the microneedle-array patch developed in the lab of Zhen Gu, Ph.D. **Zhen Gu, NC State / UNC**

Now, researchers at the University of North Carolina at Chapel Hill and North Carolina State University have devised another option: a synthetic patch filled with natural beta cells that can secrete doses of insulin to control blood sugar levels on demand with no risk of inducing hypoglycemia.

The proof-of-concept builds on an innovative technology, the "smart insulin patch," reported last year in the Proceedings of the National Academy of Sciences. Both patches are thin polymeric squares about the size of a quarter and covered in tiny needles, like a miniature bed of nails. But whereas the former approach filled these needles with manmade bubbles of insulin, this new "smart cell patch" integrates the needles with live beta cells.

Tests of this painless patch in small animal models of type-1 diabetes demonstrated that it could quickly respond to skyrocketing blood sugar levels and significantly lower them for 10 hours at a time. The results were published in Advanced Materials.

"This study provides a potential solution for the tough problem of rejection, which has long plagued studies on pancreatic cell transplants for diabetes," said senior author Zhen Gu, PhD, assistant professor in the joint UNC/NC State department of biomedical engineering. "Plus it demonstrates that we can build a bridge between the physiological signals within the body and these therapeutic cells outside the body to keep glucose levels under control."

Beta cells typically reside in the pancreas, where they act as the body's natural insulin-producing factories. In healthy people, they produce, store, and release the hormone insulin to help process sugar that builds up in the bloodstream after a meal. But in people with diabetes, these cells are either damaged or unable to produce enough insulin to keep blood sugar levels under control.

Diabetes affects more than 387 million people worldwide, and that number is expected to grow to 500 million by the year 2030. Patients with type-1 and advanced type-2 diabetes must regularly monitor their blood sugar levels and inject themselves with varying amounts of insulin, a process that is painful and imprecise. Injecting the wrong amount of medication can lead to significant complications like blindness and limb amputations, or even more disastrous consequences such as diabetic comas and death.

Since the 1970s, researchers have researched transplantation of insulin-producing cells as an alternative treatment for diabetes. The first successful transplant of human beta cells was performed in 1990, and since then hundreds of diabetic patients have undergone the procedure. Yet, only a fraction of treated patients achieved normal blood sugar levels. Most transplants are rejected, and many of the medications used to suppress the immune system wind up interfering with the activity of beta cells and insulin. More recently, researchers have been experimenting with ways to encapsulate beta cells into biocompatible polymeric cells that could be implanted in the body.

Gu, who also holds appointments in the UNC School of Medicine, the UNC Eshelman School of Pharmacy, and the UNC Diabetes Care Center, decided to create a device that would put the blood-sugar buffering properties of beta cells out of reach of the patient's immune system. Lead author Yanqi Ye, a graduate student in Gu's lab, constructed the "smart cell patches" using natural materials commonly found in cosmetics and diagnostics. She stuffed the hundreds of microneedles, each about the size of an eyelash, with culture media and thousands of beta cells that were encapsulated into microcapsules made from biocompatible

alginate. When applied to the skin, the patch's microneedles poked into the capillaries and blood vessels, forming a connection between the internal environment and the external cells of the patch.

Ye also created "glucose-signal amplifiers," which are synthetic nanovesicles filled with three chemicals to make sure the beta cells could "hear" the call from rising blood sugar levels and respond accordingly.

Gu's group showed that blood sugar levels in diabetic mice quickly declined to normal levels. To assess whether the patch could regulate blood sugar without lowering it too much, the researchers administered a second patch to the mice. As they had hoped, repeated administration of the patch did not result in excess doses of insulin, and thus did not risk hypoglycemia. Instead, the second patch extended the life of the treatment to 20 hours.

Further modifications, pre-clinical tests, and eventually clinical trials in humans will all be necessary before the patch can become a viable option for patients. But for now, the researchers believe their results provide a proof of principle for an alternative approach that could be safer and less cumbersome than current treatments.

"Managing diabetes is tough for patients because they have to think about it 24 hours a day, seven days a week, for the rest of their lives," said co-author John Buse, MD, PhD, professor of medicine at the UNC School of Medicine and director of the UNC Diabetes Care Center and the NC Translational and Clinical Sciences Institute. "These smart insulin approaches are exciting because they hold the promise of giving patients some time off with regards to their diabetes self-care. It would not be a cure but a desperately needed vacation."

The research was funded by grants from NC TraCS, home of the NIH Clinical and Translational Science Award at UNC, the American Diabetes Association, and the National Science Foundation through the ASSIST Engineering Center at NC State.

Study co-authors from UNC were Jicheng Yu, Chao Wang, Nhu-Y Nguyen, and Glenn M. Walker.

http://www.eurekalert.org/pub_releases/2016-03/b-pi031016.php

'Difficult' patients increase doctors' misdiagnosis risk regardless of case complexity

Mental effort needed to deal with behavior distracts from task in hand, say researchers

Patients regarded as 'difficult' increase doctors' risk of getting a diagnosis wrong, irrespective of the time spent or the complexity of the case, finds research published online in BMJ Quality & Safety. This is because the mental effort needed to deal with the problematic behaviour distracts from the task at hand--processing the clinical information correctly--concludes a companion study in the journal.

It is assumed that a doctor's response to patients regarded as 'difficult' could affect the accuracy of the diagnosis s/he makes, but to date there's been no empirical evidence to back that up. The researchers therefore set about testing this by providing 63 doctors in the last year of their specialty training in family medicine with one of two versions of six clinical case scenarios. One version portrayed a 'difficult' patient with one of six conditions and the other described the same patient, but without the disruptive behaviour (neutral).

The difficult behaviours portrayed included a demanding patient; an aggressive patient; one who questions the doctor's competence; one who ignores the doctor's advice; one who doesn't expect the doctor to take him seriously; and one who is utterly helpless.

The six conditions comprised: pneumonia; a blood clot in the lung (pulmonary embolism); brain inflammation (meningoencephalitis); overactive thyroid (hyperthyroidism); appendicitis; and inflammation of the pancreas caused by excess alcohol (acute alcoholic pancreatitis).

The latter three cases were deemed to be more complex. All included a brief description of the patient's medical history, their signs and symptoms, and the findings of the physical examination.

The doctors were asked to write down the most likely diagnosis as quickly as possible and then to review the same case, writing down the information for and against the diagnosis they had made, and to offer an alternative if they had got it wrong first time around. Finally, they were asked to rate the likeability of the patient, using a validated (Likert) scale.

The results showed that not unexpectedly, diagnostic accuracy was higher for simpler cases. But the doctors were 42% more likely to misdiagnose a difficult patient than a 'neutral' one in a complex case, and 6% more likely to do so in a simple case. The findings held true, irrespective of the time spent on diagnosis. Similarly, further reflection improved diagnostic accuracy, but it didn't make up for the impact of disruptive behaviours.

The average likeability ratings were significantly lower for patients portrayed as 'difficult' than they were for those portrayed as behaving neutrally.

In the second study 74 trainee hospital doctors were asked to diagnose eight clinical case scenarios, half of which involved difficult behaviours and half of which involved neutral behaviours.

The additional behaviours in this study included a patient who threatens the doctor and one who accuses the doctor of discrimination. After making the diagnosis, the doctors were asked to recall the clinical findings and behaviours of each patient.

Diagnostic accuracy was 20% lower for difficult patients, even though the time spent on diagnosis was similar. The doctors also recalled proportionally fewer clinical findings (30% compared with 32.5%) and more behaviours (25% compared with 18%) in these patients. This suggests that the mental energy needed to deal with the problematic behaviour interferes with processing the clinical information correctly, say the researchers.

They accept that vignettes don't necessarily reflect real doctor-patient interactions, and therefore clinical practice. But the potential negative impact of difficult behaviours is likely to be stronger in real life, they suggest.

And they nevertheless conclude that although the prevailing view is that doctors should be above reacting in this way to difficult patients..."the fact is, that difficult patients trigger reactions that may intrude with reasoning, adversely affect judgements, and cause errors." They suggest that efforts should be made to boost medical students' and doctors' awareness of this.

In a linked editorial, Drs Donald Redelmeier and Edward Etchells of the Centre for Quality Improvement and Patient Safety, University of Toronto, Canada, say the results echo previous analyses, suggesting that unpleasant people tend to have more unfavourable outcomes.

They suggest that doctors should engage in more reflection, teamwork, and consultation and consider checklists or computer assisted diagnostics to mitigate the effects of difficult behaviours on diagnostic accuracy.

http://www.eurekalert.org/pub_releases/2016-03/uonc-nsv031416.php

New SARS-like virus is poised to infect humans

The new virus, known as WIV1-CoV, directly binds to the same human receptor as the SARS strain that infected thousands in 2002

The new virus, known as WIV1-CoV, directly binds to the same human receptor as the SARS strain that infected thousands in 2002

(Chapel Hill, N.C. - March 14, 2016) - A SARS-like virus found in Chinese horseshoe bats may be poised to infect humans without the need for adaptation, overcoming an initial barrier that could potentially set the stage for an outbreak according to a study at the University of North Carolina at Chapel Hill.

The work, led by Ralph Baric, Ph.D., professor of epidemiology at UNC's Gillings School of Global Public Health, comes on the heels of two recent high-profile outbreaks - Ebola and Zika - for which there are no vaccines. The two outbreaks combined claimed thousands of lives and cost billions in foregone economic growth.

"The capacity of this group of viruses to jump into humans is greater than we originally thought," said Vineet Menachery, Ph.D., the study's first author. "While other adaptations may be required to produce an epidemic, several viral strains circulating in bat populations have already overcome the barrier of replication in human cells and suggest reemergence as a distinct possibility."

Baric and Menachery worked with SARS-like coronavirus sequences isolated from Chinese horseshoe bats, where SARS originated. Based on the sequences, they reconstructed the viruses to evaluate their potential to infect human cells and in mice.

They found that the newly identified virus, known as WIV1-CoV, could bind to the same receptors as SARS-CoV. They also showed that the virus readily and efficiently replicated in cultured human airway tissues, suggesting an ability to jump directly to humans.

"To be clear, this virus may never jump to humans, but if it does, WIV1-CoV has the potential to seed a new outbreak with significant consequences for both public health and the global economy," said Vineet, whose work is reported in the Mar. 13, 2016 online version of the Proceedings of the National Academy of Sciences.

The research team also found that antibodies developed to treat SARS were effective in both human and animal tissue samples against WIV1-CoV, providing a potent treatment option if there were an outbreak.

However, the limitation to treat with antibodies is the same as with ZMapp, the antibody approach used for Ebola: producing it at a large enough scale to treat many people. Also, in terms of prevention, existing vaccines against SARS would not provide protection for this new virus due to slight differences in the viral sequence.

SARS, short for severe acute respiratory syndrome, was first seen in an outbreak in 2002 and resulted in 8,000 cases and nearly 800 deaths. Spread through airborne contact, its onset presents symptoms similar to the flu with a dry cough but can accelerate rapidly to pneumonia, filling the lungs with fluid and putting extreme stress on the body's immune system.

According to the Centers for Disease Control and Prevention, SARS' mortality rate can range from less than one percent in patients below 24 years old to more than 50 percent in patients aged 60 and older. Baric and his team believe that WIV1-CoV has the potential to induce similar results with proper adaptation to humans.

"This type of work generates information about novel viruses circulating in animal populations and develops resources to help define the threat these pathogens may pose to human populations," Baric said.

"It's important to note that it's not an approach that's limited to SARS or SARS-like viruses. It can be applied to other emerging pathogens to helping us prepare for the next emergent virus, whether it be MERS, the Zika virus or something we haven't even heard of yet."

http://www.eurekalert.org/pub_releases/2016-03/dumc-nyt031416.php

Need your thyroid removed? Seek a surgeon with 25+ cases a year

Surgeons who perform 25 or more thyroidectomies a year have the least risk of complications

DURHAM, N.C. -- A new study from Duke Health suggests that patients who need to have their thyroid gland removed should seek surgeons who perform 25 or more thyroidectomies a year for the least risk of complications.

Thyroidectomy is one of the most common operations performed in the U.S, often due to cancer, over-activity, or enlargement of the gland, which is located at the base of the throat and produces hormones that regulate metabolism. But most consumers would be surprised to learn that about half (51 percent) of surgeons who perform thyroidectomy do so just once a year, according to the study published in the Annals of Surgery.

More Cases Lead to Better Surgical Outcomes

Patients of low-volume surgeons (25 or fewer thyroidectomies per year') have an increased risk for complications when compared to patients of high-volume surgeons (26 or more operations a year)

Thyroidectomies Per Year	Risk of Complication
1 case	*87 percent increased risk*
2-5 cases	*68 percent increased risk*
6-10 cases	*42 percent increased risk*
11-15 cases	*22 percent increased risk*
16-20 cases	*10 percent increased risk*
21-2:5 cases	*3 percent increased risk*

Duke Health

"This is a very technical operation, and patients should feel empowered to ask their surgeons how many procedures they do each year, on average," said Julie A. Sosa, M.D., senior author and chief of endocrine surgery at Duke. "Surgeons have an ethical responsibility to report their case numbers. While this is not a guarantee of a positive outcome, choosing a more experienced surgeon certainly can improve the odds that the patient will do well."

Although total thyroidectomy is generally safe, it can cause life-altering complications that were seen in some study patients, such as bleeding, problems with the parathyroid glands, and damage to the laryngeal nerve that can lead to difficulty speaking, breathing and swallowing. Any complication can require more care, driving up patient costs and potentially compromising quality of life.

The study evaluated data from 16,954 patients who had thyroidectomies between 1998 and 2009 and were enrolled in a national database from the Health Care Utilization Project.

In analyzing the case volumes of 4,627 surgeons, researchers found an association between the number of procedures surgeons performed each year and rates of complications. Notably, patients of surgeons who performed fewer than 25 thyroidectomies a year were 1.5 times more likely to experience complications.

As the average number of cases increased, the risk of complications for patients steadily decreased. Risks leveled out for surgeons who performed an average of 25 or more operations a year.

"Thyroid nodules, which can give rise to thyroid cancer, are a growing health issue, partly because we have better imaging and are able to discover them more easily," Sosa said. "As many as 68 percent of healthy adults have thyroid nodules, and this, in part, has significantly increased the number of biopsies and surgeries performed in the U.S."

"Surgeon volume is one factor doctors and patients should consider as we talk about value-based care -- helping patients get appropriate care at an optimized cost and with fewer complications," Sosa said.

In addition to Sosa, study authors include Mohamed Abdelgadir Adam, M.D.; Samantha Thomas; Linda Youngwirth, M.D.; Terry Hyslop, Ph.D.; Shelby D. Reed, Ph.D.; Randall P. Scheri, M.D.; and Sanziana A. Roman, M.D.

http://www.eurekalert.org/pub_releases/2016-03/kl-cii031416.php

Children in intensive care recover faster with little to no nutrition

Critically ill children are artificially fed soon after their arrival in intensive care.

This common practice is based on the assumption that it will help them recover more quickly. An international study coordinated at KU Leuven, Belgium, has now disproven this theory. The study shows that receiving little to no nutrition during the first week in intensive care makes children recover faster.

Critically ill children in intensive care are unable to eat independently. The current standard of care for such children is based mostly on the assumption that they need to eat to regain their strength. Therefore, the method that is applied worldwide is to artificially feed these children during the first days of their stay in intensive care. This artificial nutrition is meant to strengthen their muscles, prevent complications, and speed up their recovery. The artificial nutrition is infused directly into the bloodstream.

An international team of researchers from University Hospitals Leuven (Belgium), Sophia Children's Hospital Rotterdam (The Netherlands), and Stollery Children's Hospital Edmonton (Canada) has now challenged the validity of this common practice. They conducted a randomized controlled trial that involved 1,440 critically ill children. The researchers examined whether fasting or receiving very small amounts of feeding during the first week in the paediatric intensive care unit was better for the children than full feeding through an IV.

The results are remarkable. "We found that the current practice of feeding children in an early stage does not contribute to their recovery", says lead author

Professor Greet Van den Berghe from KU Leuven / University Hospitals Leuven. "On the contrary, the children who had built up a nutritional deficiency after receiving little to no feedings had fewer infections, less organ failure, and a quicker recovery than children who had been fed through the IV. The effect was present in everyone, regardless of the type of disease, the children's age, or the hospital in which they were staying." These findings provide strong evidence against current practice and can thus be expected to change paediatric intensive care worldwide.

Previous research by Professor Van den Berghe and her team (2011 and 2014) had already shown that early artificial feeding should be avoided to treat adults in intensive care.

http://bit.ly/1RafHNc

Drug may have hit wrong brain target in French clinical trial

Experimental painkiller that killed one and severely injured five others in a clinical trial may have acted on parts of the brain that it was not supposed to

An experimental painkiller that killed one volunteer and severely damaged the brains of five others in a clinical trial in Rennes, France, may have acted on parts of the brain that it was not supposed to, a committee investigating the incident has concluded. It recommends that safety rules for clinical trials be tightened up globally.

The trial was looking at a drug called BIA 10-2474, a painkiller developed by Portuguese firm Bial. In total, 90 volunteers received the drug. The six who were harmed received the highest total dose: 50 milligrams per day up to cumulative amounts of between 250 and 300 milligrams, at which point symptoms rapidly kicked in.

In its interim report, the committee appointed by the French National Agency for Medicines and Health Products Safety concluded that the damage was almost certainly “an off-target effect”.

BIA 10-2474 is meant to work by allowing the painkilling neurotransmitter anandamide to accumulate in the brain. The drug does this by blocking the enzyme FAAH, which would otherwise break anandamide down.

The investigators suspect that at the high doses some volunteers received – 40 times above what is needed to block all FAAH – the drug may start disrupting brain enzymes other than FAAH. Another possibility is that the surplus anandamide may cause damage either by activating other molecules in the brain or by breaking down into harmful substances.

The committee calls for stricter rules for trials, including a ban on doses vastly in excess of those needed to achieve the intended effect.

A fuller report will be released when the committee next meets on 24 March.

http://www.eurekalert.org/pub_releases/2016-03/icl-pma031516.php

Photosynthesis more ancient than thought, and most living things could do it

More primitive form of photosynthesis evolved in much more ancient bacteria than scientists had imagined, more than 3.5 billion years ago

Photosynthesis is the process by which plants, algae and cyanobacteria use the energy from the Sun to make sugar from water and carbon dioxide, releasing oxygen as a waste product. But a few groups of bacteria carry out a simpler form of photosynthesis that does not produce oxygen, which evolved first.

A new study by an Imperial researcher suggests that this more primitive form of photosynthesis evolved in much more ancient bacteria than scientists had imagined, more than 3.5 billion years ago.

Photosynthesis sustains life on Earth today by releasing oxygen into the atmosphere and providing energy for food chains. The rise of oxygen-producing photosynthesis allowed the evolution of complex life forms like animals and land plants around 2.4 billion years ago.

However, the first type of photosynthesis that evolved did not produce oxygen. It was known to have first evolved around 3.5-3.8 billion years ago, but until now, scientists thought that one of the groups of bacteria alive today that still uses this more primate photosynthesis was the first to evolve the ability.

But the new research reveals that a more ancient bacteria, that probably no longer exists today, was actually the first to evolve the simpler form of photosynthesis, and that this bacteria was an ancestor to most bacteria alive today. "The picture that is starting to emerge is that during the first half of Earth's history the majority of life forms were probably capable of photosynthesis," said study author Dr Tanai Cardona, from the Department of Life Sciences at Imperial College London.

The more primitive form of photosynthesis is known as anoxygenic photosynthesis, which uses molecules such as hydrogen, hydrogen sulfide, or iron as fuel - instead of water.

Traditionally, scientists had assumed that one of the groups of bacteria that still use anoxygenic photosynthesis today evolved the ability and then passed it on to other bacteria using horizontal gene transfer - the process of donating an entire set of genes, in this case those required for photosynthesis, to unrelated organisms.

However, Dr Cardona created an evolutionary tree for the bacteria by analyzing the history of a protein essential for anoxygenic photosynthesis. Through this, he was able to uncover a much more ancient origin for photosynthesis.

Instead of one group of bacteria evolving the ability and transferring it to others, Dr Cardona's analysis reveals that anoxygenic photosynthesis evolved before most

of the groups of bacteria alive today branched off and diversified. The results are published in the journal PLOS ONE.

"Pretty much every group of photosynthetic bacteria we know of has been suggested, at some point or another, to be the first innovators of photosynthesis," said Dr Cardona. "But this means that all these groups of bacteria would have to have branched off from each other before anoxygenic photosynthesis evolved, around 3.5 billion years ago.

"My analysis has instead shown that anoxygenic photosynthesis predates the diversification of bacteria into modern groups, so that they all should have been able to do it. In fact, the evolution of oxygneic photosynthesis probably led to the extinction of many groups of bacteria capable of anoxygenic photosynthesis, triggering the diversification of modern groups."

To find the origin of anoxygenic photosynthesis, Dr Cardona traced the evolution of BchF, a protein that is key in the biosynthesis of bacteriochlorophyll a, the main pigment employed in anoxygenic photosynthesis. The special characteristic of this protein is that it is exclusively found in anoxygenic photosynthetic bacteria and without it bacteriochlorophyll a cannot be made. By comparing sequences of proteins and reconstructing an evolutionary tree for BchF, he discovered that it originated before most described groups of bacteria alive today.

http://www.eurekalert.org/pub_releases/2016-03/uoc-net031116.php

No evidence that genetic tests change people's behavior

Genetic tests that estimate an individual's risk of developing diseases do not appear to motivate a change in behaviour to reduce the risk

Genetic tests that provide an estimate of an individual's risk of developing diseases such as lung cancer and heart disease do not appear to motivate a change in behaviour to reduce the risk, according to a study led by the University of Cambridge and published in The BMJ today.

Researchers at the Behaviour and Health Research Unit analysed a number of studies that looked at whether testing an individual's DNA for genetic variants that increased their risk of developing so-called 'common complex diseases' influenced their health-related behaviour. Complex diseases are those such as heart disease, most cancers and diabetes, where no single gene causes the disease, but rather it is the interaction of dozens -- possibly hundreds -- of genes together with an individual's environment and behaviour that leads to the disease.

Genome sequencing -- reading an individual's entire DNA -- has opened up the potential to provide individuals with information on whether or not they carry genes known to increase their risk of disease. Such tests are controversial -- knowing that an individual carries these variants does not mean that individual will develop the disease; however, proponents argue that if an individual knows that he or she is at a greater risk of a particular disease, they can make an informed decision about whether or not to change their behaviour.

In the early 2000s, several companies launched direct-to-consumer tests for a range of common complex disorders, and these tests continue to be sold in Canada, the United Kingdom, and other European countries. In 2013 in the United States, the Food and Drug Administration ordered the company 23andme to stop selling its testing kits because of concerns about their accuracy and usefulness, but in October 2015 the company resumed selling some health related services.

The Cambridge researchers examined over 10,000 abstracts from relevant studies and identified from these 18 studies that matched their criteria for inclusion in their analysis. By compiling the data, they found that informing individuals of their genetic risk had little or no effect on their health-related behaviour, particularly for smoking cessation and physical activity.

Professor Theresa Marteau, who led the study, says: "Expectations have been high that giving people information about their genetic risk will empower them to change their behaviour - to eat more healthily or to stop smoking, for example - but we have found no evidence that this is the case. But nor does the evidence support concerns that such information might demotivate people and discourage them from changing their behaviour."

However, the researchers recognise that DNA testing may still play a role in improving people's health. "DNA testing, alone or in combination with other assessments of disease risk, may help clinicians identify individuals at greatest risk and allow them to target interventions such as screening tests, surgery, and drug treatments," explains co-author Dr Gareth Hollands.

The team argue that these results are consistent with other evidence that risk communication typically has at best only a small effect on health behaviour.

The study was funded by the Medical Research Council and the National Institute for Health Research.

Hollands, GJ et al. The impact of communicating genetic risks of disease on risk-reducing health behaviour: systematic review with meta-analysis. BMJ; March 15, 2016; http://www.bmj.com/cgi/doi/10.1136/bmj.i1102

http://www.eurekalert.org/pub_releases/2016-03/bumc-mem031516.php

Mismatched expectations most common reason for patients not completing HPV vaccine series

Conflicting expectations between parents and medical providers about responsibility for scheduling follow-up appointments results in young girls failing to complete the HPV vaccination series

BOSTON-- Conflicting expectations between parents and medical providers about who is responsible for scheduling follow-up appointments is resulting in a failure

of young girls completing the Human Papilloma Virus (HPV) vaccination series, according to a new study led by Boston Medical Center researchers. The study, which is published online ahead of print in the journal Human Vaccines and Immunotherapeutics, involved interviews with both parents and providers in order to determine why, despite the known benefits of the vaccine, patients are not receiving all three doses.

HPV, the most common sexually transmitted infection, is diagnosed in approximately 14 million people each year in the United States and can lead to various cancers including cervical, mouth and throat cancer. The HPV vaccine is administered in a three-part series over six months and is currently recommended for boys and girls ages 11 and 12 and up to age 26. Recently, the Centers for Disease Control and Prevention (CDC) encouraged expanding the vaccine's availability to 9- and 10-year-olds if they have a history of sexual abuse and officially endorsed using the HPV-9 vaccine, which protects against nine strains of the virus.

"There has been a heightened awareness within the medical community in recent years about the need to address HPV and get more children vaccinated in order to prevent long-term health issues," said Rebecca Perkins, MD, MSc, an obstetrician at BMC and lead author of the study. "Yet, we're finding that many pre-teens aren't getting all three doses, which is imperative to preventing HPV."

Over a one-year period, researchers interviewed 65 parents whose daughters received at least one dose of the HPV vaccine and divided them into groups whose daughters had completed the series (28) and those who had not (37). Of the group whose daughters did not finish the series, 65 percent said they expected the clinic to contact them regarding scheduling additional doses. Twenty-four percent cited inconvenience, such as long commutes to the clinic, for failing to complete the series, only 4 parents made a conscious decision to halt the series.

Next, 27 providers were interviewed about their specific plans to ensure patients completed the series. Fifty-two percent said they informed parents about when the next doses were due, but relied on the parents to schedule the follow-up visits. Forty-one percent planned on scheduling the second dose when the first dose was given and 7 percent hoped to immunize patients when they returned for a different appointment. Providers stated that most failures to complete the series were due to a lack of reminder systems.

Interestingly, no provider identified the need for three doses as a barrier to completion, and more than two-thirds of the parents in both groups stated that they felt that the benefits of HPV vaccination outweighed the risks.

"What we've learned is that there is a great opportunity to close the non-completion gap by improving education and dialogue between providers and parents about scheduling future visits to finish the three-dose vaccination series," Perkins said.

Researchers had several suggestions for increasing vaccination completion rates, including scheduling follow-up appointments as the child receives the first dose; implementing reminder and recall systems in clinics, such as phone calls, educational brochures, and text messages; having patients receive reminders directly from state immunization registries, which are independent from individual medical practices; and offering vaccines at alternative sites that are more convenient for parents such as schools and pharmacies.

"By implementing a reminder system, we hope that more children will complete the vaccination series, which can help improve the overall health of our next generation," Perkins said.

http://www.eurekalert.org/pub_releases/2016-03/uoc--erp031516.php

Employee recognition programs can reduce firm-level productivity

UCR study shows costly unintended consequences from employee award programs

RIVERSIDE, Calif. - More than 80 percent of companies use award programs like "Employee of the Month" and "Top Sales Club" to motivate employees and increase performance. While the conventional wisdom is that such awards are cheap and can provide a subtle way to motivate employees, these programs might be reducing firms' overall productivity, according to a new study led by a researcher at the University of California, Riverside.

Recently accepted for publication in the journal Organization Science, "Motivational Spillovers from Awards: Crowding Out in a Multitasking Environment" is the first academic study to show that seemingly innocuous non-financial award programs can be costly to firms, primarily because they can upset the status quo and influence perceptions of equity and fairness. This can lead to internally motivated employees becoming disenfranchised.

The study was led by Timothy Gubler, assistant professor of management in UCR's School of Business Administration, together with Ian Larkin from the University of California, Los Angeles, and Lamar Pierce from Washington University in St. Louis.

For years, researchers have studied the unintentional side effects of monetary rewards that tie pay with performance. Such rewards can reduce employees' intrinsic motivation, cause workers to focus less on tasks not recognized financially, and lead to a tendency for employees to play or "game" the system. Conversely, non-monetary recognitions and small nominal awards like gift cards

are widely believed to avoid these unintended consequences and present a costless way to motivate employees.

"The common knowledge is that non-monetary awards can subtly motivate people in ways that are fundamentally different to financial reward programs, such as by increasing organizational loyalty, encouraging friendly competition, or increasing employees' self-esteem," Gubler said. "In fact, past research has focused almost exclusively on the benefits of these programs, and the costs have been considered negligible."

To explore the potential downsides of award programs, the researchers used field data from an attendance award program implemented at one of five industrial laundry plants in the Midwest United States. With the plant relying heavily on worker efficiency for overall productivity, the program was designed to recognize all employees with perfect attendance -- defined as coming on time to work and not having any unexcused absences. Each month, employees with perfect attendance were recognized at a plant-wide meeting, with one person receiving a $75 gift card through a random draw.

Using data from the company and a statistics technique called difference-in-differences (DiD), the researchers analyzed data from all five plants both before and after the award was implemented, exploring the award's effects on individual workers' performance and plant productivity as a whole. The found:

Reward-motivated employees responded positively to the awards by reducing tardiness, but gamed the system to maintain eligibility using sick days and reverted back to poor attendance behavior when they lost eligibility in a given month.

The awards crowded out intrinsic motivation in internally-motivated employees, who were already performing well by coming on time in the absence of rewards. These employees had increased tardiness after the program was implemented and they lost eligibility.

The awards decreased motivation and productivity for internally-motivated workers, suggesting these employees were unhappy because of fairness and equity concerns.

In total, the award program cost the plant 1.4 percent of daily productivity, mainly because of the lost productivity by internally-motivated employees.

Gubler said the research is among the first to show that motivational awards can be costly to firms, rather than beneficial.

"Conscientious internally-motivated employees who were performing well before the award program was introduced felt the program was unfair, as it upset the balance of what was perceived as equitable or fair in the organization. So their performance suffered -- not just in terms of their attendance but also through a motivational spillover that affected other areas of their work -- including productivity," he said.

Gubler said firms should carefully consider not only the benefits but also the costs of implementing such programs, and realize an award can cause the same issues as a bonus or other compensation.

"Employees value workplace fairness and they care about how they're perceived relative to others in the organization. To be effective, companies offering award programs need to consider not only the group they are targeting -- such as those that are coming late to work -- but also those that are already doing the right thing, as there is a possibility of demotivating some of their best employees."

http://www.eurekalert.org/pub_releases/2016-03/mri-ntf031516.php

New treatment for common incurable eye condition

MedInsight Research Institute and Ariel University Center for Drug Repurposing present new pterygium/pinguecula treatment results at Israeli Ophthalmology Conference

At the Israeli Society for Vision and Eye Research (ISVER) conference on March 10, the MedInsight Research Institute and Center for Drug Repurposing at Ariel University presented the latest findings on positive user-reported outcomes of the repurposed drug dipyridamole in treating pterygium and related dry-eye symptoms.

Dipyridamole is a cardiovascular drug, used for the past 55 years for treating angina and preventing stroke. It also has wide applicability for eye disorders, having been researched for various eye ailments over the past four decades, including diabetic retinopathy, ocular hypertension and retinal hemorrhage. In 2014, MedInsight published the first case report of a pterygium patient being successfully treated with dipyridamole eye drops.

Pterygium, or Surfer's Eye, is a benign growth that affects 10% of the population worldwide. It is more prevalent with older age. An early-stage pterygium is known as a pinguecula, and affects 50% of the population. Besides being unsightly, pterygium and pinguecula often become inflamed and cause dry eye. Eventually, they can completely obstruct vision.

In the findings presented at ISVER in Kfar Maccabia, Israel, researchers analyzed outcomes of dry-eye symptoms reported by patients with pterygium. Using a well-accepted survey known as the Ocular Surface Disease Index, OSDI, the researchers found that there was a maximum reduction in OSDI scores averaging 52.4% during the course of treatment for 25 patients. Some patients reported a complete resolution of symptoms. Photographic evidence showed marked antiangiogenic effects and regression of the pterygia.

"These results are very exciting," said Moshe Rogosnitzky, director of the Center for Drug Repurposing at Ariel University, who discovered this novel treatment. "Until now, the only known treatment for pterygium has been surgical removal,

which involves a high recurrence rate. In addition, patients are often given topical steroids to treat their symptoms, but this can result in glaucoma. Now we have a promising potential treatment for this very difficult to treat disorder, and it appears to be not only effective, but entails only a small amount of a very safe medicine. This treatment possibility offers very distinct advantages over the existing treatment offered."

Aaron Frenkel, research coordinator for MedInsight, added that studies are currently being planned at medical centers in Israel, Europe, Turkey and India. "This drug does not yet have commercial sponsorship, so studies are taking longer to initiate since research funds are dependent on donors. We are hopeful that clinical trials will begin later this year," said Frenkel.

http://www.eurekalert.org/pub_releases/2016-03/c-ub-ofa031516.php

Omega-3 fatty acids shown to exert a positive effect on the aging brain

Preventing Alzheimer's disease through supplementation with natural omega-3 fatty acids

Changes in cognitive function and memory decline form a normal part of aging. However, in neurodegenerative diseases such as Alzheimer's disease or mild cognitive impairment (the pre-dementia phase of Alzheimer's disease), these changes occur more quickly. There are currently no effective treatments for these diseases. Physicians and researchers are constantly looking for new treatment methods that will maintain their patients' cognitive performance and independence for as long as possible. Targeted prevention is another essential component when trying to preserve cognitive function for as long as possible.

"Ideally, any measures used should be aimed at long-term prevention. This means that measures must be suitable for use in healthy older adults, and should be easy to integrate into day-to-day life," says Dr. Nadine Külzow, a researcher at Charité's Department of Neurology. Nutritional supplements represent one such option. "A number of different dietary components, including omega-3 fatty acids, are currently thought to have a direct effect on nerve cell function. This is why we decided to study the effects on memory function of a daily dose of 2,200 milligrams taken for a duration of six months," says Dr. Külzow.

Study participants who received omega-3 fatty acids showed greater improvements on an object location memory task than participants who received a placebo containing sunflower oil. However, there was no evidence of improved performance on a verbal learning test. "Results from this study suggest that a long-term approach to prevention is particularly effective in preserving cognitive function in older individuals. A targeted approach involving dietary supplements can play a central role in this regard," concluded the researchers. Whether or not the improvements recorded can make a noticeable difference in day-to-day life will need to be investigated as part of a larger clinical study. As a next step, however, the researchers are planning to test the effect of supplementation with a combination of omega-3 fatty acids and vitamin B. According to research conducted at Oxford, this combination may be associated with synergistic effects.

**Nadine Külzow, Veronica Witte, Lucia Kerti, Ulrike Grittner, Jan Philipp Schuchardt, Andreas Hahn and Agnes Flöel. Impact of Omega-3 Fatty Acid Supplementation on Memory Functions in Healthy Older Adults. Journ. Alzheimers Dis. 2016 Feb 10. doi: 10.3233/JAD-150886.*

http://www.eurekalert.org/pub_releases/2016-03/jhub-ugc031516.php

Using generic cancer drug could save many millions of dollars

New research suggests little risk, huge financial upside of putting patients with chronic myeloid leukemia on generic form of Gleevec

With the expiration in January of the patent on Gleevec, the drug that 15 years ago changed chronic myeloid leukemia (CML) from a death sentence to a treatable illness, insurance companies and patients have the opportunity to realize huge cost savings, new Johns Hopkins Bloomberg School of Public Health research suggests.

The researchers, publishing online this month in the Journal of the National Cancer Institute, say that if all CML patients were started upon diagnosis on the generic form of Gleevec, known as imatinib, the cost of treatment per patient over five years would be nearly $100,000 less than it is now. Most CML patients require lifelong, daily medication.

This means that a health insurer with 100 patients with chronic myeloid leukemia could save $9.1 million over five years. CML is a relatively rare cancer that starts inside the bone marrow. Roughly 6,000 Americans are diagnosed with it every year and up to 90 percent survive five years on drugs like Gleevec, which is manufactured and sold by Novartis Pharmaceuticals Corporation.

"If we start all patients on the generic form of Gleevec and it works, then they are on a generic for the rest of their lives," says study leader William V. Padula, PhD, an assistant professor in the Department of Health Policy and Management at the Bloomberg School. "This amounts to a huge cost savings for them and their insurers."

While Gleevec was the first drug to successfully treat CML, two other drugs in the same category, known as tyrosine kinase inhibitors, have come on the market in recent years: dasatinib (sold as Sprycel) and nilotinib (sold as Tasinga). Generic versions of these drugs will not be available for many years; the branded versions cost roughly $75,000 each for a year's supply. In nearly 90 percent of cases,

patients are now started on one of these newer drugs based on each physician's preference, but research has shown that overall five-year survival rates of all three drugs are equivalent.

Also, CML patients tend to switch drugs during the course of treatment if there are side effects or if one drug doesn't appear to be effective, meaning that over the course of five years, roughly 50 percent of patients will take Gleevec for some or all of the time.

Padula and his colleagues, including Rena M. Conti, PhD, a health economist at the University of Chicago, found that if insurers decided to only pay for Gleevec as the first line drug - instead of allowing doctors to choose - the savings would be even greater than $100,000 over five years if the patient stayed on Gleevec for the entire time. This five-year time point is significant since it is the amount of time hematologists and oncologists typically use to measure progression-free survival or overall survival from remission in CML patients. With the patent protection on Gleevec lost, the researchers estimate that the per-patient, per-month cost of imatinib will likely drop 60 to 90 percent from its current cost of nearly $60,000 a year as generic manufacturers make and sell imatinib. That could mean the drug could cost less than $6,000 a year for those who stay on it.

For the study, the researchers compared cost-effectiveness of the different medications by analyzing Truven Health Analytics MarketScan data from newly diagnosed CML patients between Jan. 1, 2011 and Dec. 31, 2012.

Last year, Gleevec lost patent protection in Canada and the price of imatinib is now 18 to 26 percent of the branded drug price. The national health insurance system has mandated the use of the imatinib first, which has resulted in large cost savings.

Despite efforts to control costs, total prescription drug spending in the United States was $374 billion in 2014, up 13 percent from 2013, the highest annual growth rate since 2001, according to IMS Health.

"There is minimal risk to starting all patients on imatinib first," Padula says. "If the patient can't tolerate the medication or it seems to be ineffective in that patient, then we can switch the patient to a more expensive drug. Insurance companies have the ability to dictate which drugs physicians prescribe first, and they regularly do. Doing so here would mean very little risk to health and a lot of cost savings."

The car industry, Padula says, bases the price of its models on how much it costs to make each one, with a little bit of profit thrown in. Drug prices have little to do with the actual cost of what goes into manufacturing and distributing their product. Drug companies argue that prices take into account the cost of research and development, as well as the value provided to the patient.

"When patent protection is lost, the prices are set closer to the true cost of the drug," Padula says. "They're making 'General Motors' profits as opposed to Pharma profits and that savings can be shared with the consumer, but only if doctors and insurers work together to make sure patients are being prescribed the more cost-effective medication."

"Cost-effectiveness of Tyrosine Kinase Inhibitor Treatment Strategies for Chronic Myeloid Leukemia in Chronic Phase After Generic Entry of Imatinib in the United States" was written by William V. Padula, Richard A. Larson, Stacie B. Dusetzina, Jane F. Apperley, Rudiger Hehlmann, Michele Baccarani, Ekkehard Eigendorff, Joelle Guilhot, Francois Guilhot, Rudiger Hehlmann, Francois-Xavier Mahon, Giovanni Martinelli, Jiri Mayer, Martin C. Müller, Dietger Niederwieser, Susanne Saussele, Charles A. Schiffer, Richard T. Silver, Bengt Simonsson and Rena M. Conti.

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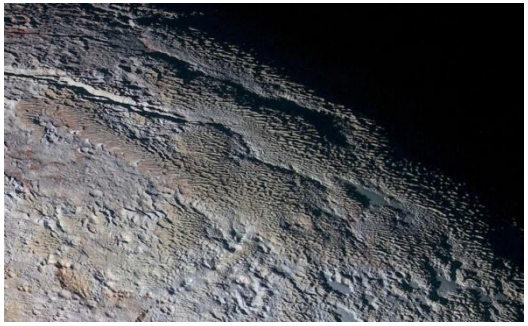
http://bit.ly/1UcbCy0

Are Pluto's Pebbled 'Snakeskin' Slopes Made of Ancient Stuff?

Pluto's mysterious "snakeskin" terrain may be made of stuff that predates the solar system's birth, scientists say.

by Mike Wall, Space.com Senior Writer | March 15, 2016 05:57pm ET

NASA's New Horizons spacecraft spotted the strange landscape — which appears pebbly and scaly from a distance — on the eastern side of Pluto's famous "heart" during the probe's epic flyby of the dwarf planet last July. Computer models created by the New Horizons team suggest that the "scales" are actually tightly packed minimountains about 1,650 feet (500 meters) tall.



Pluto's intriguing "snakeskin" terrain, which New Horizons mission team members have informally named Tartarus Dorsa. **NASA/JHUAPL/SwRI**

"Their relative spacing of about 3-5 kilometers [1.9 to 3.1 miles] makes them some of the steepest features seen on Pluto," mathematical physicist Orkan Umurhan, a New Horizons science team member based at NASA's Ames Research Center in Moffett Field, California, wrote in a blog post Friday (March 11.)

New Horizons' measurements showed that the snakeskin region — which the team has informally named Tartarus Dorsa — is dominated by methane, with

some water thrown in for good measure. So the scaly peaks could be composed of pure methane ice, or, perhaps, of methane clathrate ice — methane molecules surrounded by a "cage" of water molecules, Umurhan said.

It's unclear if pure methane ice is strong enough to maintain such steep slopes over long periods of time under Pluto conditions, Umurhan wrote. There are only two known studies that address this issue, and their findings are ambiguous; one found that pure methane would be too mushy, while the other suggested it could be stout enough, if the individual methane crystals were big enough.

And what if the snakeskin slopes are instead made of methane clathrates (which are found on Earth — for example, in the very deep ocean)? Well, that would be exciting, according to Umurhan.

Recent studies "strongly suggest that methane clathrates in the icy moons of the outer solar system and also in the Kuiper Belt were formed way back before the solar system formed — i.e., within the protosolar nebula — potentially making them probably some of the oldest materials in our solar system," Umurhan wrote in his blog post.

"Might the material comprising the bladed terrain of Tartarus Dorsa be a record of a time before the solar system ever was? That would be something!" he added.

http://huff.to/1nXmnps

Certain Carbs Could Dramatically Increase Lung Cancer Risk, Study Says

Scientists from the University of Texas MD Anderson Cancer Center have completed a study on lung cancer and the findings are rather startling.

Michael Lazar Contributor, NowItCounts.com

According to the results, processed, carb-rich foods like bagels, white bread, baguettes and even white rice can increase your risk of lung cancer by as much as 49%.

These high glycemic index foods can increase lung cancer risk regardless of whether or not you are smoker.

They published the study in the Cancer Epidemiology, Biomarkers & Prevention, earmarking the largest of its kind ever to be conducted that investigates whether the glycemic index is linked to lung cancer.

The glycemic index serves to measure the elevation of sugar levels post ingestion of certain carbohydrates. When the index is higher, blood sugar more rapidly elevates following ingestion. This process also increases insulin and glucose levels in the blood; what experts call “insulin-like growth factors.” And when this happens, it’s now directly associated with a drastically increased lung cancer risk.

The study involved 1,905 patients that had been recently diagnosed with lung cancer as well as 2,413 people who were healthy. Participants provided eating habits and health history, and then were grouped based upon the glycemic index and load as well as carb intake.

“We observed a 49% increased risk of lung cancer among subjects with the highest daily glycemic index compared to those with the lowest daily glycemic index,” explained Xifeng Wu, leading author of the study. “The associates were more pronounced among subjects who were never smokers.”

The study concluded that while glycemic load didn’t increase the risk of lung cancer, it was really what was being ingested. In this case: processed carbs.

Lung cancer is one of the deadliest diseases in the US at the present, with 150,000 new diagnoses each year and one of the highest mortality rates, according to the American Cancer Society. While smoking is a leading cause, new studies are finding that there’s plenty of other habits to be worried about, too, including your carb intake. Smokers still are at the greatest risk, according to the study, with a 31% increased chance of developing lung cancer than nonsmokers.

“The results from this study suggest that, besides maintaining healthy lifestyles, such as avoiding tobacco, limiting alcohol consumption, and being physically active, reducing the consumption of foods and beverages with high glycemic index may serve as a means to lower the risk of lung cancer,” Wu wrote.

http://bit.ly/1UHBFM6

Atrial fibrillation patients at highest stroke risk not prescribed necessary medication

Researcher describes findings as major gap in treatment and 'wake-up call'

Nearly half of all atrial fibrillation (AF) patients at the highest risk for stroke are not being prescribed blood thinners by their cardiologists, according to a new study by researchers at University of California, San Diego School of Medicine and University of California, San Francisco.

The study was published online March 16, 2016 in JAMA Cardiology.

The four-year study, which involved more than 400,000 participants, found that as stroke risk factor scores generally increased, cardiologists were more likely to prescribe blood thinners, but AF patients with the highest risk for stroke were not prescribed oral anticoagulants as frequently as guidelines suggested.

"Despite a well-known association of AF with stroke, we found a significant lack of oral anticoagulant prescribed to reduce blood clots in high-risk patients. This is a wake-up call," said lead author Jonathan C. Hsu, MD, cardiologist and assistant clinical professor of medicine at UC San Diego School of Medicine. "As the number of stroke cases in AF patients increase annually in the United States, our findings draw attention to a treatment gap in a demographic who may need these therapies the most."

The incidence of stroke for AF patients is up to seven times greater than in those without the condition. Cardioembolic stroke is one of the main complications of AF, when stagnant blood in the left atrium of the heart forms a blood clot and is released into the circulation where it blocks flow to an organ, often the brain.

In AF, electrical impulses in the upper chambers of the heart are chaotic and the atrial walls quiver rather than contract normally in moving blood to the lower chambers. As a result, blood clots may form. One in four adults over age 40 is at risk for AF with a projection of nearly 6 million people in the nation having the condition by 2050.

Standardized recommendations are used to determine and help quantify an AF patient's stroke risk and help treating physicians determine whether a prescription of oral medication, such as warfarin or newer blood thinners, may be warranted. However, in this study, researchers found just under half (48 percent) of AF patients at the highest risk for stroke were not prescribed treatment.

"Well-informed and well-intended cardiologists may struggle with a lack of data regarding optimizing risks versus benefits in patients with indications for anti-platelet drugs for their coronary artery disease and additional anticoagulants for their atrial fibrillation," said senior author Gregory Marcus, MD, cardiologist and Endowed Professor in AF Research at UC San Francisco School of Medicine. "However, while studies specifically addressing those challenging cases are needed, it is clear that identifying barriers to anticoagulant prescription, whether they involve physician education or enhanced patient access, will be the key to rectifying the situation."

The authors said there are likely multiple reasons behind the practice, including the perceived risk of prescribing blood thinners in sicker patients.

"Physicians may be avoiding additional therapy in certain patients taking antiplatelet medications because of the increased risk of bleeding associated with the oral anticoagulants," said Hsu. "It may be thought of as too dangerous for these sicker patients, but we still know that in most of these patients the benefits of blood thinning to reduce the risk of stroke outweigh the risks of bleeding."

Co-authors include Thomas M. Maddox, MD, MSc, VA Eastern Colorado Health Care System, Colorado Cardiovascular Outcomes Research Consortium, and University of Colorado School of Medicine; Kevin Kennedy, MS, Saint Luke's Mid America Heart Institute; David F. Katz, MD, and Lucas N. Marzec, MD, University of Colorado School of Medicine; Steven A. Lubitz, MD, MPH, Massachusetts General Hospital; Anil K. Gehi, MD, The University of North Carolina at Chapel Hill; and Mintu P. Turakhia, MD, MAS, VA Palo Alto Health Care System/Stanford University School of Medicine.

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http://www.eurekalert.org/pub_releases/2016-03/f-rta031016.php

Re-energizing the aging brain

The human brain has a prodigious demand for energy -- 20 to 30% of the body's energy budget.

In the course of normal aging, in people with neurodegenerative diseases or mental disorders, or in periods of physiological stress, the supply of sugars to the brain may be reduced. This leads to a reduction in the brain's energy reserves, which in turn can lead to cognitive decline and loss of memory.

But new research on mice shows that the brain's energy reserves can be increased with a daily dose of pyruvate, a small energy-rich molecule that sits at the hub of most of the energy pathways inside the cell. These results need to be replicated in human subjects, but could ultimately lead to clinical applications.

"In our new study, we show that long-term dietary supplementation with pyruvate increases the energy reserves in the brain, at least in mice, in the form of the molecules glycogen, creatine and lactate," says lead author Heikki Tanila, Professor of Molecular Neurobiology at the A. I. Virtanen Institute of the University of Eastern Finland.

What's more, dietary supplementation with pyruvate didn't only increase the brain's energy stores: it also changed the behavior of the mice in positive ways, show the researchers.

"The mice became more energetic and increased their explorative activity. It appears that these behavioral changes are directly due to the effect of pyruvate on brain function, since we didn't find that these mice had developed greater muscle force or endurance," says Tanila.

For example, chronic supplementation with pyruvate facilitated the spatial learning of middle-aged (6- to 12-months-old) mice, made them more interested in the odor of unfamiliar mice, and stimulated them to perform so-called "rearing", an exploratory behavior where mice stand on their hind legs and investigate their surroundings (photo).

The dose necessary to achieve these effects was about 800 mg pyruvate per day - which corresponds to about 10 g per day in humans -- given to the mice in normal chow over a period of 2.5 to 6 months. A single large dose of pyruvate injected directly into the blood stream had no detectable effect.

Interestingly, the positive response to dietary supplementation with pyruvate was also found in a strain of transgenic mice called APPswe/PS1dE9, often used as an animal model for the study of Alzheimer's disease. These mice exhibit many of the same symptoms as people with Alzheimer's, such as the deposition of protein plaques in the brain, neurodegeneration, and cognitive decline. These results raise

hopes that pyruvate might also benefit people with neurodegenerative disorders such as Alzheimer's and Parkinson's.

"Pyruvate supplementation may prove beneficial as an activating treatment for the elderly and in therapies for alleviating cognitive decline due to aging, neurodegenerative disease, or mental disorders. It is well tolerated and warrants further studies in humans," says Tanila.

The study, which was supported by the Alzheimer Association, is published in the open-access journal Frontiers in Aging Neuroscience.

http://www.eurekalert.org/pub_releases/2016-03/ncfa-pzv031516.php

Potential Zika virus risk estimated for 50 US cities

Weather, travel, and poverty may facilitate summertime outbreaks

BOULDER - Key factors that can combine to produce a Zika virus outbreak are expected to be present in a number of U.S. cities during peak summer months, new research shows.

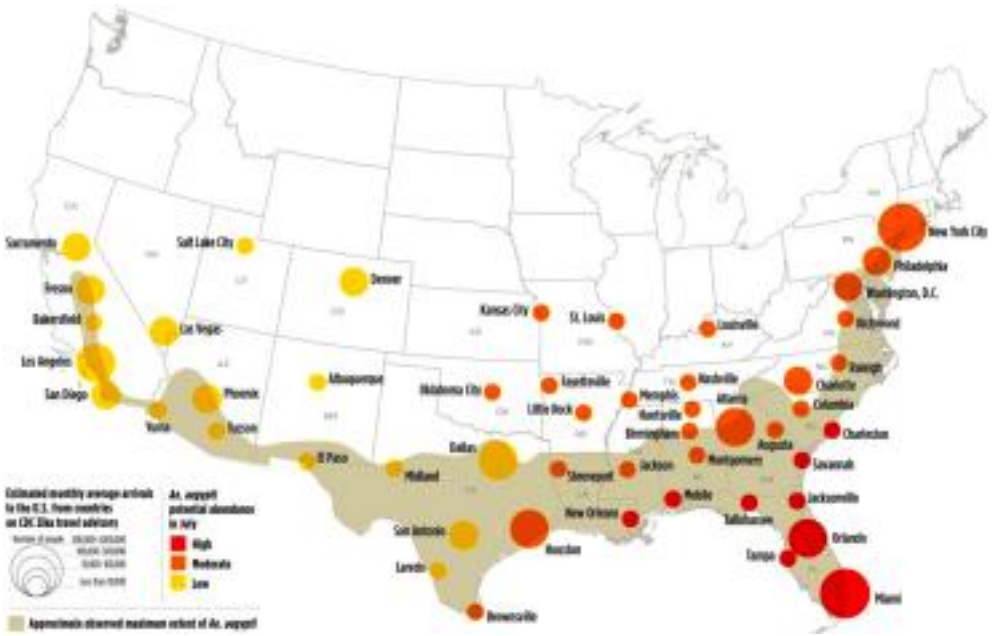
The Aedes aegypti mosquito, which is spreading the virus in much of Latin America and the Caribbean, will likely be increasingly abundant across much of the southern and eastern United States as the weather warms, according to a new study led by mosquito and disease experts at the National Center for Atmospheric Research (NCAR).

Summertime weather conditions are favorable for populations of the mosquito along the East Coast as far north as New York City and across the southern tier of the country as far west as Phoenix and Los Angeles, according to specialized computer simulations conceived and run by researchers at NCAR and the NASA Marshall Space Flight Center.

Spring and fall conditions can support low to moderate populations of the Aedes aegypti mosquito in more southern regions of its U.S. range. Wintertime weather is too cold for the species outside southern Florida and southern Texas, the study found.

By analyzing travel patterns from countries and territories with Zika outbreaks, the research team further concluded that cities in southern Florida and impoverished areas in southern Texas may be particularly vulnerable to local virus transmission.

"This research can help us anticipate the timing and location of possible Zika virus outbreaks in certain U.S. cities," said NCAR scientist Andrew Monaghan, the lead author of the study. "While there is much we still don't know about the dynamics of Zika virus transmission, understanding where the Aedes aegypti mosquito can survive in the U.S. and how its abundance fluctuates seasonally may help guide mosquito control efforts and public health preparedness."



Many US cities face potential risk in summer of low, moderate, or high populations of the mosquito species that transmits Zika virus (colored circles). The mosquito has been observed in parts of the United States (shaded portion of map) and can establish populations in additional cities because of favorable summertime meteorological conditions. In addiiton, Zika risk may be elevated in cities with more air travelers arriving from Latin America and the Caribbean (larger circles). This image is freely available for media & nonprofit use. **Image based on data mapped by Olga Wilhelmi, NCAR GIS program.**

"Even if the virus is transmitted here in the continental U.S., a quick response can reduce its impact," added NCAR scientist Mary Hayden, a medical anthropologist and co-author of the study.

Although the study does not include a specific prediction for this year, the authors note that long-range forecasts for this summer point to a 40-45% chance of warmer-than-average temperatures over most of the continental United States. Monaghan said this could lead to increased suitability for Aedes aegypti in much of the South and East, although above-normal temperatures would be less favorable for the species in the hottest regions of Texas, Arizona, and California.

Monaghan stressed that, even if Zika establishes a toehold in the mainland United States, it is unlikely to spread as widely as in Latin America and the Caribbean. This is partly because a higher percentage of Americans live and work in air-conditioned and largely sealed homes and offices.

The study was published today in the peer-reviewed journal PLOS Currents Outbreaks. It was funded by the National Institutes of Health, NASA, and the National Science Foundation (NSF), which is NCAR's sponsor. It was co-authored by scientists at the NASA Marshall Space Flight Center, North Carolina State University, Maricopa County Environmental Services Vector Control Division, University of Arizona, and Durham University.

Spreading rapidly

First identified in Uganda in 1947, the Zika virus has moved through tropical regions of the world over the past decade. It was introduced into Brazil last year and spread explosively across Latin America and the Caribbean, with more than 20 countries now facing pandemics.

About 80% of infected people do not have significant symptoms, and most of the rest suffer relatively mild flu- or cold-like symptoms that generally clear up in about a week. However, scientists are investigating whether contracting the disease during pregnancy can lead to microcephaly, a rare birth defect characterized by an abnormally small head and brain damage.

To determine the potential risk in the mainland United States, the research team ran two computer models that simulated the effect of meteorological conditions on a mosquito's entire lifecycle (egg, larval, pupal, and adult stages) in 50 cities in or near the known range of the species. Monaghan and several team members have studied Aedes aegypti for years because it also carries the viruses that cause dengue and chikungunya.

Generally, the mosquitoes need warm and relatively stable temperatures, as well as water-filled containers such as buckets, barrels, or tires, for their eggs to hatch. Once a mosquito bites an infected person, it also needs to live long enough--probably a week or more, depending on ambient temperatures--for the virus to travel from the mosquito's mid-gut to its salivary glands. Once in the saliva, the virus can then be transmitted by the mosquito biting another person.

The study results show that, as springtime weather warms, the potential abundance of the mosquito begins to increase in April in the Southeast and some Arizona cities. By June, nearly all of the 50 cities studied have the potential for at least low-to-moderate abundance, and most eastern cities are suitable for moderate-to-high abundance. Conditions become most suitable for mosquito populations in July, August and September, although the peak times vary by city. Weather conditions in southern and western cities remain suitable as late as November.

Even some cities where the Aedes aegypti mosquito has not been detected, such as St. Louis and Denver, have suitable midsummer weather conditions for the species if it were introduced via transport of used tires or other human activities, according to the computer models.

The researchers stressed that additional factors outside the scope of the study could affect populations of the species, such as mosquito control efforts, competition with other mosquito species, and the extent to which eggs can survive in borderline temperatures. However, not much is known about Aedes aegypti because researchers have not focused on observing the species in much of its U.S. range. The study noted that northern cities could become vulnerable if a related species of mosquito that is more tolerant of cold temperatures, Aedes albopictus, begins to carry the virus.

Factoring in travel, poverty

In addition to looking at meteorological conditions, the researchers studied two other key variables that could influence the potential for Zika outbreaks: travel from Zika-affected areas and socioeconomic conditions in states that may face abundant mosquito populations.

To analyze air travel, the team estimated the number of passengers arriving into U.S. cities on direct flights from airports in 22 Latin American countries and territories listed on the Centers for Disease Control and Prevention's Zika travel advisory as of January 29.

Cities that had both high potential numbers of Aedes aegypti and a large volume of air travelers included Miami, Houston, and Orlando. Since the scientists were able to obtain passenger numbers for direct flights only, they could not estimate the number of passengers continuing on to smaller cities. They noted that the summertime peak in air travel coincides with the peak season in mosquito abundance.

The study also estimated that nearly five times as many people cross the U.S.-Mexico border per month than arrive by air in all 50 cities. This could indicate a high potential for transmission in border areas from Texas to California, although the Zika virus has not been widely reported in northern Mexico.

Those border areas, as well as other parts of the South where the mosquitoes are expected to be abundant, have a high percentage of households living below the poverty line, according to 2014 U.S. Census data analyzed by the research team. Lower-income residents can be more exposed to mosquito bites if they live in non-air conditioned houses or have torn or missing screens they enable mosquitoes to enter their homes more easily. However, Aedes aegypti populations tend to thrive in densely populated urban areas, and some of the most impoverished areas are rural.

"The results of this study are a step toward providing information to the broader scientific and public health communities on the highest risk areas for Zika

emergence in the United States," said Kacey Ernst, an epidemiologist at the University of Arizona and co-author of the study. "We hope that others will build on this work as more information becomes available. All areas with an environment suitable to the establishment of Aedes aegypti should be working to enhance surveillance strategies to monitor the Aedes aegypti populations and human populations for disease emergence."

"This research highlights the complex set of human and environmental factors that determine whether a mosquito-borne disease is carried from one area to another, and how severely it affects different human populations," said Sarah Ruth, program director in NSF's Division of Atmospheric and Geospace Sciences. "By integrating information on weather, travel patterns, mosquito biology, and human behavior, the project team has improved our ability to forecast, deal with, and possibly even prevent future outbreaks of Zika and other serious diseases."

Title: On the seasonal occurrence and abundance of the Zika virus vector mosquito Aedes aegypti in the contiguous United States

Authors: Andrew Monaghan, Cory Morin, Daniel Steinhoff, Olga Wilhelmi, Mary Hayden, Dale Quattrochi, Michael Reiskind, Alun Lloyd, Kirk Smith, Christopher Schmidt, Paige Scalf, and Kacey Ernst Journal: PLOS Currents Outbreaks

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http://www.eurekalert.org/pub_releases/2016-03/cmu-mpc031616.php

Most presidential candidates speak at grade 6-8 level

Trump generally scores lowest; Lincoln remains benchmark

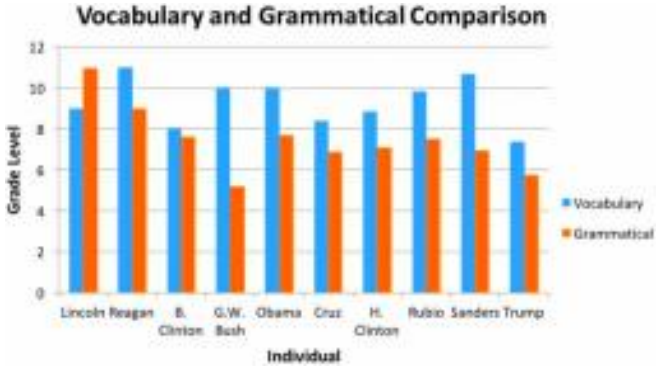
PITTSBURGH--A readability analysis of presidential candidate speeches by researchers in Carnegie Mellon University's Language Technologies Institute (LTI) finds most candidates using words and grammar typical of students in grades 6-8, though Donald Trump tends to lag behind the others.

A historical review of their word and grammar use suggests all five candidates in the analysis - Republicans Trump, Ted Cruz and Marco Rubio (who has since suspended his campaign), and Democrats Hillary Clinton and Bernie Sanders - have been using simpler language as the campaigns have progressed. Again, Trump is an outlier, with his grammar use spiking in his Iowa Caucus concession speech and his word and grammar use plummeting again during his Nevada Caucus victory speech.

"Win," after all, is more likely to appear in 3rd grade texts than "regrettably."

A comparison of the candidates with previous presidents show President Lincoln outpacing them all, boasting grammar at the 11th grade level, while President George W. Bush's 5th grade grammar was below even that of Trump.

"Assessing the readability of campaign speeches is a little tricky because most measures are geared to the written word, yet text is very different from the spoken word," said Maxine Eskenazi, LTI principal systems scientist who performed the analysis with Elliot Schumacher, a graduate student in language technologies. "When we speak, we usually use less structured language with shorter sentences."



Results of a Carnegie Mellon University readability analysis of speeches by US presidents and presidential candidates. **Elliot Schumacher/Carnegie Mellon University**

An earlier analysis by the Boston Globe used the Flesch-Kincaid readability test, which is based on average sentence length and average number of syllables per word, and found Trump speaking at a 4th grade level, two grade levels below his peers. Eskenazi and Schumacher used a readability model called REAP, which looks at how often words and grammatical constructs are used at each grade level and thus corresponds better to analysis of spoken language.

Based on vocabulary, campaign trail speeches by past and present presidents - Lincoln, Reagan, Bill Clinton, George W. Bush and Obama - were at least on the 8th grade level, while the current candidates ranged from Trump's 7th grade level to Sanders' 10th grade level. Trump and Hillary Clinton's speeches showed the greatest variation, suggesting they may work harder than the others in tailoring speeches to particular audiences, Schumacher said.

In terms of grammar, none of the presidents and presidential candidates could compare with Lincoln's Gettysburg Address - an admittedly high standard, with grammar well above the 10th grade level. The current candidates generally had scores between 6th and 7th grades, with Trump just below 6th grade level. President Bush scored at a 5th grade level.

Analyzing campaign speeches is difficult because it often is hard to obtain transcripts of speeches, Schumacher said. It is possible to generate reliable transcripts from video using automatic speech recognition (ASR) systems, such as those developed at LTI, when the speech took place in a quiet environment, but he and Eskenazi opted not to use today's automated methods because they were likely to introduce errors in the noisy environment of campaign rallies.

The study is available online at
http://reap.cs.cmu.edu/Papers/Technical_report_16-001_Schumacher_Eskenazi.pdf

http://www.eurekalert.org/pub_releases/2016-03/acs-nmc021916.php

New material could make aircraft deicers a thing of the past

Airport personnel could in the future just watch chunks slide right off without lifting a finger

SAN DIEGO - Instead of applying a deicing agent to strip ice from an aircraft's wings before stormy winter takeoffs, airport personnel could in the future just watch chunks slide right off without lifting a finger. Scientists report they have developed a liquid-like substance that can make wings and other surfaces so slippery that ice cannot adhere. The slick substance is secreted from a film on the wing's surface as temperatures drop below freezing and retreats back into the film as temperatures rise.

The researchers present their work today at the 251st National Meeting & Exposition of the American Chemical Society (ACS). ACS, the world's largest scientific society, is holding the meeting here through Thursday. It features more than 12,500 presentations on a wide range of science topics.

The liquid-secreting materials the researchers developed are called self-lubricating organogels, or SLUGs. "The SLUGs technology has a host of formulations and applications, including in a gel form that can be encapsulated in a film coating on the surface of a wing or other device," says research director Atsushi Hozumi, Ph.D.

"We came upon this idea when we observed real slugs in the environment," Chihiro Urata, Ph.D., explains. "Slugs live underground in soils when it is daytime and crawl out at night. But we never see slugs covered in dirt. They secrete a liquid mucus on their skin, which repels dirt, and the dirt slides off. From this, we started focusing on the phenomenon called syneresis, the expulsion of liquid from a gel."

The gel and the liquid-repellent substance are held in a matrix of silicone resin. The mix is cured and applied to a surface as a nearly transparent and solid film coating, Urata explains. Both Urata and Hozumi are at the National Institute of Advanced Industrial Science & Technology (Japan).

The team examined the anti-icing properties of several types of organogels under tests at various temperatures, Urata says. The discovery of the material's thermo-responsive secretion properties was an unexpected surprise. The tests also showed that the secretion was a reversible process. The syneresis gradually starts when temperatures fall below freezing. So although ice can still form, it cannot adhere to the surface and it slips off. Once the temperature rises above freezing, the liquids return back to the film.

Urata sees potential applications for SLUGs beyond aircraft and singles out antifouling coatings in packaging, paints, ship bottoms, metal molds and more. Their research is currently focusing on increasing the transparency of the SLUG's coating, Urata says. "We are planning a short-term project to apply the coating where transparency is essential. For example, we are just beginning a project to field-test the durability and visibility of SLUGs coating on signage in Japan's northern counties."

Their research is funded through a grant-in-aid for scientific research on innovative areas from the Japanese Ministry of Education, Culture, Sports, Science and Technology.

http://www.eurekalert.org/pub_releases/2016-03/cumc-sga031416.php

Scientists generate a new type of human stem cell that has half a genome

The haploid stem cells may yield new genetic screening tools and therapies

JERUSALEM and NEW YORK, NY - Scientists from The Hebrew University of Jerusalem, Columbia University Medical Center (CUMC) and The New York Stem Cell Foundation Research Institute (NYSCF) have succeeded in generating a new type of embryonic stem cell that carries a single copy of the human genome, instead of the two copies typically found in normal stem cells. The scientists reported their findings today in the journal Nature.

The stem cells described in this paper are the first human cells that are known to be capable of cell division with just one copy of the parent cell's genome.

Human cells are considered 'diploid' because they inherit two sets of chromosomes, 46 in total, 23 from the mother and 23 from the father. The only exceptions are reproductive (egg and sperm) cells, known as 'haploid' cells because they contain a single set of 23 chromosomes. These haploid cells cannot divide to make more eggs and sperm.

Previous efforts to generate embryonic stem cells using human egg cells had resulted in diploid stem cells. In this study, the scientists triggered unfertilized human egg cells into dividing. They then highlighted the DNA with a fluorescent dye and isolated the haploid stem cells, which were scattered among the more populous diploid cells.

The researchers showed that these haploid stem cells were pluripotent -- meaning they were able to differentiate into many other cell types, including nerve, heart, and pancreatic cells -- while retaining a single set of chromosomes.

"This study has given us a new type of human stem cell that will have an important impact on human genetic and medical research," said Nissim Benvenisty, MD, PhD, Director of the Azrieli Center for Stem Cells and Genetic Research at the Hebrew University of Jerusalem and principal co-author of the study. "These cells will provide researchers with a novel tool for improving our understanding of human development, and the reasons why we reproduce sexually, instead of from a single parent."

The researchers were also able to show that by virtue of having just a single copy of a gene to target, haploid human cells may constitute a powerful tool for genetic screens. Being able to affect single-copy genes in haploid human stem cells has the potential to facilitate genetic analysis in biomedical fields such as cancer research, precision and regenerative medicine.

"One of the greatest advantages of using haploid human cells is that it is much easier to edit their genes," explained Ido Sagi, the PhD student who led the research at the Azrieli Center for Stem Cells and Genetic Research at the Hebrew University of Jerusalem. In diploid cells, detecting the biological effects of a single-copy mutation is difficult, because the other copy is normal and serves as "backup."

Since the stem cells described in this study were a genetic match to the egg cell donor, they could also be used to develop cell-based therapies for diseases such as blindness, diabetes, or other conditions in which genetically identical cells offer a therapeutic advantage. Because their genetic content is equivalent to germ cells, they might also be useful for reproductive purposes.

"This work is an outstanding example of how collaborations between different institutions, on different continents, can solve fundamental problems in biomedicine," said Dieter Egli, PhD, principal co-author of the study, and Assistant Professor of Developmental Cell Biology in Pediatrics at Columbia University Medical Center and a Senior Research Fellow at the NYSCF Research Institute and a NYSCF-Robertson Investigator.

The research, supported by The New York Stem Cell Foundation, the New York State Stem Cell Science Program, and by the Azrieli Foundation, underscores the importance of private philanthropy in advancing cutting-edge science.

The paper is titled Derivation and differentiation of haploid human embryonic stem cells (doi:10.1038/nature17408). The lead authors are Nissim Benvenisty and Ido Sagi, The Azrieli Center for Stem Cells and Genetic Research, The Hebrew University, Jerusalem, and Dieter Egli, Columbia University Medical Center and New York Stem Cell Foundation Research Institute. Additional authors include Gloryn Chia, Lina Sui, and Mark Sauer of CUMC; Tamar Golan-Lev, Mordecai Peretz, Uri Weissbein and Ofra Yanuka of the Hebrew University.

http://nyti.ms/1XH1vix

Solving the Tully Monster's Cold Case

Since it was first uncovered more than a half a century ago, this kooky-looking creature known as the "Tully monster" has puzzled paleontologists who, frankly, could not make heads, tails or claws of its fossilized remains.

The creature was named after Francis Tully, the amateur who discovered it in 1958 in the Mazon Creek in Illinois. The state has designated the monster as its official fossil.

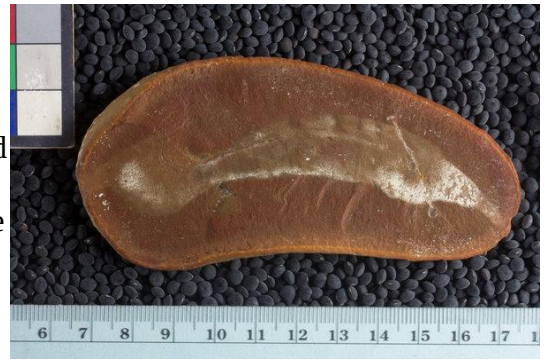
A reconstruction of the 300-million-year-old Tully Monster. **Sean McMahon**

Some thought the 300-million-year-old creature was a mollusk, like a snail. Others assumed it was an arthropod like an insect or crab. And others believed it was some sort of worm.

Now, a team of researchers from Yale University say they have figured out the monster's identity: It's a vertebrate most closely related to the lamprey, an underwater bloodsucker. They published their findings on Wednesday in Nature.

To come to their conclusion, team members first pored over 1,200 Tully monster specimens from museums. They closely examined the creature's features, like its torpedo-shaped body and triangular tail, the proboscis that looks like an elephant's trunk with sharp teeth, and the eyes on the side of its head, which resemble a hammerhead, but are similar to eye stalks found in crabs and insects.

"The frustrating thing is that these morphological features are not typical of any group," said Victoria McCoy, a paleontologist and lead author on the paper. "But they do not rule out any group very easily."



A 300-million-year-old Tully Monster fossil. **Nicole Karpus**

The clue that led them to closing the cold case was a lightly colored structure scientists had previously identified as the creature's gut. Only it wasn't a gut.

"We discovered that this feature was the notochord, the primitive backbone," said Dr. McCoy.

Most guts in the fossilized record are dark and appear three-dimensional. But the Tully monster's structure was light and appeared two-dimensional.

"It didn't make sense to us that there would be this one animal that would fossilize its gut completely differently," she said.

After finding that the creature had a primitive backbone, they could classify it as a chordate, which is a family of species that includes all vertebrates. Then they had to narrow down the type of chordate to which it was most similar. By further examining the notochord, the fossil sleuths noticed that the structure curved down as it went through the creature's tail.

In animals like sharks, the notochord curves up into the top fin of the tail, and in some fish it goes through the middle of the tail. But in lampreys the notochord curves down.

"There was no big 'Aha!' moment that pointed to the lamprey. But put together, the strongest evidence was that it could be a lamprey," Dr. McCoy said. "The coolest thing is finding out that as weird as it looks, it is part of a familiar group of animals."

http://www.eurekalert.org/pub_releases/2016-03/osu-brt031616.php

Bacterial resistance to copper in the making for thousands of years

Genetic changes pose risks to human immunity

COLUMBUS, Ohio - Human use of copper dating back to the Bronze Age has shaped the evolution of bacteria, leading to bugs that are highly resistant to the metal's antibacterial properties.

Large amounts of copper are toxic to people and to most living cells. But our immune systems use some copper to fend off bacteria that could make us sick.

More copper in the environment leads to more bacteria, including E. coli, that develop a genetic resistance. And that could pose an increased infection risk for people, said Jason Slot, who directed a new copper-resistance study and is assistant professor of plant pathology at The Ohio State University.

Today, copper is widely used, including in animal feed and to make hospital equipment - areas that could be particularly conducive to bacteria developing even greater resistance, Slot said.

Under the pressure of "copper stress," bacteria have traded DNA that enabled some to outlive the threat, said Slot, who specializes in fungal evolutionary genomics. And over centuries, the genes that lead to copper resistance have bonded, forging an especially tough opponent for the heavy metal, a cluster scientists call the "copper homeostasis and silver resistance island," or CHASRI.

Slot and his colleagues created a molecular clock, using bacterial samples collected over time and evolutionary analysis to trace the history of copper resistance. The team studied changes in bacteria and compared those to human use of copper. Their work suggests there were repeated episodes of genetic diversification within bacteria that appear to correspond to peaks in copper production. The study appears in the journal Genome Biology and Evolution.

Slot, an evolutionary biologist, first became interested in copper resistance when he learned that the genes involved weren't evolving in the way scientists would expect.

"This may have arisen at the time that humans started using a lot of copper - in the Bronze Age," Slot said. He and his collaborators speculate that the original resistance might have started in milk fermented in a copper-alloy vessel, or in the gut of an animal in a high-copper environment.

From then on, human use of copper has likely contributed to bacteria with a stronger armor against it. For instance, "About 2,000 years ago Romans were pumping a ton of copper dust into the environment," Slot said. Ice cores from Greenland have supported this theory, showing likely high copper emissions during the time.

Today, copper is widely used in industry, including in farming, where the metal is added to feed to fatten up animals. And in recent years, there's been a movement toward using copper more in medical settings because of its antibacterial properties, Slot said.

"You're enticing the bacteria in the environment to develop a mechanism that evades your immune system," Slot said. "I think overuse of anything is a bad idea, but it's really hard for people not to overuse the few weapons that we have."

Other researchers who worked on the study were Benjamin Staehlin and Thomas O'Halloran of Northwestern University and John Gibbons and Antonis Rokas of Vanderbilt University.

http://www.eurekalert.org/pub_releases/2016-03/uov-vvt031116.php

Vermont Vaccine Testing Center study reveals effective, single-dose dengue vaccine

New vaccine that is very effective at preventing dengue infection and is likely to require only a single dose

Researchers at the University of Vermont (UVM) Vaccine Testing Center, along with collaborators at the National Institute of Allergy and Infectious Diseases (NIAID) at the National Institutes of Health and Johns Hopkins Bloomberg School of Public Health, have been working since 2008 to develop a dengue vaccine that will protect against all four dengue strains. The team's latest research, published today in Science Translational Medicine, reports promising results from clinical trials on a new vaccine that is very effective at preventing dengue infection and is likely to require only a single dose.

The World Health Organization has made the development and introduction of dengue vaccines a high priority. Approximately 40 percent of the world's population - 2.5 billion people - are at risk of contracting dengue, a viral infection

spread by mosquitos in tropical and subtropical regions of the world. Dengue fever is best known for producing a high fever, rash and joint pain, but may also cause very serious disease, including hemorrhage and shock, as well as death. Development of vaccines for dengue has been complicated, since disease can be caused by any of four dengue virus serotypes and the vaccine must be tetravalent, providing equal protection against all four serotypes.

The NIH dengue vaccine was designed by Stephen Whitehead, Ph.D., a senior scientist and virologist at the Laboratory of Infectious Diseases at the NIAID. Clinical research was performed at both UVM and Johns Hopkins, where testing was led by Associate Professor Anna Durbin, M.D., corresponding author on the paper. Study volunteers were given vaccine or placebo and were tested for protection against a weakened strain of dengue that causes infection, but no or minimal symptoms. Results demonstrated that all vaccinees were protected from the "challenge" virus, but none of the volunteers receiving placebo vaccines were protected. The vaccine was well-tolerated in all volunteers.

"This work used a robust method which predicts a high likelihood of success for this critically important dengue vaccine," says UVM Professor of Medicine and Vaccine Testing Center Director Beth Kirkpatrick, M.D., who is first author on the paper. "I thank all members of the UVM, Johns Hopkins, and NIH dengue teams who have worked extremely hard over many years to develop this vaccine."

"The NIH dengue vaccine will now proceed to the ultimate test of effectiveness: large field-based trials in dengue-endemic countries," says Kristen Pierce, M.D., associate professor of medicine and UVM clinical investigator. "Beginning later this month, our team will be testing this vaccine in Dhaka, Bangladesh, and a large phase III efficacy trial has already begun in Brazil."

http://bit.ly/25fr53R

Evolution acting on older dads is protecting our genetic health

Evidence that evolution is still removing our harmful mutations

By Michael Le Page

WE'RE running just to stay still. A study of more than a million people going back four centuries shows that we are still evolving – not into superhumans, but to stay as we are.

Almost all children in rich countries now survive to adulthood. That has led some biologists to suggest that evolution has essentially stopped. The thinking is that if children are less likely to die, those with lots of adverse new mutations are more likely to pass these on, so natural selection is no longer stopping these genetic changes from building up in the population.

According to geneticist Michael Lynch of Indiana University in Bloomington, this process could affect our health and intelligence in just a few generations. Some have claimed that our genetic potential for intelligence is already eroding, and that IQ scores should have risen even more than they have over the past century due to better health and education.

But now there's evidence that evolution is still removing our harmful mutations. Ruben Arslan of the University of Göttingen in Germany and his colleagues made this discovery by analysing church records from the 15th and 16th centuries from three areas – in Germany, Sweden and Quebec in Canada – and also in modern Swedish health records.

Studies have shown that for every extra year of their father's life before they were conceived, a child has about two extra mutations. But Arslan's team has found that the mutations of children born to older fathers are less likely to be passed on, because these children grow up to have fewer children themselves. Compared with a sibling born 10 years earlier, individuals born when the fathers were older had on average 5 per cent fewer children who survived beyond infancy (*bioRxiv*, doi.org/bdd3).

The team thinks this is because the additional mutations are preventing the children of older fathers from reproducing as much as those born to younger dads. In this way, evolution still seems to be weeding out harmful mutations from human populations, stopping them from accumulating over generations.

But Lynch points out that even though there may be some evolution taking place, this selection may be weaker than it used to be. This means that over longer periods of time, mutations could still build up in human populations, albeit more slowly.

Even so, Arslan's work suggests that we can worry less about recent trends towards having children later in life. Although the age at which men first become fathers has crept upwards in the past half-century, the average age of each child's father is still lower now than it was in the 16th century, the study found.

This is because people used to have more children, starting their families earlier, but continuing to reproduce until late in life. In Sweden, between 1737 and 1880, the average age of a baby's father at their time of birth was 35, a couple of years older than dads in Sweden today.

http://bit.ly/22rW264

Rats learn to sense infrared in hours thanks to brain implants

Rat brains quickly adapted to use data from four infrared sensors, allowing them to "see" in the dark and paving the way for augmenting the human brain

By Andy Coghlan

BRAINS get data about the world through senses – sight, hearing, taste, smell and touch. In a lab in North Carolina, a group of rats is getting an extra one. Thanks to implants in their brains, they have learned to sense and react to infrared light. The

rats show the brain's ability to process unfamiliar data– an early step towards augmenting the human brain.

Miguel Nicolelis of Duke University School of Medicine is leading the experiment. His team implanted four clusters of electrodes in the rats' barrel cortex – the part of the brain that handles whisker sensation (doi.org/bdb6). Each cluster is connected to a sensor that converts infrared light into an electrical signal. Feeding stations placed at the four corners of the rats' cage take turns emitting infrared signals that guide the rats to them, releasing a reward only when the rats press a button on the feeding station that is emiting the infrared signal.

In an older, single sensor version of the experiment, it took the rats one month to adapt. With four sensors, it took them just three days.

"This is a truly remarkable demonstration of the plasticity of the mammalian brain," says Christopher James of the University of Warwick, UK.

All the extra data that goes into making the rats' new sense doesn't appear to diminish their original senses. "The results show that nature has apparently designed the adult mammalian brain with the possibility of upgrades, and Nicolelis' team is leading the way showing how to do it," says Andrea Stocco of the University of Washington in Seattle.

Nicolelis says unpublished data from a follow-up experiment shows that rats learn even faster when the sensors feed directly into their visual cortex, taking just 6 or 7 hours. Nicolelis thinks the speed-up comes from using a part of the brain that already interprets light. He is planning a subsequent experiment in which the rats can only get a reward if they "see" both parts of the spectrum at once, visual and infrared. And if it could be done with infrared, why not with ultraviolet light, microwaves, or other inputs? "It would be a fusion, total vision," says Nicolelis.

"Now there's no doubt that it's easy for the mammalian brain, even in adulthood, to adaptively use a novel, never-experienced sense, such as infrared," says Yuji Ikegaya of the University of Tokyo in Japan.

Nicolelis' brain interfaces will probably find their first application in the medical world, but they are part of a trend that erodes the boundary between our brain and the outside world. Human beings already implant sensors and chips in their flesh, and although implanting in the brain is dangerous, the benefits may outweigh the risks someday.

"Is it safe, and are these capabilities we necessarily want to develop?" asks Filippa Lentzos of King's College London. "Could it be abused by the military, to enhance battlefield performance or degrade enemy performance?"

But Lentzos points out that implants such as hearing aids are widely offered to patients. "We do a lot of this already, so whether completely new senses would be acceptable is a very interesting debate."

http://www.eurekalert.org/pub_releases/2016-03/kcl-spm031716.php

Scientists pinpoint molecular signal that drives and enables spinal cord repair

Researchers from King's College London and the University of Oxford have identified a molecular signal, known as 'neuregulin-1', which drives and enables the spinal cord's natural capacity for repair after injury.

The findings, published today in Brain, could one day lead to new treatments which enhance this spontaneous repair mechanism by manipulating the neuregulin-1 signal.

Every year more than 130,000 people suffer traumatic spinal cord injury (usually from a road traffic accident, fall or sporting injury) and related healthcare costs are among the highest of any medical condition - yet there is still no cure or adequate treatment. Spinal cord injury has devastating consequences for muscle and limb function, but the central nervous system does possess some limited capacity to repair itself naturally.

Understanding what drives this repair mechanism could aid the development of new treatment strategies aimed at boosting the self-healing capacity of the injured spinal cord by taking advantage of 'tools' that the spinal cord already possesses.

For the first time researchers from King's and Oxford have identified one of these tools, neuregulin-1, which signals from the surface of damaged nerve fibres during a process called 'spontaneous remyelination.'

Spontaneous remyelination is a period of natural regeneration that happens in the weeks following a spinal cord injury. The process takes place as a result of damage to spinal nerve fibres which have lost their insulating 'myelin sheath'. This myelin sheath is crucial for efficient communication between the brain and the body.

However, this natural capacity for repair is not sufficient for full recovery and may account for the compromised function of surviving nerve fibres, which can affect balance, coordination and movement.

The researchers found that, in mice lacking the neuregulin-1 gene, spontaneous myelin repair was completely prevented and spinal nerve fibres remained demyelinated (i.e. unable to send nerve signals along the spinal cord).

They also discovered that mice without neuregulin-1 showed worse outcomes after spinal cord injury compared to mice with the gene intact, particularly in walking, balance and coordinated movements.

Not only did neuregulin-1 drive spontaneous remyelination, but it also served as a molecular switch for cells within the spinal cord to transform themselves into cells with remyelinating capacity. This is unusual, according to the researchers,

because the 'Schwann' cells with new remyelinating capacity normally only myelinate nerve fibres in the peripheral nervous system - not the central nervous system, as observed here.

Elizabeth Bradbury, Professor of Regenerative Medicine & Neuroplasticity at the Institute of Psychiatry, Psychology & Neuroscience (IoPPN), King's College London, and Medical Research Council Senior Fellow, said: 'Spinal cord injury could happen to anyone, at any time. In an instant your life could change and you could lose all feeling and function below the level of the injury. 'Existing treatments are largely ineffective, so there is a pressing need for new regenerative therapies to repair tissue damage and restore function after spinal cord injury.

'These new findings advance our understanding of the molecular mechanisms which may orchestrate the body's remarkable capacity for natural repair.'

Professor Bradbury added: 'By enhancing this spontaneous response, we may be able to significantly improve spinal cord function after injury. Our research also has wider implications for other disorders of the central nervous system which share this demyelinating pathology, such as multiple sclerosis.'

Dr Katalin Bartus, also from the IoPPN at King's College London, said: 'We hope this work will provide a platform for future research, in which it will be important to test how enhancing levels of neuregulin-1 will improve functional outcome after spinal cord injury.'

This research is a collaboration between scientists at King's - led by Professor Elizabeth Bradbury - who work on repairing traumatic injuries of the central nervous system, and a group of researchers at Oxford - led by Professor David Bennett - who work on nerve injury and myelination within the peripheral nervous system. The study was funded by the Medical Research Council, Wings for Life Spinal Cord Research Foundation, the Wellcome Trust and the International Spinal Research Trust and Henry Smith Charity.

http://www.eurekalert.org/pub_releases/2016-03/uomh-dms031516.php

Drug makes stem cells become 'embryonic' again

Research in mice shows for the first time that erasing epigenetic markers on chromatin can return stem cells to original state

ANN ARBOR, Mich. -- If you want to harness the full power of stem cells, all you might need is an eraser.

Not an ordinary eraser, of course. More of a drug, really. But if you use it right, it can erase the tiny labels that tell cells where to start reading important chapters in DNA, their inner instruction manual.

And if they can't read that manual, the cells regain their full stem cell power - the power to become any kind of cell in the body.

In a surprising new finding, University of Michigan Medical School scientists have shown that a drug developed at U-M can achieve this -- at least in mice.

It's the first time that scientists have shown they can get stem cells to revert to their original state by erasing specific labels called epigenetic markers. The drug specifically targets markers on histones, the protein "spools" that DNA coils around to create structures called chromatin.

"Magic" eraser

Writing in the journal Cell Stem Cell, the team reports that more than half of mouse epiblast stem cells treated with the drug reversed course within three days, and regained an embryonic "be anything" state, also called pluripotency.

In addition to generating pluripotent stem cells, the team showed that mice bred using the cells grew up healthy.

"We've demonstrated that we don't have to manipulate the pluripotent genes to get to the ground state, but rather that we can block all other options of where the cell 'wants' to go. Then the only option is going back to the ground, or naïve, pluripotent state," says Yali Dou, Ph.D., senior author of the new paper and an associate professor of pathology and biological chemistry at U-M.

The researchers used a relatively new compound called MM-401, which U-M scientists originally designed for use in treating leukemia. Now, they're working to see if the MM-401 eraser technique works with human stem cells that bear some resemblance to mouse epiblast stem cells. They will share the drug with any other researchers who want to try the technique.

However, it's far too early to see the approach as a way to avoid the use of human embryos for research or potential treatments. Currently, embryos left over from infertility treatments are the only source of human embryonic stem cells.

Other techniques can reprogram "adult" cells in the human body taken from skin, for example -- but the cells still carry baggage from their previous state.

Still, the new achievement shows the power of altering the epigenetic labels that dot the chromatin packaging, without altering the DNA itself. Past attempts by other teams to restore pluripotency to mouse cells from the epiblast stem cell state have yielded far lower amounts, or non-viable cells. And, they've required cocktails of multiple drugs, given over the long term, to achieve it.

The U-M team shows that using MM-401 for just a few days, and then stopping its use, is enough. The first author of the new paper is Hui Zhang, Ph.D., a postdoctoral fellow in Dou's laboratory.

Epigenetic maneuvers

Epigenetic labels signal to the cell's DNA-reading machinery where they should start uncoiling a chromosome in order to read it. The U-M-developed drug targets the labels that come from the activity of a gene called MLL1.

MLL1 plays a key role in the uncontrolled explosion of white blood cells that's the hallmark of leukemia, which is why U-M researchers originally developed

MM-401 to interfere with it. But it also plays a much more mundane role in regular cell development, and the formation of blood cells and the cells that form the spinal cord in later-stage embryos.

It does this by placing tiny tags -- called methyl groups -- on histones. Without those labels, the cell's DNA-reading machinery doesn't know where to start reading. It's as if the invitation to open the instruction manual had vanished.

Stem cells don't harness the power of MLL1 until they're older. So using MM-401 to block MLL1's normal activity in cells that had started down the path to adulthood meant that histone marks were missing before the cell needed them. The cells couldn't continue on their journey to becoming different types of cells. But they could still function as healthy pluripotent stem cells.

"People have been focused on other epigenetic changes that are more dramatic, but ignored methylation by the MLL family," says Dou. "Deleting MLL1 entirely causes failure later in differentiation. But inhibiting it with a drug temporarily leaves no trace behind."

The U-M team that designed MM-401 is led by co-author Shaomeng Wang, Ph.D., the Warner-Lambert/Parke-Davis Professor at the Medical School who holds appointments in internal medicine and pharmacology, as well as an appointment in the U-M College of Pharmacy. The team also included Sundeep Kalantry, Ph.D., an assistant professor of human genetics at U-M who showed that female stem cells treated with MM-401 had un-silenced one of their X chromosomes. This step is crucial for showing that cells have returned to true pluripotency.

Alexey Nesvizhskii, Ph.D., and his colleagues in Pathology and Computational Medicine and Bioinformatics contributed important analysis to show how changes in MLL1 expression affects other gene expression in cells.

The work was funded by the National Institutes of Health (GM082856, OD008646, GM094231, CA117307) and by the Leukemia and Lymphoma Society. U-M holds a patent on MM-401 and has licensed it to Ascentage Pharma, a China-based company co-founded by Wang in which the university holds equity.

Reference: Cell Stem Cell , http://dx.doi.org/10.1016/j.stem.2016.02.004.

http://www.eurekalert.org/pub_releases/2016-03/asu-nrt031516.php

Natural resilience to major life stressors is not as common as thought

Natural resilience may not be as common as once thought: many people can struggle considerably and for longer periods of time

Tempe, Ariz. - When someone goes through a rough period in their life, say a divorce or losing their job, the common thought has been that this is a test of the person's natural resilience or ability to bounce back. "Give the person time to heal" has been the common mantra. This oftentimes meant that when these people struggled they would be left to deal with their situation largely on their own.

Most psychological studies have supported the idea of a person's innate resilience to the struggles of life. Prior research reinforced the idea that humans by and large are naturally resilient to major events that result in qualitative shifts in their life circumstances. As a result, people stay on an even keel even through trying times.

But now, new research from Arizona State University finds that natural resilience may not be as common as once thought and that when confronted with a major life-altering event many people can struggle considerably and for longer periods of time. The new research questions prior claims that resilience is the "usual" response to major life stressors by looking at longitudinal data in a more nuanced way and making less generalization about the human response to such dramatic events.

A paper detailing the research, "Resilience to major life stressors is not as common as thought," is published in the current issue of Perspectives on Psychological Science.

"We show that contrary to an extensive body of research, when individuals are confronted with major life stressors, such as spousal loss, divorce or unemployment, they are likely to show substantial declines in well-being and these declines can linger for several years," said Frank Infurna, an ASU assistant professor of psychology and co-author of the new study.

"Previous research largely claimed that individuals are typically resilient to major life stressors," he said. "Whereas when we test these assumptions more thoroughly, we find that most individuals are deeply affected and it can take several years for them to recover and get back to previous levels of functioning."

Infurna and co-author Suniya Luthar, an ASU Foundation Professor in psychology, were seeking to replicate prior work that showed among adults, resilience - which is described as stable healthy levels of well being, and the absence of negative outcomes during or following potentially harmful circumstances - is the prototypical trajectory after potentially traumatic events. Previous work by others in the field involving people going through traumas ranging from bereavement and deployment in military service to spinal cord injury and natural disasters, have reported that resilience is the most common response following significant negative life events.

"Our findings go against the grain and show there can be more to the picture than that," Infurna said. "It may not be the case that most people are unperturbed and doing fine."

Infurna and Luthar used existing longitudinal data from Germany (the German socioeconomic panel study), which is an on going survey that began in 1984 and

annually assesses participants over a wide range of measures. The outcome that they focused on was life satisfaction, which assesses how satisfied individuals are with their lives, all things considered, as they pass through years of their lives.

Essentially, Infurna and Luthar documented that "rates of resilience" vary substantially based on assumptions applied while running the statistical models. They explain that in essence, the question that was addressed in previous studies was not, "How many people are resilient?" But instead, "Assuming A and B, how many people are resilient?"

And what were the A and B assumptions applied in previous studies?

One was about how much the groups (resilient and others) differed but within one another. Previous studies assumed that whereas resilient and non-resilient groups differed in life satisfaction changes over time - steady and high in the former but not the latter - trajectories of change were the same for all people within all of the groups. To illustrate with four hypothetical people, this would mean that Rita and Ralph, in the resilient group, both showed the same steady high life-satisfaction over time; whereas Norma and Nate, both in a non-resilient group who showed declines as a function of their major life event, showed declines exactly at the same time, and then rebounded at exactly the same time. Infurna and Luthar allowed for the possibility that Nate might have recovered two years after the adverse event and Norma immediately after the event (for example, when divorce signaled release from a particularly unhappy marriage).

The second assumption in earlier studies was that "peaks and valleys" over time would be the same within the resilient and non-resilient groups, that is, the degree to which people showed extreme highs and lows around the average of their own sub-groups. Back to the illustrative example, this assumption would mean that in prior studies, life satisfaction scores across all 10 years ranged between 4 and 8 (out of 10) for resilient and for non-resilient groups. Infurna and Luthar, by contrast, allowed for the possibility that Ralph and Rita may have stayed within the range of 6 to 8 over 10 years (that is the definition of resilience -- stable good functioning) but that Norma and Nate may have been as low as 2 in one or two years, and as high as 10 in others; again, by definition, these people are "not stable."

Merely removing the restrictive assumptions applied in previous studies dramatically changed the percentage of people found to be resilient. Using exactly the same database, rates of resilience in the face of unemployment were reported to be 81 percent. With the restrictive assumptions removed, Infurna and Luthar found the rates to be much lower, around 48 percent.

"We used previous research as a basis and analyzed the data based on their specifications," Infurna explained. "Then we used our own specifications that we feel are more in line with conceptual assumptions and we found contrasting results."

"The previous research postulated that most people, anywhere from 50 to 70 percent, would show a trajectory characterized by no change. They are largely unperturbed by life's major events," Infurna said. "We found that it usually took people much longer, several years, to return to their previous levels of functioning."

A finding that means giving a person time alone to deal with the stressor might not be the best approach to getting them back to full functionality, Infurna said.

"These are major qualitative shifts in a person's life and it can have a lasting impact on their lives," he said. "It provides some evidence that if most people are affected then interventions certainly should be utilized in terms of helping these individuals in response to these events."

The findings have implications not just for science but for public policy. According to Infurna, sweeping scientific claims that "most people are resilient" carry dangers of blaming the victims (those who do not rebound immediately), and more seriously, suggest that external interventions are not necessary to help people hit by traumatic events.

"Previously it was thought such interventions may not be a good utilization of resources or could be detrimental to the person," he added. "But based on our findings, we may need to rethink that and to think after the event: What are the best ways that we can help individuals to move forward?"

http://www.eurekalert.org/pub_releases/2016-03/uoc--ybm031716.php

Your brain might be hard-wired for altruism

UCLA neuroscience research suggests an avenue for treating the empathically challenged

It's an age-old quandary: Are we born "noble savages" whose best intentions are corrupted by civilization, as the 18th century Swiss philosopher Jean-Jacques Rousseau contended? Or are we fundamentally selfish brutes who need civilization to rein in our base impulses, as the 17th century English philosopher Thomas Hobbes argued?

After exploring the areas of the brain that fuel our empathetic impulses -- and temporarily disabling other regions that oppose those impulses -- two UCLA neuroscientists are coming down on the optimistic side of human nature.

"Our altruism may be more hard-wired than previously thought," said Leonardo Christov-Moore, a postdoctoral fellow at UCLA's Semel Institute of Neuroscience and Human Behavior.

The findings, reported in two recent studies, also point to a possible way to make people behave in less selfish and more altruistic ways, said senior author Marco

Iacoboni, a UCLA psychiatry professor. "This is potentially groundbreaking," he said.

For the first study, which was published in February in Human Brain Mapping, 20 people were shown a video of a hand being poked with a pin and then asked to imitate photographs of faces displaying a range of emotions -- happy, sad, angry and excited. Meanwhile, the researchers scanned participants' brains with functional magnetic resonance imaging, paying close attention to activity in several areas of the brain.

One cluster they analyzed -- the amygdala, somatosensory cortex and anterior insula -- is associated with experiencing pain and emotion and with imitating others. Two other areas are in the prefrontal cortex, which is responsible for regulating behavior and controlling impulses.

In a separate activity, participants played the dictator game, which economists and other social scientists often use to study decision-making. Participants are given a certain amount of money to either keep for themselves or share with a stranger. In the UCLA study, participants were given $10 per round for 24 rounds, and the recipients were actual Los Angeles residents whose names were changed for the game, but whose actual ages and income levels were used. After each participant had completed the game, researchers compared their payouts with brain scans.

Participants with the most activity in the prefrontal cortex proved to be the stingiest, giving away an average of only $1 to $3 per round.

But the one-third of the participants who had the strongest responses in the areas of the brain associated with perceiving pain and emotion and imitating others were the most generous: On average, subjects in that group gave away approximately 75 percent of their bounty. Researchers referred to this tendency as "prosocial resonance" or mirroring impulse, and they believe the impulse to be a primary driving force behind altruism.

"It's almost like these areas of the brain behave according to a neural Golden Rule," Christov-Moore said. "The more we tend to vicariously experience the states of others, the more we appear to be inclined to treat them as we would ourselves."

In the second study, published earlier this month in Social Neuroscience, the researchers set out to determine whether the same portions of the prefrontal cortex might be blocking the altruistic mirroring impulse.

In this study, 58 study participants were subjected to 40 seconds of a noninvasive procedure called theta-burst Transcranial Magnetic Stimulation, which temporarily dampens activity in specific regions of the brain. In the 20 participants assigned to the control group, a portion of the brain that had to do with sight was weakened on the theory it would have no effect on generosity. But in the others, the researchers dampened either the dorsolateral prefrontal cortex or the dorsomedial prefrontal cortex, which combine to block impulses of all varieties.

Christov-Moore said that if people really were inherently selfish, weakening those areas of the brain would free people to act more selfishly. In fact, though, study participants with disrupted activity in the brain's impulse control center were 50 percent more generous than members of the control group.

"Knocking out these areas appears to free your ability to feel for others," Christov-Moore said.

The researchers also found that who people chose to give their money to changed depending on which part of the prefrontal cortex was dampened. Participants whose dorsomedial prefrontal cortex was dampened, meanwhile, tended to be more generous overall. But those whose dorsolateral prefrontal cortex was dampened tended to be more generous to recipients with higher incomes -- people who appeared to be less in need of a handout.

"Normally, participants would have been expected to give according to need, but with that area of the brain dampened, they temporarily lost the ability for social judgments to affect their behavior," Christov-Moore said. "By dampening this area, we believe we laid bare how altruistic each study participant naturally was."

The findings of both studies suggest potential avenues for increasing empathy, which is especially critical in treating people who have experienced desensitizing situations like prison or war.

"The study is important proof of principle that with a noninvasive procedure you can make people behave in a more prosocial way," Iacoboni said.

http://bit.ly/22s8CST

New Study Details Interbreeding of Ancient Humans With Evolutionary Cousins

Genetic analysis shows multiple periods of inbreeding—trysts that may have given ancient humans the genetic tools they needed to survive

By Jason Daley

Scientists have known for a while that early humans interbred with their ancient Neanderthal and Denisovan cousins. Chunks of their DNA can still be found in most non-African populations. But just how often and where this interbreeding took place has remained a mystery—until now.

A new study published in the journal *Science* is starting to unravel that timeline, showing that the periods of mating between evolutionary cousins took place multiple times over a 60,000 year period on several different continents.

Cari Romm at *The Atlantic* reports that researchers analyzed the DNA from 1,523 modern people of various ethnic backgrounds. Using a new statistical method, the

team classified which DNA came from Neanderthals or Denisovans and whether that ancient DNA came from one encounter or separate periods of interbreeding.

The study led to an interesting chronology, writes Ann Gibbons for *Science Magazine*. It revealed that most of the ancient DNA in Melanesians—the people who live in Papua New Guinea and the surrounding islands in the South Pacific—came from Denisovans, a close cousin of the Neanderthal known from some molars and a single pinky bone found in a cave in Siberia.

While researcher knew Melanesians had Denisovan DNA, they did not think the percentage would be so high, roughly 1.9 to 3.4 percent of their total genome. Melanesians also have Neanderthal DNA from one encounter period, which probably took place soon after *Homo sapiens* left Africa. It's thought the Melanesian ancestors then moved on, picking up the Denisovan DNA somewhere in Asia.

"That's pretty strange," Joshua Akey, a population geneticist at the University of Washington in Seattle and a lead author on the study tells Charles Q. Choi at *LiveScience*. "What we know of Denisovans comes from a pinky bone from a cave in northern Siberia, yet the only modern human population with appreciable levels of Denisovan ancestry is a couple of thousand miles away from that cave, in Melanesia."

A second tryst with Neanderthals is recorded in the DNA of Europeans, South Asians and East Asians, which likely took place somewhere in the Middle East. The genome also shows that East Asians had a third dalliance with Neanderthals sometime after breaking away from Europeans and South Asians.

"The most exciting new thing about the paper is that it confirms that there have been multiple Neanderthal introgression events independently on several different human evolutionary lineages," Rasmus Nielsen, a researcher at the University of California, Berkeley, not involved in the project, tells Eva Botkin-Kowaki at *The Christian Science Monitor*. "Instead of thinking of Neanderthal admixture as something that happened just once or twice, we are now forced to consider the possibility that there has been extensive admixture between Neanderthals and humans in the entire range in which they overlapped."

The interspecies breeding may have also helped *Homo sapiens* gain a few useful genes as they radiated out of Africa reports Gibbons. As early humans moved north and east, they encountered new climates, new food sources, and new diseases. Mating with Neanderthals and Denisovans may have given them the genetic tools to survive. In fact, the researchers identified 21 chunks of ancient DNA in modern humans which include genes that recognize viruses, help handle blood glucose and code for proteins that break down fat.

"The immune system is a pretty frequent target of evolution," Akey tells Choi. "As our ancestors were spreading to new environments all over the world, hybridization would have provided an efficient way to pick up copies of genes adapted to local environmental conditions, and immune-related genes probably helped our ancestors handle new pathogens they were exposed to."

Needless to say the human gene pool is getting deeper and over the next couple years scientists may learn that it is even more jumbled than we thought. Carl Zimmer at *The New York Times* points out a report released last month in *Genome Research* indicating that pieces of DNA in African pygmies come from an unknown ancestor that mated with humans within the last 30,000 years.

Akey's team will soon take a look at that too, adding another unexpected branch to the increasingly full human family tree.

http://www.bbc.com/news/magazine-35766627

'I nearly died in a medical drug trial'

When Rob Oldfield signed up for a drugs trial at Northwick Park Hospital in 2006, he thought he had found a way to earn some easy money, and do his bit for medical science. But the trial went disastrously wrong, leaving him and five other healthy men fighting for their lives.

By Jason Caffrey BBC World Service

On the morning of 13 March 2006 Oldfield joined seven other test subjects at an independent clinic at Northwick Park Hospital run by Parexel, a company which conducts drug trials for pharmaceutical companies. He was taking part in the first human trial of what was known as TGN1412, a drug that manipulated the immune system.

The German company that developed the drug hoped it would revolutionise treatment of leukaemia and rheumatoid arthritis. But within minutes of having the drug administered, all of the test subjects began feeling unwell. "I was injected at about 8am," says Oldfield. "Around midnight I was taken to intensive care."

The group of eight people had initially been split into two groups of four, who were put in separate rooms. One person in each room was given a placebo. The remaining six were given TGN1412. "They administered to everybody in the other room," recalls Oldfield, who was subject number seven, "then they came into our room." "We all had a catheter fitted to our arm and an electronic syringe. They came around, plugged in the syringe and pressed go.

"People started feeling cold. Everyone was starting to look a bit under the weather, freezing cold, a bit of the shivers. I thought 'it'll be OK, I'll probably be a placebo'."

Oldfield had no such luck. Subject number eight was given the placebo and went home shortly afterwards. "They activated the needle - injected me - then I began

to feel cold," recalls Oldfield. "The nurses didn't know what was going on really. They were faffing around looking for blankets to keep us warm.

"I remember being sick into a biohazard bag, and all of us being very ill. But the worrying point for me was when one guy, they drew the curtains around him, then these guys with gowns came up, like from an operating theatre. "They went behind the curtain, then went away and came back with all this equipment - life-support stuff."

Oldfield had signed up to the trial for a fee of £2,000. He had spent two months in the US training as a screen actor, and returned to the UK with some debts he wanted to clear. "A friend of mine had told me about medical trials before I'd gone. I thought I may as well take of advantage of it. Plus I thought I could be a kind of ambassador for medical science."

Like the other men taking part, he filled out an 11-page consent form which detailed the risks of taking part. But he had no inkling that the "potential hazards" could have resulted in him needing life-support. "I didn't know it was dangerous. I had no idea it altered the immune system."

But TGN1412 had a catastrophic effect on the six men's bodies. Headaches and chills rapidly gave way to vomiting, severe pain and shortness of breath. Swollen tissue, plummeting blood pressure and multiple organ failure followed. One by one, all six were transferred to intensive care.

"I remember quite vividly being pushed through those corridors that hospitals have, and when they go outside and it's like a glass enclosure. "I remember the cool air hitting me and feeling faint because of the temperature change."

Oldfield ended up in an area where people recover after surgery. Intensive care was short of room. "There were six of us in this triage space, and that's where they started putting machines on us - haemo-filtration, cleaning your blood."

Despite the drama, it took Oldfield some time to grasp the danger he was in. He was given steroids, which masked his symptoms, and for a time he thought the adverse reaction to TGN1412 was within expectations - it was a trial after all, and the medical staff treating him were not being explicit about his situation.

"They were just saying we need to put this in the top of your leg, put a big tube into the neck, just to give drugs - it wasn't like 'you are seriously ill'."

At about 02:00, some 18 hours after Oldfield was injected, medical staff called his mother and told her she should come to the hospital. In the middle of the night, she started driving from her home in Bristol to Northwick Park. "The doctors were saying this is your goodbye perhaps - this person could die," he says.

When his mother arrived, the look in her eyes told him that he was in a bad condition. "I now know that I was very puffy because of the steroids," he says. "The whites of my eyes were orange because of the toxins. I didn't look well."

How trials are regulated

People running clinical trials have legal obligations that are set out in Medicines for Human Use (Clinical Trials) Regulations 2004. conditions include:

- ***Anyone taking part in a trial must have a full understanding of the objectives of the research, and any risks and potential inconveniences they may experience when taking part. This information will be given to them at a meeting with a member of the research team***
- ***A point of contact must be provided so patients can obtain more information about the trial***

Before a clinical trial of a new medicine can begin, all of the following needs to be in place:

- ***The science the research is based on must be reviewed by experts***
- ***The researchers must secure funding***
- ***An organisation, such as a hospital or research institute, must agree to provide a home base for the trial***
- ***The Medicines and Healthcare Products Regulatory Agency (MHRA) needs to review and approve trials of a medicine and issue a clinical trial authorisation (CTA)***
- ***A recognised ethics committee must review the trial and allow it to proceed***

Find out more at NHS Choices

For two weeks, Oldfield's blood was filtered 24 hours a day, he recalls. His immune system had crashed, and his liver, kidneys and lungs were failing. Fluid seeped into his lungs and he had to breathe air through a mask, while a direct line pumped vital drugs into his heart. Thankfully, like all of the men injected with TGN1412 that day, Oldfield survived. After three weeks in hospital, including seven days in intensive care, he emerged alive.

His short-term memory was impaired - for months afterwards he would forget conversations and appointments - and his immune system made extremely weak. Doctors advised him not to use public transport, and avoid other places where he might be exposed to viruses. But he was, relatively speaking, fortunate.

At least one of the other men in the test experienced severe swelling of the head, leading to the episode being dubbed the "elephant man" trial. Another spent four months in hospital, and had his toes and parts of his fingers amputated.

Oldfield received substantial cash payments over the course of two years as compensation. He used some of the money to hire a personal trainer to help "get myself in shape and feel more active".

Although he doesn't want to make public the amount of money he received, he believes the compensation was inadequate. He is also critical of Parexel. He notes that Parexel's own document about the trial said TGN1412 could cause a cytokine storm - the dangerous reaction the men experienced.

The speed at which TGN1412 had been administered was criticised at the time, with one scientist, Prof Terry Hamblin of Southampton University, describing it as "reckless". The eight men in the test were injected at two-minute intervals, leaving very little time to assess its impact on one person before moving on to the next.

An interim review by the Medicines and Healthcare products Regulatory Agency found that Parexel had acted within protocols. But its final report said the trial had not properly considered the safe dosage of the drug for humans - a consideration that at the time was not required by law. It was also noted that there was no formal system in place to provide 24-hour medical cover.

Parexel says it "cannot discuss the specifics of any one patient-related matter to ensure the privacy for our patients and confidentiality for our clients". Patient safety is the firm's top priority, it says. "Carefully designed and conducted clinical trials are essential in evaluating investigational compounds and treatment regimens."

Oldfield has pursued a career as an actor, and feels his health is reasonable, if not perfect. "I think my immunity is a bit damaged. I get mouth ulcers more than I ever used to. The specialists say that after two years we should be at the same level as everybody. I don't see how that could be accurate.

"I try to be healthy in general, but who knows?"

http://read.bi/22zahm3

Surgeons in China used a pig's cornea to give a 14-year-old boy his sight back

Corneal transplants are common operations to restore eyesight but they can only be done with a donor cornea.

Marcus Hondro, Digital Journal

That is a problem in China, and elsewhere, where demand is high. But doctors there are solving the problem — by using pig's corneas.

Corneal transplant

A medical team at Zhongshan University in Guangdong, China successfully gave a 14-year-old boy sight back into his right eye by using a pig's cornea.

It's not the first time it's been done and doctors are hopeful such operations will restore eyesight to many of those around the world with damaged corneas.

The cornea covers the outer layer of our eyes, protecting them and serving as a lens; damage or disease can cloud the cornea and lead to reduced eyesight or blindness.

Using a pig's cornea may now become the norm in China where so many go without because of the lack of eye banks with sufficient human corneas. Other countries may also turn to pig's corneas. In the U.S. there are some 40,000 cornea transplants yearly but they come from human corneas available in eye banks.

Eye transplant success

The South China Morning Post reports the youngster lost the sight in his right eye after suffering an injury from a firecracker earlier this year while at a New Year's celebration.

The paper said the teen, from Jiangxi province in southeast China, is doing well and doctors say his eyesight continues to improve. He's regained most of the sight in the damaged eye since the operation, which was performed in late February. The operation is only now being reported in Chinese media.

The bio-engineering company China Regenerative Medicine International (CRMI) is at the forefront of the research that is leading the way in using pig's corneas for human eye transplants.

http://www.eurekalert.org/pub_releases/2016-03/varc-bas030816.php

Beyond Alzheimer's: Study reveals how mix of brain ailments drives dementia

Most compelling evidence yet that dementia commonly results from a blend of brain ailments

A new analysis based on two long-term aging studies--one of Roman Catholic nuns, the other of Japanese American men--provides what may be the most compelling evidence yet that dementia commonly results from a blend of brain ailments, rather than from a single condition. This is often the case even when an Alzheimer's diagnosis has been given, say the researchers.

A team led by Dr. Lon White, with the University of Hawaii and the Veterans Affairs-affiliated Pacific Health Research and Education Institute, analyzed data on more than 1,100 people who had taken part in the Nun Study or the Honolulu-Asia Aging Study. Both studies followed hundreds of aging adults and included brain autopsies upon their death.

The analysis by White's team appears in the March 15, 2016, issue of Neurology.

"The impact on clinical dementia and impairment is largely unrelated to the type of lesion, or type of lesion combination," said White in an email interview. "Rather, the driving factor seems to be just the total burden of disease."

The observation is not new. Based on several studies in the past few years, experts have begun to recognize "mixed pathology" dementia as a relevant model to explain the cognitive losses of older people. White notes that "even the lay public seems to now be appreciating that dementia is often the result not of a single disease process, but of a combination."

But the new study led by the Hawaii team offers the largest-scale, most comprehensive documentation of the trend to date.

The study included data on 334 nuns and 774 Japanese American men, all of whom completed multiple cognitive assessments as they grew older, and whose brains were autopsied after they died. The average age at death was around 90 for the nuns and 88 for the men.

Based on the autopsies, White's team found predictable rates of five different brain pathologies, all of which can bring on dementia. These included Alzheimer's disease, Lewy bodies, hippocampal sclerosis, microinfarcts, and low brain weight.

The researchers found signs of Alzheimer's in about half the brains. But only in about half of those cases was it the main lesion type. Among 279 participants who had severe Alzheimer's pathology, more than three-quarters had at least one other type of lesion.

Along with this, the researchers observed that most of the participants who had displayed significant levels of cognitive impairment during their final years had few or no Alzheimer's-type abnormalities.

By and large, it was combinations of ailments--rather than any single condition--that correlated most strongly with cognitive impairment. Such combinations had a "dramatic" impact on dementia risk, wrote the researchers.

The nuns with the highest level of comorbidity--the most lesion types, with the greatest overall severity--were 99 times more likely to have cognitive impairment, compared with those with no pathology.

The study documented many different combinations. There were no overarching patterns.

"There are a huge number of possible combinations of lesion types, reflecting what appears to be nearly random linkages among the types," said White. "The probability of each is largely unrelated to the probabilities of the others."

White, a neuroepidemiologist, said the effect of comorbidity appears to be multiplicative, rather than additive. This means, for example, if one type of lesion normally raises the risk of cognitive impairment by a factor of three, and another also raises it threefold, the combined risk increase from the two lesions would be not three plus three, but three times three. In other words, the older person with both lesion types would have a nine-fold risk of cognitive impairment, compared with someone without either pathology.

Says White: "I believe it's because all of these lesion types seem to be broadly distributed around the brain, each involving different neuron types and fields. So the result of their summation reflects the wiping out of multiple different systems within the brain, each required for optimal cognition."

"The bad news," he sums up, "is that it is much worse to have comorbid lesions than to have a single lesion type."

By the same token, White says, the upshot of the findings is that the opportunity to ward off dementia may be broader than currently thought.

"The good news is that preventing any [of the pathologies] will be of benefit to the process of aging-related cognitive decline. We can prevent illnesses currently diagnosed as Alzheimer's disease by preventing any of the other four lesion types, even if we cannot directly prevent the Alzheimer's lesions."

White admits there is not currently an abundance of clinical or lifestyle strategies shown to do that.

But he does underscore the importance of maintaining healthy blood pressure. High blood pressure has been implicated as a contributing factor in most of the lesion types his group studied.

"At this point," says White, "prevention by effective treatment of hypertension in midlife seems to be the only solid approach."

White is with the University of Hawaii and the Pacific Health Research and Education Institute, an independent nonprofit affiliated with the VA Pacific Islands Health Care System and the VA Central California Health Care System. His coauthors on the study were from the University of Hawaii; National Institute on Aging; University of California, San Diego; University of Minnesota; Geriatric Research, Education, and Clinical Center at the Minneapolis VA Health Care System; University of Washington; University of Southern California; University of Utah; VA Pacific Islands; and Kuakini Medical Center in Honolulu.

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http://www.eurekalert.org/pub_releases/2016-03/uos-dml032116.php

DNA markers link season of birth and allergy risk

Researchers at the University of Southampton have discovered specific markers on DNA that link the season of birth to risk of allergy in later life.

The season a person is born in influences a wide range of things: from risk of allergic disease, to height and lifespan. Yet little is known about how a one-time exposure like the season of birth has such lasting effects.

The Southampton study, published in the journal Allergy, conducted epigenetic scanning on DNA samples from a group of people born on the Isle of Wight. They found that particular epigenetic marks (specifically, DNA methylation) were associated with season of birth and still present 18 years later. The research team was also able to link these birth season epigenetic marks to allergic disease, for example people born in autumn had an increased risk of eczema compared to those born in spring. The results were validated in a cohort of Dutch children.

John Holloway, Professor of Allergy and Respiratory Genetics at the University and one of the study's authors, comments: "These are really interesting results. We

know that season of birth has an effect on people throughout their lives. For example generally, people born in autumn and winter are at increased risk for allergic diseases such as asthma. However, until now, we did not know how the effects can be so long lasting.

"Epigenetic marks are attached onto DNA, and can influence gene expression (the process by which specific genes are activated to produce a required protein) for years, maybe even into the next generation. Our study has linked specific epigenetic marks with season of birth and risk of allergy. However, while these results have clinical implications in mediating against allergy risk, we are not advising altering pregnancy timing."

Dr Gabrielle Lockett, of the University of Southampton and first author of the study, adds: "It might sound like a horoscope by the seasons, but now we have scientific evidence for how that horoscope could work. Because season of birth influences so many things, the epigenetic marks discovered in this study could also potentially be the mechanism for other seasonally influenced diseases and traits too, not just allergy."

The team say that further research is needed to understand what it is about the different seasons of the year that leads to altered disease risk, and whether specific differences in the seasons including temperature, sunlight levels and diets play a part. More study is also needed on the relationship between DNA methylation and allergic disease, and whether other environmental exposures also alter the epigenome, with potential disease implications.