http://www.eurekalert.org/pub_releases/2015-08/whoi-etf081815.php

Examining the fate of Fukushima contaminants

A fraction of buried, ocean sediment uncovered by typhoons, carried offshore by currents

The research aids in understanding what happens to Fukushima contaminants after they are buried on the seafloor off coastal Japan.

Led by Ken Buesseler, a senior scientist and marine chemist at the Woods Hole Oceanographic Institution (WHOI), the team found that a small fraction of contaminated seafloor sediments off Fukushima are moved offshore by typhoons that resuspend radioactive particles in the water, which then travel laterally with southeasterly currents into the Pacific Ocean.

"Cesium is one of the dominant radionuclides that was released in unprecedented amounts with contaminated water from Japan's Fukushima Daiichi nuclear power plant following the March 11, 2011, earthquake and tsunami," says Buesseler. "A little over 99 percent of it moved with the water offshore, but a very small fraction - less than one percent - ended up on the sea floor as buried sediment."

"We've been looking at the fate of that buried sediment on the continental shelf and tracking how much of that contaminated sediment gets offshore through re-suspension from the ocean bottom," he adds.

The research team, which included colleagues from the Japan Agency for Marine-Earth Science and Technology and the Japan Atomic Energy Agency, analyzed three years' worth of data collected from time-series sediment traps.

Researchers deployed the pre-programmed, funnel-shaped instruments 115 kilometers (approximately 70 miles) southeast of the nuclear power plant at depths of 500 meters (1,640 feet) and 1,000 meters (3,280 feet). The two traps began collecting samples on July 19, 2011 - 130 days after the March 11th earthquake and tsunami - and were recovered and reset annually.

After analyzing the data, researchers found radiocesium from the Fukushima Daiichi Nuclear Power Plant accident in the sediment samples along with a high fraction of clay material, which is characteristic of shelf and slope sediments suggesting a near shore source.

"This was a bit of a surprise because when we think of sediment in the ocean, we think of it as sinking vertically, originating from someplace above. But what this study clearly shows is that the only place that the material in our sediment traps could have come from was the continental shelf and slope buried nearshore. We know this because the coastal sediments from the shelf have a unique Fukushima radioactive and mineral signal," says Buesseler.

The data also revealed that peak movements of the sediments with radiocesium coincided with passing typhoons which likely triggered the resuspension of coastal sediments. Radiocesium was still detected in sediment samples from July 2014.

"The total transport is small, though it is readily detectable. One percent or less of the contaminated sediment that's moving offshore every year means things aren't going to change very fast," Buesseler says. "What's buried is going to stay buried for decades to come. And that's what may be contributing to elevated levels of cesium in fish - particularly bottom-dwelling fish off Japan."

While there were hundreds of different radionuclides released from the Fukushima Daiichi Nuclear Power Plant during the disaster, after the initial decay of contaminants with half lives (the time it takes for one half of a given amount of radionuclide to decay) less than days to weeks, much of the attention has remained focused on cesium-137 and-134 - two of the more abundant contaminants. Cesium-134 has a half-life of a little over two years, and so any found in the ocean could come only from the reactors at Fukushima. Cesium-137 has a half-life of roughly 30 years and is also known to have entered the Pacific as a result of aboveground nuclear weapons tests in the 1950s and '60s, providing a benchmark against which to measure any additional releases from the reactors.

In October, Buesseler and the research team will return to Japan to redeploy more sediment traps. The continued study will help estimate how long it takes to decrease the level of radiocesium in seafloor sediments near the Fukushima Daiichi Nuclear Power Plant.

The research was funded initially by a Rapid Response Grant from the National Science Foundation, and continued for three years through support from the Deerbook Charitable Trust and Gordon and Betty Moore Foundation.

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Hot chili may unlock a new treatment for obesity

University of Adelaide researchers have discovered a high-fat diet may impair important receptors located in the stomach that signal fullness.

Published today* in the journal PLOS ONE, researchers from the University's Centre for Nutrition and Gastrointestinal Diseases (based at the South Australian Health and Medical Research Institute) investigated the association between hot chilli pepper receptors (TRPV1) in the stomach and the feeling of fullness, in laboratory studies.

"The stomach stretches when it is full, which activates nerves in the stomach to tell the body that it has had enough food. We found that this activation is regulated through hot chilli pepper or TRPV1 receptors," says Associate Professor Amanda Page, Senior Research Fellow in the University of Adelaide's School of Medicine and lead author on the paper.

"It is known from previous studies that capsaicin, found in hot chillies, reduces food intake in humans. And what we've discovered is that deletion of TRPV1 receptors dampens the response of gastric nerves to stretch - resulting in a delayed feeling of fullness and the consumption of more food. Therefore part of the effect of capsaicin on food intake may be mediated via the stomach.

"We also found that TRPV1 receptors can be disrupted in high fat diet induced obesity," she says.

Dr Stephen Kentish says these findings will inform further studies and the development of new therapies.

"It's exciting that we now know more about the TRPV1 receptor pathway and that the consumption of capsaicin may be able to prevent overeating through an action on nerves in the stomach," says Dr Kentish, National Health and Medical Research Council (NHMRC) Fellow from the University of Adelaide's School of Medicine.

"The next stage of research will involve investigation of the mechanisms behind TRPV1 receptor activation with the aim of developing a more palatable therapy.

"We will also do further work to determine why a high-fat diet de-sensitises TRPV1 receptors and investigate if we can reverse the damage," he says.

This research was funded by the Blue Gum bequest, Royal Adelaide Hospital.

http://www.eurekalert.org/pub_releases/2015-08/uu-tto081815.php

The Tree of Life may be a bush

Evolution is more complex than the current model would have it; the tree is actually more akin to a bush.

New species evolve whenever a lineage splits off into several. Because of this, the kinship between species is often described in terms of a 'tree of life', where every branch constitutes a species. Now, researchers at Uppsala University have found that evolution is more complex than this model would have it, and that the tree is actually more akin to a bush.

Less than a year ago, a consortium of some hundred researchers reported that the relationship between all major bird clades had been mapped out by analysing the complete genome of around 50 bird species. This included the exact order in which the various lineages had diverged.

Since then, two of the members of the consortium, Alexander Suh and Hans Ellegren at the Uppsala University Evolutionary Biology Centre, have expanded upon this model by analysing the avian genome through a new method, which hinges on so-called 'jumping genes'. Their results paint a partially contrasting picture of the kinship between the various species.

'We can see that the very rapid rate at which various bird species started evolving once the dinosaurs went extinct, i.e. around 65 million years ago, meant that the genome failed to split into separate lineages during the process of speciation', Hans Ellegren says.

This is because evolution moved quickly, and many species arose in quick succession. When this happens, different parts of the genome can tell disparate tales of the kinship between the new species. The phenomenon has previously been explained theoretically and is a result of the genetic variation passing from one species to another. If new species then continue to evolve quickly, random chance can end up determining which original genetic variants end up in each lineage. The phenomenon is called incomplete lineage sorting.

'Previously, the difficulty resided in finding instances of incomplete lineage sorting far back in time', Hans Ellegren says. 'Therefore, it's been unknown if this phenomenon has affected evolution to any appreciable extent'.

By using the jumping genes, or so-called retrotransposed elements, the Uppsala researchers have found that, for instance, a cuckoo can be more closely related to a hummingbird than a pigeon in a certain part of its genome, while the opposite holds true in another part. The study found numerous examples to corroborate the existence of the phenomenon.

This is one of the first cases in evolutionary research where researchers have been able to document and quantify incomplete lineage sorting far back in time. It is likely a far more common occurrence than previously thought.

'The more complex kinship patterns that result from this phenomenon mean that the Tree of Life should often be understood as a Bush of Life', Alexander Suh and Hans Ellegren say.

The results will be published in the leading research journal PLoS Biology. The authors and their study are also featured in the leading editorial.

Read the article in PLoS Biology: http://dx.doi.org/10.1371/journal.pbio.1002224

http://www.eurekalert.org/pub_releases/2015-08/uu-tto081815.php

Bacteria's secret weapon against pesticides and antibiotics revealed

Bacteria have therefore developed advanced mechanisms to extract phosphate from other substances

All living things need phosphate to grow, which is why several hundred million tons of phosphate fertilisers are used every year in agriculture throughout the world. The nutrient content is so low in many parts of the world's oceans that all growth comes to a halt, and bacteria have therefore developed advanced mechanisms to extract phosphate from other substances. These are known as phosphonate compounds, which are produced by many primitive organisms and account for the largest known stock of phosphorus in the marine environment (see figure).

Many of these compounds are formed as toxins (antibiotics) as part of the ongoing battle for survival among marine organisms. Several million kilograms of glyphosate (Roundup®) are used as pesticide in agriculture every year, and the accumulation of residues of this phosphonate compound in groundwater has led to growing concern in recent years.

Bacteria capable of converting phosphonate compounds into phosphate to boost their growth have developed an arsenal of fourteen proteins for this purpose, approximately half of which are enzymes required for the chemical transformation of the substances. Five of these enzymes accumulate in the cells in a large complex called the C-P lyase complex, which can catalyse two of the total of five reactions required to use the phosphonate compound for growth.

An international team consisting of researchers from both the Department of Molecular Biology and Genetics, Aarhus University, and the Medical Research Council (MRC) in Cambridge, UK, have now determined the precise molecular structure of the C-P lyase complex, making it possible for the first time to understand how the secret weapon used by bacteria actually works.

Using X-ray crystallography and electron microscopy, the researchers were able to achieve extremely detailed insight into the structure of four of the enzymes, as well as the location of the fifth enzyme in the complex. The results have just been published in the highly esteemed scientific journal Nature and they are expected to revolutionise our understanding of the way bacteria can survive under harsh natural conditions, as well as their ability to break down certain antibiotics.

In the long term, the results could potentially be used to develop techniques for removing pesticide residues from drinking water, to avoid bacterial resistance to antibiotics, and to understand how the greenhouse effect is caused, as a significant amount of methane emission is due to bacterial conversion of methyl phosphonate in the world's oceans.

Link to the scientific article in Nature: Structural insights into the bacterial carbon-phosphorus lyase machinery, Paulina Seweryn, Lan Bich Van, Morten Kjeldgaard, Christopher J. Russo, Lori A. Passmore, Bjarne Hove-Jensen, Bjarne Jochimsen & Ditlev E. Brodersen: http://www.nature.com/nature/journal/vaop/ncurrent/full/nature14683.html

http://www.eurekalert.org/pub_releases/2015-08/acs-s072115.php

Solar cell efficiency could double with novel 'green' antenna

Unique, "green" antenna developed that could potentially double the efficiencies of certain kinds of solar cells

BOSTON - The use of solar energy in the U.S. is growing, but panels on rooftops are still a rare sight. They cost thousands of dollars, and homeowners don't recoup costs for years even in the sunniest or best-subsidized locales. But scientists may have a solution. They report today the development of a unique, "green" antenna that could potentially double the efficiencies of certain kinds of solar cells and make them more affordable.

The researchers are presenting their work at the 250th 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 9,000 presentations on a wide range of science topics. "Most of the light from the sun is emitted over a very broad window of wavelengths," says Challa V. Kumar, Ph.D. "If you want to use solar energy to produce electric current, you want to harvest as much of that spectrum as possible."

But the silicon solar cells people buy today are not very efficient in the blue part of the light spectrum. So Kumar's team at the University of Connecticut built an antenna that collects those unused blue photons and then converts them to lower energy photons that the silicon can then turn into current.

"Many groups around the world are working hard to make this kind of antenna, and ours is the first of its kind in the whole world," he says.

Commercial solar cells do a good job of converting light from about 600 to 1,000 nanometers (nm) into electric current but not from the 350 to 600 nm range. That's part of the reason solar cells on the market today are only about 11 to 15 percent efficient. High-end panels can reach 25 percent efficiency but are unaffordable for most customers. Lab prototypes can reach even higher efficiencies but are difficult to scale up.

Converting the mostly unused portion of the light spectrum to wavelengths solar cells can use in an affordable way is far from a simple task. To tackle this problem, Kumar turned to organic dyes. Photons in light excite dye molecules, which can then, under the right circumstances, relax and emit less energetic but more silicon-friendly photons.

But to get dye molecules to work together, they need to be wrapped individually and densely, while satisfying certain quantum mechanical requirements. To address this issue, they embed the dyes inside a protein-lipid hydrogel by mixing them together, warming them up and then cooling them to room temperature. With this simple process, the material wraps around individual dye molecules, keeping them separated while packing them densely. Rather than creating a radio-like antenna, however, the procedure results in a thin, pinkish film that can be coated on top of a solar cell.

"It's very simple chemistry," Kumar says. "It can be done in the kitchen or in a remote village. That makes it inexpensive to produce." These antennas are made with biological and non-toxic materials that are edible in theory, Kumar says. "Not that you would want to eat your solar cells, but they should be compostable so they won't accumulate in the environment," he says.

Now his team is working with a Connecticut company to figure out how to apply the artificial antenna to commercial solar cells. In other projects, they also are figuring out ways to use the versatile hydrogel for drug delivery and white light-emitting diodes.

Kumar acknowledges funding from the University of Connecticut and the National Science Foundation.

Edible or digestible artificial light antennas: Hydrogels of dye-loaded bovine serum albumin and medium chain fatty acids

Abstract

With the goal of producing solar energy conversion devices that are environmentally friendly, green and sustainable, we are designing and evaluating artificial light antenna systems using biological soft materials. For example, well-controlled stoichiometric mixtures of four different dyes, bovine serum albumin and medium chain fatty acids form soft hydrogels when the mixtures are heated to 90 ?C for 8-10 minutes. These gels contain roughly 90% water and they are transparent to the eye when the dyes are absent. This is a robust and facile strategy to prepare biocompatible hydrogels composed of a protein, dyes and fatty acids which are digestible, in principle. The gelation was triggered by the weak physical interactions between partially unfolded protein and the fatty acid but unperturbed by the presence of added dye molecules or the type of dye molecules used. We postulate that the dyes are embedded in these hydrogels at discrete binding sites as monomeric entities and their concentrations are adjusted for efficient energy transfer from the highest energy donor to the lower energy acceptors. Thus, an energy transfer cascade system among four different singlet energy states are constructed, and excitation of any of the dyes results in intense emission from the lowest energy acceptor state. The transparent and mechanically strong hydrogels could be simply prepared by annealing their physical mixtures. The resulting hydrogels with a shear thin-recovery behavior were syringe-injectable for device or biomedical applications. These gels may also be suitable for implantable scaffolds for the long-term release of drug molecules in vivo, where the dyes are replaced by drug molecules, or they may function as light-harvesting complexes when loaded with appropriate donor and acceptor dye molecules.

http://www.eurekalert.org/pub_releases/2015-08/uonc-ddm081715.php

Diabetes drug metformin's primary effect is in the gut, not the bloodstream

New study in Diabetes Care suggests new delayed-release metformin could help 40 percent of type 2 diabetes patients that currently can't take metformin.

CHAPEL HILL NC - Although metformin was introduced as a treatment for type 2 diabetes nearly 60 years ago and is now the recommended first-line treatment for newly diagnosed patients, researchers still debate precisely how the drug works. Now, a study published online today in Diabetes Care by researchers at the University of North Carolina School of Medicine, Elcelyx Therapeutics, and other leading endocrinologists provides strong evidence that metformin's primary effect occurs in the gut, not the bloodstream. The paper outlines results from phase 1 and phase 2 studies involving the investigational drug Metformin Delayed Release (Metformin DR), which is designed to target the lower bowel and limit absorption into the blood.

"Our clinical trials show that metformin works largely in the lower intestine, reversing half a century of conventional thinking," said John Buse, MD, PhD, first author of the paper, professor of medicine, and director of the Diabetes Care Center at the University of North Carolina School of Medicine. "These findings create an opportunity to develop a new metformin treatment option for the 40 percent of patients that currently can't take this first-line drug of choice."

Buse added, "One of the top reasons metformin isn't used for all people with type 2 diabetes is that patients with impaired kidneys accumulate too much drug in the blood, and this can result in life-threatening lactic acidosis. These studies provide evidence that delivering Metformin DR to the lower bowel significantly reduces the amount of metformin in the blood, while maintaining its glucose-lowering effect."

Because of this, Metformin DR may prove to be a treatment option for the four million type 2 diabetes patients in the United States with impaired kidney function.

In the phase 1 study, single daily doses of Metformin DR were compared to immediate-release metformin (Metformin IR) and extended-release metformin (Metformin XR) in healthy volunteers. The amount of metformin in the bloodstream after Metformin DR treatment was approximately half the amount seen with Metformin IR or Metformin XR. The phase 1 randomized study involved 20 healthy subjects.

In the phase 2 study, various doses of Metformin DR were compared to placebo or Metformin XR in patients with type 2 diabetes. Metformin DR exhibited a 40 percent increase in apparent potency compared to Metformin XR. Also, Metformin DR exhibited statistically significant and sustained reductions in fasting plasma glucose levels over 12 weeks compared to placebo. Treatment was generally well tolerated, with adverse events consistent with those for currently available metformin products.

The phase 2 randomized trial included 240 patients with type 2 diabetes at multiple study centers. Patients received either 600, 800 or 1,000 mg of Metformin DR once daily, blinded placebo, or unblinded Metformin XR at 1,000 or 2,000 mg per day. Patients previously on metformin (88 percent of subjects) had their metformin therapy withheld for two weeks prior to randomization.

The published paper is titled "The Primary Glucose-Lowering Effect of Metformin Resides in the Gut, Not the Circulation. Results From Short-term Pharmacokinetic and 12-Week Dose-

Ranging Studies," and is available at http://care.diabetesjournals.org/content/early/recent. The results of these studies were previously presented at meetings of the American Diabetes Association and the European Association for the Study of Diabetes.

http://www.eurekalert.org/pub_releases/2015-08/tu-mi081715.php

Meteorite impacts can create DNA building blocks

A new study shown that meteorite impacts on ancient oceans may have created nucleobases and amino acids.

Researchers from Tohoku University, National Institute for Materials Science and Hiroshima University discovered this after conducting impact experiments simulating a meteorite hitting an ancient ocean.

With precise analysis of the products recovered after impacts, the team found the formation of nucleobases and amino acids from inorganic compounds. The research is reported this week in the journal Earth and Planetary Science Letters.

All the genetic information of modern life is stored in DNA as sequences of nucleobases. However, formation of nucleobases from inorganic compounds available on prebiotic Earth had been considered to be difficult.

In 2009, this team reported the formation of the simplest amino acid, glycine, by simulating meteorite impacts. This time, they replaced the carbon source with bicarbonate and conducted hypervelocity impact experiments at 1 km/s using a single stage propellant gun.

They found the formation of a far larger variety of life's building blocks, including two kinds of nucleobases and nine kinds of proteinogenic amino acids. The results suggest a new route for how genetic molecules may have first formed on Earth.

Nucleobases and amino acids formation through impacts of meteorites on the early ocea. Furukawa Y., Nakazawa H., Sekine T., Kobayashi T., Kakegawa T. Earth and Planetary Science Letters (2015), http://www.sciencedirect.com/science/article/pii/S0012821X15004926

http://bit.ly/1JuaAXM

Oldest hand hints we came down from trees earlier than thought

1.8-million-year-old pinky bone suggests that modern human hands evolved earlier than we thought

THE discovery of a 1.8-million-year-old pinky bone suggests that modern human hands, good at tool use but bad at tree climbing, evolved earlier than we thought.

The bone found in Tanzania's Olduvai Gorge is the earliest modern-human-like hand bone ever found, and pushes back the origin of our dexterous digits by some 400,000 years.

The find suggests that by 1.8 million years ago, a Homo sapiens-like species had already made the transition to terrestrial living, and coexisted with smaller, more tree-dwelling Homo habilis and Paranthropus boisei.

"This bone belongs to somebody who's not spending any time in the trees at all," says Manuel Dominguez-Rodrigo from the Institute of Evolution in Africa, in Madrid, whose team analysed the bone. Hanging from branches bends bones like this one that extend from the knuckle, whereas in modern humans – and in this case – they are straighter (Nature Communications, DOI: 10.1038/ncomms8987).

"This provides good evidence supporting the hypothesis that, by about 2 million years ago, our early ancestors lost the anatomy linked to our tree-climbing past," says Brian Richmond of the American Museum of Natural History in New York.

But Richard Potts of the Smithsonian Human Origins Program in Washington DC says that a single bone is not enough to conclude that the hand it came from truly resembles that of a modern human, even though it is clearly different from those of the ape-like Australopithecines.

http://www.bbc.com/news/health-33986250

Stroke 'more likely' with long hours

People working long hours are more likely to have a stroke, according to analysis of more than half a million people.

By James Gallagher Health editor, BBC News website

The data, published in the Lancet medical journal, showed the chance of a stroke increased beyond the traditional 9am to 5pm. The link is uncertain, but theories include a stressful job and the damaging impact on lifestyle.

Experts said people working long hours should monitor their blood pressure

The study showed that in comparison to a 35-40 hour week, doing up to 48 hours increased the risk by 10%, up to 54 hours by 27% and over 55 hours by 33%.

Dr Mika Kivimaki, from University College London, said that in the 35-40 hour group there were fewer than five strokes per 1,000 employees per decade.

And that increased to six strokes per 1,000 employees per decade in those working 55 hours or more. Dr Kivimaki admitted researchers were still at the "early stages" of understanding what was going on.

Ideas include the extra stress of working long hours or that sitting down for long periods is bad for health and may increase the risk of a stroke.

However, it could just be a marker for poor health with those chained to the office not having enough time to prepare healthy meals or exercise. Dr Kivimaki told the BBC News website: "People need to be extra careful that they still maintain a healthy lifestyle and ensure their blood pressure does not increase."

The Stroke Association's Dr Shamim Quadir commented: "Working long hours can involve sitting for long periods of time, experiencing stress and leads to less time available to look after yourself. "We advise that you have regular blood pressure checks, if you're at all concerned about your stroke risk you should make an appointment with your GP or health professional."

Dr Tim Chico, a consultant cardiologist based at the University of Sheffield, said: "Most of us could reduce the amount of time we spend sitting down, increase our physical activity and improve our diet while working and this might be more important the more time we spend at work."

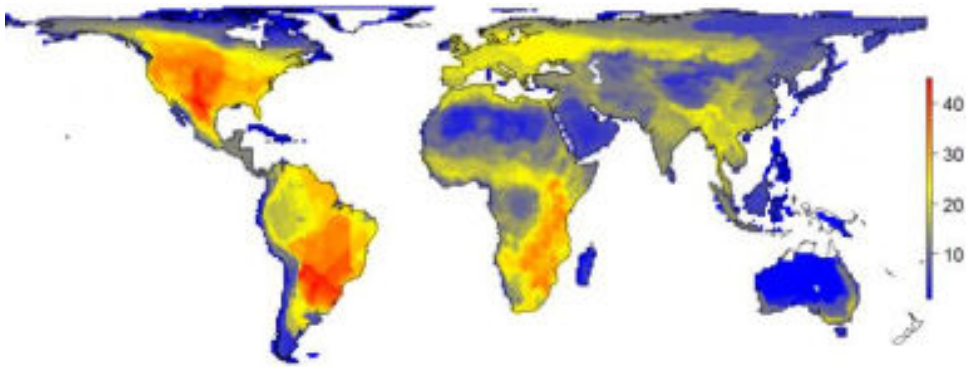
http://www.eurekalert.org/pub_releases/2015-08/au-wht082015.php

Without humans, the whole world could look like Serengeti

New study shows what the natural worldwide diversity patterns of mammals would be like in the absence of past and present human impacts

The fact that the greatest diversity of large mammals is found in Africa reflects past human activities - and not climatic or other environmental constraints. This is determined in a new study, which presents what the world map of mammals would look like if modern man (Homo sapiens) had never existed.

In a world without humans, most of northern Europe would probably now be home to not only wolves, Eurasian elk (moose) and bears, but also animals such as elephants and rhinoceroses.



The natural diversity of large mammals is shown as it would appear without the impact of modern man (Homo sapiens). The figure shows the variation in the number of large mammals (45 kg or larger) that would have occurred per 100 x 100 kilometer grid cell. The numbers on the scale indicate the number of species. **Illustration: Soren Faurby**

This is demonstrated in a new study conducted by researchers from Aarhus University, Denmark. In a previous analysis, they have shown that the mass extinction of large mammals during the Last Ice Age and in subsequent millennia (the late-Quaternary megafauna extinction) is largely explainable from the expansion of modern man (Homo sapiens) across the world. In this follow-up study, they investigate what the natural worldwide diversity patterns of mammals would be like in the absence of past and present human impacts, based on estimates of the natural distribution of each species according to its ecology, biogeography and the current natural environmental template. They provide the first estimate of how the mammal diversity world map would have appeared without the impact of modern man.

"Northern Europe is far from the only place in which humans have reduced the diversity of mammals - it's a worldwide phenomenon. And, in most places, there's a very large deficit in mammal diversity relative to what it would naturally have been", says Professor Jens-Christian Svenning, Department of Bioscience, Aarhus University, who is one of the researchers behind the study.

Africa is the last refuge

The current world map of mammal diversity shows that Africa is virtually the only place with a high diversity of large mammals. However, the world map constructed by the researchers of the natural diversity of large mammals shows far greater distribution of high large-mammal diversity across most of the world, with particularly high levels in North and South America, areas that are currently relatively poor in large mammals.

"Most safaris today take place in Africa, but under natural circumstances, as many or even more large animals would no doubt have existed in other places, e.g., notably parts of the New World such as Texas and neighboring areas and the region around northern Argentina-Southern Brazil. The reason that many safaris target Africa is not because the continent is naturally abnormally rich in species of mammals. Instead it reflects that it's one of the only places where human activities have not yet wiped out most of the large animals," says Postdoctoral Fellow Soren Faurby, Department of Bioscience, Aarhus University, who is the lead author on the study.

The existence of Africa's many species of mammals is thus not due to an optimal climate and environment, but rather because it is the only place where they have not yet been eradicated by humans. The underlying reason includes evolutionary adaptation of large mammals to humans as well as greater pest pressure on human populations in long-inhabited Africa in the past.

Better understanding helps nature preservation

The study's openly accessible data set of natural range maps for all late-Quatenary mammals provides researchers with the first opportunity to analyse the natural patterns in the species diversity and composition of mammals worldwide. Hereby, it can be used to provide a better understanding of the natural factors that determine the biodiversity in a specific area.

Today, there is a particularly large number of mammal species in mountainous areas. This is often interpreted as a consequence of environmental variation, where different species have evolved in deep valleys and high mountains. According to the new study, however, this trend is much weaker when the natural patterns are considered.

"The current high level of biodiversity in mountainous areas is partly due to the fact that the mountains have acted as a refuge for species in relation to hunting and habitat destruction, rather than being a purely natural pattern. An example in Europe is the brown bear, which now virtually only live in mountainous regions because it has been exterminated from the more accessible and most often more densely populated lowland areas," explains Soren Faurby. Hereby, this new study can provide an important base-line for nature restoration and conservation.

The study has been published in the scientific journal Diversity and Distributions.

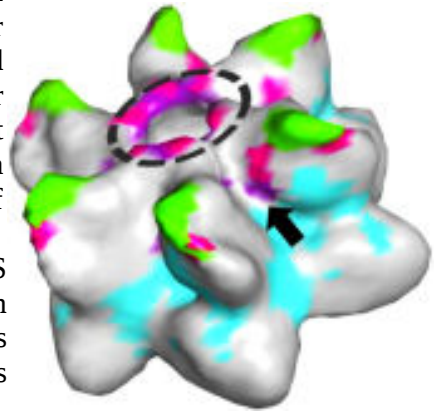
http://www.eurekalert.org/pub_releases/2015-08/p-hlh081315.php

How long have primates been infected with viruses related to HIV?

Lentiviruses closely related to HIV have infected primates in Africa as far back as 16 million years

Disease-causing viruses engage their hosts in ongoing arms races: positive selection for antiviral genes increases host fitness and survival, and viruses in turn select for mutations that counteract the antiviral host factors. Studying such adaptive mutations can provide insights into the distant history of host-virus interactions.

A study published on August 20th in PLOS Pathogens of antiviral gene sequences in African monkeys suggests that lentiviruses closely related to HIV have infected primates in Africa as far back as 16 million years.



Model of a retrovirus capsid hexamer, showing the conserved beta-hairpin domains common to most kinds of retroviruses (circled) and a pocket containing additional sites thought to affect recognition of lentiviruses by the TRIM5 anti-viral defense proteins of old world monkeys (arrow). **Johnson et al, CC-BY**

Interested in the history of lentiviruses--the group of retroviruses to which HIV and its simian (monkey) relatives, the SIVs belong--Welkin Johnson, from Boston College, USA, and colleagues focused on an antiviral gene called TRIM5.

TRIM5 is part of a group of antiviral genes called "restriction factors", which have evolved to protect host cells from infection by viruses.

Its product, the TRIM5 protein, interacts directly with the outer shell of lentivirus particles after they enter the host cells and prevents the virus from multiplying there.

(The human version of TRIM5 does not interfere with--and therefore not protect against--HIV, but many monkeys have TRIM5 variants that do render HIV harmless and are therefore immune to HIV/AIDS.)

Because of its unique specificity for retroviruses (whereas other restriction factors often have broader antiviral activity), the researchers hypothesized that the evolution of TRIM5 in African monkeys should reveal selection by lentiviruses closely related to modern SIVs.

To derive an evolutionary tree of the TRIM5 gene, they analyzed and compared its complete protein-coding DNA sequences from 22 African primate species.

They identified a cluster of adaptive changes unique to the TRIM5 proteins of a subset of African monkeys--the Cercopithecinae, which include macaques, mangabeys, and baboons--that suggests that ancestral lentiviruses closely related to modern SIVs began colonizing primates in Africa as far back as 11-16 million years ago.

The scientists also generated a panel of (reconstructed) ancestral and existing TRIM5 genes (19 total), expressed them in cultured cell lines, and exposed the cells to 16 different retroviruses (lentiviruses and others) to see which TRIM5 versions conferred resistance to which viruses.

These experiments confirmed that the observed cluster of adaptations resulted in resistance specifically to cercopithecine lentiviruses, but had no effect on restriction of other retroviruses, including lentiviruses of other, non-cercopithecine primates.

The researchers conclude "The correlation between lineage specific adaptations and ability to restrict viruses endemic to the same hosts supports the hypothesis that lentiviruses closely related to modern SIVs were present in Africa and infecting the ancestors of cercopithecine primates as far back as 16 million years ago, and provides insight into the evolution of TRIM5 specificity."

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http://www.eurekalert.org/pub_releases/2015-08/usgs-era081315.php

Ecologists roll a century's work on food-webs into a single model

What is the mathematical structure of the natural world?

SANTA BARBARA, Calif. - In a paper released today in Science, a new model presents a common mathematical structure that underlies the full range of feeding strategies of plants and animals: from familiar parasites, predators, and scavengers to more obscure parasitic castrators and decomposers. Now ecologists can view all food-web interactions through the same lens using a common language to understand the natural world.

"Physicists use 'string theory' to decipher the universe, economists use complex regression methods to model the global economy, but what about the animals and plants that supply our food and that clean and produce the air we breathe?" said co-author Andrew Dobson, a professor in Princeton University's Department of Ecology and Evolutionary Biology.

The model captures the structure of all the consumer-resource links, plants capturing sunlight, predators eating prey, and parasites eating hosts, that connect species in food webs. "It rolls a century's worth of food-web mathematics into a single model," said U.S. Geological Survey Ecologist and lead author Kevin Lafferty.

Although ecologists have previously assumed that different food web links had different structure, for example lions eating zebras operate in different ways than viruses causing disease, this new research finds that they share a common structure, but with distinct characteristics. Insights from past ecological research as well as new ecological models can now be viewed through a common framework akin to physics or chemistry. Co-author Armand Kuris of University of California Santa Barbara considers this "the first development of a unifying theory for ecology. With this approach we can now see the entire elephant, not just some of its parts."

"Ecologists have long used mathematical equations to study how predators and diseases affect plant, animal and human populations," said co-author Cheryl Briggs of UC Santa Barbara, "But these approaches have been idiosyncratic, limited in scope and full of hidden assumptions."

The model emerged from a National Science Foundation sponsored working group organized by Lafferty and Dobson at the National Center for Ecological Analysis and Synthesis, a think tank at UC Santa Barbara where ecologists tackle big problems about the environment. The group first set out to reveal the hidden role of parasites in food webs. Early discussions took the group down the same road travelled by others - trying to find different functions to fit different types of parasites and predators.

After several years, the group realized that there was a consistent mathematical backbone underlying their efforts. Out of a jumble of seemingly unrelated and complicated mathematical expressions, they found a simple solution that generalized across a comprehensive range of ecological reactions and revealed previously unobserved similarities and hidden assumptions in classic ecological models. The solution provides a general mathematical framework for food-webs. Ecologists can use this general model to develop a deeper understanding of how the world functions ecologically; this will have profound implications for infectious diseases, fisheries, conservation and humans manage natural ecosystems.

The team anticipates their work will lead to a new generation of food web models that examine ecological structure more acutely and how that structure is responding to global change.

The paper "A General Consumer-Resource Population Model" published today in Science included authors from UC Santa Barbara, Stanford University, University of Bristol, Princeton University and the Santa Fe Institute.

http://www.eurekalert.org/pub_releases/2015-08/hsop-bme081715.php

Breastfeeding may expose infants to toxic chemicals

Widely used class of industrial chemicals linked to cancer and interference with immune function appears to build up in infants each month they're breastfed

Boston, MA -- A widely used class of industrial chemicals linked with cancer and interference with immune function--perfluorinated alkylate substances, or PFASs--appears to build up in infants by 20%-30% for each month they're breastfed, according to a new study co-authored by experts from Harvard T.H. Chan School of Public Health. It is the first study to show the extent to which PFASs are transferred to babies through breast milk, and to quantify their levels over time.

"We knew that small amounts of PFAS can occur in breast milk, but our serial blood analyses now show a buildup in the infants, the longer they are breastfed," said Philippe Grandjean, adjunct professor of environmental health at Harvard Chan School.

The study appeared online August 20, 2015 in Environmental Science & Technology. Other study authors were from Danish universities and the Faroese Hospital System.

PFASs are used to make products resistant to water, grease, and stains. They've been in use for more than 60 years in products such as stain-proof textiles, waterproof clothing, some food packaging, paints, and lubricants, and are known to contaminate drinking water in the U.S. near various production facilities. These compounds--which tend to bioaccumulate in food chains and can persist for a long time in the body--are found regularly in the blood of animals and humans

worldwide, and have been linked with reproductive toxicity, endocrine disruption, and immune system dysfunction.

The researchers followed 81 children who were born in the Faroe Islands between 1997-2000, looking at levels of five types of PFASs in their blood at birth and ages 11 months, 18 months, and 5 years. They also looked at PFAS levels in mothers of the children at week 32 of pregnancy. They found that, in children who were exclusively breastfed, PFAS concentrations in the blood increased by roughly 20%-30% each month, with lower increases among children who were partially breastfed. In some cases, by the end of breastfeeding, children's serum concentration levels of PFASs exceeded that of their mothers'.

One type of PFAS--perfluorohexanesulfonate--did not increase with breastfeeding. After breastfeeding was stopped, concentrations of all of five types of PFASs decreased. The results suggest that breast milk is a major source of PFAS exposure during infancy. "There is no reason to discourage breastfeeding, but we are concerned that these pollutants are transferred to the next generation at a very vulnerable age. Unfortunately, the current U.S. legislation does not require any testing of chemical substances like PFASs for their transfer to babies and any related adverse effects," Grandjean said.

Funding for the study came from the National Institute of Environmental Health Sciences, NIH (ES012199); the U.S. Environmental Protection Agency (R830758); the Danish Council for Strategic Research (09-063094); and the Danish Environmental Protection Agency as part of the environmental support program DANCEA (Danish Cooperation for Environment in the Arctic).

"Breastfeeding as an Exposure Pathway for Perfluorinated Alkylates," Ulla B. Mogensen, Philippe Grandjean, Flemming Nielsen, Pal Weihe, and Esben Budtz-Jørgensen, Environmental Science & Technology, August 20, 2015, doi: 10.1021/acs.est.5b02237

http://www.eurekalert.org/pub_releases/2015-08/tl-tln081915.php

The Lancet Neurology: Experts claim number of people with dementia in some Western European countries could be stabilizing

Risk of dementia may be falling due to improved education and living conditions, and better prevention and treatment of vascular diseases, highlighting the need for policies to improve health across the lifecourse

In a Policy View published in The Lancet Neurology journal, a group of leading experts on the epidemiology of dementia state that the number of people with dementia - both new cases and total numbers with the disease - in some Western European countries is stabilising despite population ageing, in direct contrast to the "dementia epidemic" reported in some recent studies.

The Policy View discusses data from five large epidemiological studies done in Sweden, the Netherlands, the UK, and Spain that compare dementia occurrence in old people across two periods of time using the same methods of diagnosing dementia in the same geographical regions (figure 1 [1]). The findings suggest that prevalence (ie, the percentage of the population with dementia) and incidence (the number of new dementia cases over a given time) of dementia in specific age groups are falling across time and generations (figure 3 and panel 3).

Estimates of the proportion of dementia cases within countries are needed to plan for the provision of care, yet much of the evidence used at both national and local levels (eg, the UK's NHS primary care targets) is based on research started in the 1980s. "These old studies support the idea of a continuing 'dementia epidemic', but are now out of date because of changes in life expectancy, living conditions, and improvements in health care and lifestyle," [2] says Carol Brayne, lead author and Professor of Public Health Medicine at the Cambridge Institute of Public Health (CIPH), University of Cambridge in the UK.

Findings from four of the five studies analysed in the Policy View showed non-significant changes in overall dementia occurrence over the past 20 to 30 years. The UK study showed a significant reduction (about 22%) in overall prevalence in people aged 65 years in 2011 than the predicted estimates in 1990, resulting in stabilisation of estimated numbers of people with dementia. Results from the study done in Zaragoza (Spain) showed a significant decline in dementia prevalence in men aged 65 and older (about 43%) between 1987 and 1996. The studies done in Stockholm (Sweden) and Rotterdam (the Netherlands) showed that the age-specific incidence of dementia is falling in these regions.

"The suggested decrease in dementia occurrence coincides with improvements in protective factors (such as education and living conditions) for dementia and a general reduction in risk factors (such as vascular diseases) over recent decades," explains Brayne. "Incidence and deaths from major cardiovascular diseases have decreased in high-income countries since the 1980s. We are now potentially seeing the results of improvements in prevention and treatment of key cardiovascular risk factors such as high blood pressure and cholesterol reflected in the risk of developing dementia." [2]

According to the researchers, although the decrease in dementia occurrence is a positive sign, dementia care will remain a crucial challenge for many years because of population ageing. "It is important to remember that the number of people over age 85 is the fastest growing age demographic, with about 40% currently estimated to be affected by dementia," [2] says co-author Yu-Tzu Wu from CIPH, University of Cambridge in the UK.

Professor Brayne concludes, "Our up-to-date evidence suggests a relatively optimistic picture of possible future trends in dementia occurrence and strengthens the need to shift more of our societal and research focus to primary prevention across the lifecourse, with a rebalancing from what could be seen as the current overemphasis on diagnostics and drug interventions for dementia (which detect early or later assumed pathology). Policies which address determinants of health in earlier life stages and enhance cognitive reserve for populations may have the greatest long term impact on reduction of dementia risk at given ages in later life as well as on population health more generally." [2]

[1] The studies allow meaningful comparisons of prevalence and incidence over time because they use the same methods of diagnosing dementia between two time-points.

[2] Quotes direct from authors and cannot be found in text of Policy View.

http://www.eurekalert.org/pub_releases/2015-08/uom-bpb082015.php

Brief postnatal blindness triggers long-lasting reorganization in the brain

Temporary visual deprivation shortly after birth induces permanent auditory responses in the visual area of the brain, highlighting a crossmodal competition for brain territories during the early sensitive period of brain development

A brief period of postnatal visual deprivation, when early in life, drives a rewiring of the brain areas involved in visual processing, even if the visual restoration is completed well before the baby reaches one year of age, researchers at the University of Trento, McMaster University, and the University of Montreal revealed today in Current Biology.

Scientists have long known that the functional neural architecture for perception and cognition strongly depends upon plasticity: in other words, our brain has the capacity to change and adapt as a result of experience.

As a number of neuroimaging studies show, the early onset of permanent blindness alters the response of the neurons of the visual cortex and causes a cortical compensatory re-organization in the occipital lobe. This lobe, where visual functions are typically located, becomes active during the processing of auditory stimuli. The recruitment of visual areas for auditory tasks is sometimes thought to underlie the better performance in processing inputs from other senses observed in congenitally blind people.

What was not clear yet was whether a short and transient period of postnatal visual deprivation is sufficient to trigger crossmodal reorganization that persists after years of visual experience. In order to answer that question, the researchers characterized the brain responses to auditory stimuli in 11 adults who had been treated for congenital cataracts in both eyes.

These adults had been deprived of all patterned vision from birth until the cataracts were removed surgically and the eyes fitted with appropriate contact lenses that restored nearly normal visual input. The age at treatment varied from 9 days to just under 8 months of age. The control group consisted of 11 visually normal adults.

"The cataract-recovery participants had been blind for less than 8 months, but their blindness occurred at birth, during the most sensitive period for brain development.

They showed enhanced auditory-driven activity in focal visual regions", explained study leader Olivier Collignon, who undertook the work at University of Trento and the University of Montreal. "Thus, a short and transient period of visual deprivation early in life leads to enduring large-scale crossmodal reorganization of the brain circuitry typically dedicated to vision. This compellingly highlights the role early postnatal experience plays in shaping the functional architecture of the brain".

Crossmodal plasticity in the case of blindness is a vital brain mechanism for compensating for visual deprivation, but the mechanism can have also negative effects on visual restoration, because it might interfere, to a certain extent, with the optimal resettlement of the regained sensory inputs. "Crossmodal plasticity may therefore be considered as a two-edged sword", Collignon added.

The existence of auditory responses in the occipital cortex of cataract-recovery patients, as observed in the study, therefore poses crucial questions regarding how these non-visual inputs coexist or even interfere with visual functions. Olivier Collignon and his collaborators are now investigating further how this crossmodal reorganization might contribute to the impaired visual abilities observed in cataract-reversal patients. Resolving this crucial question may impact on how visual training programs are developed for visual restoration.

Professor Olivier Collignon is founder of the Crossmodal Perception and Plasticity Group of the Center for Mind/Brain Sciences (CIMeC) of the University of Trento and a researcher affiliated with the University of Montreal's Department of Psychology. Collignon and his colleagues, Giulia Dormal (University of Montreal, University of Hamburg), Adelaide de Heering (McMaster University, University of Louvain), Franco Lepore (University of Montreal), Terri Lewis (McMaster University, The Hospital for Sick Children, and Daphne Maurer (McMaster University, The Hospital for Sick Children), published "Long-Lasting Crossmodal Cortical Reorganization Triggered by Brief Postnatal Visual Deprivation" in Current Biology on August 20, 2015. This research received funding from by the Quebec Bio-Imaging Network "pilot project" grant, the Canadian Institutes of Health Research, the Sainte-Justine Hospital Fundation, the Belgian National Funds for Scientific Research and the "MADVIS" European Research Council starting grant.

http://www.eurekalert.org/pub_releases/2015-08/mskc-msk082015.php

Memorial Sloan Kettering Cancer Center researchers publish landmark 'basket study'

Researchers from Memorial Sloan Kettering Cancer Center (MSK) have announced results from the first published basket study, a new form of clinical trial design that explores responses to drugs based on the specific mutations in patients' tumors rather than where their cancer originated.

Published in the New England Journal of Medicine, the early phase II study, led by MSK Physician-in-Chief and Chief Medical Officer José Baselga, MD, PhD, looked at the effect of vemurafenib (Zelboraf®) in multiple nonmelanoma BRAFV600-mutated cancers in 122 patients from 23 centers around the world. Vemurafenib previously has been proven to treat BRAFV600-mutated melanoma. People with lung, colorectal, and ovarian cancers were among those included in the study as well as people with rare diseases, such as Erdheim-Chester disease. Until this point, the efficacy of vemurafenib in nonmelanoma cancers has remained unexplored despite significant therapeutic potential.

"This study is the first deliverable of precision medicine. We have proven that histology-independent, biomarker-selected basket studies are feasible and can serve as a tool for developing molecularly targeted cancer therapy," said Dr. Baselga, the study's senior author.

"While we can -- and should -- be cautiously optimistic, this is what the future of precision medicine looks like."

Basket studies permit the detection of early signals of activity across multiple tumor types simultaneously, while allowing for the possibility that tumor lineage might influence drug sensitivity.

The first to follow this model, this new study aims to explore treatment responses among tumors based on their mutation types and to identify promising signals of activity in individual tumor types that could be pursued in subsequent studies.

The results will ultimately guide researchers in looking for different drug targets or developing therapies that combine vemurafenib with complementary treatments. Basket studies also have the ability to greatly increase the number of patients eligible to receive certain drugs.

The mixed efficacy seen in this study proves that drugs can reach patients beyond the current approved use but, expectedly, do not work for everyone.

As a pioneering trial, this data demonstrates the promising benefits of basket studies and the need for more work to be done with these types of trials.

The findings illustrate the preliminary clinical efficacy of vemurafenib in multiple nonmelanoma BRAFV600-mutated cancers. Of the 122 trial participants, clinical activity was observed in various tumor types.

Preliminary vemurafenib activity was observed in non-small cell lung cancer as well as Erdheim-Chester disease and Langherhans cell histiocytosis. Response rate and median progression-free survival in non-small cell lung cancer was 42 percent and 7.3 months, respectively.

In Erdheim-Chester disease and Langherhans cell histiocytosis, response rate was 43 percent; despite median treatment duration of 5.9 months, no patients progressed during therapy.

Anecdotal responses were seen in anaplastic pleomorphic xanthoastrocytoma, anaplastic thyroid cancer, cholangiocarcinoma, salivary duct cancer, ovarian cancer, clear cell sarcoma, and colorectal cancer (cetuximab combination only).

"This kind of study is a beneficial way to do rare tumor research because it allows us to open the study to patients with diseases that are completely underrepresented in clinical trials in general, such as anaplastic thyroid cancer and glioblastoma," said David Hyman, MD, the study's first author and Acting Director of Developmental Therapeutics at MSK.

"By broadening eligibility, we are translating potential benefits to as large a patient population as possible."

This clinical trial is the first in an impending wave of such studies focused on cancer-related mutations identified through the huge amounts of genomic data generated in recent years.

It highlights the importance of further investigation into precision medicine, a promising area that has recently received attention from President Obama and the National Cancer Institute, among others.

Last May, MSK launched an initiative in this space -- the Marie-Josée and Henry R. Kravis Center for Molecular Oncology -- that works to transform cancer care through genomic analysis of patient-derived tumors.

Currently the center is analyzing 410 of the most important cancer genes in thousands of patients.

"We now have the landscape of all the most frequent cancer-causing mutations in the majority of tumor types, and we know there are a number of genes that are frequently mutated in some tumors and less frequently in others," explained Dr. Baselga.

"The next step is exploring appropriate drug combinations, knowing that these cells have a finite number of pathways."

Full findings from the study can be found in the August 20 issue of the New England Journal of Medicine.

http://www.eurekalert.org/pub_releases/2015-08/mcog-tpw082015.php

Two proteins work together to help cells eliminate trash and Parkinson's may result

Two proteins that share the ability to help cells deal with their trash appear to need each other to do their jobs and when they don't connect, it appears to contribute to development of Parkinson's disease, scientists report.

Much like a community's network for garbage handling, cells also have garbage sites called lysosomes, where proteins, which are functioning badly because of age or other reasons, go for degradation and potential recycling, said Dr. Wen-Cheng Xiong, developmental neurobiologist and Weiss Research Professor at the Medical College of Georgia at Georgia Regents University.

Inside lysosomes, other proteins, called proteases, help cut up proteins that can no longer do their job and enable salvaging of things like precious amino acids.

It's a normal cell degradation process called autophagy that actually helps cells survive and is particularly important in cells such as neurons, which regenerate extremely slowly, said Xiong, corresponding author of the study in The Journal of Neuroscience.

Key to the process - and as scientists have shown, to each other - are two more proteins, VPS35 and Lamp2a. VPS35 is essential for retrieving membrane proteins vital to cell function.

Levels naturally decrease with age, and mutations in the VPS35 gene have been found in patients with a rare form of Parkinson's.

VPS35 also is a critical part of a protein complex called a retromer, which has a major role in recycling inside cells. Lamp2a enables unfit proteins to be chewed up and degraded inside lysosomes.

If the two sound like a natural couple, scientists now have more evidence that they are.

They have shown that without VPS35 to retrieve Lamp2a from the trash site for reuse, Lamp2a, or lysosomal-associated membrane protein 2, will be degraded and its vital function lost.

When the scientists generated VPS35-deficient mice, the mice exhibited Parkinson's-like deficits, including impaired motor control.

When they looked further, they found the lysosomes inside dopamine neurons, which are targets in Parkinson's, didn't function properly in the mice.

In fact, without VPS35, the degradation of Lamp2a itself is accelerated. Consequently, yet another protein, alpha-synuclein, which is normally destroyed by Lamp2a, is increased.

Alpha-synuclein is a major component of abnormal protein clumps, called Lewy bodies, found in the brains of patients with Parkinson's. "If alpha-synuclein is not degraded, it just accumulates. If VPS35 function is normal, we won't see its accumulation," Xiong said.

Conversely, when MCG scientists increased expression of Lamp2a in the dopamine neurons of the VPS35-deficient mice, alpha-synuclein levels were reduced, a finding that further supports the linkage of the three proteins in the essential ability of the neurons to deal with undesirables in their lysosomes.

Without lamp2a, dopamine neurons essentially start producing more garbage rather than eliminating it. Recycling of valuables such as amino acids basically stops, and alpha-synuclein is free to roam to other places in the cell or other brain regions where it can damage still viable proteins.

The bottom line is dopamine neurons are lost instead of preserved. Brain scans document the empty spaces where neurons used to be in patients with neurodegenerative diseases such as Parkinson's and Alzheimer's.

One of the many problems with treatment of these diseases is that by the time the empty spaces and sometimes the associated symptoms are apparent, much damage has occurred, Xiong said.

Putting these pieces together provides several new, early targets for disease intervention. "Everything is linked," Xiong said.

Dopamine is a brain chemical with many roles, including motor control, and patients with Parkinson's have a loss of the neurons that secrete this neurotransmitter.

At least in mice, VPS35 is naturally expressed in dopamine neurons in areas of the brain affected by Parkinson's.

Xiong and her colleagues reported in 2011 that reduced expression of VPS35 enables activity of the dormant-in-healthy-adults protein BACE1 to increase along with accumulation of the brain plaque that is a hallmark of Alzheimer's. Xiong said then that impaired VPS35 function likely also was a factor in Parkinson's.

In a definite vicious circle, trash starts overwhelming the brain cell's natural garbage disposal system.

Proteins start getting misfolded and dysfunctional, potentially destructive proteins such as BACE1 and Lamp2a end up in the wrong place and get activated/inactivated, while good proteins get chopped up and/or bad proteins accumulate.

Parkinson's disease is characterized by uncontrolled shaking, an unstable gait and cognitive loss.

The research was funded by the National Institutes of Health and the Department of Veterans Affairs. Postdoctoral Fellow Dr. Fulei Tang is the study's first author.

http://www.eurekalert.org/pub_releases/2015-08/asfm-ldt082015.php

Long distance travelers likely contributing to antibiotic resistance's spread

Unseen diversity of resistance genes enriched in the gut microbiome of long-distance travelers

Washington, DC - Swedish exchange students who studied in India and in central Africa returned from their sojourns with an increased diversity of antibiotic resistance genes in their gut microbiomes. The research is published 10 August in Antimicrobial Agents and Chemotherapy, a journal of the American Society for Microbiology.

In the study, the investigators found a 2.6-fold increase in genes encoding resistance to sulfonamide, a 7.7-fold increase in trimethoprim resistance genes, and a 2.6-fold increase in resistance to beta-lactams, all of this without any exposure to antibiotics among the 35 exchange students. These resistance genes were not particularly abundant in the students prior to their travels, but the increases are nonetheless quite significant.

The germ of the research was concern about the burgeoning increase in antibiotic resistance. "I am a physician specializing in infectious diseases, and I have seen antibiotics that I could safely rely on ten years ago being unable to cure my patients," said principal investigator Anders Johansson, MD, PhD, Chief, Infection Control, Umeå University and the County Council of Västerbotten, Sweden.

However, Johansson also questioned the conventional wisdom that overuse of antibiotics was entirely responsible for the surge in resistance, despite the fact that overuse is a huge problem. "Currently, I head an infection control department, and from this position it is very evident that resistance is no longer generated primarily in the hospital," he explained. Instead, patients bring bacteria carrying resistance genes into the hospital as part of their own microbial communities, he said. "We hypothesized that the gut microbiome of humans serves as a vehicle for moving many different resistance genes very large distances, even in the absence of antibiotic treatment."

And in fact, the increases the investigators observed in abundance and diversity of resistance genes occurred despite the fact that none of the students took antibiotics either before or during travel. The increase seen in resistance genes could have resulted from ingesting food containing resistant bacteria, or from contaminated water, the investigators write. Providing further support for the hypothesis that resistance genes increased during travel, genes for extended spectrum beta-lactamase, which dismembers penicillin and related antibiotics, was present in just one of the 35 students prior to travel, but in 12 students after they returned to Sweden.

Collecting samples of resistance genes was simple. "We asked students going abroad on exchange programs to provide a sample of their feces before and after traveling," said Johansson. But the study was different from previous studies of this issue in using metagenomics sequencing, a modern method. That enabled the investigators to sample the entire microbiome of each student, and to sequence every resistance gene therein, rather than focusing on resistance genes in those few bacterial species that grow well on culture plates.

"Our results spotlight that to reduce antibiotic resistance we need to minimize dispersal rates from the healthcare system, and importantly, at the societal level," said Johansson. Suppressing further spread after travelers return to their home countries is crucial, and depends, he added, upon having well-informed citizens and a well-functioning public health system.

The article can be found online at http://aac.asm.org/cgi/reprint/AAC.00933-15v1?ijkey=ApED6UHo8GluE&keytype=ref&siteid=asmjournals.

http://www.bbc.com/news/health-33974816

Vaccine for Mers coronavirus 'looks promising'

A prototype vaccine against the lung infection Mers coronavirus has shown promising results, scientists say.

By Smitha Mundasad Health reporter

The study, published in the journal Science Translational Medicine, suggests the vaccine guards against the disease in monkeys and camels. Researchers hope with more work it could be turned into a jab for humans.

Mers has infected 1,400 people and claimed 500 lives since 2012. But no specific treatment or preventative medicines exist. In the majority of cases, individuals are thought to have caught Mers (Middle-East respiratory syndrome) through close contact with infected patients in hospital.

Two-prong approach

But experts suspect camels also play an important role - acting as a host for the disease. The researchers, led by University of Pennsylvania, say their experimental vaccine could be a "valuable tool" in two different ways - first, to immunise camels to stop it spreading to human populations and, secondly, as a jab to protect individuals at risk of getting Mers.

In the trial, the vaccine was tested on blood samples taken from camels and appeared to kick-start the production of antibody proteins that may help mount a defence against the virus. And when it was given to macaque monkeys later exposed to Mers, the animals did not become ill.

Prof Andrew Easton, from Warwick University, described the research as a "significant step forward in the generation of a vaccine to prevent Mers disease".

He added: "The data show that the vaccine is capable of generating protective antibodies in laboratory studies and also in camels. "This is very promising as a possible way to reduce virus spread in camels and therefore to reduce the risk of infection in humans."

Other experts caution that since the virus tends to affect macaques less severely than humans, it is not yet clear whether it could definitely be used as a vaccine in human populations.

The research was funded in part by the National Institute of Allergy and Infectious Diseases in the US and Inovio Pharmaceuticals.

http://www.eurekalert.org/pub_releases/2015-08/aaos-sft082115.php

Study finds that genetic ancestry partially explains 1 racial sleep difference

Study is first to show that race differences in slow-wave sleep may have an independent and significant genetic basis

DARIEN, IL - A new study clearly establishes a partial genetic basis underlying racial differences in slow-wave sleep, suggesting that it may be possible to develop sleep-related therapies that target specific genetic variants.

Using a panel of 1,698 ancestry informative genetic markers, the study found that greater African genetic ancestry was associated with lower amounts of slow-wave sleep in African-American adults. African ancestry explained 11 percent of the variation in slow-wave sleep after adjustment for potential confounders. Although a similar association was observed for delta power, no association with African ancestry was observed for sleep duration and efficiency.

"Our data are the first to show that race differences in slow-wave sleep may have an independent and significant genetic basis," said senior author Martica Hall, professor of psychiatry at the University of Pittsburgh. "Although all humans have the same set of genes, variations within the genes sometimes follow population-specific patterns. By identifying the specific genetic variants that influence slow-wave sleep, we can eventually develop population-specific treatment approaches and therapies for sleep."

Study results are published in the August issue of the journal Sleep.

Led by Hall and lead author Indrani Halder, the research team analyzed data from a community-based sample of 70 African-American adults and 101 European Americans with a mean age of about 60 years. Objective sleep data were gathered by polysomnography. Blood samples for genotyping were collected, and DNA was isolated following standard protocols.

According to the authors, African-Americans have varying proportions of genetic admixture and exhibit a wide range of African genetic ancestry. Among African-American study participants, percentage of African ancestry ranged between 10 percent and 88 percent, with a mean of 67 percent.

The study was supported by the Pennsylvania Department of Health and grants from the National Institutes of Health (NIH).

To request a copy of the study, "African Genetic Ancestry is Associated with Sleep Depth in Older African Americans," or the commentary, "Parsing Race by Genetic Ancestry," or to arrange an interview with the study author or an AASM spokesperson, please contact Communications Coordinator Lynn Celmer at 630-737-9700, ext. 9364, or lcelmer@aasmnet.org.

http://www.eurekalert.org/pub_releases/2015-08/osu-ggc081915.php

Greenhouse gases caused glacial retreat during last Ice Age

A recalculation of the dates at which boulders were uncovered by melting glaciers at the end of the last Ice Age has conclusively shown that the glacial retreat was due to rising levels of carbon dioxide and other greenhouse gases, as opposed to other types of forces.

CORVALLIS, Ore. - Carbon dioxide levels are now significantly higher than they were at that time, as a result of the Industrial Revolution and other human activities since then. Because of that, the study confirms predictions of future glacial retreat, and that most of the world's glaciers may disappear in the next few centuries.

The findings were published today in Nature Communications by researchers from Oregon State University, Boston College and other institutions. They erase some of the uncertainties about glacial melting that had been due to a misinterpretation of data from some of these boulders, which were exposed to the atmosphere more than 11,500 years ago.

"This shows that at the end of the last Ice Age, it was only the increase in carbon dioxide and other greenhouse gases that could have caused the loss of glaciers around the world at the same time," said Peter Clark, a professor in the OSU College of Earth, Ocean and Atmospheric Sciences, and co-author on the study.

"This study validates predictions that future glacial loss will occur due to the ongoing increase in greenhouse gas levels from human activities," Clark said. "We could lose 80-90 percent of the world's glaciers in the next several centuries if greenhouse gases continue to rise at the current rate."

Glacial loss in the future will contribute to rising sea levels and, in some cases, have impacts on local water supplies.

As the last Ice Age ended during a period of about 7,000 years, starting around 19,000 years ago, the levels of carbon dioxide in the atmosphere increased from

180 parts per million to 280 parts per million. But just in the past 150 years, they have surged from 280 to about 400 parts per million, far higher than what was required to put an end to the last Ice Age. The new findings, Clark said, were based on a recalculation of the ages at which more than 1,100 glacial boulders from 159 glacial moraines around the world were exposed to the atmosphere after being buried for thousands of years under ice.

The exposure of the boulders to cosmic rays produced cosmogenic nuclides, which had been previously measured and used to date the event. But advances have been made in how to calibrate ages based on that data. Based on the new calculations, the rise in carbon dioxide levels - determined from ancient ice cores - matches up nicely with the time at which glacial retreat took place.

"There had been a long-standing mystery about why these boulders were uncovered at the time they were, because it didn't properly match the increase in greenhouse gases," said Jeremy Shakun, a professor at Boston College and lead author on the study. "We found that the previous ages assigned to this event were inaccurate. The data now show that as soon as the greenhouse gas levels began to rise, the glaciers began to melt and retreat."

There are other forces that can also cause glacial melting on a local or regional scale, the researchers noted, such as changes in the Earth's orbit around the sun, or shifts in ocean heat distribution. These factors probably did have localized effects. But the scientists determined that only the change in greenhouse gas levels could have explained the broader global retreat of glaciers all at the same time.

In the study of climate change, glaciers have always been of considerable interest, because their long-term behavior is a more reliable barometer that helps sort out the ups-and-downs caused by year-to-year weather variability, including short-term shifts in temperature and precipitation.

Other collaborators on this research were from the University of Wisconsin, Purdue University, and the National Center for Atmospheric Research. The work was supported by the National Oceanic and Atmospheric Administration and the National Science Foundation.

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New drug protects against the deadly effects of nuclear radiation 24 hours after exposure

New breakthrough in countering the deadly effects of radiation exposure

An interdisciplinary research team led by The University of Texas Medical Branch at Galveston reports a new breakthrough in countering the deadly effects of radiation exposure. A single injection of a regenerative peptide was shown to significantly increase survival in mice when given 24 hours after nuclear radiation exposure. The study currently appears in Laboratory Investigation, a journal in the Nature Publishing group.

UTMB lead author Carla Kantara, postdoctoral fellow in biochemistry and molecular biology, said that a single injection of the investigative peptide drug TP508 given 24 hours after a potentially-lethal exposure to radiation appears to significantly increase survival and delay mortality in mice by counteracting damage to the gastrointestinal system.

The threat of a nuclear incident, with the potential to kill or injure thousands of people, has raised global awareness about the need for medical countermeasures that can prevent radiation-induced bodily damage and keep people alive, even if given a day or more after contact with nuclear radiation.

Exposure to high doses of radiation triggers a number of potentially lethal effects. Among the most severe of these effects is the gastrointestinal, or GI, toxicity syndrome that is caused by radiation-induced destruction of the intestinal lining. This type of GI damage decreases the ability of the body to absorb water and causes electrolyte imbalances, bacterial infection, intestinal leakage, sepsis and death.

The GI toxicity syndrome is triggered by radiation-induced damage to crypt cells in the small intestines and colon that must continuously replenish in order for the GI tract to work properly. Crypt cells are especially susceptible to radiation damage and serve as an indicator of whether someone will survive after total body radiation exposure.

"The lack of available treatments that can effectively protect against radiation-induced damage has prompted a search for countermeasures that can minimize the effects of radiation after exposure, accelerate tissue repair in radiation-exposed individuals and increase the chances for survival following a nuclear event," said Darrell Carney, UTMB adjunct professor in biochemistry and molecular biology and CEO of Chrysalis BioTherapeutics, Inc. "Because radiation-induced damage to the intestines plays such a key role in how well a person recovers from radiation exposure, it's crucial to develop novel medications capable of preventing GI damage."

The peptide drug TP508 was developed for use in stimulating repair of skin, bone and muscle tissues. It has previously been shown to begin tissue repair by stimulating proper blood flow, reducing inflammation and reducing cell death. In human clinical trials, the drug has been reported to increase healing of diabetic foot ulcers and wrist fractures with no drug-related adverse events.

"The current results suggest that the peptide may be an effective emergency nuclear countermeasure that could be delivered within 24 hours after exposure to increase survival and delay mortality, giving victims time to reach facilities for advanced medical treatment," Kantara said.

Authors include UTMB's Carla Kantara, Stephanie Moya, Robert Ullrich, Pomila Singh and Darrell Carney; Courtney Houchen from the University of Oklahoma Health Sciences Center and Shahid Umar from the University of Kansas Medical Center. Carney is also affiliated with Chrysalis BioTherapeutics, Inc. Chrysalis BioTherapeutics, Inc. has licensed worldwide exclusive rights to TP508 for treatment directed towards radiation induced damage from The University of Texas Medical Branch at Galveston.

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Anti-aging tricks from dietary supplement seen in mice

Alpha-lipoic acid stimulates telomerase in vascular smooth muscle

In human cells, shortened telomeres, the protective caps at the ends of chromosomes, are both a sign of aging and contribute to it. Scientists at Emory University School of Medicine have found that the dietary supplement alpha lipoic acid (ALA) can stimulate telomerase, the enzyme that lengthens telomeres, with positive effects in a mouse model of atherosclerosis.

The discovery highlights a potential avenue for the treatment for chronic diseases. The results were published Thursday, August 20 in Cell Reports.

"Alpha-lipoic acid has an essential role in mitochondria, the energy-generating elements of the cell," says senior author Wayne Alexander, MD, PhD, professor of medicine at Emory University School of Medicine. "It is widely available and has been called a 'natural antioxidant'. Yet ALA's effects in human clinical studies have been a mixed bag."

ALA appears to exert its effects against atherosclerosis by spurring the smooth muscle cells that surround blood vessels to make PGC1 (peroxisome proliferator-activated receptor gamma co-activator 1)-alpha. PGC1-alpha was already well known to scientists as controlling several aspects of how skeletal muscles respond to exercise. While the Emory researchers did not directly assess the effects of exercise in their experiments, their findings provide molecular clues to how exercise might slow the effects of aging or chronic disease in some cell types.

"The effects of chronic diseases such as atherosclerosis and diabetes on blood vessels can be traced back to telomere shortening," Alexander says. "This means that treatments that can restore healthy telomeres have great potential."

"What's new here is that we show that PGC1-alpha is regulating telomerase, and that has real beneficial effects on cellular stress in a mouse model of atherosclerosis," says Shiqin Xiong, PhD, instructor in the division of cardiology and first author of the paper.

Xiong and Alexander used a model of atherosclerosis where mice lacked the ApoE cholesterol processing gene and were fed a high-fat diet. In this model, mice also lacking PGC1-alpha have more advanced plaques in their blood vessels, but only in older animals, the authors show.

Consistent with the poorer state of their blood vessels, aortic cells from PGC1-alpha-disrupted mice had shorter telomeres and reduced telomerase activity. Having shortened telomeres led the smooth muscle cells to display more oxidative stress and damage to the rest of their DNA.

The authors show that introducing PGC1-alpha back into vascular smooth muscle cells lacking that gene with a gene-therapy adenovirus could restore telomerase activity and lengthen the cells' telomeres.

Telomerase is off in most healthy cell types and only becomes turned on when cells proliferate. Because telomerase is active in cancer cells and enables their continued growth, researchers have been concerned that stimulating telomerase in all cells might encourage cancer growth or have other adverse effects.

As a way to boost PGC1-alpha in cells more conveniently, Xiong and Alexander turned to alpha lipoic acid or ALA. ALA is a sulfur-containing fatty acid used to treat diabetic neuropathy in Germany, and has previously been shown to combat atherosclerosis in animal models.

Treating isolated smooth muscle cells with ALA for one day could both stimulate PGC1-alpha and telomerase, the authors found. ALA's effects on vascular smooth muscle cells could also be seen when it was injected into mice. Xiong and Alexander say they are now investigating the effects of ALA on other tissues in mice. They have not observed increased cancers in ALA-treated mice, but say more thorough investigation is needed to fully assess cancer risk.

"While ALA is present in many foods and its effects in animal models look promising, it may be problematic for clinical use because of its poor solubility, stability and bioavailability," Xiong says. "We are designing new ways to formulate and deliver ALA-related compounds to resolve these issues."

Co-authors include assistant professor Lu Hilenski, PhD, Nikolay Patrushev, MD and Farshad Forouzandeh, MD, PhD.

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US has 5 percent of world's population, but had 31 percent of its public mass shooters from 1966-2012

United States was the attack site for a disproportionate 31 percent of public mass shooters globally 1966-2012

CHICAGO -- Despite having only about 5 percent of the world's population, the United States was the attack site for a disproportionate 31 percent of public mass shooters globally from 1966-2012, according to new research that will be presented at the 110th Annual Meeting of the American Sociological Association (ASA).

"The United States, Yemen, Switzerland, Finland, and Serbia are ranked as the Top 5 countries in firearms owned per capita, according to the 2007 Small Arms Survey, and my study found that all five are ranked in the Top 15 countries in public mass shooters per capita," said study author Adam Lankford, an associate professor of criminal justice at the University of Alabama. "That is not a coincidence."

Lankford's study, which examines the period from 1966-2012, relies on data from the New York City Police Department's 2012 active shooter report, the FBI's 2014 active shooter report, and multiple international sources. It is the first quantitative analysis of all reported public mass shootings around the world that resulted in the deaths of four or more people. By definition, these shootings do not include incidents that occurred solely in domestic settings or were primarily gang-related, drive-by shootings, hostage taking incidents, or robberies.

"My study provides empirical evidence, based on my quantitative assessment of 171 countries, that a nation's civilian firearm ownership rate is the strongest predictor of its number of public mass shooters," Lankford said. "Until now, everyone was simply speculating about the relationship between firearms and public mass shootings. My study provides empirical evidence of a positive association between the two."

As part of his study, Lankford explored how public mass shootings in the U.S. differed from those abroad. He found that public mass shooters in other countries were 3.6 times less likely to have used multiple weapons (typically multiple guns, but occasionally a gun plus another weapon or weapons) than those in the U.S., where more than half of shooters used at least two weapons.

"Given the fact that the United States has over 200 million more firearms in circulation than any other country, it's not surprising that our public mass shooters would be more likely to arm themselves with multiple weapons than foreign offenders," Lankford said. "I was surprised, however, that the average number of victims killed by each shooter was actually higher in other countries (8.81 victims) than it was in the United States (6.87 victims) because so many horrific attacks have occurred here."

The side-effect of America having experienced so many mass shootings may be that our police are better trained to respond to these incidents than law enforcement in other countries, which reduces the number of casualties, Lankford suggested. In addition to killing fewer people and using more weapons, U.S. public mass shooters were also more likely to attack in schools, factories/warehouses, and office buildings than offenders in other countries. But compared to U.S. shooters, attackers abroad were significantly more likely to strike in military settings, such as bases, barracks, and checkpoints.

While Lankford's study revealed a strong link between the civilian firearm ownership rate and the large number of public mass shooters in the United States, he said there could be other factors that make the U.S. especially prone to public mass shooting incidents.

"In the United States, where many individuals are socialized to assume that they will reach great levels of success and achieve 'the American Dream,' there may be particularly high levels of strain among those who encounter blocked goals or have negative social interactions with their peers, coworkers, or bosses," Lankford explained. "When we add depression, schizophrenia, paranoia, or narcissism into the mix, this could explain why the U.S. has such a disproportionate number of public mass shooters. Other countries certainly have their share of people who struggle with these problems, but they may be less likely to indulge in the delusions of grandeur that are common among these offenders in the U.S., and, of course, less likely to get their hands on the guns necessary for such attacks."

In terms of the study's policy implications, Lankford said, "The most obvious implication is that the United States could likely reduce its number of school shootings, workplace shootings, and public mass shootings in other places if it reduced the number of guns in circulation."

There is evidence that such an approach could be successful, according to Lankford. "From 1987-1996, four public mass shootings occurred in Australia," Lankford said. "Just 12 days after a mass shooter killed 35 people in the last of these attacks, Australia agreed to pass comprehensive gun control laws. It also launched a major buyback program that reduced Australia's total number of firearms by 20 percent. My study shows that in the wake of these policies, Australia has yet to experience another public mass shooting."

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New study indicates magnetic stimulation effective in reducing bed-wetting

Non-invasive treatment shows promise in a new Restorative Neurology and Neuroscience report

Amsterdam, NL - Bedwetting, or nocturnal enuresis, causes distress in children and young adults, as well as for their parents or caregivers. The causes are not fully understood and there may be both physiological and psychological components to the condition.

In a new study published in Restorative Neurology and Neuroscience, researchers report that repetitive sacral root magnetic stimulation (rSMS) can reduce the frequency of nighttime bedwetting and improve quality-of-life for sufferers.

In a study conducted by researchers at the Assiut University Hospital, Assiut, Egypt, 41 patients experiencing nocturnal enuresis were divided into two groups receiving either real magnetic stimulation or a sham stimulation using the same equipment and procedures.

The identities of the real vs. sham patients were unknown to both the researchers and the patients. Each participant received 10 sessions, five per week. A magnetic stimulator was placed over the sacral vertebrae in the lower back and 15 Hz pulses were applied for 10 seconds on and 30 seconds off.

For the sham procedure, the stimulator was internally adjusted so that little magnetic stimulation could reach the underlying tissue. All patients had been taking the tricyclic antidepressant drug imipramine (25mg once at night /day) for at least three months without satisfactory results and they continued taking their prescribed medication throughout the study.

"It seems likely that rSMS produced some of its effect in the present patients by a direct effect on bladder control," explained lead investigator Eman M. Khedr, MD, Professor, Department of Neurology, Assiut University Hospital.

"In the present study rSMS could have increased arousal or enhanced inhibition of neuronal re-uptake of noradrenaline and serotonin. We have previously reported that patients with nocturnal enuresis have pathologically increased excitability and reduced inhibitory processing in the motor cortex and it is possible that rSMS could affect these measures as well."

The average number of weekly nocturnal bedwetting episodes fell from 5.7 to 0.3 per week after the end of the treatment sessions for the real group compared to 6.5 to 1.8 per week after sham stimulation. Although the sham procedure resulted in improvement (placebo effect), the improvement in the real group continued one month later (1 per week) whereas the sham group returned to baseline behaviour (5.2 per week).

All patients were asked to complete a Visual Analogue Scale (VAS) and a generic Health Survey (SF-36v2). The VAS assesses how bedwetting affects the patient's life, while the Health Survey measures physical health and mental well-being in eight different health domains.

This treatment resulted in significant improvements in the mental health scores including social functioning, vitality, mental health, and component mental health summation in the real group compared to the sham group. While further trials will be needed to determine the optimum stimulation protocols, the potential benefits to young patients and their caregivers are clear.

http://www.eurekalert.org/pub_releases/2015-08/uotm-ghm082115.php

Generic heart medication shown to prolong ovarian cancer patients' survival

Even despite prognostic factors and co-morbidities associated with poorer outcomes

In a first-of-its-kind study, researchers demonstrate a benefit in overall survival among epithelial ovarian cancer (EOC) patients receiving generic heart medications known as beta-blockers. Survival was shown to be greatest among those prescribed first-generation nonselective beta-blockers. According to The University of Texas MD Anderson Cancer Center investigators, the drugs block the effects of stress pathways involved in tumor growth and spread. With further research, they may also prove beneficial in conjunction with other treatment regimens and across other cancer types.

Published today in the journal CANCER, the findings are the result of a multi-institutional retrospective analysis of the medical records of 1,425 women with ovarian cancer treated between 2000 and 2010. Researchers compared overall survival among patients with documented beta-blocker use during chemotherapy and those without. Among the 269 patients who received beta-blockers, 193 (71.7 percent) received beta-1-adrenergic receptor selective agents (SBBs) and the remaining patients received nonselective beta antagonists (NSBBs). The research team found:

For patients receiving any beta-blocker, the median overall survival was 47.8 months versus 42 months for nonusers.

Median overall survival based on beta-blocker receptor selectivity was 94.9 months for those receiving NSBBs versus 38 months for those receiving SBBs.

Even among patients with hypertension, a longer median overall survival was observed among users of NSBBs compared with nonusers (90 months versus 38.2 months).

This study builds on a large body of research by principal investigator Anil Sood, M.D., professor in Gynecologic Medical Oncology and Cancer Biology at MD Anderson. It showed that stress hormones fuel progression of ovarian and other cancers, and that beta-blockers - among the most proven drugs in cardiovascular medicine - might be a new way to stifle that effect.

"Beta-blockers treat a variety of conditions, such as heart disease, high-blood pressure, glaucoma and migraines. They target a receptor protein in heart muscle that causes the heart to beat harder and faster when activated by stress hormones," Sood said. "Our research has shown that the same stress mechanisms impact

ovarian cancer progression, so these drugs could play a new role in cancer treatment."

According to Sood, the usefulness of beta-blockers was unclear until now. "The ability to show improved survival using nonselective agents - which inhibit a specific stress pathway - is the culmination of years of research into ovarian cancer biology and pathogenesis."

He added that beta-blocker users in the study presented at a higher stage of disease, had an increased average BMI and were more likely to be hypertensive. All these factors were associated with decreased survival, yet those who received beta-blockers had either equivalent or improved overall survival. Further examination revealed that NSBB users had improved overall survival regardless of the presence of such prognostic factors or comorbidities. This was not true for patients who took SBBs.

Although further study is needed, these results highlight the importance of adrenergic receptor-β2 (ADRB2), a signaling pathway important to ovarian carcinogenesis and targeted by NSBBs (versus the ADRB1 pathway targeted by SBBs).

Ovarian cancer is the 5th most deadly cancer among women, accounting for more deaths than any other female reproductive system cancer. An estimated 21,290 new cases are diagnosed, and some 14,180 women die from the disease each year in the U.S., according to the American Cancer Society.

Future trials will seek to identify patients who would benefit most from beta-blocker use and the best beta-blocker for a specific tumor type based on adrenergic receptor expression. Then they potentially could be used as an adjuvant therapy during surgical recovery and chemotherapy to decrease tumor growth, delays in wound healing and metastasis. Beta-blockers may also reduce cancer-related psychological distress in newly diagnosed patients, according to the study authors.

There are currently two clinical trials, one led by MD Anderson, evaluating the combination of chemotherapy and propranolol (a type of NSBB) on cancer biology and on stress modulators in patients with newly diagnosed EOC. According to Sood, the preliminary data from these feasibility trials will be used to design prospective, randomized clinical trials examining NSBBs on patient outcomes.

"The stratification of patients by beta-blocker use and selectivity in this study makes it unique among all other studies examining the impact of these drugs on cancer. It also builds on the mounting evidence that beta-blockers may become a key treatment component for many patients in the future," said Sood.

Portions of this study were supported by National Institutes of Health grants (CA140933, CA104825, CA109298, P50CA083639, U54CA151688, U54CA96300, U54CA96297, and CA016672), an Ovarian Cancer Research Fund program Project Development Grant, the Department of Defense (grants OC073399, W81XWJ-10-0158, and OC100237), the Betty Ann Asche Murray Distinguished Professorship, the RGK Foundation, the Gilder Foundation, the Blanton-Davis Ovarian Cancer Research Program, and a Gynecologic Cancer Foundation-St. Louis Ovarian Cancer Awareness grant. One of the researchers has acted as a paid consultant for Incyte Pharmaceuticals and received research funding from Egen Pharmaceuticals.

Other researchers contributing to this study include: Robert L. Coleman, M.D., Alpa M. Nick, M.D., Pedro T. Ramirez, M.D., Lois M. Ramondetta, M.D., Diana Urbauer, Jack L. Watkins, all from MD Anderson; Susan K. Lutgendorf, Ph.D. from University of Iowa; Sanjeev Kumar, M.B., B.S. from the Mayo Clinic; Koji Matsuo, M.D., from Mercy Medical Center; Kathryn Squires, M.D. and Premal H. Thaker, M.D., M.S. from Washington University School of Medicine.