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Spurred by food allergies, 2 esophagus conditions stump doctors

Researchers at the UNC School of Medicine found that two on-the-rise esophagus conditions are so similar that even a biopsy is not enough to distinguish one disease from the other.

CHAPEL HILL, N.C. – One condition is called eosinophilic esophagitis, or EoE. The other is PPI-responsive esophageal eosinophilia, or PPI-REE. Symptoms for each condition include difficulty swallowing, persistent heartburn, and getting food stuck in the throat. Both are diagnosed with an endoscopy, which reveals high numbers of a certain type of white blood cell – an eosinophil – in biopsies of both conditions. But finding a lot of white blood cells does not distinguish EoE from PPI-REE, said Evan Dellon, MD, MPH, associate professor of medicine and epidemiology and lead author of a study published in the American Journal of Gastroenterology.

Dellon says that both conditions can be the result of a food allergy, but they require different treatments. Patients whose white blood cell count can be lowered by antacid medications, also called proton-pump inhibitor (PPI) medications, are diagnosed with PPI-REE. However, finding out if the white blood cell count was lowered requires a second endoscopy and biopsy. If the count remained high, then patients are diagnosed with EoE and require an anti-inflammatory medication, such as a steroid typically used to treat asthma. "Unfortunately, right now the only way to differentiate between the conditions is to do the PPI medication trial and then repeat the endoscopy," Dellon said.

During his study, Dellon's team wanted to see if any symptoms, endoscopic views of the esophagus, or tissue samples could help him differentiate the two conditions so that future patients wouldn't have to go through an eight-week antacid trial and a second endoscopic biopsy, an invasive procedure that is safe but costly and requires sedation.

The study enrolled 223 patients with esophageal complaints. Dellon's team took small samples of tissue from the patients and examined them for the presence of eosinophils—white blood cells. Patients with a high eosinophil count were given an 8-week course of antacids. The study showed that approximately 30 to 40 percent of the participants responded to the antacid medication. They were diagnosed with PPI-REE. Patients who did not respond to antacids were diagnosed with EoE. There are no FDA-approved medicines for EoE, so the steroids that doctors prescribe are considered off-label use. There are, however, several randomized, double-blind studies that show that these medications work for EoE.

"The other option for treating EoE is to try a variety of elimination diets to remove the most common food triggers, such as wheat, dairy, soy, or eggs," Dellon said. "We know that it's mostly an allergic reaction because if you take away all allergens, nearly everyone will get better very quickly. But that isn't a practical treatment for many people."

After rigorous analysis, Dellon and his colleagues did not find any clinical or endoscopic characteristics that could reliably distinguish the two conditions. This means patients will still need to undergo the PPI trial and repeat endoscopy in order to be properly diagnosed.

Dellon's team is working on an extension of this study that uses a special stain on the cell biopsies that he hopes will predict who will respond to antacids. Dellon also wants to investigate patient genetics as a possible diagnostic tool. "This whole antacid response and even the existence of PPI-REE as a condition weren't really described well until two years ago," Dellon said. "So the diagnostics are still very much in flux right now."

This research was funded through a grant from the National Institutes of Health and a Junior Faculty Development Award from the American College of Gastroenterology. Evan Dellon, MD, MPH, associate professor of medicine in the UNC School of Medicine and adjunct associate professor of epidemiology in UNC's Gillings School of Global Public Health, won a Hettleman Prize for scholarship achievement in 2012.

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Do patients in a vegetative state recognize loved ones?

Tel Aviv University researchers find unresponsive patients' brains may recognize photographs of their family and friends

Patients in a vegetative state are awake, breathe on their own, and seem to go in and out of sleep. But they do not respond to what is happening around them and exhibit no signs of conscious awareness. With communication impossible, friends and family are left wondering if the patients even know they are there. Now, using functional magnetic resonance imaging (fMRI), Dr. Haggai Sharon and Dr. Yotam Pasternak of Tel Aviv University's Functional Brain Center and Sackler Faculty of Medicine and the Tel Aviv Sourasky Medical Center have shown that the brains of patients in a vegetative state emotionally react to photographs of people they know personally as though they recognize them.

"We showed that patients in a vegetative state can react differently to different stimuli in the environment depending on their emotional value," said Dr. Sharon. "It's not a generic thing; it's personal and autobiographical. We engaged the person, the individual, inside the patient."

The findings, published in PLOS ONE, deepen our understanding of the vegetative state and may offer hope for better care and the development of novel treatments. Researchers from TAU's School of Psychological Sciences, Department of Neurology, and Sagol School of Neuroscience and the Loewenstein Hospital in Ranaana contributed to the research.

Talking to the brain

For many years, patients in a vegetative state were believed to have no awareness of self or environment. But in recent years, doctors have made use of fMRI to examine brain activity in such patients. They have found that some patients in a vegetative state can perform complex cognitive tasks on command, like imagining a physical activity such as playing tennis, or, in one case, even answering yes-or-no questions. But these cases are rare and don't provide any indication as to whether patients are having personal emotional experiences in such a state.

To gain insight into "what it feels like to be in a vegetative state," the researchers worked with four patients in a persistent (defined as "month-long") or permanent (persisting for more than three months) vegetative state. They showed them photographs of people they did and did not personally know, then gauged the patients' reactions using fMRI, which measures blood flow in the brain to detect areas of neurological activity in real time. In response to all the photographs, a region specific to facial recognition was activated in the patients' brains, indicating that their brains had correctly identified that they were looking at faces.

But in response to the photographs of close family members and friends, brain regions involved in emotional significance and autobiographical information were also activated in the patients' brains. In other words, the patients reacted with activations of brain centers involved in processing emotion, as though they knew the people in the photographs. The results suggest patients in a vegetative state can register and categorize complex visual information and connect it to memories – a groundbreaking finding.

The ghost in the machine

However, the researchers could not be sure if the patients were conscious of their emotions or just reacting spontaneously. So they then verbally asked the patients to imagine their parents' faces. Surprisingly, one patient, a 60-year-old kindergarten teacher who was hit by a car while crossing the street, exhibited complex brain activity in the face- and emotion-specific brain regions, identical to brain activity seen in healthy people. The researchers say her response is the strongest evidence yet that vegetative-state patients can be "emotionally aware." A second patient, a 23-year-old woman, exhibited activity just in the emotion-specific brain regions. (Significantly, both patients woke up within two months of the tests. They did not remember being in a vegetative state.)

"This experiment, a first of its kind, demonstrates that some vegetative patients may not only possess emotional awareness of the environment but also experience emotional awareness driven by internal processes, such as images," said Dr. Sharon

Research focused on the "emotional awareness" of patients in a vegetative state is only a few years old. The researchers hope their work will eventually contribute to improved care and treatment. They have also begun working with patients in a minimally conscious state to better understand how regions of the brain interact in response to familiar cues. Emotions, they say, could help unlock the secrets of consciousness.

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Cat domestication traced to Chinese farmers 5,300 years ago

Cats were attracted to ancient farming villages by small animals, such as rodents that were living on the grain that farmers grew, ate and stored

Five-thousand years before it was immortalized in a British nursery rhyme, the cat that caught the rat that ate the malt was doing just fine living alongside farmers in the ancient Chinese village of Quanhucun, a forthcoming study in the Proceedings of the National Academy of Sciences has confirmed.

"At least three different lines of scientific inquiry allow us to tell a story about cat domestication that is reminiscent of the old 'house that Jack built' nursery rhyme," said study co-author Fiona Marshall, PhD, a professor of archaeology in Arts & Sciences at Washington University in St. Louis.



The Near Eastern Wildcat, native to Western Asia and Africa, is believed to be the primary ancestor of all domestic cats now living around the globe. Wikipedia Commons

"Our data suggest that cats were attracted to ancient farming villages by small animals, such as rodents that were living on the grain that the farmers grew, ate and stored."

Set for early online publication in PNAS during the week of Dec. 16, the study provides the first direct evidence for the processes of cat domestication.

"Results of this study show that the village of Quanhucun was a source of food for the cats 5,300 years ago, and the relationship between humans and cats was commensal, or advantageous for the cats," Marshall said. "Even if these cats were not yet domesticated, our evidence confirms that they lived in close proximity to farmers, and that the relationship had mutual benefits."

Cat remains rarely are found in ancient archaeological sites, and little is known about how they were domesticated. Cats were thought to have first been domesticated in ancient Egypt, where they were kept some 4,000 years ago, but more recent research suggests close relations with humans may have occurred much earlier, including the discovery of a wild cat buried with a human nearly 10,000 years ago in Cyprus.

While it often has been argued that cats were attracted to rodents and other food in early farming villages and domesticated themselves, there has been little evidence for this theory.

The evidence for this study is derived from research in China led by Yaowu Hu and colleagues at the Chinese Academy of Sciences. Hu and his team analyzed eight bones from at least two cats excavated from the site.

Using radiocarbon dating and isotopic analyses of carbon and nitrogen traces in the bones of cats, dogs, deer and other wildlife unearthed near Quanhucun, the research team demonstrated how a breed of once-wild cats carved a niche for themselves in a society that thrived on the widespread cultivation of the grain millet.

Carbon isotopes indicate that rodents, domestic dogs and pigs from the ancient village were eating millet, but deer were not. Carbon and nitrogen isotopes show that cats were preying on animals that lived on farmed millet, probably rodents.

At the same time, an ancient rodent burrow into a storage pit and the rodent-proof design of grain storage pots indicate that farmers had problems with rodents in the grain stores.

Other clues gleaned from the Quanhucun food web suggest the relationship between cats and humans had begun to grow closer. One of the cats was aged, showing that it survived well in the village. Another ate fewer animals and more millet than expected, suggesting that it scavenged human food or was fed.

Recent DNA studies suggest that most of the estimated 600 million domestic cats now living around the globe are descendants most directly of the Near Eastern Wildcat, one of the five *Felis sylvestris lybica* wildcat subspecies still found around the Old World.

Marshall, an expert on animal domestication, said there currently is no DNA evidence to show whether the cats found at Quanhucun are descendants of the Near Eastern Wildcat, a subspecies not native to the area. If the Quanhucun cats turn out to be close descendents of the Near Eastern strain, it would suggest they were domesticated elsewhere and later introduced to the region.

"We do not yet know whether these cats came to China from the Near East, whether they interbred with Chinese wild-cat species, or even whether cats from China played a previously unsuspected role in domestication," Marshall said.

This question is now being pursued by researchers based in China and in France.

Other members of the research team include Xianglong Chen, Changsui Wang and Liangliang Hou, all affiliated with the Chinese Academy of Sciences' Key Laboratory of Vertebrate Evolution and Human Origins and the Institute of Vertebrate Paleontology and Paleoanthropology; Songmei Hu, of the Archaeological Research Institute of Shaanxi Province, Xi'an, China; and Xiaohong Wu, of the Department of Archaeology, Peking University, in Beijing.

Changsui Wang designed the research project. Songmei Hu, a zooarchaeologist, conducted the biometric measurement of cat bones. Weilin Wang, an archaeologist, excavated the Quanhucun site and supplied the archaeological context, including pottery cited in the paper. Xianglong Chen and Liangliang Hou prepared collagen samples for testing, and Xiaohong Wu conducted the radiocarbon dating.

http://www.eurekalert.org/pub_releases/2013-12/vumc-vs121013.php

Vanderbilt study: Ancient chemical bond may aid cancer therapy

Researchers included 48 middle- and high-school students in five states, from Arkansas to Maine

A chemical bond discovered by Vanderbilt University scientists that is essential for animal life and which hastened the "dawn of the animal kingdom" could lead to new therapies for cancer and other diseases.

The report, published online today by the Proceedings of the National Academy of Sciences (PNAS), was co-authored by 83 participants in the "Aspironaut" K-20 STEM pipeline program for diversity. Six were middle school students when the study was conducted, 42 were high school students, 30 were college undergraduates and five were graduate students.

Because many of the high school students grew up in poverty in rural communities, "they're invisible. They're an untapped talent pool," said Billy Hudson, Ph.D., who founded the Aspirnaut program with his wife and co-senior author Julie Hudson, M.D. "Aspirnaut connects the 'Forgotten Student' to STEM opportunities." The study demonstrates that the sulfilimine bond, which Hudson's group discovered in 2009, is part of a "primordial innovation" dating back more than 500 million years to the ancestor of jellyfish. The bond stabilizes the collagen IV scaffold and is essential for more advanced tissue formation.

The bond is formed by hypohalous acids, a form of household bleach, generated by peroxidasin, an ancient enzyme embedded in the extracellular environment. This "oxidant generator" is key to forming new blood vessels that feed tumors, making it an attractive target for developing new drugs for cancer therapy, the researchers said.

The involvement of so many young students in a scientific publication is "rare, the first that I know of," said PNAS Editor-in-Chief Inder Verma, Ph.D. "It is a remarkable achievement," added Mina Bissell, Ph.D., who conducted the initial review of the manuscript for the journal.

During the summers of 2009 to 2013, the students participated in an "Expedition to the Dawn of the Animal Kingdom," a summer research program at Vanderbilt to search for the evolutionary origin of the sulfilimine chemical bond.

They contributed to experiments that showed the sulfilimine bond and the peroxidasin-based mechanism by which it forms can be traced to a common ancestor dating back more than 500 million years ago.

Of the 42 high-school researchers, 31 have now graduated. Thirty are attending or have completed college, 26 with STEM (science, technology, engineering and mathematics) majors.

The Aspirnaut program provides a summer research experience at Vanderbilt for students from underrepresented groups, many of whom are low-income.

http://www.eurekalert.org/pub_releases/2013-12/uom-do1121213.php

Discovery of 1.4 million-year-old fossil human hand bone closes human evolution gap

Bone suspected to belong to the early human species, Homo erectus

COLUMBIA, Mo. – Humans have a distinctive hand anatomy that allows them to make and use tools. Apes and other nonhuman primates do not have these distinctive anatomical features in their hands, and the point in time at which these features first appeared in human evolution is unknown. Now, a University of Missouri researcher and her international team of colleagues have found a new hand bone from a human ancestor who roamed the earth in East Africa approximately 1.42 million years ago. They suspect the bone belonged to the early human species, *Homo erectus*. The discovery of this bone is the earliest evidence of a modern human-like hand, indicating that this anatomical feature existed more than half a million years earlier than previously known.

"This bone is the third metacarpal in the hand, which connects to the middle finger. It was discovered at the 'Kaitio' site in West Turkana, Kenya," said Carol Ward, professor of pathology and anatomical sciences at MU. The discovery was made by a West Turkana Paleo Project team, led by Ward's colleague and co-author Fredrick Manthi of the National Museums of Kenya.



The styloid process is a projection of bone. Ward and her team found a styloid process at the end of a wrist bone more than 1.42 million years old, indicating this anatomical feature existed more than half a million years earlier than previously known. University of Missouri

"What makes this bone so distinct is that the presence of a styloid process, or projection of bone, at the end that connects to the wrist. Until now, this styloid process has been found only in us, Neandertals and other archaic humans."

The styloid process helps the hand bone lock into the wrist bones, allowing for greater amounts of pressure to be applied to the wrist and hand from a grasping thumb and fingers. Ward and her colleagues note that a lack of the styloid process created challenges for apes and earlier humans when they attempted to make and use tools. This lack of a styloid process may have increased the chances of having arthritis earlier, Ward said.

The bone was found near sites where the earliest Acheulian tools have appeared. Acheulian tools are ancient, shaped stone tools that include stone hand axes more than 1.6 million years old. Being able to make such precise tools indicates that these early humans were almost certainly using their hands for many other complex tasks as well, Ward said.

"The styloid process reflects an increased dexterity that allowed early human species to use powerful yet precise grips when manipulating objects. This was something that their predecessors couldn't do as well due to

the lack of this styloid process and its associated anatomy," Ward said. "With this discovery, we are closing the gap on the evolutionary history of the human hand. This may not be the first appearance of the modern human hand, but we believe that it is close to the origin, given that we do not see this anatomy in any human fossils older than 1.8 million years. Our specialized, dexterous hands have been with us for most of the evolutionary history of our genus, Homo. They are – and have been for almost 1.5 million years – fundamental to our survival."

The study was published in the Proceedings of the National Academy of Science this week. Members of Ward's team who helped discover and analyze the bone include: Matthew Tocheri, National Museum of Natural History in the Smithsonian Institution; J. Michael Plavcan, University of Arkansas; Francis Brown, University of Utah; and Fredrick Manthi, National Museums of Kenya.

http://www.eurekalert.org/pub_releases/2013-12/uoc--rsh121613.php

Research shows how household dogs protect against asthma and infection

Study led by UCSF, U Michigan scientists points to changes in gut microbes

Children's risk for developing allergies and asthma is reduced when they are exposed in early infancy to a dog in the household, and now researchers have discovered a reason why.

Exposure of mice to dust from houses where canine pets are permitted both indoors and outdoors can reshape the community of microbes that live in the mouse gut — collectively known as the gastrointestinal microbiome — and also diminish immune system reactivity to common allergens, according to a new study by researchers led by Susan Lynch, PhD, associate professor with the Division of Gastroenterology at UC San Francisco, and Nicholas Lukacs, PhD, professor with the Department of Pathology at the U Michigan. The scientists also identified a specific bacterial species within the gut that is critical to protecting the airways against both allergens and viral respiratory infection.

The study, funded by the National Institute of Allergy and Infectious Diseases (NIAID), is published online this week in the Proceedings of the National Academy of Sciences (PNAS) and involves a multi-disciplinary group of researchers from UCSF, the University of Michigan, Henry Ford Health System and Georgia Regents University.

The results were obtained in studies of mice challenged with allergens after earlier exposure to dust from homes with dogs, but the results also are likely to explain the reduced allergy risk among children raised with dogs from birth, according to the study leaders.

In their study the scientists exposed mice to cockroach or protein allergens. They discovered that asthma-associated inflammatory responses in the lungs were greatly reduced in mice previously exposed to dog-associated dust, in comparison to mice that were exposed to dust from homes without pets or mice not exposed to any dust.

Among the bacterial species in the gut microbiome of these protected mice, the researchers homed in on one, *Lactobacillus johnsonii*. When they fed it alone to mice, they found it could prevent airway inflammation due to allergens or even respiratory syncytial virus (RSV) infection. Severe RSV infection in infancy is associated with elevated asthma risk. The researchers showed in this experiment that protection of the lungs' airways was associated with reduced numbers and activity of asthma-associated immune cells.

The level of protection with this single species was less than that obtained with the full complement of dust microbes from dog owners' homes, indicating that other, environmentally sourced bacterial species probably are necessary for full airway protection, Lynch said. This result suggests that *Lactobacillus johnsonii* or other species of "good" bacteria might one day be used to reshape the gut microbiome in ways that can prevent the development of asthma or allergies, or perhaps even to treat existing cases, she said.

Lynch's own work and research by several others in the field has led her to become convinced that "the composition and function of the gut microbiome strongly influence immune reactions and present a novel avenue for development of therapeutics for both allergic asthma and a range of other diseases."

The current study demonstrates that changes in the gut microbiome can have wide-reaching effects on immune function beyond the gut, at sites elsewhere in the body, Lynch said.

The team had previously demonstrated that the presence of a dog that roams both inside and outside was associated with a significantly more diverse house dust microbiome that was enriched for species found in the gastrointestinal tract of humans.

After teaming up with Lukacs, an expert on immune responses in lung disease, Lynch said, "We set out to investigate whether being exposed to a distinct house dust microbiome associated with indoor/outdoor dogs mediated a protective effect through manipulation of the gut microbiome and, by extension, the host immune response."

"The results of our study indicate that this is likely to be one mechanism through which the environment influences immune responses in early life, and it is something we are currently examining using human samples in a large multi-institutional collaborative study funded by the NIAID."

"Gut microbiome manipulation represents a promising new therapeutic strategy to protect individuals against both pulmonary infection and allergic airway disease," Lynch said.

Others who conducted experiments and wrote the PNAS study include UCSF associate research specialist Kei Fujimura, PhD, who profiled and analyzed microbiomes, and University of Michigan postdoctoral fellows Tine Demoor, PhD, and Sihyug Jang, PhD, who completed mouse experiments and measured airway symptomology. Marcus Rauch, PhD, an associate research specialist at UCSF, isolated the Lactobacillus species from the mouse gut, and assistant research specialist Ali Faruqi analyzed data for the study. The study also included UCSF asthma expert Homer Boushey, MD, as well as Christine Cole Johnson PhD an epidemiologist, and Edward Zoratti, MD, an allergist-immunologist, both from Henry Ford Health System in Detroit, and Dennis Ownby MD, a professor of pediatrics at Georgia Regents University in Augusta.

<http://phys.org/news/2013-12-alzheimer-substance-nanomaterial-tomorrow.html>

Alzheimer substance may be the nanomaterial of tomorrow

Amyloid protein causes diseases like Alzheimer's, Parkinson's and Creutzfeldt-Jakob disease.

But amyloid also carries unique characteristics that may lead to the development of new composite materials for the nano processors and data storage of tomorrow, and even make objects invisible.

Researchers from Chalmers University of Technology recently unveiled an unexpected discovery about amyloid in an article published in the Nature Photonics journal. Amyloids are misfolded variants of proteins that occur naturally in the body. The researchers have now shown that the misfolded variants react to multiphoton irradiation, a type of laser effect, whereas the healthy proteins do not.

The discovery could be useful in a variety of fields. Not only can it lead to new methods to detect and treat the brain diseases that amyloid causes, amyloid may also be used as a building block for future nanomaterials.

"It is possible to create these protein aggregates artificially in a laboratory", says Piotr Hanczyc, one of the researchers who made the discovery. "By combining them with other molecules, one could create materials with unique characteristics."

The amyloid aggregates are as hard and rigid as steel. The difference is that steel is much heavier and has defined material properties, whereas amyloids can be tuned for specific purposes. By attaching a material's molecules to the dense amyloid, its characteristics change.

"This was already known, but what has not been known is that the amyloids react to multiphoton irradiation," says Piotr Hanczyc. "This opens up new possibilities to also change the nature of the material attached to the amyloids."

The amyloids are shaped like discs, densely piled upon each other. When a material gets merged with these discs, its molecules end up so densely and regularly placed that they can communicate and exchange information. This means completely new possibilities to change a material's characteristics.

Piotr Hanczyc now sees opportunities for collaboration with the material science researchers at Chalmers, for example on solar cell technology.

And although it may still be science fiction, he also believes that one day scientists may use the material properties of amyloid fibrils in research on invisible meta materials.

"An object's ability to reflect light could be altered so that what's behind it gets reflected instead of the object itself, in principle changing the index of light refraction. Kind of like when light hits the surface of water."

More information: "Multiphoton absorption in amyloid protein fibres." Piotr Hanczyc, Marek Samoc, Bengt Norden. Nature Photonics 7, 969–972 (2013). DOI: 10.1038/nphoton.2013.282

<http://phys.org/news/2013-12-evidence-mass-extinction-central-asia.html>

Researchers collect evidence of mass extinction that occurred in Central Asia

Members of a U.N.-sponsored research team with members from Appalachian State University's Department of Geology have found evidence for catastrophic oceanographic events associated with climate change and a mass extinction 375 million years ago that devastated tropical marine ecosystems.

"The Late Devonian mass extinction was one of the five largest mass extinction events in the history of life," said Professor Johnny Waters, who is a co-leader of the five-year, U.N. International Geoscience Programme project that began in 2011. The research team, which includes Assistant Professor Sarah Carmichael, is examining the relationship between climate change and changes in the ecosystems in the Devonian period, from 419 to 359 million years ago. "This is the third most significant mass extinction and it was caused by plants," Waters said. "Unlike the dinosaur mass extinction, which was related to an asteroid impact, this one was environmentally related."

In the Devonian period, Waters explained, the world was experiencing super greenhouse climate conditions. This means that it was very warm, there probably were no ice caps, there was a lot carbon dioxide in the atmosphere (with estimates of 4,000 parts per million).

"As plant communities expanded onto land to form the first forests, they depleted the carbon dioxide (CO₂) that was in the atmosphere," Waters said. "CO₂ levels dropped to 400 ppm toward the end of the Devonian. It got colder. There were glaciation events and the rapid change in the climate caused severe extinction in the tropics and the existing coral reefs became extinct." By comparison, the world's current CO₂ level is very close to 400 ppm.

Researchers collect evidence of mass extinction that occurred in Central Asia

Mongolian soldiers and Professor Johnny A. Waters, center, pose for a photograph at a border outpost in Southwest Mongolia. Waters and a team of international scientists conducted fieldwork in the mountainous area along the Chinese/ Mongolian border. The soldiers ensured that the scientists did not stray into China. Credit: Johnny A. Waters

Most of the knowledge that geologists have about this mass extinction comes from North America and Europe. Although these two land masses are far apart now, in the Devonian they were very close to each other.

Scientists have tried to make inferences about worldwide events based on sample locations that are really quite limited in terms of their geographic history, or paleogeography. Therefore, it is vitally important to obtain samples from locations outside this region for understanding global climate change during this time period.

Waters' international team of geoscientists has conducted field work in remote areas of western China for many years, in addition to two recent field seasons in western Mongolia near the Russian and Chinese borders. The changing political climate in China, Russia and Mongolia in recent years has now made it possible to do fieldwork in these locations. The strength of these field collaborations is that they draw on the expertise of scientists from a variety of disciplines to add critical climatic information to a limited database. U.N. researchers associated with this project are also collecting related data in Thailand, Myanmar, Vietnam and Northern China.

"The reason we are working in central Asia is that there is a lot of good evidence of what happened at and after this mass extinction – this is an area that has not been well studied," Waters said. "It's all a part of our work finding the places that give us the best information in sorting out what happened in the extinction event and in its aftermath."

Answers about the earth's climate during and after this mass extinction are contained within rock samples from these new field sites, which were once part of the ocean floor, as geochemical signals preserved in the rocks record devastating climate change. The paleogeography of the field sites indicate that Devonian climate change not only had environmental impacts on life associated with large land masses, but also on life in the open ocean.

"We now have evidence that the radiation of surviving life following the mass extinction was centered in Central Asia," Waters said.

Researchers collect evidence of mass extinction that occurred in Central Asia

Professor Johnny A. Waters stands on an outcropping near the Gobi Altai Mountains in Mongolia. The area, once covered by a vast ocean, contains clues to the earth's climate history. Credit: Johnny A. Waters

The geochemistry of the samples is being analyzed primarily by students in Appalachian's Department of Geology under Carmichael's supervision, with additional analyses being conducted at UNC-Chapel Hill and a university in Austria. "We are using geochemistry to tie it all together all across Central Asia, which used to be an open ocean, and compare our new data to established sequences in Europe and North America, in order to develop a global understanding of the climate change associated with this mass extinction," Waters said.

"Today we are looking at increases in carbon dioxide causing warming and the negative impacts to the ecosystem. In the Devonian period, we are looking at a rapid loss of carbon dioxide, which in geologic time occurred over millions of years rather than hundreds of years," Waters said. "But the lessons are actually quite similar. We clearly are concerned today about climate change and its impact on the environment and its effect on the ecosystem, and the geologic record is really the only record where we can see these events and compare what happened before and after."

Waters and Carmichael will present the preliminary results of their research at the Geological Society of America's Annual Meeting in Denver in October and at the American Geophysical Union's annual meeting in San Francisco in December.

Next summer, Waters will lead a 20-member team, including Dr. Sarah Carmichael and two students from Appalachian's Department of Geology, for continued field work in Mongolia.

Provided by Appalachian State University

<http://phys.org/news/2013-12-continent-world-frogs-lot-common.html>

No matter the continent, the world's frogs have a lot in common, biologist finds

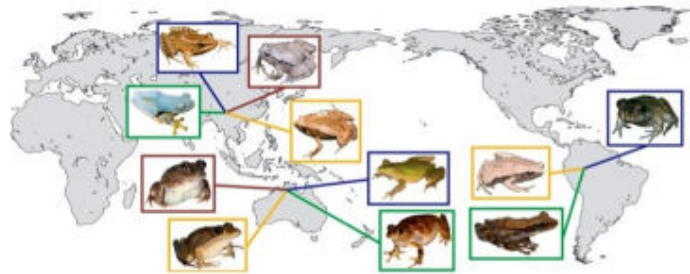
Striking similarity in frog species on different continents

Phys.org - A University of Arizona biologist researching frog evolution has discovered striking similarity in frog species on different continents and proposes two very different ways that this similarity comes about.

In a study published in the journal *Proceedings of the Royal Society B: Biological Sciences*, ecology and evolutionary biology professor John Wiens and collaborators suggest that the similarity in frog species across continents has two explanations. In some cases, different groups of frogs evolved similar characteristics in parallel on different continents, while in other cases the same group of frogs maintained similar characteristics over huge distances and vast periods of time as they moved between continents.

Wiens worked with collaborators Dan Moen and Duncan Irschick in studying frogs from three different sites on three continents, in China, Colombia and Australia. They quantified how well different frog species performed the same tasks, including jumping, swimming, and clinging to a slick surface. They also measured anatomical traits related to these tasks, like leg length and muscle mass.

"All around the world, any given location is likely to have frogs that either climb trees, burrow, live on the ground or live in water," Wiens says. "One of the things we've found is that frogs that use the same microhabitat tend to be very similar, both in their morphology and in their performance. For example, all around the world, frogs that live in trees usually have expanded pads at the tips of their fingers and toes that help them cling to smooth surfaces. Similarly, frogs that live in water have thick leg muscles and heavily webbed feet that help them swim faster."



John Wiens and his collaborators studied frogs on three continents.

Wiens says that in some cases, this similarity in species across continents is explained by groups of species staying the same over time but moving over huge distances.

"In one interesting case, there are species in a group called the narrow-mouthed frogs that are very similar in both South America and China, and this is because they've changed very little over 65 million years and as they've spread around the world," he says. "Another example is a group of tree frogs that originated in South America and have spread to both China and Australia."

This pattern of evolutionary conservatism over time coupled with long-distance dispersal can explain similarity in many different organisms from all around the world, Wiens says. However, the pattern remains relatively poorly studied.

Other groups of frogs have followed a very different path. Instead of staying the same over time and moving, they have evolved to use different microhabitats while staying in the same place.

"The really cool thing we found is what happened in Australia. There all the different habitat types have all evolved from tree frogs. After the tree frogs went from South America to Australia, some stayed in the trees, but others became burrowing, aquatic and terrestrial frogs," Wiens says. "The species of tree frogs that evolved to use these new microhabitats show no trace of their tree frog ancestry, and are basically indistinguishable from unrelated burrowing, terrestrial and aquatic species on other continents."

Explore further: Torrent frog has advantage attaching to rough, wet surfaces

Journal reference: Proceedings of the Royal Society B

<http://www.wired.com/wiredscience/2013/12/plate-tectonics-on-europa/>

Icy Europa May Have First Evidence For Active Plate Tectonics on an Alien World

Scientists may have spotted the first evidence for active plate tectonics on another world. Jupiter's moon Europa is covered in an ice crust bearing scars that may reveal movement similar to that of Earth's rocky plates.

By Betsy Mason

SAN FRANCISCO - Europa was already considered to be among the most scientifically intriguing bodies in the solar system and one of the most promising places to hunt for life in the solar system because of the liquid ocean that resides beneath its crust. If the latest findings turn out to be true, it could be another point in favor of the moon's potential habitability by providing a way to get nutrients from the surface down into the ocean.

“What’s exciting is that this would be the only other place outside of Earth where a plate-tectonic-style system is occurring,” said planetary scientist Alyssa Rhoden, a NASA postdoctoral program fellow who studies Europa, but was not involved in the new research.

Europa’s icy surface has been estimated to be between 40 million and 90 million years old, making it one of the youngest surfaces in the solar system, and far younger than the moon itself, which is more than 4 billion years old. This means that somehow the crust is being refreshed either by resurfacing or recycling of old crust.

Scientists believe new ice is being formed on Europa along linear features called dilational bands. There are thousands of kilometers of these bands on the planet, potentially creating significant amounts of new ice crust. The problem is that nobody knows where all the old crust is disappearing.

“Unless Europa has been expanding within the last 40 to 90 million years, there has to be some process on this icy moon that’s able to accommodate a large amount of new surface area being created at dilational bands,” planetary scientist Simon Kattenhorn of the University of Idaho said during a presentation about the new research Dec. 13 at the American Geophysical Union meeting.

On Earth new crust is created along seams on plates that underlie the oceans, known as mid-ocean ridges. Here, the two sides of the plate move away from each other as molten material rises from the mantle below the crust to fill the gap, cool and form new crust. A similar process is thought to create new ice along Europa’s dilational bands.

Now Kattenhorn and his colleague Louise Prockter of Johns Hopkins University think they have found something similar to Earth’s subduction zones on Europa. By mapping the criss-crossing fractures and other linear features on a 106,000-square-kilometer section of Europa’s surface using imagery from the Galileo mission, the scientists identified potential zones where the ice crust is being pushed down below the surface. If Europa’s crust is being recycled by being pushed down along subsumption bands and recreated along dilational bands, it could provide a way to get potential nutrients from the surface into the water ocean below where they could be critical for harboring life.

“Having that mixing seems to be pretty important for establishing life,” said Rhoden, who cofounded Destination Europa to push for a mission to the moon.

Kattenhorn and Prockter located the subsumption bands by trying to unravel geologic time to reconstruct the original geology before the missing crust disappeared. They found features that had been separated and shifted by movement of the crust, and when they matched those features all up again, there was a large area of crust missing.

“Once the reconstruction is done, we have this big area here that is missing, 92 kilometers wide, that is alongside one of these zones that we refer to using the term subsumption bands,” Kattenhorn said in his presentation.

They say the crust in the area they mapped was pushed down underneath an overriding section of crust along a 23-kilometer-wide subsumption band, which would be analogous to a subduction zone on Earth.

“It’s an important thing to look for,” planetary scientist Michael Manga of the University of California, Berkeley told WIRED. “We see expansion at the surface so there must be contraction somewhere.”

But Manga’s not yet convinced the subsumption bands are the answer, and says there are some potential problems with the idea. For one, if a buoyant plate is pushed down into denser liquid, it should bow upward to compensate for the buoyancy. “If there is contraction or compression things should be lifted upwards,” he said. Uplift occurs along subduction zones on Earth, for example, but the subsumption bands are basically topographically flat. Though Kattenhorn suggested in his presentation that this could be explained by the ice being pushed down at a relatively shallow angle.

Artist’s concept of the Europa Clipper mission investigating Jupiter’s icy moon Europa. (NASA/JPL-Caltech) Rhoden thinks Kattenhorn and Prockter’s reconstructions do seem to show that there’s no way to recreate the original geology without the surface having been subsumed. But, she says, it’s hard to extrapolate from the small study area to a global system. The problem is that only about 10 percent of Europa’s surface has imagery good enough to do these kinds of detailed reconstructions.

“I think we are going to be hard pressed to make any global map of tectonics with our current data set,” Rhoden told WIRED. This is a good argument for a new mission to Europa, which could also help us understand Earth better, she says. There is still a lot of disagreement among scientists about what drives plate tectonics on Earth, and even if the driving force on Europa is different, it could be enlightening.

And while Europa is far away, it does have some advantages over Earth as a study subject. “On Europa, there’s a lot less vegetation, a lot less cities, a lot less obscuring the evidence of what has gone on in Europa’s past,” Rhoden said.

<http://www.bbc.co.uk/news/world-us-canada-25405037>

US health watchdog cracks down on antibacterial soaps

The US health regulator has warned that antibacterial chemicals in soaps and body washes may pose health risks.

The Food and Drug Administration (FDA) called for a safety review of such products. It proposed a rule requiring manufacturers to prove such soaps are safe and more effective against infection than plain soap and water. Recent studies indicate an ingredient in such products could scramble hormone levels and boost drug-proof bacteria.

The proposal rule does not apply to alcohol-based hand sanitizers and products used in healthcare settings. Manufacturers have until the end of 2014 to submit the results of clinical trials on their products, the FDA said. The new regulations would be finalised in 2016.

'Unanticipated hormonal effects'

"New data suggest that the risks associated with long-term, daily use of antibacterial soaps may outweigh the benefits," Colleen Rogers, an FDA microbiologist, wrote in a statement on Monday. Certain ingredients in such products - such as triclosan in liquid soaps and triclocarban in bar soaps - may contribute to bacterial resistance to antibiotics, the agency added.

Such products may also have "unanticipated hormonal effects that are of concern", according to the statement. Recent studies of such chemicals on animals have shown they may alter hormones, the FDA said, but such results have not yet been proven in humans. "Because so many consumers use them, FDA believes that there should be clearly demonstrated benefits to balance any potential risks," the statement added. If the FDA's proposed rule is finalised, companies would be required to provide data to support their product's health claims. If they cannot, the products would be reformulated or relabelled in order to remain on the market.

In March, a federal appeals court approved a lawsuit by the non-profit Natural Resources Defense Council, aimed at forcing the FDA to review the health impacts of triclosan.

<http://www.sciencedaily.com/releases/2013/12/131216204023.htm>

Ear Acupuncture Can Help Shed Pounds

Using continuous stimulation of five acupuncture points may be better at reducing abdominal fat (the midriff bulge) than single point stimulation, the findings suggest.

Auricular acupuncture therapy is based on the understanding that the outer ear represents all parts of the body. It was first used in France in 1956 by Dr Paul Nogier who noticed that a patient's back-ache was cured after s/he sustained a burn on the ear.

Since then the approach has been used to treat drug addiction and help people give up smoking and lose weight. The Korean researchers compared acupuncture of five points on the outer ear -- shen-men (divine gate); spleen, stomach, hunger, and endocrine -- and one point (hunger) -- with sham treatment on 91 overweight adults (BMI of 23 or more). Participants were asked to follow a restrictive (although not weight loss) diet and not to take any extra exercise during the eight week period of their treatment.

Thirty one people were randomly assigned to the five point treatment, which involved the insertion of acupuncture needles 2mm deep into the outer ear. These were kept in place with surgical tape for a week, after which the same treatment was applied to the other ear, with the process repeated over eight weeks. Another 30 people were assigned to the same treatment process, but at just the one hunger point. And a further 30 were given sham treatment -- with the same process and timescales, but with the removal of the needles immediately after insertion.

All participants were weighed and measured at the start and end of treatment, and four weeks in, to include BMI, waist circumference, body fat mass, percentage body fat, and blood pressure to see what impact acupuncture might have. Twenty four people dropped out before the eight weeks were up, 15 of whom were in the sham treatment group, suggesting that perhaps they found it harder to regulate their desire to eat and cope with the restrictive diet, say the authors.

But among those who kept going for the entire period, significant differences were apparent after four weeks, with the active treatment groups showing a 6.1% (5-point treatment) and 5.7% (1-point treatment) reduction, respectively, in BMI compared with the sham treatment group among whom there was no reduction in BMI. Weight also differed significantly after four weeks in both active treatment groups compared with the sham treatment group.

Waist circumference fell, with the largest drop seen in the group on the 5-point treatment compared with the sham groups, although this difference disappeared after taking account of age. Measures of body fat also fell after eight weeks, but only in those receiving the 5-point treatment. There were no significant differences in

blood pressure among the groups. The authors conclude that both five and one point approaches can help treat overweight, but that the five point approach may be more appropriate for tackling abdominal fat.

http://www.eurekalert.org/pub_releases/2013-12/ohs-sma121713.php

Study: Moderate alcohol consumption boosts body's immune system

Moderate drinking may actually bolster our immune system and help it fight off infection.

PORTLAND, Ore. — Medical science has known for years that people who drink moderate amounts of alcohol actually have a reduced risk of death. In general, they are healthier and have better cardiovascular function than those who don't drink alcohol at all.

Now, new research from Oregon Health & Science University adds a fascinating twist: moderate drinking may actually bolster our immune system and help it fight off infection.

The research, published Dec. 17 in the journal *Vaccine*, not only opens a new window into scientific understanding of the immune system, it also could help scientists find new ways to improve the human body's ability to respond to vaccines and infections.

The scientists did their research in rhesus macaques, which have an immune system very similar to humans. To conduct the study, the researchers trained a group of 12 rhesus macaques to consume alcohol — a 4 percent ethanol mixture — of their own accord.

Researchers vaccinated the monkeys against small pox as part of the study. They then separated the animals into two groups — those with access to the 4 percent ethanol and those with access to sugar water. All of the animals had regular access to pure water, and to food.

The researchers then monitored the animals' daily ethanol consumption for 14 months. And the animals were vaccinated again, seven months after the experiment began.

"Like humans, rhesus macaques showed highly variable drinking behavior," said Ilhem Messaoudi, the lead author of the paper, a former assistant professor at the Vaccine and Gene Therapy Institute at OHSU and assistant scientist in the Division of Pathobiology and Immunology at the Oregon National Primate Research Center and now an associate professor of biomedical sciences at the University of California, Riverside. "Some animals drank large volumes of ethanol, while others drank in moderation."

The monkeys' voluntary ethanol consumption segregated them into two groups. One group was made up of heavy drinkers, those that had an average blood ethanol concentration greater than 0.08 percent — the legal limit for humans to be able to drive a vehicle. The other group was made up of moderate drinkers, with an average blood ethanol concentration of 0.02 to 0.04 percent.

Prior to consuming the alcohol, all of the animals showed comparable responses to the vaccination. But after exposure to the alcohol, the two groups of monkeys responded in very different ways to the vaccination.

The heavy drinkers showed greatly diminished vaccine responses compared with the control group of monkeys who drank the sugar water. But the more surprising finding: the moderate-drinking monkeys displayed enhanced responses to the vaccine compared to the control group. Moderate drinking bolstered their bodies' immune systems.

"It seems that some of the benefits that we know of from moderate drinking might be related in some way to our immune system being boosted by that alcohol consumption," said Kathy Grant, Ph.D., senior author on the paper, a professor of behavioral neuroscience at OHSU and a senior scientist at the ONPRC.

The researchers stressed that excessive alcohol consumption was injurious to the monkeys' immune systems — just as excessive alcohol consumption is bad for human bodies in many ways.

"If you have a family history of alcohol abuse, or are at risk, or have been an abuser in the past, we are not recommending you go out and drink to improve your immune system," Messaoudi said. "But for the average person who has, say, a glass of wine with dinner, it does seem in general to improve health and cardiovascular function. And now we can add the immune system to that list."

The next steps for the researchers will be to better understand why the immune system reacts as it does to moderate alcohol. That may lead to a pharmaceutical alternative that could provide the same benefits as the moderate alcohol consumption.

The study was funded by the National Institutes of Health (grant #8P51 ODO11092-53) and the National Institute on Alcohol Abuse and Alcoholism within the NIH (grant # R21AA021947).

The study was carried out under strict accordance with the recommendations outlined in the Guide for the Care and Use of Laboratory Animals of the National Institutes of Health, the Office of Animal Welfare and the U.S. Department of Agriculture. The study also was approved by the Oregon National Primate Research Center Institutional Animal Care and Use Committee.

http://www.eurekalert.org/pub_releases/2013-12/uoc--ngs121613.php

Neanderthal genome shows early human interbreeding, inbreeding

First high-quality genome sequence allows comparison with human, Denisovan DNA

The most complete sequence to date of the Neanderthal genome, using DNA extracted from a woman's toe bone that dates back 50,000 years, reveals a long history of interbreeding among at least four different types of early humans living in Europe and Asia at that time, according to University of California, Berkeley, scientists. Population geneticist Montgomery Slatkin, graduate student Fernando Racimo and post-doctoral student Flora Jay were part of an international team of anthropologists and geneticists who generated a high-quality sequence of the Neanderthal genome and compared it with the genomes of modern humans and a recently recognized group of early humans called Denisovans.

The comparison shows that Neanderthals and Denisovans are very closely related, and that their common ancestor split off from the ancestors of modern humans about 400,000 years ago. Neanderthals and Denisovans split about 300,000 years ago. Though Denisovans and Neanderthals eventually died out, they left behind bits of their genetic heritage because they occasionally interbred with modern humans. The research team estimates that between 1.5 and 2.1 percent of the genomes of modern non-Africans can be traced to Neanderthals.

Denisovans also left genetic traces in modern humans, though only in some Oceanic and Asian populations.

The genomes of Australian aborigines, New Guineans and some Pacific Islanders are about 6 percent

Denisovan genes, according to earlier studies. The new analysis finds that the genomes of Han Chinese and

other mainland Asian populations, as well as of native Americans, contain about 0.2 percent Denisovan genes.

The genome comparisons also show that Denisovans interbred with a mysterious fourth group of early humans also living in Eurasia at the time. That group had split from the others more than a million years ago, and may have been the group of human ancestors known as *Homo erectus*, which fossils show was living in Europe and Asia a million or more years ago. "The paper really shows that the history of humans and hominins during this period was very complicated," said Slatkin, a UC Berkeley professor of integrative biology. "There was a lot of interbreeding that we know about and probably other interbreeding we haven't yet discovered."

The genome analysis will be published in the Dec. 19 issue of the journal *Nature*. Slatkin, Racimo and Jay are members of a large team led by former UC Berkeley post-doc Svante Pääbo, who is now at the Max Planck Institute for Evolutionary Anthropology in Leipzig, Germany.

In another analysis, Jay discovered that the Neanderthal woman whose toe bone provided the DNA was highly inbred. The woman's genome indicates that she was the daughter of a very closely related mother and father who either were half-siblings who shared the same mother, an uncle and niece or aunt and nephew, a grandparent and grandchild, or double first-cousins (the offspring of two siblings who married siblings).

Further analyses suggest that the population sizes of Neanderthals and Denisovans were small and that inbreeding may have been more common in Neanderthal groups than in modern populations.

As part of the new study, Racimo was able to identify at least 87 specific genes in modern humans that are significantly different from related genes in Neanderthals and Denisovans, and that may hold clues to the behavioral differences distinguishing us from early human populations that died out.

"There is no gene we can point to and say, 'This accounts for language or some other unique feature of modern humans,'" Slatkin said. "But from this list of genes, we will learn something about the changes that occurred on the human lineage, though those changes will probably be very subtle."

According to Pääbo, the list of genes "is a catalog of genetic features that sets all modern humans apart from all other organisms, living or extinct. I believe that in it hide some of the things that made the enormous expansion of human populations and human culture and technology in the last 100,000 years possible".

The Pääbo group last year produced a high-quality Denisovan genome based on DNA from a pinky finger bone discovered in 2008 in Denisova Cave in the Altai Mountains of Southern Siberia. That bone is from a young woman who lived about 40,000 years ago. The Neanderthal toe bone was found in the same cave in 2010, though in a deeper layer of sediment that is thought to be about 10,000-20,000 years older. The cave also contains modern human artifacts, meaning that at least three groups of early humans occupied the cave at different times. The Pääbo group developed new techniques to extract DNA from these old bones.

Slatkin noted that no one is sure how long the various now-extinct groups lasted, but that there is evidence that Neanderthals and modern humans coexisted in Europe and Asia for at least 30,000 years. Interbreeding was infrequent, though how infrequent is unclear given the genomic information available today. "We don't know if interbreeding took place once, where a group of Neanderthals got mixed in with modern humans, and it didn't happen again, or whether groups lived side by side, and there was interbreeding over a prolonged period," he said.

http://www.eurekalert.org/pub_releases/2013-12/aga-uba121713.php

Use biologic agents to induce remission in patients with moderately severe Crohn's disease *New American Gastroenterological Association guidelines provide guidance on most effective treatment pathway*

Bethesda, MD - The anti-TNF- α biologic agents, such as infliximab or adalimumab, are recommended to induce remission in patients with moderately severe Crohn's disease, according to a new guideline from the American Gastroenterological Association (AGA). Additionally, the guidelines recommend against using thiopurines or methotrexate alone to induce remission in these patients. The new guideline¹ and accompanying technical review² have been published in *Gastroenterology*, the official journal of the AGA Institute. The AGA Clinical Decision Support Tool, based on the guideline, can be reviewed at <http://gastro.org/crohnsdecisiontool>.

"Crohn's disease is a lifelong, relapsing disorder that can damage the bowel and lead to multiple abdominal operations over time. Deciding which medications are the best is a common dilemma for gastroenterologists and the Crohn's patients we treat. The disease can be disabling, but the drugs to control the disease can be toxic too and they can be costly. Balancing the benefits and the risks of the drugs and determining which medicines are most likely to keep the patient healthy is critical," according to Jonathan P. Terdiman, MD, lead author of the guidelines, and Chief of the Gastroenterology Service at the University of California, San Francisco Medical Center. "The new AGA guideline and clinical decision support tool will ease the decision process by providing transparent and actionable recommendations."

Crohn's disease is a chronic inflammatory bowel disease that causes significant morbidity and represents a considerable burden to society. It is estimated that 300,000 to 500,000 Americans suffer from Crohn's disease, costing the health-care system between \$2.5 and \$4 billion per year.

These guidelines are the first to make medication recommendations based on methodology that includes review of risks and benefits, patient preferences, and the quality of clinical evidence.

For the induction of remission, the guidelines recommend:

Using anti-TNF- α drugs to induce remission in patients with moderately severe Crohn's disease (strong recommendation, moderate-quality evidence).

Using anti-TNF- α monotherapy over thiopurine monotherapy to induce remission in patients who have moderately severe Crohn's disease (strong recommendation, moderate-quality evidence).

Using anti-TNF- α drugs in combination with thiopurines over thiopurine monotherapy to induce remission in patients who have moderately severe Crohn's disease (strong recommendation, high-quality evidence).

For maintenance of remission, the guidelines recommend:

Using thiopurines over no immunomodulator therapy to maintain a steroid-induced remission in patients with Crohn's disease (strong recommendation, moderate-quality evidence).

Using anti-TNF- α drugs over no anti-TNF- α drugs to maintain a steroid or anti-TNF- α drug-induced remission in patients with Crohn's disease (strong recommendation, high-quality evidence).

Read the "American Gastroenterological Association Institute Guideline on the Use of Thiopurines, Methotrexate, and Anti-TNF- α Biologic Drugs for the Induction and Maintenance of Remission in Inflammatory Crohn's Disease" to review all of the treatment recommendations.

¹ Terdiman J P et al. American Gastroenterological Association Institute Guideline on the Use of Thiopurines, Methotrexate, and Anti-TNF- α Biologic Drugs for the Induction and Maintenance of Remission in Inflammatory Crohn's Disease. *Gastroenterology* 2013;145:1459.

² Dassopoulos T et al. American Gastroenterological Association Institute Technical Review on the Use of Thiopurines, Methotrexate, and Anti-TNF- α Biologic Drugs for the Induction and Maintenance of Remission in Inflammatory Crohn's Disease. *Gastroenterology* 2013;145:1464.

http://www.eurekalert.org/pub_releases/2013-12/uoc--usc121713.php

UCLA study challenges long-held hypothesis that iron promotes atherosclerosis *A UCLA research team has found no evidence of an association between iron levels in the body and the risk of atherosclerosis, the hardening and narrowing of the arteries that leads to cardiovascular disease, the No. 1 killer in the U.S.*

The discovery, based on a comprehensive study in a mouse model of atherosclerosis, contradicts a long-held hypothesis about the role of iron in the disease and carries important implications for patients with chronic kidney disease or anemia related to inflammatory disorders, many of whom receive high-dose iron supplementation therapy. The findings currently appear online in the peer-reviewed journal *Cell Reports*.

"Understanding risk factors for atherosclerosis progression is important for better prevention and treatment of the disease," said senior author Elizabetha Nemeth, a professor of medicine at the David Geffen School of Medicine at UCLA and co-director of the UCLA Center for Iron Disorders. "For many years, there has been a belief that higher iron levels might contribute to, or worsen, atherosclerosis. We found no such connection."

The observation that men and postmenopausal women have both higher body iron levels and higher rates of atherosclerosis than premenopausal women led more than 30 years ago to the "iron hypothesis" — the notion that higher iron levels might promote atherosclerosis by generating more oxidative stress and promoting inflammation. However, subsequent studies noted that in diseases characterized by excessive iron in the body, atherosclerosis rates were no higher than normal.

The hypothesis was refined over the last decade because of the discovery of hepcidin, a hormone that plays a central role in iron metabolism, much like the role of glucose in regulating the body's insulin levels. The refined iron hypothesis held that hepcidin is increased by the inflammation associated with atherosclerosis and that the higher hepcidin levels promote the accumulation of iron in macrophages — key cells in the development of atherosclerosis.

Unexpectedly, the UCLA researchers discovered that the level of hepcidin was not increased in mice at any stage of atherosclerosis progression. Moreover, when the scientists increased the levels of iron in the macrophage cells, they found no effect on the progression of atherosclerosis. The study is the first to evaluate hepcidin expression during atherosclerosis progression in mice, as well as the first to weigh the impact on atherosclerosis of iron-loading macrophages through genetic manipulation and/or injection of intravenous iron. "The surprise was that we found no evidence that iron excess exacerbates atherosclerosis or that hepcidin is influenced at all by atherosclerosis," said Léon Kautz, a postdoctoral fellow in Nemeth's laboratory and the study's first author. "However, it is important to keep in mind that this is a mouse model. We need to see whether the same is true in humans."

Other research groups have begun analyzing hepcidin in atherosclerosis patients, Nemeth noted. Among the additional questions raised by the study is whether significantly lowering iron below normal levels could have a positive atherosclerosis-related effect.

The study was funded by the National Institutes of Health. Nemeth is a cofounder of Intrinsic LifeSciences, a company developing hepcidin diagnostics, and a consultant for Xenon Pharma, a company developing iron-related therapeutics. The research was a collaboration between Nemeth's lab and the lab of study author Jake Lusis, a professor of medicine and human genetics and of microbiology, immunology and molecular genetics at the David Geffen School of Medicine at UCLA. Additional authors included Victoria Gabayan, Xuping Wang, Judy Wu, James Onwuzurike, Grace Jung and Dr. Bo Qiao, all of the UCLA Department of Medicine, and Dr. Tomas Ganz, of the UCLA Department of Pathology.

<http://www.bbc.co.uk/news/uk-wales-south-west-wales-25412939>

Fungus could control mosquitoes, research suggests

Researchers at Swansea University say a fungus could be the key to controlling mosquitoes.

Fungus *Metarhizium anisopliae* lives in soil and kills a whole range of insects and researchers say it also affects mosquito larvae if added to the water where the insect breeds.

The insects carry diseases such as yellow fever and malaria.

According to the World Health Organisation malaria causes 800,000 deaths a year world-wide.

The team at Swansea University's department of bioscience said initial trials are very promising.

"The fungus occurs in soil and kills a whole range of insects but we've put it in the water where mosquito larvae breed and it is ingested by the insect and they die," team member Professor Tariq Butt told BBC Radio Wales.

"Normally what happens is the fungus attaches to its hosts, germinates and penetrates the body of the insect, colonises the insect and in the process the insect dies.

"But, in this case it doesn't germinate it just stays as spores packed in the body, in the gut, of the insect where it causes stress which activates a number of genes which trigger a whole range of responses leading to the death of the insect."

Malaria and yellow fever

Further research is now needed to see how the fungus can be introduced as initially it was hoped it would be passed from one insect to another, he added.

"In the past we were hoping the fungus was going to emerge from the body of the insect then the spores would be carried over to the healthy larvae and create an epidemic, but now what we're seeing is we'd have to apply the fungus frequently," he added.

The hope is the research will find a way to control the insect which spreads diseases such as malaria and yellow fever.

"It is reported that 300 children die each hour in Africa because of Malaria, but other diseases which are emerging such as dengue (fever) results in thousands of deaths reported across the world and also some of these diseases have been reported in Europe," said Prof Butt.

"We've done a number of trials and it looks very, very promising. Also, it's quite nice that we're killing three of the major species of mosquito transmitting a whole range of diseases."

<http://www.sciencedaily.com/releases/2013/12/131217104227.htm>

Discovery of 'Teen Gene' Could Hold Promise for Combating Severe Mental Illnesses

Researchers have isolated a gene responsible for dopamine connectivity in the medial prefrontal cortex during adolescence, providing the first clues towards understanding this phase of brain development

As many parents of mentally ill adults will confirm anecdotally, the first symptoms of "something not quite right" with their children begin to appear during the teen years. It is known that during this teenaged phase of brain development, adolescents are particularly vulnerable to psychiatric disorders, including schizophrenia, depression and drug addiction.

Researchers at the Douglas Institute Research Centre, affiliated with McGill University, have isolated a gene, DCC, which is responsible for dopamine connectivity in the medial prefrontal cortex during adolescence. Working with mice models, they have shown that dysfunction of this gene during adolescence has behavioral consequences which carry into adulthood.

The breakthrough provides the first clues towards a fuller understanding of this important phase of brain development. "Certain psychiatric disorders can be related to alterations in the function of the prefrontal cortex and to changes in the activity of the brain chemical dopamine," says Cecilia Flores, senior author on the study and professor at McGill's Department of Psychiatry, "Prefrontal cortex wiring continues to develop into early adulthood, although the mechanisms were, until now, entirely unknown."

Even subtle variations in DCC during adolescence produce significant alterations in prefrontal cortex function later on. To determine whether the findings of such basic research can translate to human subjects, researchers examined DCC expression in postmortem brains of people who had committed suicide. Remarkably, these brains showed higher levels of DCC expression -- some 48 per cent higher when compared to control subjects. Prefrontal cortex is associated with judgment

"The prefrontal cortex is associated with judgment, decision making, and mental flexibility -- or with the ability to change plans when faced with an obstacle," explained Dr. Flores, "Its functioning is important for learning, motivation, and cognitive processes. Given its prolonged development into adulthood, this region is particularly susceptible to being shaped by life experiences in adolescence, such as stress and drugs of abuse. Such alterations in prefrontal cortex development can have long term consequences later on in life."

Hope to reverse the course of an illness

By identifying the first molecule involved in how the prefrontal dopamine system matures, researchers now have a target for further investigation for developing pharmacological and other types of therapies. "We know that the DCC gene can be altered by experiences during adolescence," said Dr. Flores. "This already gives us hope, because therapy, including social support, is itself a type of experience which might modify the function of the DCC gene during this critical time and perhaps reduce vulnerability to an illness."

The psychiatric consensus is that early therapy and support in adolescence, as soon as a mental health issue first manifests itself, has dramatically greater potential for a successful outcome -- and for a healthy adulthood.

This discovery is reported in *Translational Psychiatry*.

C Manitt, C Eng, M Pokinko, R T Ryan, A Torres-Berrio, J P Lopez, S V Yogendran, M J J Daubaras, A Grant, E R E Schmidt, F Tronche, P Krimpenfort, H M Cooper, R J Pasterkamp, B Kolb, G Turecki, T P Wong, E J Nestler, B Giros, C Flores. dcc orchestrates the development of the prefrontal cortex during adolescence and is altered in psychiatric patients. Translational Psychiatry, 2013; 3 (12): e338 DOI: 10.1038/tp.2013.105

<http://www.bbc.co.uk/news/science-environment-25417441>

New findings hint at diamond deposits in Antarctica

Scientists say they have discovered compelling evidence that diamonds exist in the icy mountains of Antarctica.

By Matt McGrath Environment correspondent, BBC News

The researchers have identified a type of rock in the permanently frozen region that is known to contain the precious stones. However recovering any Antarctic mineral resources for commercial purposes is currently forbidden. The research is published in the journal *Nature Communications*.

Ice under ice

Diamonds are formed from pure carbon under extreme heat and pressure at depths of about 150km in the Earth's crust. Volcanic eruptions bring the valuable crystals to the surface, usually preserved in another type of bluish rock called kimberlite. The presence of kimberlite has been a clue to significant deposits of diamonds in several parts of the world, including Africa, Siberia and Australia. Now researchers have, for the first time, found evidence of kimberlite in Antarctica.

The team found three samples on the slopes of Mount Meredith in the northern Prince Charles Mountains.

"The fact they are reporting Group One kimberlites is an important one as diamonds are more likely to be found in this style of kimberlite eruption," said Dr Teal Riley, a survey geologist with the British Antarctic Survey. "However even amongst the Group One kimberlites, only 10% or so are economically viable, so it's still a big step to extrapolate this latest finding to any diamond mining activity in Antarctica."

Even if diamonds were plentiful in this inhospitable region, there are still some significant legal barriers to their extraction. The Protocol on Environmental Protection to the Antarctic Treaty, added in 1991, explicitly bans any extraction activity relating to mineral resources, except for scientific purposes. However it is up for review in 2041 and could be subject to change.

"We do not know what the Treaty Parties' views will be on mining after 2041 or what technologies might exist that could make extraction of Antarctic minerals economically viable," said Dr Kevin Hughes from the Scientific Committee on Antarctic Research. "An additional issue is that nations outside the Protocol are not bound by its provisions, including the ban on mineral resource activities."

<http://arstechnica.com/science/2013/12/caffeine-alcohol-keeps-your-chromosomes-just-right/>

Caffeine + alcohol keeps your chromosomes just right

The ends of your chromosomes are sensitive to a variety of environmental factors.

by Diana Gitig - Dec 18 2013, 3:05am TST

When cells divide, they must first replicate all of their genetic material. DNA replication is a very tightly controlled process; the double helix must be unwound, and the many enzymes involved must be coordinated to ensure that every nucleotide in each of our 46 chromosomes is copied exactly and only once. The system generally works pretty well, but the DNA replication machinery has a hard time with the ends of chromosomes, called telomeres.

Now, researchers have found that caffeine makes it more difficult for cells to copy the ends of their chromosomes. But that may be OK, since they also found that booze has the opposite effect.

Telomeres protect the ends of chromosome. Embryonic cells have a special enzyme, telomerase, that lengthens telomeres; after the cells specialize, however, they stop expressing telomerase. From there on, telomeres get shorter with each cell division since they are so difficult to replicate. Once telomeres reach a critically short length, the cell stops dividing altogether. Shorter telomeres are thus a hallmark of aging. Tumor cells start re-expressing telomerase, and their lengthened telomeres are one factor that allows them to divide indefinitely. Psychological stress and poor socioeconomic status have been linked to shortened telomeres. (Remember: longer telomeres = cancer, shorter telomeres = age.) However, it has not yet been determined if these stresses actually cause a change in telomere length, and if so, how that might occur; it's possible that they simply accelerate the normal trend of aging.

To explore the effects of stress on telomere length, a group at Tel Aviv University turned to yeast, a simpler organism that also maintains telomeres. To find any molecular mechanisms involved in changing telomere length, they grew yeast in the presence of thirteen different environmental stresses, measured the lengths of their telomeres, and then analyzed their gene expression profiles. They found that caffeine (and high temperatures) shorten telomeres, and alcohol (and acetic acid) lengthen them. Oxidative stress had no effect. At least six percent of yeast genes—some 400 genes—are involved in regulating telomere length. To home in on which genes might be important in these stress responses, the researchers looked at mutants that showed atypical stress responses—yeast strains with telomeres that did not get shorter when they were exposed coffee (the yeast strains, not the researchers). The most prominent of these genes was Rif-1, a negative regulator of telomerase. They found that exposure to ethanol (and isopropanol, and methanol) reduced the recruitment of Rif1 to telomeres. About ten other genes were also identified as playing roles.

Some telomeres are too long, and some are too short. Perhaps striking the right balance of caffeine and alcohol is the key to keeping them just right—as if you needed an excuse to have another hot toddy.

PLoS Genetics, 2013. DOI: 10.1371/journal.pgen.1003721 (About DOIs).

<http://www.sciencedaily.com/releases/2013/12/131217134706.htm>

Radiation Therapy to Treat Uterine Cancer Linked to Increased Risk of Bladder Cancer Later in Life

Radiation therapy used to treat uterine cancer may increase a patient's risk of developing bladder cancer.

That is the conclusion of a recent study published in *BJU International*. The findings indicate the importance of monitoring patients for potential signs of bladder cancer to ensure early diagnosis and treatment.

In the United States, uterine cancer is the fourth most common cancer in women, with an estimated 49,560 women diagnosed in 2013. In addition to surgery, 38 percent of patients undergo pelvic radiation therapy to decrease uterine cancer recurrence. Studies have found that women treated with radiation therapy for uterine

cancer, like men who received radiation therapy for prostate cancer, have an increased risk of developing bladder cancer later in life.

To investigate the issue, Guan Wu, MD, PhD, of the University of Rochester Medical Center, and his colleagues analyzed the records of 56,681 patients diagnosed with uterine cancer as their first primary malignancy between 1980 and 2005. The information was obtained from the Surveillance, Epidemiology and End-Results (SEER) database.

With an average follow-up of 15 years, bladder cancer incidence in uterine cancer patients treated with pelvic radiation therapy was twice as high as that seen in patients treated without radiation. Similarly, the death rate from bladder cancer was nearly three times higher in patients treated with pelvic radiation than in those who did not receive radiation. It is commonly thought that bladder cancers that develop after pelvic radiation tend to be aggressive, with high grades and stages, but this study found that the types, grades, and stages of bladder cancer that developed were similar in patients treated with and without radiation therapy.

"Physicians who care for patients with a history of uterine cancer and pelvic radiation treatment should keep in mind the increased risk of bladder cancer," said Dr. Wu. "Proper clinical evaluation should be performed to avoid delayed diagnosis, which may improve the quality of care for this group of patients."

Janet E. Baack Kukreja, Emil Scosyrev, Ralph A. Brasacchio, Eugene P. Toy, Edward M Messing, Guan Wu. Bladder Cancer Incidence and Mortality in Patients Treated with Radiation for Uterine Cancer. BJU International, 2013; DOI: 10.1111/bju.12543

<http://bit.ly/197uPVK>

Did Rock Weathering Trigger 'Snowball Earth'?

A global ice age that lasted more than 50 million years may have been triggered by volcanic rocks trapping carbon dioxide that would otherwise warm the planet, researchers say in a new study detailed in the Dec. 16 journal Proceedings of the National Academy of Sciences.

Dec 17, 2013 02:20 PM ET // by Charles Choi, LiveScience

Although ice is now found mostly in Earth's polar regions, analysis of ancient rocks suggests it could at times cover the entire globe. The causes of these "snowball Earth" periods remain mysterious, with the cause of one episode 2.3 billion years ago perhaps being the widespread emergence of oxygen in the atmosphere, which destroyed greenhouse gases keeping Earth warm.

For the new study, scientists focused on a snowball Earth period that began about 717 million years ago known as the Sturtian glaciation. This global ice age was preceded by more than 1 billion years without glaciers, making the Sturtian a transition from a longtime ice-free world to a snowball Earth, the most dramatic episode of climate change in the geological record. The researchers noted the Sturtian broadly coincided with rifts tearing apart the ancient supercontinent Rodinia, as well as major volcanic activity in equatorial regions. This suggested the Sturtian might have its roots in tectonic activity.

The scientists investigated ancient rocks in the Mackenzie Mountains of northwest Canada known as glaciogenic diamictites, which are sedimentary rocks that are deposited by glaciers as they move over the Earth. They analyzed rocks both above and below these glaciogenic deposits to find out the deposits' ages.

"For me, this type of work combines the best parts of geology — fieldwork in remote and beautiful places, such as the Mackenzie Mountains of northern Canada, and working in a geochemistry lab," said study lead author Alan Rooney, a geologist at Harvard University. "The fieldwork is crucial to provide context for any data you may generate in the lab."

Specifically, the researchers analyzed levels of the elements rhenium and osmium within the sedimentary rocks bracketing the glaciogenic deposits. Rhenium breaks down via radioactive decay, generating osmium over time. By analyzing the ratios of rhenium and osmium isotopes within the rocks, the investigators could determine their age. (Isotopes are different forms of elements, where the atoms have different numbers of neutrons in their nuclei.) The scientists found the Sturtian lasted about 55 million years. "The most surprising aspect of these results is the duration of this glacial epoch," Rooney told LiveScience's OurAmazingPlanet.

The researchers also investigated osmium and strontium isotopes within rocks before, during and after the Sturtian. The levels of various isotopes in rocks depends on whether or not they came from radioactive sources such as eroded volcanic rock.

Based on their analysis, the researchers suggest a "fire and ice" scenario cooled the planet. As volcanic rock that erupted before the Sturtian eroded, it absorbed carbon dioxide, trapping it within sediments that washed into the oceans. Carbon dioxide is a greenhouse gas that traps heat — by removing it from the atmosphere, global cooling resulted.

Future research can analyze whether the Sturtian was one long-lasting snowball or a series of glacial and warmer periods with one final global snowball, Rooney said. Research can also investigate the environment right before the Sturtian to unearth even more details about its development.

<http://www.bbc.co.uk/news/business-25415485>

GSK to stop paying doctors to make speeches

GlaxoSmithKline (GSK) is making major changes to its incentive schemes following a damaging corruption scandal in China.

The pharmaceuticals firm will stop paying doctors to promote its products through speaking engagements. Members of its sales force will also no longer have individual sales targets. Earlier this year, Chinese police said GSK had transferred 3bn yuan (\$489m; £321m) to travel agencies and consultancies to help bribe doctors. But the company says the latest measures are not related to that continuing investigation. Instead, it says, they are part of a wider effort to improve transparency.

'Greater clarity'

In a statement, Sir Andrew Witty, chief executive of GSK, said: "Today we are outlining a further set of measures to modernise our relationship with healthcare professionals. "These are designed to bring greater clarity and confidence that whenever we talk to a doctor, nurse or other prescriber, it is patients' interests that always come first." As well as stopping payments to doctors for making speeches, GSK is also ending payments to healthcare professionals for attending medical conferences.

A spokesperson told the BBC that there were "perceived conflicts of interest with that way of working". GSK plans a new system under which independent organisations, such as universities, can approach GSK for a grant if they want a particular doctor to attend a medical conference.

Doctors 'satisfied'

In a statement, Dr Vivienne Nathanson, head of science and ethics at the British Medical Association (BMA), which represents doctors, said: "Whilst we agree that GSK should not directly sponsor doctors going to meetings, we are satisfied that they will continue to financially support education.

"It is pleasing to see a large pharmaceutical company like GlaxoSmithKline recognise that it can reduce the possibility of undue influence by rewarding employees for providing high-quality information and education for doctors, rather than for their sales figures."

GSK says sales representatives will be rewarded for "technical knowledge" and the "quality of the service they deliver to support improved patient care". Their compensation will also be linked to the overall performance of GSK. Salespeople in the US have already been working under those conditions since 2011. A spokesperson from GSK said: "It was always our intent to roll it out globally."

Paying doctors to make speeches and attend conferences is common in the pharmaceuticals industry, but there is growing demand for reform. "Where GSK leads we must hope that other companies will follow," Fiona Godlee, editor of the British Medical Journal and a campaigner against industry influence in medicine, told the Reuters news agency. "But there is a long way to go if we are truly to extricate medicine from commercial influence. Doctors and their societies have been too ready to compromise themselves."

'Non-trivial'

Ben Goldacre, author of the book *Bad Pharma*, is concerned about the quality of advice received by doctors. He told BBC Radio 4: "Doctors get a lot of their education about which treatment works best from the pharmaceutical industry itself - from doctors who have been paid to give lectures about which drug is best. "This free education has been shown to be biased in research and it's non-trivial."

Andrew Powrie-Smith, director at the Association of the British Pharmaceutical Industry, told BBC Radio 4: "A number of companies I think are looking at this area and different models of education are emerging." He stressed that by 2016 companies would have to disclose how much they pay individual doctors.

http://www.eurekalert.org/pub_releases/2013-12/acs-121813.php

First plant-based 'microswimmers' could propel drugs to the right location

Corkscrew structures from plants are incorporated into a new kind of helical "microswimmer"

In the quest to shrink motors so they can maneuver in tiny spaces like inside and between human cells, scientists have taken inspiration from millions of years of plant evolution and incorporated, for the first time, corkscrew structures from plants into a new kind of helical "microswimmer." The low-cost development, which appears in ACS' journal *Nano Letters*, could be used on a large scale in targeted drug delivery and other applications

Joseph Wang and colleagues point out that nanomotors have tremendous potential in diverse applications from delivering drugs to precise locations in the body to making biosensors. To realize this potential, scientists have

recently taken inspiration from microorganisms that have tiny, hair-like structures that they whip around to propel themselves. But copying these nature-engineered nanomotors requires advanced instruments and costly processing techniques that make them a challenge to produce on a large scale. To address these issues of practicality, Wang's group also drew inspiration from nature, but turned to plants instead.

They isolated spiral microstructures packed by the million in small pieces of a plant's stem. The scientists coated these tiny coils that are about the width of a fine cotton fiber with thin layers of titanium and magnetic nickel. The plant material makes these microswimmers biodegradable and less likely to be rejected by the human body. The magnetic layer allows scientists to control the motors' movement. When the scientists placed the coated spirals in water or human blood serum and applied a magnetic field, the nanomotors efficiently spun their way through the liquids. The scientists conclude that the microswimmers show great promise for future biomedical uses.

The authors acknowledge funding from the Defense Threat Reduction Agency-Joint Science and Technology Office for Chemical and Biological Defense.

http://www.eurekalert.org/pub_releases/2013-12/ctco-ptf121813.php

Preferable treatment for MS found in allogenic bone marrow stem cells

MSCs isolated from MS patients have decreased suppressive function compared to those of healthy counterparts

Putnam Valley, NY. Multiple sclerosis (MS), an inflammatory autoimmune disease affecting more than one million people worldwide, is caused by an immune reaction to myelin proteins, the proteins that help form the myelin insulating substance around nerves. Demyelination and MS are a consequence of this immune reaction. Bone marrow mesenchymal stem cells (MSCs) have been considered as an important source for cell therapy for autoimmune diseases such as MS because of their immunosuppressive properties.

Now, a research team in Brazil has compared MSCs isolated from MS patients and from healthy donors to determine if the MSCs from MS patients are normal or defective. The study will be published in a future issue of Cell Transplantation but is currently freely available on-line as an unedited early e-pub at:

<http://www.ingentaconnect.com/content/cog/ct/pre-prints/content-ct1131>.

"The ability of MSCs to modulate the immune response suggests a possible role of these cells in tolerance induction in patients with autoimmune diseases, and also supports the rationale for MSC application in the treatment of MS," said study corresponding author Dr. Gislane Lelis Vilela de Oliveira of the Center for Cell-Based Research at the University of Sao Paulo. "We found that MS patient-derived MSCs present higher senescence, or biological aging, and decreased expression of important immune system markers as well as a different transcriptional profile when compared to their healthy counterparts."

The researchers suggested that further clinical studies should be conducted using transplanted allogenic (other-donated) MSCs derived from healthy donors to determine if the MSCs have a therapeutic effect over transplanted autologous (self-donated) MSCs from patients.

"Several reports have shown that bone marrow-derived MSCs are able to modulate innate and adaptive immunity cell responses and induce tolerance, thus supporting the rationale for their application in treating autoimmune diseases," said the researchers.

They also noted that studies have shown that transplanted MSCs migrate to demyelinated areas as well as induce generation and expansion of regulatory T cells, important in immunity.

"We found that the transcriptional profile of patient MSCs after transplantation was closer to that of their pre-transplant MSC samples than those from their healthy counterparts, suggesting that treatment with patient self-donated MSCs does not reverse the alterations we observed in MSCs from MS patients," they concluded.

The researchers further noted that their results might not be representative of "typical" MS patients because their study included only patients who were refractory to conventional treatments.

"This study highlights one of the potential problems with autologous stem cell transplants" said Dr. Paul R. Sanberg, distinguished professor at the Center of Excellence for Aging and Brain Repair, Morsani College of Medicine, University of South Florida, Tampa, FL. "Autologous cells are frequently affected by the disease etiology thus reducing their ability to be effective, meaning that allogenic transplants maybe preferable to maximize their potential benefit if other concerns such as rejection can be overcome."

Citation: de Oliveira, G. L. V.; de Lima, K. W. A.; Colombini, A. M.; Pinheiro, D. G.; Panepucci, R. A.; Palma, P. V. B.; Brum, D. G.; Covas, D. T.; Simões, B. P.; de Oliveira, M. C.; Donadi, E. A.; Malmegrim, K. C. R. Bone marrow mesenchymal stromal cells isolated from multiple sclerosis patients have distinct gene expression profile and decreased suppressive function compared with healthy counterparts. Cell Transplant. Appeared or available online: November 20, 2013

<http://phys.org/news/2013-12-japan-tsunami-exacerbated-landslide.html>

Japan tsunami exacerbated by landslide

The 2011 Japan tsunami, which killed up to 20,000 people and caused the partial meltdown of the Fukushima nuclear plant, was made worse by an underwater landslide, according to scientists.

Until now, the lethal waves have been blamed solely on the magnitude-nine earthquake which struck at sea, 43 miles east of the country's northern Tohoku peninsula. But an international team, led by Professor Dave Tappin of NERC's British Geological Survey, say the earthquake can't explain the full extent of the waves. 'The earthquake alone cannot explain the height of the waves along the Sanriku coast of northern Honshu Island,' says Tappin. 'They were generated by a submarine landslide.'

According to Tappin, the research raises a 'big problem' for early-warning systems. Where the risk of landslides goes unrecognised, tsunamis generated by similar earthquakes could be badly underestimated.

It's well known that landslides can generate tsunamis on their own, and research on the Papua New Guinea event of 1998 showed that landslides triggered by small earthquakes could also produce devastating tsunamis. But this research, presented at last week's Fall Meeting of the American Geophysical Union, is the first to recognise the significant contribution that underwater landslides can make to tsunamis generated by giant quakes.

'With the Japan tsunami, for the first time we had offshore wave data recorded at GPS buoys,' says Tappin. 'This allowed us to identify the most likely location of the landslide.'

'Using maps of the seabed, we identified a landslide that was 40 kilometres wide, 20 kilometres long and 2 kilometres thick. That makes it 500 cubic kilometres, so it's pretty big.' 'We then used computer models to simulate the tsunami from a dual source; the earthquake and the landslide, and this gave us the high water levels along the north Honshu coast.' 'An additional check on the landslide source was from an analysis of the wave frequency at the buoys, which showed a high-frequency component that could only be from the landslide.' Tappin says the landslide also explains helicopter video footage of the tsunami which appears to show two separate wave trains, around 20-30 minutes apart.

The earthquake hit on the afternoon of March 11 2011. It was the most powerful ever known to have struck Japan, and was strong enough to shift the Earth slightly on its axis. The sheer scale of the tsunami took Japan by surprise. The Japanese Meteorological Agency had predicted a tsunami of just six metres. But when the waves arrived, they reached heights of up to 12 metres, overtopping seawalls and sweeping away entire towns behind them. The Sanriku coastline was particularly hard-hit. In Minamisanriku, a town of 17,000 people, over 95 per cent of the buildings were destroyed, and more than 800 people lost their lives.

<http://www.sciencedaily.com/releases/2013/12/131218100141.htm>

Algae to Crude Oil: Million-Year Natural Process Takes Minutes in the Lab

Engineers have created a continuous chemical process that produces useful crude oil minutes after they pour in harvested algae -- a verdant green paste with the consistency of pea soup.

The research by engineers at the Department of Energy's Pacific Northwest National Laboratory was reported recently in the journal *Algal Research*. A biofuels company, Utah-based Genifuel Corp., has licensed the technology and is working with an industrial partner to build a pilot plant using the technology.

In the PNNL process, a slurry of wet algae is pumped into the front end of a chemical reactor. Once the system is up and running, out comes crude oil in less than an hour, along with water and a byproduct stream of material containing phosphorus that can be recycled to grow more algae.

With additional conventional refining, the crude algae oil is converted into aviation fuel, gasoline or diesel fuel. And the waste water is processed further, yielding burnable gas and substances like potassium and nitrogen, which, along with the cleansed water, can also be recycled to grow more algae.

While algae has long been considered a potential source of biofuel, and several companies have produced algae-based fuels on a research scale, the fuel is projected to be expensive. The PNNL technology harnesses algae's energy potential efficiently and incorporates a number of methods to reduce the cost of producing algae fuel.

"Cost is the big roadblock for algae-based fuel," said Douglas Elliott, the laboratory fellow who led the PNNL team's research. "We believe that the process we've created will help make algae biofuels much more economical."

PNNL scientists and engineers simplified the production of crude oil from algae by combining several chemical steps into one continuous process. The most important cost-saving step is that the process works with wet algae. Most current processes require the algae to be dried -- a process that takes a lot of energy and is expensive. The new process works with an algae slurry that contains as much as 80 to 90 percent water.

"Not having to dry the algae is a big win in this process; that cuts the cost a great deal," said Elliott. "Then there are bonuses, like being able to extract usable gas from the water and then recycle the remaining water and nutrients to help grow more algae, which further reduces costs."

While a few other groups have tested similar processes to create biofuel from wet algae, most of that work is done one batch at a time. The PNNL system runs continuously, processing about 1.5 liters of algae slurry in the research reactor per hour. While that doesn't seem like much, it's much closer to the type of continuous system required for large-scale commercial production.

The PNNL system also eliminates another step required in today's most common algae-processing method: the need for complex processing with solvents like hexane to extract the energy-rich oils from the rest of the algae. Instead, the PNNL team works with the whole algae, subjecting it to very hot water under high pressure to tear apart the substance, converting most of the biomass into liquid and gas fuels.

The system runs at around 350 degrees Celsius (662 degrees Fahrenheit) at a pressure of around 3,000 PSI, combining processes known as hydrothermal liquefaction and catalytic hydrothermal gasification. Elliott says such a high-pressure system is not easy or cheap to build, which is one drawback to the technology, though the cost savings on the back end more than makes up for the investment.

"It's a bit like using a pressure cooker, only the pressures and temperatures we use are much higher," said Elliott. "In a sense, we are duplicating the process in the Earth that converted algae into oil over the course of millions of years. We're just doing it much, much faster."

The products of the process are:

- *Crude oil, which can be converted to aviation fuel, gasoline or diesel fuel. In the team's experiments, generally more than 50 percent of the algae's carbon is converted to energy in crude oil -- sometimes as much as 70 percent.*
- *Clean water, which can be re-used to grow more algae.*
- *Fuel gas, which can be burned to make electricity or cleaned to make natural gas for vehicle fuel in the form of compressed natural gas.*
- *Nutrients such as nitrogen, phosphorus, and potassium -- the key nutrients for growing algae.*

Elliott has worked on hydrothermal technology for nearly 40 years, applying it to a variety of substances, including wood chips and other substances. Because of the mix of earthy materials in his laboratory, and the constant chemical processing, he jokes that his laboratory sometimes smells "like a mix of dirty socks, rotten eggs and wood smoke" -- an accurate assessment.

Genifuel Corp. has worked closely with Elliott's team since 2008, licensing the technology and working initially with PNNL through DOE's Technology Assistance Program to assess the technology.

"This has really been a fruitful collaboration for both Genifuel and PNNL," said James Oyler, president of Genifuel. "The hydrothermal liquefaction process that PNNL developed for biomass makes the conversion of algae to biofuel much more economical. Genifuel has been a partner to improve the technology and make it feasible for use in a commercial system.

"It's a formidable challenge, to make a biofuel that is cost-competitive with established petroleum-based fuels," Oyler added. "This is a huge step in the right direction."

The recent work is part of DOE's National Alliance for Advanced Biofuels & Bioproducts, or NAABB. This project was funded with American Recovery and Reinvestment Act funds by DOE's Office of Energy Efficiency and Renewable Energy. Both PNNL and Genifuel have been partners in the NAABB program.

A short video clip about the process is at <https://www.youtube.com/watch?v=Qs0QZJ0rea0>.

Douglas C. Elliott, Todd R. Hart, Andrew J. Schmidt, Gary G. Neuenschwander, Leslie J. Rotness, Mariefel V. Olarte, Alan H. Zacher, Karl O. Albrecht, Richard T. Hallen, Johnathan E. Holladay. *Process development for hydrothermal liquefaction of algae feedstocks in a continuous-flow reactor. Algal Research, 2013; DOI: 10.1016/j.algal.2013.08.005*

<http://www.astrobio.net/exclusive/5876/organics-preserved-in-ancient-meteorite-formed-glass->

Organics Preserved in Ancient Meteorite-Formed Glass

Scientists have found organics from Earth's swamp trapped inside glass that had been created by a meteor impact almost a million years ago.

Author: Nola Taylor Redd

Scientists have found organics from Earth's swamp trapped inside of glass created by a meteor impact almost a million years ago. The tiny pockets, only micrometers across, contain material such as cellulose and proteins. Though the impact glass was found on Earth, scientists say that similar samples could have been thrown into space by this or other blasts, allowing organics to be transported from one planet to another.

Impact glass

Approximately 800,000 years ago, a rock 100 to 160 feet (30 to 50 meters) across crashed down in Western Tasmania, Australia. As it slammed into the Earth, temperatures exceeded 1,700 degrees Celsius (3,100 degrees

Fahrenheit), melting rock and creating glass sphericals, as well as a quarter-mile wide hole known as the Darwin Crater.

"The reason the glass is so abundant seems likely to relate to the presence of volatiles like water at the surface when the impact occurred," lead author Kieren Howard of the City University of New York told Astrobiology by email. "A bit like when water from your spatula drips into a frying pan, having the right amount of water at the surface during impact may have increased the magnitude of the explosion, and the production and dispersal of the melt."

In Tasmania, the land was covered by swamps and rainforest, offering sufficient water to create the glass. According to the authors, glass from the Darwin Crater is the most abundant and widely dispersed impact glass on Earth, relative to the crater's size, with glass scattered across 150 square miles (400 square kilometers). In fact, the widespread glass led to the discovery of the crater, which is now filled with younger sediments, in 1972.

Varying types of glass form from impacts, depending on the rocks laying at the surface. Darwin contains quartz-rich rocks that create white colors, though other rock mixes in to create different shades.

"The greater the proportion of shale molten to make the glass, the darker in color it gets—from white through light green, dark green, to black," Howard said.

The white glass blends in with quartzite samples in the area, making them a challenge to pick out. White Darwin glass fragments make up less than 3 percent of all finds. The authors suggest that, in less well-preserved fields, the tiny fraction of white glass could easily remain undiscovered.



Samples of Darwin glass range in size and color. White glass make up less than 3 percent of all finds. K. Howard

An organic surprise

Howard and his team weren't originally looking for organics. But when they examined the glass, they found surprising evidence of crystalline quartz. "I went looking for crystals in the glass, only to discover the spherical inclusions," Howard said.

Inside the tiny crystal pockets, spheres up to 200 micrometers in diameter contained organics including cellulose, lignin, aliphatic biopolymer, and protein. The signature from the biomarkers suggested that fragments of peat were trapped in the molten glass, rapidly heating and degassing to create a frothy, bubble-like texture. Trapped inside of glass, the organics would have been prevented from breaking down via oxidation. Howard's samples showed no signs of fossilizations, indicating that such trapped organics could last as long as the glass around them.

"Providing the glass seal isn't broken, it's a good preservation method," said organic geochemist Stephen Bowden at the University of Aberdeen in Scotland. Bowden, who was not involved in the research, has previously studied fossil organic matter within impact rocks and its survival during atmosphere re-entry.

"[It's] like setting something in resin or amber—like a scorpion novelty in a glass paperweight."

Fossil organic matter—fossil fuels—have been found in rocks formed by meteorite impacts and glasses from experimental collisions, but never before organics with such a well-preserved biological character. The research was published in the journal *Nature Geoscience* on November 10.

Organic transportation

Finding organics inside of glass could have extensive ramifications. Though Howard found glass spheres that crashed back to Earth, other spheres could have been hurled into space, if their velocities were high enough.

"Survival in or transfer to ejecta is a 'big deal' because of the conditions of its formation—it's surprising—and the fact that it can leave Earth's atmosphere," Bowden said.

Organics launched off the planet could have traveled through space to seed other bodies, suggesting a possible method of travel for panspermia. This theory suggests that life did not originate on Earth, but traveled here from elsewhere in the universe.

Rocky bodies such as Mars, the Moon, and Titan could potentially have organics trapped after impacts hit their surface, though Bowden says that without further evidence, "this is still speculation." Even if ejecta from icy moons such as Jupiter's Europa formed around organics, they would be composed of ice, which would easily be breached when they melted. Bowden went on to point out the difficulty of locating such finds on Earth.

"The volume of organic matter is small in comparison to the volumes of rock and sediment that are thrown up," he said. "After a few seconds in the hot ejecta, it's an even smaller volume of organic matter being diluted by a lot of rock and sediment."

But although the white glass only makes up a small percentage of the Darwin ejecta, Howard remained positive about the potential for similar discoveries of preserved organic biomarkers in other impact glasses and tektites here, and perhaps elsewhere. "Impacts are the most common geologic process in the solar system. Mars is littered with craters and known to have impact glasses across its surface," Howard said. "We've shown these glasses are potentially some of the most stable organic repositories imaginable, so yes, if looking for biomarker evidence of life on Mars—or any other planet—impact glasses are prospective targets."

The challenge, he noted, is discovering the tiny inclusions. Still, on Earth at least, the capture of organics could be more abundant than previous finds have indicated. "To the uniformitarian mind of a geologist, finding a discovery like ours suggests it's a product of a common process," Howard said. "Ultimately, impacts are impacts and organics are abundant -- and apparently more resilient than we ever predicted, at least in terrestrial settings."

<http://www.sciencedaily.com/releases/2013/12/131218130259.htm>

Brain Area Attacked by Alzheimer's Links Learning, Rewards

One of the first areas of the brain to be attacked by Alzheimer's disease is more active when the brain isn't working very hard, and quiets down during the brain's peak performance.

The question that Duke University graduate student Sarah Heilbronner wanted to resolve was whether this brain region, called the posterior cingulate cortex, or PCC, actively dampens cognitive performance, say by allowing the mind to wander, or is instead monitoring performance and trying to improve it when needed.

If the PCC were monitoring and improving performance, increased activity there would be the result of poor performance, not the cause of it.

The PCC connects to both learning and reward systems, Heilbronner said, and is a part of the "default mode network." It lies along a mid-line between the ears, where many structures related to rewards can be found. "It's kind of a nexus for multiple systems," said Heilbronner, who is currently a postdoctoral researcher in neuroanatomy at the University of Rochester.

"As this area begins to deteriorate, people begin to show the early signs of cognitive decline -- problems learning and remembering things, getting lost, trouble planning -- that ultimately manifest as outright dementia," said Michael Platt, director of the Duke Institute for Brain Sciences, who supervised Heilbronner's 2012 dissertation. Their findings appear Dec. 18 in the journal *Neuron*.

Heilbronner's experiment to better understand the PCC's role in learning and remembering relied on two rhesus macaque monkeys fitted with electrodes to read out the activity of individual neurons in their brains. Their task was akin to playing video games with their eyes. The monkeys were shown a series of photographs each day marked with dots at the upper left and lower right corners. To get a rewarding squirt of juice, they had to move their gaze to the correct target dot on a photo, and they learned by trial and error which dot would yield the reward for each photo.

Each day, they were shown up to 12 photos from an assortment of Heilbronner's vacation snaps at Yellowstone National Park and the Grand Canyon. Some of each day's images were familiar with a known reward target, and others were new. As the monkeys responded with their gaze, the researchers watched the activity of dozens of neurons in each monkey's brain immediately following correct and incorrect responses. They also altered the amount of juice dispensed in some cases, creating a sense of high-reward and low-reward answers.

If the PCC actively dampened performance, the researchers would expect to see it active before a choice is made or the feedback is received. Instead, they saw it working after the feedback, lasting sometimes until the next image was presented. Neurons in the PCC responded strongly when the monkeys needed to learn something new, especially when they made errors or didn't earn enough reward to keep motivated.

The researchers also ran the task after administering a drug, muscimol, that impaired the function of the PCC temporarily during testing. With the center inactivated by the drug, the monkeys could recall earlier learning regardless of the size of the reward. Learning a new item was still possible when the reward was large, but the monkeys couldn't learn anything new when rewards were small. "Maybe it didn't seem worth it," Heilbronner said.

The dampening experiment also reinforced what the researchers had seen in the timing of the PCC's response. If this center's role is to let the mind wander, performance should have improved when the muscimol was administered, but the opposite was true. Heilbronner concludes that the PCC summons more resources for a

challenging cognitive task. So rather than being the cause of poor performance on a task, PCC actually steps in during a challenge to improve the situation.

"This study tells us that a healthy PCC is required for monitoring performance and keeping motivated during learning, particularly when problems are challenging," Platt said.

Heilbronner is now interested in finding out whether the PCC is more important to learning than it is to recall, and how motivation interacts with PCC abnormalities seen in Alzheimer's disease.

Sarah R. Heilbronner, Michael L. Platt. Causal Evidence of Performance Monitoring by Neurons in Posterior Cingulate Cortex during Learning. Neuron, 2013; 80 (6): 1384 DOI: 10.1016/j.neuron.2013.09.028

http://www.eurekalert.org/pub_releases/2013-12/ded-ss-121713.php

Salty surprise -- ordinary table salt turns into 'forbidden' forms

High-pressure X-ray experiments violate textbook rules of chemistry

High-pressure experiments with ordinary table salt have produced new chemical compounds that should not exist according to the textbook rules of chemistry. The study at DESY's X-ray source PETRA III and at other research centres could pave the way to a more universal understanding of chemistry and to novel applications, as the international research team, led by Prof. Artem Oganov of Stony Brook University (State University of New York) and Prof. Alexander Goncharov of Carnegie Institution, report in the scientific journal *Science*. Table salt, also known as sodium chloride or NaCl, is one of the best-known and most studied chemical compounds. It crystallises in a cubic unit cell and is very stable. Its chemical composition is simple - one sodium atom (Na) and one chlorine atom (Cl). Or at least that's true under ambient conditions. Other compounds of the two elements are forbidden by the classical rules of chemistry. For instance, according to the octet rule all chemical elements strive to fill their outermost shell with eight electrons, which is the most stable configuration, found in noble gases. Sodium has one extra electron and chlorine is missing one, so sodium donates one electron to chlorine, leaving both atoms with an outer shell containing eight electrons and forming a strong ionic bond.

But when the scientists put table salt under high pressure of 200,000 atmospheres and more at PETRA III and added an extra dash of either sodium or chlorine, "forbidden" compounds like Na₃Cl and NaCl₃ turned up.

"Following the theoretical prediction, we heated the samples under pressure with lasers for a while," explains co-author Dr. Zuzana Konôpková of DESY, who supported the experiments at DESY's Extreme Conditions Beamline P02 (ECB). "We found other stable compounds of Na and Cl which came as a surprise." This is not supposed to happen, as these compounds require a completely different form of chemical bonding with higher energy, and nature always favours the lowest state of energy.

But Oganov's team had calculated before that exotic compounds might form under extreme conditions and remain stable under these conditions. "We have predicted and made crazy compounds that violate textbook rules: NaCl₃, NaCl₇, Na₃Cl₂, Na₂Cl, and Na₃Cl," says Dr. Weiwei Zhang, the lead author of the paper and a visiting scholar at Oganov's lab at Stony Brook. At PETRA III and at Carnegie Institution the scientists tested the predictions in what they call "cook and look" experiments, targeting Na₃Cl and NaCl₃, the two compounds that were predicted to be more easily made than others, and indeed found them. "These compounds are thermodynamically stable and once made, remain so indefinitely," says Zhang. "Classical chemistry forbids their very existence. Classical chemistry also says atoms try to fulfil the octet rule - elements gain or lose electrons to attain an electron configuration of the nearest noble gas, with complete outer electron shells that make them very stable. Well, here that rule is not satisfied."

The experiments help to explore a broader view of chemistry. "I think this work is the beginning of a revolution in chemistry," Oganov says. "We found, at low pressures achievable in the lab, perfectly stable compounds that contradict the classical rules of chemistry. If you apply rather modest pressure, 200,000 atmospheres – for comparison purposes, the pressure at the centre of the Earth is 3.6 million atmospheres – much of what we know from chemistry textbooks falls apart."

One reason for the surprising discovery is that textbook chemistry usually applies to what we call ambient conditions. "Here on the surface of the earth, these conditions might be default, but they are rather special if you look at the universe as a whole," Konôpková explains. What may be "forbidden" under ambient conditions on earth, can become possible under more extreme conditions. "'Impossible' really means that the energy is going to be high," Oganov says. "The rules of chemistry are not like mathematical theorems, which cannot be broken. The rules of chemistry can be broken, because impossible means softly impossible. You just need to find the conditions where the energy balance shifts and the rules hold no more."

Apart from its fundamental meaning, the discovery can also produce new practical applications. "When you change the theoretical underpinnings of chemistry, that's a big deal," Goncharov says. "But what it also means is that we can make new materials with exotic properties." Among the compounds Oganov and his team created

are two-dimensional metals, where electricity is conducted along the layers of the structure. "One of these materials – Na₃Cl – has a fascinating structure," Oganov says. "It is comprised of layers of NaCl and layers of pure sodium. The NaCl layers act as insulators; the pure sodium layers conduct electricity. Systems with two-dimensional electrical conductivity have attracted a lot of interest."

The experiments with table salt might only be the beginning of the discovery of completely new compounds. "If this simple system is capable of turning into such a diverse array of compounds under high-pressure conditions, then others likely are, too," Goncharov explains. "This could help answer outstanding questions about early planetary cores, as well as to create new materials with practical uses."

"Unexpected stable stoichiometries of sodium chloride"; Weiwei Zhang, Artem R. Oganov, Alexander F. Goncharov, Qiang Zhu, Salah Eddine Boulfelfel, Andriy O. Lyakhov, Elissaios Stavrou, Maddury Somayazulu, Vitali B. Prakapenka, Zuzana Konôpková; Science (2013); DOI: 10.1126/science.1244989

http://www.eurekalert.org/pub_releases/2013-12/ps-bra121713.php

Brain repair after injury and Alzheimer's disease

Technology developed to regenerate functional neurons (In vivo reprogramming of reactive glial cells into functional neurons)

Researchers at Penn State University have developed an innovative technology to regenerate functional neurons after brain injury, and also in model systems used for research on Alzheimer's disease. The scientists have used supporting cells of the central nervous system, glial cells, to regenerate healthy, functional neurons, which are critical for transmitting signals in the brain.

Gong Chen, a professor of biology, the Verne M. Willaman Chair in Life Sciences at Penn State, and the leader of the research team, calls the method a breakthrough in the long journey toward brain repair. "This technology may be developed into a new therapeutic treatment for traumatic brain and spinal cord injuries, stroke, Alzheimer's disease, Parkinson's disease, and other neurological disorders," Chen said. The research will be posted online by the journal *Cell Stem Cell* on 19 December 2013.

When the brain is harmed by injury or disease, neurons often die or degenerate, but glial cells become more branched and numerous. These "reactive glial cells" initially build a defense system to prevent bacteria and toxins from invading healthy tissues, but this process eventually forms glial scars that limit the growth of healthy neurons. "A brain-injury site is like a car-crash site," Chen explained. "Reactive glial cells are like police vehicles, ambulances, and fire trucks immediately rushing in to help -- but these rescue vehicles can cause problems if too many of them get stuck at the scene. The problem with reactive glial cells is that they often stay at the injury site, forming a glial scar and preventing neurons from growing back into the injured areas," he explained.

So several years ago, Chen's lab tested new ways to transform glial scar tissue back to normal neural tissue. "There are more reactive glial cells and fewer functional neurons in the injury site," Chen said, "so we hypothesized that we might be able to convert glial cells in the scar into functional neurons at the site of injury in the brain. This research was inspired by the Nobel prize-winning technology of induced pluripotent stem cells (iPSCs) developed in Shinya Yamanaka's group, which showed how to reprogram skin cells into stem cells," Chen recalled.

Chen and his team began by studying how reactive glial cells respond to a specific protein, NeuroD1, which is known to be important in the formation of nerve cells in the hippocampus area of adult brains. They hypothesized that expressing NeuroD1 protein into the reactive glial cells at the injury site might help to generate new neurons -- just as it does in the hippocampus. To test this hypothesis, his team infected reactive glial cells with a retrovirus that specifies the genetic code for the NeuroD1 protein. "The retrovirus we used is replication-deficient and thus cannot kill infected cells like other viruses found in the wild," Chen said. "More importantly, a retrovirus can infect only dividing cells such as reactive glial cells, but it does not affect neurons, which makes it ideal for therapeutic use with minimal side effect on normal brain functions."

In a first test, Chen and his team investigated whether reactive glial cells can be converted into functional neurons after injecting NeuroD1 retrovirus into the cortex area of adult mice. The scientists found that two types of reactive glial cells -- star-shaped astroglial cells and NG2 glial cells -- were reprogrammed into neurons within one week after being infected with the NeuroD1 retrovirus. "Interestingly, the reactive astroglial cells were reprogrammed into excitatory neurons, whereas the NG2 cells were reprogrammed into both excitatory and inhibitory neurons, making it possible to achieve an excitation-inhibition balance in the brain after reprogramming," Chen said. His lab also performed electrophysiological tests, which demonstrated that the new neurons converted by the NeuroD1 retrovirus could receive neurotransmitter signals from other nerve cells, suggesting that the newly converted neurons had successfully integrated into local neural circuits.

In a second test, Chen and his team used a transgenic-mouse model for Alzheimer's disease, and demonstrated that reactive glial cells in the mouse's diseased brain also can be converted into functional neurons. Furthermore, the team demonstrated that even in 14-month-old mice with Alzheimer's disease -- an age roughly equivalent to 60 years old for humans -- injection of the NeuroD1 retrovirus into a mouse cortex can still induce a large number of newborn neurons reprogrammed from reactive glial cells. "Therefore, the conversion technology that we have demonstrated in the brains of mice potentially may be used to regenerate functional neurons in people with Alzheimer's disease," Chen said.

To ensure that the glial cell-to-neuron conversion method is not limited to rodent animals, Chen and his team further tested the method on cultured human glial cells. "Within 3 weeks after expression of the NeuroD1 protein, we saw in the microscope that human glial cells were reinventing themselves: they changed their shape from flat sheet-like glial cells into normal-looking neurons with axon and dendritic branches," Chen said. The scientists further tested the function of these newly converted human neurons and found that, indeed, they were capable of both releasing and responding to neurotransmitters.

"Our dream is to develop this in vivo conversion method into a useful therapy to treat people suffering from neural injury or neurological disorders," Chen said. "Our passionate motivation for this research is the idea that an Alzheimer's patient, who for a long time was not able to remember things, could start to have new memories after regenerating new neurons as a result of our in vivo conversion method, and that a stroke victim who could not even move his legs might start to walk again."

In addition to Chen, other scientists who contributed to this research include Ziyuan Guo, Lei Zhang, Zheng Wu, Yuchen Chen, and Fan Wang, all from Penn State.

The research was funded by Penn State University and the National Institutes of Health.

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<http://www.bbc.co.uk/news/health-25445748>

Youth-drug can 'reverse' ageing in animal studies

US scientists have performed a dramatic reversal of the ageing process in animal studies.

By James Gallagher Health and science reporter, BBC News

They used a chemical to rejuvenate muscle in mice and said it was the equivalent of transforming a 60-year-old's muscle to that of a 20-year-old - but muscle strength did not improve. Their study, in the journal *Cell*, identified an entirely new mechanism of ageing and then reversed it. Other researchers said it was an "exciting finding".

Ageing is considered a one-way street, but now researchers at Harvard Medical School have shown that some aspects can be reversed. Their research focused on a chemical called NAD. Its levels naturally drop in all cells of the body with age. The team showed this disrupted the function of the cell's in-built powerstations, mitochondria, leading to lower energy production and ageing. Experiments showed that boosting NAD levels, by giving mice a chemical which they naturally convert into NAD, could reverse the sands of time.

One week of youth-medication in two-year-old mice meant their muscles became akin to those of a six-month-old in terms of mitochondrial function, muscle wastage, inflammation and insulin resistance.

Dr Ana Gomes, from the department of genetics at Harvard Medical School, said: "We believe this is quite an important finding." She argues muscle strength may return with a longer course of treatment.

A cure?

However, this could never be a cure-all for ageing. Other aspects such as shortening of telomeres or damage to DNA would not be reversed. Dr Gomes told the BBC: "Ageing is multi-factorial, it's not just one component we can fix, so it's hard to target the whole thing. "I believe there is a lot of cross-talk in cells and energy is very important in a cell and likely to be a very big component of ageing that might cause some of the other things that happen with ageing." The research group wants to begin clinical trials in 2015.

Dr Gomes said human therapies were a distant prospect but: "From what we know so far we don't think you'd have to take it from 20 years until we die. "It seems we can start when we're already old, but not too old that we're already damaged. "If started at 40 you would probably have a much nicer window of health ageing - but I would guess that, we have to do clinical trials."

Prof Tim Spector, from Kings College London, commented: "This is an intriguing and exciting finding that some aspects of the ageing process are reversible. "It is however a long and tough way to go from these nice mouse experiments to showing real anti-ageing effects in humans without side effects."

Dr Ali Tavassoli, from the University of Southampton argued: "It is important to note, that they did not see any changes in the mouse itself. "This could be for one of two reasons. Either they need to treat for longer so that the changes occurring in the cells have time to affect the whole organism, or alternatively, the biochemical

changes by themselves are not sufficient to reverse the physical changes associated with ageing in the mouse. "More experiments are necessary to see which of these cases are true."

<http://www.sciencedaily.com/releases/2013/12/131219130742.htm>

Research Linking Autism Symptoms to Gut Microbes Called 'Groundbreaking'

First to show that a specific probiotic may be capable of reversing autism-like behaviors

A new study showing that feeding mice a beneficial type of bacteria can ameliorate autism-like symptoms is "groundbreaking," according to University of Colorado Boulder Professor Rob Knight, who co-authored a commentary piece about the research appearing in the current issue of the journal *Cell*.

The autism study, published today in the same issue of *Cell*, strengthens the recent scientific understanding that the microbes that live in your gut may affect what goes on in your brain. It is also the first to show that a specific probiotic may be capable of reversing autism-like behaviors in mice.

"The broader potential of this research is obviously an analogous probiotic that could treat subsets of individuals with autism spectrum disorder," wrote the commentary authors, who also included CU-Boulder Research Associate Dorota Porazinska and doctoral student Sophie Weiss.

The study underscores the importance of the work being undertaken by the newly formed Autism Microbiome Consortium, which includes Knight as well as commentary co-authors Jack Gilbert of the University of Chicago and Rosa Krajmalnik-Brown of Arizona State University. The interdisciplinary consortium -- which taps experts in a range of disciplines from psychology to epidemiology -- is investigating the autism-gut microbiome link.

For the new *Cell* study, led by Elaine Hsiao of the California Institute of Technology, the researchers used a technique called maternal immune activation in pregnant mice to induce autism-like behavior and neurology in their offspring. The researchers found that the gut microbial community of the offspring differed markedly compared with a control group of mice. When the mice with autism-like symptoms were fed *Bacteriodes fragilis*, a microbe known to bolster the immune system, the aberrant behaviors were reduced.

Scientific evidence is mounting that the trillions of microbes that call the human body home can influence our gut-linked health, affecting our risk of obesity, diabetes and colon cancer, for example. But more recently, researchers are discovering that gut microbes also may affect neurology -- possibly impacting a person's cognition, emotions and mental health, said Knight, also a Howard Hughes Medical Institute Early Career Scientist and an investigator at CU-Boulder's BioFrontiers Institute.

The Autism Microbiome Consortium hopes to broaden this understanding by further studying the microbial community of autistic people, who tend to suffer from more gastrointestinal problems than the general public. People with autism spectrum disorder who would like to have their gut microbes sequenced can do so now through the American Gut Project, a crowdfunded research effort led by Knight.

The consortium also includes Catherine Lozupone and Kimberly Johnson of CU-Boulder, James Adams of Arizona State University, Mady Hornig of Columbia University, Sarkis Mazmanian of the California Institute of Technology, John Alverdy of the University of Chicago and Janet Jansson of Lawrence Berkeley Lab.

Jack A. Gilbert, Rosa Krajmalnik-Brown, Dorota L. Porazinska, Sophie J. Weiss, Rob Knight. Toward Effective Probiotics for Autism and Other Neurodevelopmental Disorders. Cell, 2013; 155 (7): 1446 DOI: 10.1016/j.cell.2013.11.035

<http://nyti.ms/1kBn3LG>

What Happens in the Brain After a Concussion

A remarkable recent experiment allowed scientists to see inside the skull and brain of animals that had just experienced a concussion, providing sobering new evidence of how damaging even minor brain impacts can be.

By GRETCHEN REYNOLDS

While the results, which were published in *Nature*, are worrisome, they also hint at the possibility of treating concussions and lessening their harm.

Concussions occur when the brain bounces against the skull after someone's head is bumped or jolted. Such injuries are fairly common in contact sports, like football and hockey, and there is growing concern that repeated concussions might contribute to lingering problems with thinking or memory. This concern was heightened this week by reports that the brain of the late major league baseball player Ryan Freel showed symptoms of chronic traumatic encephalopathy, a degenerative condition. He reportedly had been hit in the head multiple times during his career.

But scientists did not know exactly what happens at a molecular level inside the brain during and after a concussion. The living brain is notoriously difficult to study, since it shelters behind the thick, bony skull and other protective barriers. In some earlier studies, scientists had removed portions of lab animals' skulls to view

what happened to their brains during subsequent impacts. But removing part of the skull causes its own tissue damage and physiological response, muddying any findings about how the brain is affected by concussions. So scientists at the National Institute of Neurological Disorders and Stroke, a division of the National Institutes of Health, decided to develop a less destructive means of seeing inside skulls and came up with the deceptively simple method of shaving away microscopic layers of a lab mouse's skull, thinning it to the point that powerful microscopic lenses could see through it, even as the skull remained essentially intact.

They then gently compressed a portion of the skull toward the brain, imitating (in reverse) the thumping that the brain endures when it strikes the skull during a concussive head injury, such as might occur after a jarring football tackle or if your head slams against the slope when you fall while skiing. Meanwhile, microscopic lenses positioned atop the animals' thinned skulls documented in real-time everything that subsequently occurred around and within the brain as a result of the concussion.

The brain is, in many ways, the body's best-protected organ. Besides the skull, it is shielded by multiple layers of membranes located just beneath the skull that block out harmful molecules. But, as the N.I.H. researchers saw, these membranes became slightly ripped and frayed by the force of the concussion, leaving them leaky and the brain potentially vulnerable to the influx of molecules.

And such molecules soon appeared. "We saw a very quick build-up of reactive oxygen species" in the space between the skull and the brain after the concussion, said Dorian B. McGavern, a senior N.I.H. investigator who oversaw the study. Reactive oxygen species, which are also called free radicals, are known to play a role in various normal tissue processes, including the inflammatory response to any injury, but in excess they can contribute to cell death and tissue damage.

In the case of concussion, the body mounted a brave repair campaign, sending specialized immune cells from the blood and the brain to patch and fill in the frayed membranes. But the process was too slow, allowing an excess of free radicals to pass through the weakened membranes and migrate into the brain tissue, where they soon caused the death of brain cells far from the original impact site.

While concerning, this development also suggested to the scientists the possibility of treatment. If they could reduce the number of free radicals clustering near the brain, they reasoned, they could lessen the subsequent damage. So, in follow-up experiments, they inserted large amounts of a powerful antioxidant into the space between the animals' skull and brain. Antioxidants soak up free radicals and, it turned out, dramatically blunted the trauma associated with impacts to the brain. In animals that received the treatment immediately after a concussion, almost 70 percent fewer brain cells died than in untreated mice.

These findings are "promising and intriguing," Dr. McGavern said, although they are extremely preliminary and, for now, applicable only to mouse brains, not those of humans. But he and his N.I.H. colleagues are mounting a number of follow-up experiments to learn more about what precisely happens inside a concussed brain and how potentially to treat the injury. They are, for instance, looking at whether antioxidant patches applied to the scalp might be as effective at reducing concussion-related brain-cell death as more invasive approaches. Results should start rolling in next year.

<http://www.bbc.co.uk/news/science-environment-25465102>

Neanderthals could speak like modern humans, study suggests

An analysis of a Neanderthal's fossilised hyoid bone - a horseshoe-shaped structure in the neck - suggests the species had the ability to speak.

By **Melissa Hogenboom** Science reporter, BBC News

This has been suspected since the 1989 discovery of a Neanderthal hyoid that looks just like a modern human's. But now computer modelling of how it works has shown this bone was also used in a very similar way.

Writing in journal Plos One, scientists say its study is "highly suggestive" of complex speech in Neanderthals. The hyoid bone is crucial for speaking as it supports the root of the tongue. In non-human primates, it is not placed in the right position to vocalise like humans.

An international team of researchers analysed a fossil Neanderthal throat bone using 3D x-ray imaging and mechanical modelling.

This model allowed the group to see how the hyoid behaved in relation to the other surrounding bones. Stephen Wroe, from the University of New England, Armidale, NSW, Australia, said: "We would argue that this is a very significant step forward. It shows that the Kebara 2 hyoid doesn't just look like those of modern humans - it was used in a very similar way."

He told BBC News that it not only changed our understanding of Neanderthals, but also of ourselves.

"Many would argue that our capacity for speech and language is among the most fundamental of characteristics that make us human. If Neanderthals also had language then they were truly human, too."

It was commonly believed that complex language did not evolve until about 100,000 years ago and that modern humans were the only ones capable of complex speech.

But that changed with the discovery of a Neanderthal hyoid bone in 1989. It was found in the Kebara Cave in Israel and is very similar to our own,

Much older hyoid fossils have also recently been discovered, attributed to the human and Neanderthal relative *Homo heidelbergensis*. They were found in Spain and are over 500,000 years old.

These have yet to be modelled, but Prof Wroe said they were likely to be very similar to those of modern humans and Neanderthals, so could take back the origins of speech still further.

He added that his work would not necessarily be accepted as proof that Neanderthals spoke.

"We were very careful not to suggest that we had proven anything beyond doubt, but I do think it will help to convince a good number of specialists and tip the weight of opinion."

Neanderthals were stockier and shorter than modern humans, with no chin and backwards sloping foreheads. They are not regarded as direct human ancestors but DNA analysis has revealed that between 1% and 4% of the Eurasian human genome seems to come from Neanderthals.

Dan Dediu, from the Max Plank Institute for Psycholinguistics, Netherlands, published a review article earlier this year suggesting that Neanderthals and modern humans shared a similar capacity for language.

He said that the current study brought more weight to the conclusions that Neanderthals had very similar hyoid bones to us, "not only in form but also in what concerns their mechanical properties".

"The authors themselves are understandably cautious in drawing strong conclusions, but I think that their work clearly supports the contention that speech and language is an old feature of our lineage going back at least to the last common ancestor that we shared with the Neanderthals," Dr Dediu told BBC News.

He stressed, though, that the latest study was only a first step and that future work on other living primates were necessary to better understand the range of variation within modern humans.

http://www.eurekalert.org/pub_releases/2013-12/giot-sas122013.php

Scientists anticipated size and location of 2012 Costa Rica earthquake

Scientists using GPS to study changes in the Earth's shape accurately forecasted the size and location of the magnitude 7.6 Nicoya earthquake that occurred in 2012 in Costa Rica.

The Nicoya Peninsula in Costa Rica is one of the few places where land sits atop the portion of a subduction zone where the Earth's greatest earthquakes take place. Costa Rica's location therefore makes it the perfect spot for learning how large earthquakes rupture. Because earthquakes greater than about magnitude 7.5 have occurred in this region roughly every 50 years, with the previous event striking in 1950, scientists have been preparing for this earthquake through a number of geophysical studies. The most recent study used GPS to map out the area along the fault storing energy for release in a large earthquake.

"This is the first place where we've been able to map out the likely extent of an earthquake rupture along the subduction megathrust beforehand," said Andrew Newman, an associate professor in the School of Earth and Atmospheric Sciences at the Georgia Institute of Technology.

The study was published online Dec. 22, 2013, in the journal *Nature Geoscience*. The research was supported by the National Science Foundation and was a collaboration of researchers from Georgia Tech, the Costa Rica Volcanological and Seismological Observatory (OVSICORI) at Universidad Nacional, University California, Santa Cruz, and the University of South Florida.

Subduction zones are locations where one tectonic plate is forced under another one. The collision of tectonic plates during this process can unleash devastating earthquakes, and sometimes devastating tsunamis. The magnitude 9.0 earthquake off the coast of Japan in 2011 was due to just such a subduction zone earthquake.

The Cascadia subduction zone in the Pacific Northwest is capable of unleashing a similarly sized quake.

Damage from the Nicoya earthquake was not as bad as might be expected from a magnitude 7.6 quake.

"Fortunately there was very little damage considering the earthquake's size," said Marino Protti of OVSICORI and the study's lead author. "The historical pattern of earthquakes not only allowed us to get our instruments ready, it also allowed Costa Ricans to upgrade their buildings to be earthquake safe."

Plate tectonics are the driving force for subduction zones. As tectonic plates converge, strain temporarily accumulates across the plate boundary when portions of the interface between these tectonic plates, called a megathrust, become locked together. The strain can accumulate to dangerous levels before eventually being released as a massive earthquake.

"The Nicoya Peninsula is an ideal natural lab for studying these events, because the coastline geometry uniquely allows us to get our equipment close to the zone of active strain accumulation," said Susan Schwartz, professor of earth sciences at the University of California, Santa Cruz, and a co-author of the study.

Through a series of studies starting in the early 1990s using land-based tools, the researchers mapped regions where tectonic plates were completely locked along the subduction interface. Detailed geophysical observations of the region allowed the researchers to create an image of where the faults had locked.

The researchers published a study a few months before the earthquake, describing the particular locked patch with the clearest potential for the next large earthquake in the region. The team projected the total amount of energy that could have developed across that region and forecasted that if the locking remained similar since the last major earthquake in 1950, then there is presently enough energy for an earthquake on the order of magnitude 7.8 there.

Because of limits in technology and scientific understanding about processes controlling fault locking and release, scientists cannot say much about precisely where or when earthquakes will occur. However, earthquakes in Nicoya have occurred about every 50 years, so seismologists had been anticipating another one around 2000, give or take 20 years, Newman said. The earthquake occurred in September of 2012 as a magnitude 7.6 quake.

"It occurred right in the area we determined to be locked and it had almost the size we expected," Newman said. The researchers hope to apply what they've learned in Costa Rica to other environments. Virtually every damaging subduction zone earthquake occurs far offshore.

"Nicoya is the only place on Earth where we've actually been able to get a very accurate image of the locked patch because it occurs directly under land," Newman said. "If we really want to understand the seismic potential for most of the world, we have to go offshore."

Scientists have been able to reasonably map portions of these locked areas offshore using data on land, but the resolution is poor, particularly in the regions that are most responsible for generating tsunamis, Newman said. He hopes that his group's work in Nicoya will be a driver for geodetic studies on the seafloor to observe such Earth deformation. These seafloor geodetic studies are rare and expensive today.

"If we want to understand the potential for large earthquakes, then we really need to start doing more seafloor observations," Newman said. "It's a growing push in our community and this study highlights the type of results that one might be able to obtain for most other dangerous environments, including offshore the Pacific Northwest."

http://www.eurekalert.org/pub_releases/2013-12/jhm-aro121913.php

Acupuncture, real or sham, eases hot flashes due to breast cancer chemo

Both real and sham weekly acupuncture treatments eased hot flashes and other side effects of anticancer drug treatment in a small, preliminary study of breast cancer patients, Baltimore researchers have found.

The results, they say, add to previous reports that even the sensation of skin pricks used to simulate genuine acupuncture needle sticks might be enough to generate natural chemicals that improve symptoms.

Investigators at the University of Maryland Greenebaum Cancer Center and the Johns Hopkins Kimmel Cancer Center set out to see if acupuncture could reduce the severity of side effects linked to aromatase inhibitors (AI), drugs used to treat breast cancer or prevent it from recurring after surgery. Because AIs block estrogen synthesis in postmenopausal patients, they can cause moderate to severe hot flashes, similar to those experienced during menopause, and musculoskeletal problems, such as joint and muscle pain.

For the study, investigators enrolled 47 postmenopausal women with stage 0 through III hormone receptor-positive breast cancer who had been receiving AI therapy for at least a month and who reported some AI-associated musculoskeletal symptoms. Patients were randomly assigned to receive eight weekly real or sham acupuncture treatments; 23 patients received real acupuncture and 24 received sham acupuncture.

In addition, the research team collected weekly hot-flash diaries during weeks 0 through 8 and in week 12.

Other questionnaires addressing menopausal symptoms, mood, sleep quality, depression, anxiety and quality of life were collected at the study's start and four, eight and 12 weeks later.

Among those receiving real acupuncture, researchers said there were statistically significant improvements in depression, hot-flash severity and frequency, hot flash-related daily interference and other menopausal symptoms. Among those receiving sham acupuncture, researchers noted statistically significant improvements in quality of life, hot flash-related daily interference, and menopausal symptoms. Women in both groups saw an average reduction in hot-flash severity of 31 percent to 54 percent, respectively, from the real and sham acupuncture treatments.

To compare the effects of real acupuncture sessions with those of sham acupuncture, for the latter, the team used non-penetrating, retractable needles placed in 14 locations on the skin between points used for real acupuncture. The non-penetrating needles produce a pricking sensation on the skin so that research subjects could not tell if they are getting the real treatment or not. Study results, published online Dec. 23 in the journal

Cancer, showed few differences overall in benefits between those receiving real and sham acupuncture, and no patients experienced significant side effects from acupuncture.

Although the researchers were not specifically studying racial differences in patients' response, they found that African-American women more often had less frequent or severe hot flashes after real acupuncture, but not after the sham treatments. However, only nine African-Americans participated in the study, not enough, the researchers said, to draw firm conclusions.

The fact that some women had benefits from sham acupuncture raised the question of whether the pricking sensation of sham acupuncture triggers physiological effects, says lead author Ting Bao, M.D., D.A.B.M.A., M.S., assistant professor of medicine at the University of Maryland Greenebaum Cancer Center.

An estimated 60 percent of the acupuncture points used in the study, primarily to treat musculoskeletal symptoms, overlap with those used in treating hot flashes.

Another study published by the researchers earlier this year in the journal *Breast Cancer Research and Treatment* showed that both real and sham acupuncture treatments helped improve AI-associated musculoskeletal symptoms, including a statistically significant reduction in the inflammatory protein IL-17.

"The current interventions for musculoskeletal side effects are limited to oral analgesics and exercise," Bao says. "But the efficacy of these approaches is limited, and long-term use of oral analgesics can be challenging. If patients are open to acupuncture, this is a reasonable alternative for them."

Studies indicate that up to 60 percent of women with early stage breast cancer who receive AIs experience hot flashes, says Vered Stearns, M.D., senior study author and co-director of the breast cancer program at the Johns Hopkins Kimmel Cancer Center. Conventional hot-flash treatments include drugs, though their use is limited because of side effects, underscoring a demand for more non-pharmacological interventions, she says. "These women have had a lot of different treatments, and some really try to avoid additional medications," she added. The authors caution that their study was small and needs verification. They are planning a randomized controlled trial to look further into the racial differences seen in response to real versus sham acupuncture.

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<http://phys.org/news/2013-12-adult-stem-cells-suppress-cancer.html>

Adult stem cells found to suppress cancer while dormant

Mechanism by which certain adult stem cells suppress their ability to initiate skin cancer during their dormant phase

Researchers at UCLA's Eli and Edythe Broad Center of Regenerative Medicine and Stem Cell Research have discovered a mechanism by which certain adult stem cells suppress their ability to initiate skin cancer during their dormant phase—an understanding that could be exploited for better cancer-prevention strategies.

The study, which was led by UCLA postdoctoral fellow Andrew White and William Lowry, an associate professor of molecular, cell and developmental biology who holds the Maria Rowena Ross Term Chair in Cell Biology in the UCLA College of Letters and Science, was published online Dec. 15 in the journal *Nature Cell Biology*.

Hair follicle stem cells, the tissue-specific adult stem cells that generate the hair follicles, are also the cells of origin for cutaneous squamous cell carcinoma, a common skin cancer. These stem cells cycle between periods of activation (during which they can grow) and quiescence (when they remain dormant).

Using mouse models, White and Lowry applied known cancer-causing genes to hair follicle stem cells and found that during their dormant phase, the cells could not be made to initiate skin cancer. Once they were in their active period, however, they began growing cancer.

"We found that this tumor suppression via adult stem cell quiescence was mediated by PTEN, a gene important in regulating the cell's response to signaling pathways," White said. "Therefore, stem cell quiescence is a novel form of tumor suppression in hair follicle stem cells, and PTEN must be present for the suppression to work." Understanding cancer suppression through quiescence could better inform preventative strategies for certain patients, such as organ transplant recipients, who are particularly susceptible to squamous cell carcinoma, and for those taking the drug vemurafenib for melanoma, another type of skin cancer. The study also may reveal parallels between squamous cell carcinoma and other cancers in which stem cells have a quiescent phase.