http://www.eurekalert.org/pub_releases/2014-11/epfd-hba103114.php

## How bile acids could fight diabetes

***Bile acids activate a little-known receptor to overcome the loss of insulin sensitivity***

The growing epidemic of obesity across the world is associated with an equivalent increase in type-2 diabetes, which results from the body's ineffective use of insulin. Obese people often develop inflammation in their fat tissue, which, in turn, can reduce the sensitivity of fat cells to insulin, resulting in type-2 diabetes. EPFL scientists, working with researchers from Italy and the Netherlands, have shown that bile acids activate a little-known receptor to overcome the loss of insulin sensitivity, forming the basis for a new class of drug against type-2 diabetes. The work is published in the Journal of Clinical Investigation.

Diabetes develops when the body has problems with insulin, a hormone that regulates sugar levels in the blood. This results either because the pancreas cannot produce enough insulin or when the body cannot use insulin efficiently. There are two types of diabetes: type 1, which usually starts at young age, and type 2, which accounts for 90% of all diabetics and is generally caused by obesity.

One of the major problems of type-2 diabetes is that it often coincides with chronic inflammation in the body's fat tissue. This inflammation arises from the activity of immune cells called macrophages within the fat tissue, which recruit even more macrophages through chemical signals. The accumulation of macrophages interferes with the ability of fat cells to respond appropriately to insulin; this condition is known as "insulin resistance". Consequently, pharmaceutical companies are urgently searching for treatments that can minimize the accumulation of macrophages in fat tissue.

A research team led by Kristina Schoonjans at EPFL has discovered that a receptor located on macrophages can inhibit the inflammation of type-2 diabetes. Receptors are proteins that bind chemicals and initiate cascades of events in the cell. The macrophage receptor in this study is called TGR5, and is activated by chemicals in our bile, collectively referred to as "bile acids".

Bile acids have traditionally been thought to be restricted to the small intestine, helping with the digestion of lipids. But recent studies - many led by Schoonjans - have shown that bile acids also enter the bloodstream and behave like hormones, acting on receptors like TGR5, and affecting the behavior of different types of cells.

The researchers found that TGR5 can block the chemical signals macrophages send to attract more of their number into fat tissue. When they activated the receptor with compounds that were similar to bile acids, TGR5 triggered a molecular cascade in the cells that reduced the accumulation of macrophages, significantly minimizing the inflammation associated with type-2 diabetes.

This discovery opens a new way for addressing inflammation in type-2 diabetes. Molecules that can mimic the effect of bile acids on macrophage TGR5 can become new anti-obesity and diabetes drugs. "Of course, we don't want to use bile acids for treatment of diabetes," says Alessia Perino who is the lead author on the study. "We are very interested in finding molecules that can mimic the effects of bile acids, and we have already discovered several small molecules that can do that."

*This study represents a collaboration between EPFL's Institute of Bioengineering, the University of Amsterdam, and the University of Perugia.*

*Perino A, Pols TWH, Nomura M, Stein S, Pellicciari R, Schoonjans K. TGR5 reduces macrophage migration through mTOR-induced C/EBPβ differential translation. J Clin Invest. 2014; 124(12). DOI: 10.1172/JCI76289.*

http://www.eurekalert.org/pub_releases/2014-11/ind-lcd110314.php

## Lung cancer diagnosed before it is detected by imaging

***Possible to detect circulating cancer cells months or years before cancer becomes detectable by CT scanning***

A team of researchers from Inserm led by Paul Hofman (Inserm Unit 1081/University of Nice) has just made a significant advance in the area of early diagnosis of invasive cancers. In a study which has just been published in the journal PLOS ONE, the team shows that it is possible to detect, in patients at risk of developing lung cancer, early signs, in the form of circulating cancer cells, several months, and in some cases several years, before the cancer becomes detectable by CT scanning. This warning could play a key role in early surgical intervention, thereby making it possible to attempt the early eradication of the primary cancer site.

Studies carried out in animals have clearly shown that invasive tumours shed cancer cells into the bloodstream from the very earliest stages of their formation, even before the tumours are detectable by diagnostic imaging. The possibility of identifying these "sentinel" cells is considered a major asset in the race against time for the early detection, and hence treatment, of cancer. Circulating cancer cells are extremely rare in the bloodstream, are very heterogeneous and fragile, and are difficult to isolate without bias or loss.

The team of researchers led by Paul Hofman used a blood test developed during French research[1], which isolates all types of tumour cells from the bloodstream, without any loss, leaving them intact. The team studied a group of 245 people without cancer, including 168 patients at risk of later developing lung cancer because they had Chronic Obstructive Pulmonary Disease (COPD). Participants

systematically underwent the blood test and standard diagnostic imaging tests. Using the blood test, circulating cancer cells were identified in 5 patients (3%), whereas imaging did not show any nodules in the lungs.

In these 5 patients, a nodule became detectable 1-4 years after detection of circulating cancer cells by the blood test. They immediately underwent surgery, and analysis of the nodule confirmed the diagnosis of lung cancer. Monitoring of the patients for a minimum of one year after surgery showed no sign of recurrence in the 5 patients, leading one to hope that the cancer had been eradicated. At the same time, no nodules were detected during monitoring of subjects who did not have circulating cancer cells, and no cancer cells were detected in the bloodstream of "control" subjects without COPD.

Detection of these circulating cells via this blood test could play a key role in early surgical intervention, thus making it possible to aim for early eradication of the primary cancer site.

Lung cancer is one of the most lethal cancers. According to the American Cancer Society (ACS), one-year survival among these patients is 44%, and 5-year survival only 16%. Only 15% of these cancers are presently diagnosed at a stage where the disease is localised. Early detection could both improve patient survival and help to improve health economics. COPD is the 3rd leading cause of deaths in the USA, and is mainly caused by smoking.

*[1] known as ISET (Isolation by SizE of Tumour cells), and developed by Rarecells Diagnostics.*

**Sources**

*"Sentinel" Circulating Tumor Cells allow early diagnosis of lung cancer in patients with chronic obstructive pulmonary disease*

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***http://www.eurekalert.org/pub_releases/2014-11/aaop-nsv110314.php***

## Nasal spray vaccine has potential for long-lasting protection from Ebola virus

***Pioneering research to be featured at 2014 AAPS Annual Meeting and Exposition***

San Diego - A nasal vaccine in development by researchers at The University of Texas at Austin has been shown to provide long-term protection for non-human primates against the deadly Ebola virus. Results from a small pre-clinical study represent the only proof to date that a single dose of a non-injectable vaccine platform for Ebola is long-lasting, which could have significant global implications in controlling future outbreaks. This work is being presented Nov. 5 at the 2014 American Association of Pharmaceutical Scientists (AAPS) Annual Meeting and Exposition, the world's largest pharmaceutical sciences meeting, in San Diego, Nov. 2-6.

The Ebola virus is an often fatal illness that is spread among the human population via direct contact with blood or bodily fluids from an infected individual. The current Ebola outbreak in Western Africa is the largest and most complex epidemic since the virus was first discovered in 1976, according to the World Health Organization. With a fatality rate currently as high as 70%, officials are declaring this outbreak a public health emergency of international concern.

Maria Croyle, a professor in the College of Pharmacy at The University of Texas at Austin, Kristina Jonsson-Schmunk, a graduate student in pharmacy, and colleagues at the university developed a nasal formulation that improved survival of immunized non-human primates from 67 percent (2 out of 3) to 100 percent (3 out of 3) after challenge with 1,000 plaque forming units of Ebola Zaire 150 days after immunization. This is important since only 50 percent of the primates given the vaccine by the standard route (intramuscular injection) survived challenge.

"Ebola causes devastating outbreaks with fatality rates of 25 - 90 percent in Africa and Asia. Although progress has been made in understanding the virus' biology, no licensed vaccines or treatments currently exist. There is a desperate need for a vaccine that not only prevents the continued transmission from person to person, but also aids in controlling future incidences," said Jonsson-Schmunk. "The main advantage of our vaccine platform over the others in clinical testing is the long-lasting protection after a single intranasal dose. This is important since the longevity of other vaccines for Ebola that are currently being evaluated is not fully understood. Moreover, the nasal spray immunization method is more attractive than a needle vaccine given the costs associated with syringe distribution and safety."

The next stage of Dr. Croyle's research is a Phase I clinical trial that tests the effectiveness of their vaccine in human subjects. They will also further explore preliminary data they have collected for administration of the vaccine as a thin film under the tongue in non-human primates.

*This work was supported by a grant from the National Institutes of Health awarded to Dr. Croyle (U01 AI078045).*

***http://www.eurekalert.org/pub_releases/2014-11/bc-mfm102714.php***

## Malaria from monkeys now dominant cause of human malaria hospitalizations in Malaysia

***New study released at ASTMH annual meeting targets deforestation as a possible problem for increasing human encounters with macaques***

NEW ORLEANS - The majority of malaria hospitalizations in Malaysia are now caused by a dangerous and potentially deadly monkey-borne parasite once rarely seen in humans, and deforestation is the potential culprit in a growing number of infections that could allow this virulent malaria strain to jump from macaque monkeys to human hosts, according to research presented today at the American Society of Tropical Medicine and Hygiene (ASTMH) Annual Meeting.

An analysis of malaria patients hospitalized in Malaysian Borneo in 2013 showed that 68 percent had been sickened by Plasmodium knowlesi, said Balbir Singh, PhD, director of the Malaria Research Center at the University of Malaysia in Sarawak. The parasite is increasingly associated with malaria deaths and is three times more frequent as a cause of severe malaria in Borneo than the more common P. falciparum parasite that is currently considered the world's most deadly form of the disease.

The main host of knowlesi malaria has been the long-tailed and pig-tailed macaques found in the tropical forests of Malaysia and elsewhere in Southeast Asia. The infections are concentrated in areas of Malaysia where over the last decade massive loss of native forest to timber and palm oil production has led to substantially increased human interactions with macaques. That puts knowlesi malaria in the company of a growing list of dangerous emerging and re-emerging diseases - including Ebola and AIDS - that are being passed from animals to humans as development peels back more and more layers of tropical forest previously uninhabited by humans.

"This is a form of malaria that was once rarely seen in people, but today, in some remote areas of the country, all of the indigenous malaria cases we are seeing are caused by the P. knowlesi parasite," Singh said. "If the number of cases continue to increase, human-to-human transmission by mosquitoes becomes possible. In fact, this may already have happened, which would allow P. knowlesi malaria to spread more easily throughout Southeast Asia."

Evidence to date has strongly suggested that victims of P. knowlesi malaria have been bitten by mosquitoes that had first bitten an infected macaque, making humans a dead-end host for the parasite. Of concern, however, is recent research that the parasite could change so that it can jump from person to person via mosquito bites, without requiring a monkey as part of its life cycle. Laboratory tests in the 1960s indicated that a mosquito variety in Malaysian Borneo that carries the two most common human malaria parasites - P. falciparum and P. vivax - also can spread the knowlesi parasite. Moreover, P. knowlesi was recently found in Vietnam in mosquitoes that transmit falciparum and vivax malaria, raising the possibility that human-to-human transmission is already occurring.

P. knowlesi is the fifth species of malaria known to infect humans in nature. The parasite causes only mild malaria in macaques, Singh said, but in people it is the fastest replicating malaria parasite, multiplying every 24 hours in the blood.

The majority of the macaques carrying the parasite once lived in remote forested regions that saw little human activity or settlements. This has changed over the last ten years as a result of significant deforestation in Malaysia. According to a 2013 study in the journal Science, Malaysia lost about 47,000 square kilometers of forest between 2000 and 2012, or about 14 percent of its total land area, which environmentalists blame on logging and conversion of native forests to palm oil plantations.

At the ASTMH meeting, a team from the London School Hygiene and Tropical Medicine is presenting preliminary findings from an ongoing study that is outfitting people in the Sabah region of Malaysia with GPS tracking devices to explore the role of human movements into different macaque and mosquito habitats on the spread of P. knowlesi infections.

Researchers have been warning for decades that more frequent human incursions into undeveloped tropical forests will significantly increase the threat from diseases that could spread far beyond the forest canopy. The current Ebola outbreak is linked to a growing number of people living and hunting in forested areas and consuming "bush meat" from infected animals, chiefly chimpanzees. Meanwhile, illegal mining operations in tropical forests have been linked to the recent resurgence of malaria in Venezuela and may have intensified the rise of drug resistant malaria in Thailand.

These interactions are prompting a growing interest in research that probes the threat of disease from multiple vantage points - including economical, biological, and anthropological - an approach known as One Health.

Singh said that P. knowlesi malaria is currently a major public health problem in Malaysia, as it is causing illness serious enough to require medical treatment in about two thousand people a year.

"But the P. knowlesi strain of malaria should stay within Southeast Asia as there are no mosquitoes outside the region capable of carrying these parasites," he said.
Singh also pointed out that, in terms of overall burden of disease, knowlesi malaria still ranks far behind dengue fever. Infections and deaths with that mosquito-borne disease have more than tripled in Malaysia in just the last year.
The rising threat of the P. knowlesi parasite, however, which is carried by mosquitoes that prey on humans when they are outdoors, presents a new challenge for the broader effort to control and eliminate malaria in Southeast Asia - a fight that has been focused on using bed nets and indoor spraying to prevent malaria infections caused mainly by mosquitoes that attack indoors and at night. Malaria control campaigns also have not faced a malaria strain that is entrenched in a large animal population. "Controlling a zoonotic - meaning an animal-to-human infection - carried by outdoor feeding mosquitoes is almost impossible with currently used methods," Singh said.
"These intriguing results are yet another example of the complexity and diversity of the interaction between man, his activities, parasites, and mosquitoes. P. knowlesi is now a significant cause of human malaria in Malaysian Borneo that must be addressed across multiple levels: research, development, implementation, funding and evidence-based policies," said Alan J. Magill, MD, FASTMH, president of the American Society of Tropical Medicine and Hygiene.

***http://www.eurekalert.org/pub_releases/2014-11/cmaj-edt102914.php***

## End-of-life discussions: The top 5 things to talk about with patients and their families

***What are the most important things for health care teams to talk about in end-of-life discussions with patients in hospital and their families?***

A new study published in CMAJ (Canadian Medical Association Journal) asked older patients and their families for their top priorities and found gaps between what patients would like and the care they actually receive.
"Our findings could be used to identify important opportunities to improve end-of-life communication and decision-making in the hospital setting," states Dr. John You, lead author of the study and associate professor of medicine, and clinical epidemiology and biostatistics at McMaster University, and a staff physician at Hamilton Health Sciences, Hamilton, Ontario.
Current guidelines list 11 key elements for health care providers to discuss regarding end-of-life care, although these are based mainly on expert opinion and not on patient and family feedback.
A team of researchers with backgrounds in general internal medicine, critical care medicine and palliative care surveyed 233 older adults in hospital with serious illnesses and 205 family members about the importance of the 11 guideline-recommended elements of end-of-life care. The patients had been admitted to 9 hospitals in British Columbia, Alberta, Ontario and Quebec.
Top 5 things to discuss in end-of-life care, according to patients and families:

***preferences of care in event of life-threatening illness***
***patient values***
***prognosis of illness***
***fears or concerns***
***additional questions regarding care.***

"However, we found that these elements are infrequently discussed and that concordance between preferred and prescribed goals of care is low," state the authors.
Patients reported that of the 11 key elements, an average of only 1.4 had been discussed with the health care team within the first few days after admission to hospital. The more elements of care that physicians discussed with patients, the higher the satisfaction patients and their families reported about care received.
"Our results suggest that concordance between preferences and prescribed goals of care, as well as satisfaction with end-of-life communication, increase with the number of elements discussed," write the authors.
They hope that their findings will help improve end-of-life care for patients in hospital.
The authors have previously published a related guide in CMAJ called "Just Ask" to help physicians initiate end-of-life discussions with patients and their families.

***http://www.eurekalert.org/pub_releases/2014-11/osu-co110314.php***

## 'Mild' control of systolic blood pressure in older adults is adequate: 150 is good enough

***In the elderly, there's no clear benefit to more aggressive use of medications to achieve a lower pressure***

CORVALLIS, Ore. – A broad review of the use of medications to reduce blood pressure has confirmed that "mild" control of systolic pressure is adequate for adults age 65 or older - in the elderly, there's no clear benefit to more aggressive use of medications to achieve a lower pressure.
Historically, most medical practitioners tried to achieve control of systolic pressure – the higher of the two blood pressure readings – to 140 or less. Recently changed guidelines now suggest that for adults over 60, keeping the systolic pressure at 150 or less is adequate, and this extensive analysis confirms that.
However, researchers also say in the report that more work needs to be done studying blood pressure in older populations, since most of the research, and the medical guidelines based on them, were done using predominately younger adults.

The review was just published in Drugs & Aging, a professional journal, by scientists from the College of Pharmacy at Oregon State University and Oregon Health & Science University.

"The goal of a systolic pressure at or below 140 has been around a long time, and there's still skepticism among some practitioners about accepting a higher blood pressure," said Leah Goeres, an OSU postdoctoral fellow and lead author on the publication.

"Keeping systolic blood pressure in older adults below 150 is important, it's what we consider a mild level of control," Goeres said. "But for older people that level is also good enough. After an extensive review, there was no significant evidence that more intensive management is necessary."

The issue about how low is low enough, researchers say, is important because blood pressure medications can have unwanted side effects that increase as higher dosages of medications are used. The problem is common – in the United States, about 70 percent of adults age 65 or older have hypertension, and millions of people take medication to control it.

One of the more significant side effects is what's called "orthostatic hypotension," a condition in which a person's blood pressure can suddenly fall when they rise or stand, making them feel light-headed or dizzy, and sometimes leading to dangerous falls. More than 30 percent of people over the age of 80 have this problem.

High blood pressure is a serious health concern, but also one of the most treatable with medication, if such things as diet, exercise, weight management or lifestyle change prove inadequate. Hypertension is often called the "silent killer" because it causes few obvious symptoms, but it weakens blood vessels and has been linked to higher levels of heart attacks, kidney disease and especially stroke.

"There's clearly a value to controlling blood pressure, enough to keep it at 150 or less," said David Lee, an OSU assistant professor of pharmacy practice. "Keeping blood pressure within acceptable levels will lower death rates. But as people get older, there's less clear evidence that stringent control of systolic blood pressure is as important."

The researchers said a goal for the future should be to do more studies specifically with older adult populations and try to identify health situations and conditions that might benefit from different types of management. Such "individualized" treatments, they said, would consider a person's entire health situation instead of treating them based on findings made with large groups.

In this study, the researchers did not find that one approach or another to lowering blood pressure stood out and was clearly better than other alternatives. A variety of medications can be used to treat the condition.

http://www.eurekalert.org/pub_releases/2014-11/wkh-mlt110314.php

## Migraine linked to defective 'insulation' around nerve fibers, suggests study in Plastic and Reconstructive Surgery

***Differences in nerve structure and function may help to explain how migraine headaches occur***

A new study shows cellular-level changes in nerve structure and function that may contribute to the development of migraine headaches, reports the November issue of Plastic and Reconstructive Surgery®, the official medical journal of the American Society of Plastic Surgeons (ASPS).

Nerve specimens from patients with migraine show abnormalities of the myelin sheath that serves as "insulation" around the nerve fibers," according to the study by ASPS Member Surgeon Bahman Guyuron, MD, of Case Western Reserve University, Cleveland. The findings help to explain why a plastic surgery procedure provides effective pain relief for migraine patients - and may provide useful clues for developing new approaches to migraine treatment.

Nerve Fiber Abnormalities in Patients with Migraine...

The researchers performed in-depth studies on tiny specimens of the trigeminal nerve (one of the cranial nerves), from 15 patients who underwent surgical treatment for migraine. Sample from 15 patients undergoing a cosmetic forehead lift procedure were studied for comparison. The study - conducted through collaboration by three independent departments at Case Western Reserve School of Medicine - included electron microscopy to assess nerve cell structure and proteomic analysis to assess the presence and function of proteins.

The results showed important differences in nerve structure between the migraine and cosmetic surgery patients. "Essentially, the protective layer surrounding and insulating the normal nerves, called myelin, is missing or is defective on the nerves of the patients with migraine headaches," said Dr. Guyuron.

He likens the myelin sheath to the plastic coating used as insulation material around electrical wires and cables. "If the insulation becomes cracked or damaged by conditions in the environment, that's going to affect the cable's ability to perform its normal function," said Dr Guyuron. "In a similar way, damage to the myelin sheath may make the nerves more prone to irritation by the dynamic structure surrounding them, such as muscle and blood vessels, potentially triggering migraine attacks."

Organization of the cellular elements in nerve fibers also differed between groups. Healthy nerves were tightly organized with elements uniformly distributed through the nerve, while nerves from migraine patients showed discontinuous, "patchy" distribution.

**...Suggest Reasons Why Migraine Surgery May Be Effective**

Dr Guyuron developed migraine surgery techniques after noticing that some migraine patients had reduced headache activity after cosmetic forehead-lifting, which involved removal of some muscle and vessel tissue surrounding the cranial nerves. The new study lends some important new clues for understanding the mechanisms by which migraine headaches occur. It also adds new evidence that the peripheral nerves play an important role in triggering the complex cascade of migraine attacks that ultimately involve the central nervous system.

By showing pathological changes of a cranial nerve involved in triggering migraine headaches, the study may help to explain why migraine surgery is effective. Dr Guyuron and coauthors write, "These findings may also lead to other opportunities to treat patients with migraine headaches non-invasively, or with less invasive procedures that repair the defective myelin around nerves, lending additional protection for the nerves."

The new findings on nerve cell abnormalities associated with migraine are discussed in this month's introductory video by Rod J. Rohrich, MD, Editor-in-Chief, on the Plastic and Reconstructive Surgery website. "This type of cutting edge research...is just one way plastic surgeons are constantly trying to improve patients' outcomes," Dr Rohrich concludes.

*Click here to read "Electron Microscopic and Proteomic Comparison of Terminal Branches of the Trigeminal Nerve in Patients with and without Migraine Headaches."*

***http://www.eurekalert.org/pub_releases/2014-11/cru-sas110314.php***

## Swallowing a sponge on a string could replace endoscopy as pre-cancer test

***Swallowing a sponge on a string could replace traditional endoscopy as an equally effective but less invasive way of diagnosing a condition that can be a forerunner of oesophageal cancer.***

The results of a Cancer Research UK trial involving more than 1,000 people are being presented today (Tuesday) at the National Cancer Research Institute's annual conference in Liverpool. The trial invited more than 600 patients with Barrett's Oesophagus – a condition that can sometimes lead to oesophageal cancer – to swallow the Cytosponge and to undergo an endoscopy. Almost 500 more people with symptoms like reflux and persistent heartburn did the same tests.

The Cytosponge proved to be a very accurate way of diagnosing Barrett's Oesophagus. More than 94 per cent of people swallowed the sponge and reported no serious side effects. Patients who were not sedated for endoscopy were more likely to rate the Cytosponge as a preferable experience.

Lead author Professor Rebecca Fitzgerald, based at the MRC Cancer Unit at the University of Cambridge, said: "The Cytosponge test is safe, acceptable and has very good accuracy for diagnosing Barrett's Oesophagus. It should be considered as an alternative to endoscopy for diagnosing the condition and could possibly be used as a screening test in primary care."

Barrett's Oesophagus is caused by acid coming back up the food pipe from the stomach – known as acid reflux – which can cause symptoms like indigestion and heartburn. Over time people with these symptoms may develop changes in the cells that line the oesophagus. These cells can become cancerous and so patients with Barrett's Oesophagus are tested every couple of years.

Barrett's Oesophagus is usually diagnosed by having a biopsy during an endoscopy. This can be uncomfortable and carries some risks – and it's not always practical for everyone who has symptoms like reflux and heartburn.

Oesophageal cancer is the thirteenth most common cancer in the UK. Around 5,600 men develop the disease each year compared with 2,750 women. And each year around 5,200 men and 2,460 women die from the disease.

Dr Julie Sharp, Cancer Research UK's head of health information, said: "These results are very encouraging and it will be good news if such a simple and cheap test can replace endoscopy for Barrett's oesophagus.

"Death rates are unacceptably high in oesophageal cancer so early diagnosis is vital. Tackling oesophageal cancer is a priority for Cancer Research UK and research such as this will help doctors to diagnose people who are at risk quickly and easily."

*http://conference.ncri.org.uk/abstracts/2014/abstracts/clinicalshowcase04.html*

*Watch how sponge on a string works: https://www.youtube.com/watch?v=s7X9z6qlNUI*

*Read more about the trial on the Cancer Research UK Blog: https://scienceblog.cancerresearchuk.org/2011/07/25/sponge-on-a-string-trial-launches/*

***http://bit.ly/1y84y6F***

## Breast milk stem cells may be incorporated into baby

***BREAST milk is known for being full of goodies – but could that include stem cells from mum that go on to transform into parts of the baby's body?***

**14:53 03 November 2014 by Clare Wilson**

Preliminary evidence has shown this happens in mice, suggesting it also does in people. Stem cells have the unusual ability to regenerate themselves and develop into a variety of tissues. Several sources of stem cells are being developed for therapeutic use, including embryos, umbilical-cord blood and adult tissues.

It was discovered seven years ago that human breast milk also contains a kind of stem cell. The question was whether these cells do anything useful for the baby or if they simply leak unavoidably into breast milk.

The latest findings, presented at the National Breastfeeding and Lactation Symposium in London last week, suggest that in mice at least, breast milk stem

cells cross into the offspring's blood from their stomach and play a functional role later in life.

Foteini Hassiotou at the University of Western Australia and her colleagues showed this by first creating genetically modified mice whose cells contain a gene called *tdTomato*, which makes them glow red under fluorescent light.

The female mice were mated but then after giving birth were given unmodified baby mice to suckle. So any red cells that ended up in the pups must have come via the milk.

Sure enough, when the offspring reached adulthood, red cells were found in their blood and many of their tissues, including the brain, thymus, pancreas, liver, spleen and kidneys. Using other techniques, Hassiotou's team also found that the stem cells had developed into mature cells. The ones in the brain, for instance, had the characteristic shape of neurons; the ones in the liver were making the liver protein albumin, and the ones in the pancreas were making insulin. "They seem to integrate and become functional cells," she says.

Is it simply that these stem cells play a role in normal growth and development, or might they also be, say, helping offspring to tolerate their mother's cells and proteins, reducing the chances of an allergic reaction to her breast milk? "There must be some evolutionary advantage," says Hassiotou. The finding that breast milk stem cells are capable of making different tissues makes it more likely they could be used for therapeutic applications, says Hassiotou. Chris Mason of University College London adds: "If these intriguing cells are functional, they could be a novel option for producing future cell therapies."

Breast milk stem cells seem to have less capacity for unlimited cell division than embryonic stem cells. "But that's actually a good thing," says Hassiotou. They do not form tumours when injected into mice, for example, so they may be less likely to trigger cancer if used to treat people. Hassiotou points out that this kind of work cannot be done in humans, but she is planning to repeat it in macaques.

***http://www.eurekalert.org/pub_releases/2014-11/cums-rco102314.php***

## Report card on complementary therapies for breast cancer

***First clear guidelines on use of complementary therapies for breast cancer;***

Meditation and yoga get 'A' grade for easing anxiety and mood

Over eighty percent of breast cancer patients in the United States use complementary therapies following a breast cancer diagnosis, but there has been little science-based guidance to inform clinicians and patients about their safety and effectiveness. In newly published guidelines from the Society for Integrative Oncology, researchers at Columbia University's Mailman School of Public Health and the Herbert Irving Comprehensive Cancer Center with colleagues at MD Anderson Cancer Center, University of Michigan, Memorial Sloan Kettering, and other institutions in the U.S. and Canada, analyzed which integrative treatments appear to be most effective and safe for patients. They evaluated more than 80 different therapies.

Meditation, yoga, and relaxation with imagery were found to have the strongest evidence supporting their use. They received an "A" grade and are recommended for routine use for anxiety and other mood disorders common to breast cancer patients. The same practices received a "B" grade for reducing stress, depression, and fatigue, but are also endorsed for most breast cancer patients. Acupuncture received a "B" grade for controlling chemotherapy induced nausea and vomiting and can be recommended to most patients. More than 30 interventions, including some natural products and acupuncture for other conditions, had weaker evidence of benefit due to either small study sizes or conflicting study results, and received a "C" grade. Seven other therapies were deemed unlikely to provide any benefit and are not recommended. One therapy was found to be harmful: acetyl-l-carnitine, which is marketed to prevent chemotherapy-related neuropathy, and actually increased risk for the condition.

Results will appear online in the Journal of the National Cancer Institute Monograph and be presented Monday, October 27th at the Society for Integrative Oncology's 11th International Conference held in Houston, Texas.

To conduct their analysis, the researchers used a set of nine biomedical publication databases to review randomized controlled clinical trials conducted from 1990 through 2013 among breast cancer patients that tested complementary therapies together with standard cancer care - defined as surgery, chemotherapy, radiation therapy, and hormonal therapy. Based on a set of guidelines developed by the Institute of Medicine, the researchers considered the magnitude and type of benefit and harm along with trial quality and size. Of 4,900 research articles reviewed, 203 met the criteria for the final analysis. Recommendations were organized by clinical outcome and graded using the U.S. Preventive Services Task Force grading system.

"Most breast cancer patients have experimented with integrative therapies to manage symptoms and improve quality of life. But of the dozens of products and practices marketed to patients, we found evidence that only a handful currently have a strong evidence base," said Heather Greenlee, ND, PhD, assistant professor of Epidemiology at Columbia's Mailman School of Public Health and president of the Society for Integrative Oncology. A number of interventions did not have sufficient evidence to support specific recommendations. "This does not mean that they don't work, this means that we don't yet know if they work, in what form, or what dose is the most effective. The vast majority of therapies require further investigation through well-designed controlled clinical trials," said Dr. Greenlee.

"A challenge in assessing the safety and effectiveness of complementary therapies was the lack of standardization of interventions across trials using similar therapeutic approaches," said Debu Tripathy, MD, professor and chair of breast medical oncology at MD Anderson Cancer Center. "In addition, some integrative therapies are applied in a variety of settings - early vs. advanced stages of disease and a spectrum of symptom severity - such that the clinical criteria for using some therapies may not be straightforward." However, the researchers also found that many of the complementary therapies were low risk, and the lack of means to measure them may not greatly influence their clinical application.

"These guidelines provide an important tool for breast cancer patients and their clinicians as they make decisions on what integrative therapies to use and not use. The guidelines clearly demonstrate that clinicians and patients should adopt shared decision-making approaches when assessing the risk-benefit ratio for each therapy. It is important to personalize the recommendations based upon patients' clinical characteristics and values. What's right for one patient, may be wrong for another," said Dr. Greenlee.

*Co-author institutions: Columbia University, MD Anderson Cancer Center, University of Michigan, Memorial Sloan Kettering Cancer Center, University of California San Francisco, University of British Columbia, University of Calgary, Georgia Center for Oncology Research and Education, and the Ottawa Integrative Cancer Center.*

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*The authors report no conflicts of interest.*

***http://bit.ly/10s76kN***

## Heritage of Water Ice in the Solar System

***New research from astronomers at the Harvard-Smithsonian Center for Astrophysics reveals that water in our solar system almost certainly derives in large part from interstellar water, rather than forming locally, and that consequently other stellar systems would be expected to contain water as well.***

Water, the key ingredient for life, is not only abundant on Earth, it is also ubiquitous across the solar system. Either as ice or sometimes as liquid, water has been spotted in comets, the icy moons of the giant planets, and even in the shadowed basins of Mercury.

Water has left its mark in hydrated minerals in meteorites that penetrated our atmosphere, in lunar basalts retrieved by the astronauts, and in Martian melt inclusions recovered from rock samples ejected from Mars that found their way to Earth. Comets and asteroids (as traced by meteorites) remain the oldest, most primitive objects with water. They provide a natural time capsule of the conditions present during the Sun's epoch of planet formation.

No one knows for sure when and where these ices formed. Water might have been present in the dense interstellar medium from which Sun formed or it might have been made somehow within the solar nebula after it developed. Astronomers are trying to determine which applies because the former suggests that all planet-forming systems will have abundant water ices, whereas the latter presumably means that the abundance of water can vary dramatically from stellar system to system.

***An image of the stellar nursery in NGC 3603 where stars are actively forming from the nebula's extended clouds of gas and dust.*** **Credit: ESO**

Water is usually made with two atoms of hydrogen and one of oxygen, as H2O, but it can also come in deuterated form in which a deuterium atom replaces one hydrogen atom. The fraction of deuterated water in a sample is a powerful measure of the age and origin of the sample: Interstellar ices are highly enriched in the deuterated species because the chemistry of interstellar space – ionizing radiation in particular – preferentially destroys normal H2O water. Ice in interstellar space can have a two to thirty times higher fraction of deuterated water than is found on Earth.

CfA astronomer Karin Oberg and her colleagues did comprehensive modeling of the proto-planetary disk that forms around new stars, including the effects of ultraviolet ionization and the influence of radioactive elements in the material. In the latest issue of Science, the team reports a number of key results, including that the young solar nebula must have contained some pristine interstellar ice. A considerable fraction of the solar system's water therefore predates the Sun. If the solar system is typical, the scientists conclude, then interstellar ices in a stellar birth cloud should be widely available to all young protoplanetary systems.

***Publication***: *L. Ilsedore Cleeves, et al., "The Ancient Heritage of Water Ice in the Solar System," Science 26 September 2014: Vol. 345 no. 6204 pp. 1590-1593;*

***PDF Copy of the Study***: *The Ancient Heritage of Water Ice in the Solar System*

***http://bit.ly/1x6JiS5***

## Crater Hunters Find New Clues to Ancient Impact Storm

***Back when Wisconsin and western Russia once shared an address south of the equator, a violent collision in the asteroid belt blasted Earth with meteorites.***

**by Becky Oskin, Senior Writer | October 31, 2014 01:55pm ET**

The space rock smashup showered Earth with up to 100 times more meteorites than today's rate (a rock the size of a football field hits the planet about every

10,000 years). Yet, only a dozen or so impact craters have been found from the ancient bombardment 470 million years ago, during the Ordovician Period. Most are in North America, Sweden and western Russia. There are only about 185 known impact craters on Earth of any age, while the moon has more than 100,000. But the number of Ordovician craters may soon take off. That's because it's easier and cheaper than ever to hunt down evidence that confirms an impact. The clinchers include shocked minerals, deformed rocks and structural features that match other craters.

"Google Earth images are not good enough to identify an impact structure," noted planetary geologist Christian Köeberl on Oct. 22, at the Geological Society of America's annual meeting in Vancouver, British Columbia. During the Vancouver meeting, researchers presented new clues that bring suspected craters in Wisconsin, Kentucky and Tennessee closer to official listings as Ordovician impact craters.

***A meteor crater in northern Quebec, Canada.*** **Credit: NASA Earth Observatory**

The three enigmatic structures retain their circular shape, but have lost most of their original features through erosion. In the last century, quarrying has also slowly dismantled the Wisconsin crater. Only the central uplift seems to persist. When a meteorite hits, the impact's force causes the underlying rock to rebound upward, leaving a topographic high in the center of the crater.

In each state, researchers looked for traces of minerals shattered or heated by the impact. So far, no one has found one of the smoking guns in crater research: shatter cones, the finely fractured rocks created when the shock wave travels through the ground. The fractures are often arranged in a conical shape, like an ice cream cone.

**Three little craters**

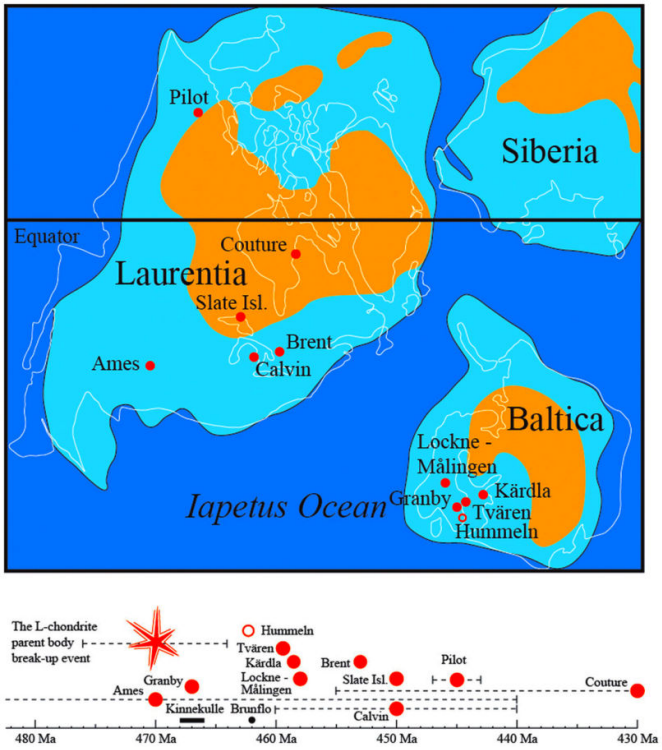
But even without a smoking gun, at Brussels Hill in Door County, Wisconsin, a meteorite impact is the best explanation for the perfectly round, 130-foot-tall (40 meters) hill, said Emily Zawacki, an undergraduate at Lawrence University in Appleton, Wisconsin. The flat-topped peak is filled with fractured blocks of Cambrian sandstone that should lie some 1,300 feet below the younger carbonate rocks. The fragmented rocks all tilt toward the center of the hill, and a series of faults radiate outward from its center.

The evidence all points to a deeply eroded impact crater, Zawacki said. "This is a highly disturbed area in otherwise flat-lying stratigraphy," Zawacki said. "It very clearly is anomalous and we feel a meteoritic impact best explains it."

In the middle of Tennessee, the Howell Structure has confounded geologists for decades. The bowl-shaped basin is about the same diameter as Brussels Hill (about 1.2 miles, or 2 km). In this case, however, the suspected crater is weaker than the surrounding rocks, creating a depression. A pile of fragmented carbonate and other craterlike features suggests an impact origin.

Keith Milam, a professor at Ohio University in Athens, recently uncovered a rare trove of rock cores drilled at Howell in the 1960s. John Bensko, a retired lunar geologist from NASA's Marshall Space Flight Center, provided the 15 segments. Bensko oversaw the testing of drilling equipment intended for the canceled Apollo 18 program. The first tests on the rock cores suggest the fragmented carbonate rocks were shocked by a meteorite impact, Milam reported at the Vancouver meeting.

Finally, the Jeptha Knob structure in Kentucky is a site that stands out on Google Earth and just needs the right mineral evidence to certify its impact origin. "I don't think you can say for sure this is an impact structure yet," said Eric Gibbs, an undergraduate at Ohio University in Athens.




***A partial map of Ordovician continents and impact craters.*** **Credit: Jens Ormö et al., Scientific Reports**

Gibbs is testing the X-ray diffraction pattern produced by minerals from the crater. The pattern shortens and widens with increasing shock, he said.

The initial tests, presented at the Vancouver geology meeting, support an impact origin for the hill. Jeptha Knob is the highest point in Kentucky's Bluegrass Region, rising some 300 feet (90 m) above the surrounding farms. The round crater is ringed by faults and busted-up Ordovician limestone, but topped by flat layers of younger carbonate rocks. The apparent alignment of many of these craters makes it seem that some coincidence favored Earth's tropical latitudes during the big Ordovician bombardment.

At the time, North America was flipped backward and sitting across the equator. The Baltica continent - western Russia, Sweden and Finland - was just to the south. There are six confirmed Ordovician craters in the central United States and more in the middle of Canada. There are five confirmed craters in Sweden; and this month a double crater was identified in central Sweden at Lockne and Malinga, according to a study published Oct. 24 in the journal Scientific Reports. Who knows how many more are buried under the protective limestones and shales of the huge Ordovician seas?

***http://www.eurekalert.org/pub_releases/2014-11/ef-hoe110414.php***

## Half of elderly people are more than happy to consume new foods

***Elderly people are regarded as traditional consumers, but the AZTI study reveals that there are more and more elderly people who are happy to accept new foods.***

However, these consumers insist that the new proposals should be similar to or evoke traditional products and flavours and, at the same time, be health-enhancing, have the right nutrient profile for their age, and be flavoursome.

To come up with new foods adapted to the needs of the population over 65, AZTI –in collaboration with the ADIMEN group of sociologists and with the support of chefs in the R&D AZTI and Mugaritz team– is working to produce various food prototypes. The research is also being expanded in the quest for new foods designed for people between 40 and 50, known as pre-seniors or young seniors.

One of the key aspects in the quest for new foods is that the moment of eating should become a moment of pleasure. The technicians and chefs in the R&D AZTI-Mugaritz team are exploring combinations of aromas, flavours and textures that evoke pleasurable memories linked to food. So it boils down to relating food with moments of happiness.

The results, the outcome of the interaction between methodologies of the sensory sciences and the consumer together with other more classical ones to do with sociological behaviour, have provided clear proof that 50% of the seniors consulted readily accept new foods.

The AZTI research to get to know senior consumers also reflects the significant degree of concern about health matters among people between 50 and 70. This group is seeking a solution in foods to prevent the problems that emerge with the passing years. Among the disorders identified in the study as the ones giving cause for concern are cardiovascular disease, cancer and those relating to digestive health.

The R&D centre believes that elderly people are a group of great interest for the food industry, as they constitute a target group with purchasing capacity and prepared to try new things. To come up with fresh initiatives for this sector, AZTI is working on the design of new foods that do not forgo taste and tradition and which are accompanied by labelling that incorporates clear messages and which details all the benefits that can result from consuming them. In this respect, the AZTI study has revealed that the senior consumer does not feel identified with the products currently available on the market. Specifically, the study reveals that the messages on the labels neither address their needs nor coincide with the perception they have about their own health.

**Seniors: A Growing Market**

As the population ages, the over-sixties are becoming an increasingly important segment for many industries, including the food industry. Coming up with the foods and ingredients that address the needs of this new market will be crucial in the near future, and this is the challenge that the second edition of the symposium Growing Young will be endeavouring to address. The symposium is being organised by AZTI and is due to take place in Bilbao on 26-27 May, 2015.

***http://www.eurekalert.org/pub_releases/2014-11/bc-nru102814.php***

## New research: Undiagnosed, undertreated Chagas disease emerging as US public health threat

***ASTMH Annual Meeting presentations highlight massive treatment gap***

NEW ORLEANS - Across a broad swath of the southern United States, residents face a tangible but mostly unrecognized risk of contracting Chagas disease - a stealthy parasitic infection that can lead to severe heart disease and death - according to new research presented today at the American Society of Tropical Medicine and Hygiene (ASTMH) Annual Meeting.

Chagas disease (American trypanosomiasis) is typically spread to people through the feces of blood-sucking triatomine bugs sometimes called "kissing bugs" because they feed on people's faces during the night. The disease, which can also be spread through blood supply, affects 7 to 8 million people worldwide and can be cured - if it is caught early. Often considered a problem only in Mexico, Central America and South America, Chagas disease is being seen in Texas and recognized at higher levels than previously believed, reported researchers from Baylor College of Medicine in Houston. Among those infected are a high

percentage believed to have contracted the disease within the U.S. border, according to the scientists whose findings will also be published in the *American Journal of Tropical Medicine and Hygiene*.

"We were astonished to not only find such a high rate of individuals testing positive for Chagas in their blood, but also high rates of heart disease that appear to be Chagas-related," said Baylor epidemiologist Melissa Nolan Garcia, one of the researchers who presented findings from a series of studies. "We've been working with physicians around the state to increase awareness and diagnosis of this important emerging infectious disease."

And while this research was conducted in Texas, kissing bugs are found across half of the United States, according to the U.S. Centers for Disease Control. Bites from these insects may be infecting people who are never diagnosed, due to a lack of awareness of Chagas disease by healthcare personnel and the U.S. healthcare system.

**Chagas Infection Rate Underreported; Often Overlooked as Risk Factor For Heart Disease**

Garcia's team conducted an analysis of routine testing of Texas blood donors for Chagas between 2008 and 2012. In that study published in *Epidemiology and Infection* (August 2014), the researchers found that one in every 6,500 blood donors tested positive for exposure to the parasite that causes Chagas disease. That figure is 50 times higher than the CDC's estimated infection rate of one in 300,000 nationally, but according to Garcia, a rate that is consistent with other studies in the southern United States indicating a substantial national disease burden. Since 2007, all potential blood donors within the United States are screened for exposure to the Chagas disease parasite.

"We think of Chagas disease as a silent killer," Garcia said. "People don't normally feel sick, so they don't seek medical care, but it ultimately ends up causing heart disease in about 30 percent of those who are infected."

Symptoms can range from non-existent to severe with fever, fatigue, body aches, and serious cardiac and intestinal complications. Positive blood donors, who would likely develop chronic Chagas disease over time, could cost about US $3.8 million for health care and lost wages for those individuals, according to the researchers' calculations. And according to a recent study published in the *The Lancet Infectious Diseases*, societal and healthcare costs for each infected person in the United States averages $91,531.

"We're the first to actively follow up with positive blood donors to assess their cardiac outcomes and to determine where southeastern Texas donors may have been exposed to Chagas," Garcia said. "We are concerned that individuals who test positive are not seeking medical care or being evaluated for treatment. And even if they do seek medical care, we heard from some patients that their primary care doctors assumed the positive test represented a 'false positive' due to low physician awareness of local transmission risk."

Garcia shared the findings from separate pilot studies conducted by the Baylor team, which followed 17 Houston-area residents who were infected. They found that 41 percent of them had signs of heart disease caused by the infection, including swollen, weakened heart muscle and irregular heart rhythms caused by the parasite burrowing into heart tissue. Most of these individuals lived in rural areas or spent a significant amount of time outside. One of the individuals was an avid hunter and outdoorsman. At least six of them had insignificant travel outside the United States and they didn't have mothers from foreign countries, indicating they had likely become infected locally in Texas.

As blood donor screening is currently the only active screening program in the United States, they provide an insight into the characteristics of who might be at risk for disease. "People who give blood are usually generally healthy adults. The people that we worry about in terms of burden of disease here are from rural settings and people who live in severe poverty. So the burden of disease may be even higher than what we see in this study," said Kristy Murray, DVM, PhD, a co-author on the study and associate professor of tropical medicine at Baylor.

**Local Kissing Bugs Spreading Disease**

Kissing bugs emerge at night to feed. Once they have bitten and ingested blood, they defecate on their victim and the parasites then enter the body through breaks in the skin. While no firm data exists on how many bugs in the United States may carry the parasite, another pilot study conducted by the research team at Baylor, and presented as a poster during the ASTMH meeting, may shed some light on the issue. In that study, researchers collected a random sample of 40 kissing bugs found near homes in 11 central-southern Texas counties. They found 73 percent of the insects carried the parasite and half of the positive bugs had dined on human blood in addition to a dozen types of animals including dogs, rabbits, and raccoons.

"The high rate of infectious bugs, combined with the high rate of feeding on humans, should be a cause of concern and should prompt physicians to consider the possibility of Chagas disease in U.S. patients with heart rhythm abnormalities and no obvious underlying conditions," said Murray.

**New Analysis of CDC Data and National Blood Bank Data Uncovers Large Treatment Gap**

Another ASTMH Annual Meeting presentation shows people who test positive for Chagas disease mostly go untreated. Jennifer Manne-Goehler, MD, a clinical fellow at Harvard Medical School and Beth Israel Deaconess Medical Center,

collected data from the CDC and the American Association of Blood Banks and compared the almost 2,000 people who tested positive through the blood banking system to the mere 422 doses of medications administered by the CDC from 2007 to 2013.

"This highlights an enormous treatment gap," said Manne-Goehler. "In some of the areas of the country we know there are a lot of positive blood donors, yet people still don't get care. We don't know what happens to them because there is no follow up."

In the United States, most physicians are unfamiliar with the disease, and some who have heard of it mistakenly dismiss Chagas disease as a not-so-serious health concern, even in parts of the country where many people may be living with Chagas symptoms, she said at an ASTMH presentation on access to treatment.

Further complicating the situation, in the United States the currently available medicines used to treat Chagas disease have not been approved by the U.S. Food and Drug Administration. Physicians seeking treatment for their patients are referred to the CDC, which makes two drugs - nifurtimox and benznidazole - available, both of which carry the risk of side effects including nausea, weight loss and possible nerve damage.

In addition to data collection, Manne-Goehler conducted interviews with physicians, state health directors, and other healthcare workers treating patients diagnosed with Chagas disease in states with higher numbers of cases: Texas, California, Florida, Virginia, New York and Massachusetts. The findings revealed a disjointed, ad hoc approach to both diagnosing and treating the disease. Most of the doctors interviewed had never treated a patient whose infection had been identified through the blood donor system.

Manne-Goehler and her colleagues Michael Reich, PhD, of the Harvard School of Public Health and Veronika Wirtz PhD, of the Boston University Center for Global Health and Development, are calling for the creation of an independent expert panel to define clinical screening guidelines to help improve identification of patients with Chagas disease in the United States. In addition, they argue for creation of a physician-referral network so that physicians who are unfamiliar with the disease can send patients to providers who regularly diagnose and treat cases of Chagas disease.

Several ASTMH presenters also argued for a more comprehensive system of surveillance beyond testing of blood donors.

"So little surveillance has been done that we don't know the true disease burden here in the United States," said Murray. "The next step is to study populations considered high risk. There is still a lot to be learned in terms of who is contracting the disease within the United States."

***http://www.eurekalert.org/pub_releases/2014-11/s-tow110414.php***

## Tell-tales of war: Traditional stories highlight how ancient women survived

### *'Stockholm Syndrome' could have ancient roots*

New York | Heidelberg, - Through the ages, women have suffered greatly because of wars. Consequently, to protect themselves and their offspring, our female ancestors may have evolved survival strategies specific to problems posed by warfare, says Michelle Scalise Sugiyama of the University of Oregon in the US. Her findings, based on the comprehensive analysis of traditional stories from across the world, are published in Springer's journal Human Nature. The work is of interest because research to date has focused on the problems warfare poses for men, and how these problems shaped human male cognition.

Scalise Sugiyama studied a sample of forager and forager-horticulturalist societies by looking at archaeological and ethnographic research on lethal raiding. This helped her to compile a list of five 'fitness costs' – ways in which warfare impedes women's chances of surviving and reproducing. These occur when a woman is killed, a woman is captured, her offspring is killed, a mate is killed or captured, or an adult male kinsman is killed or captured.

The study then reviewed traditional stories about lethal raids that had been handed down for generations by word of mouth. Scalise Sugiyama analyzed a cross-cultural sample of war stories from 45 societies and found that the five fitness costs often feature within these story lines. The war stories included tales from various North American Indian tribes, the Eskimo of the Arctic, Aborigine groups of Australia, the San of Southern Africa and certain South American tribal societies.

Based on the fitness costs documented in these stories, Scalise Sugiyama believes that ancestral women may have developed certain strategies to increase their odds of survival and their ability to manage their reproduction in the face of warfare. These include manipulating male behavior, determining whether the enemy's intent was to kill or capture them, and using defensive and evasive tactics to sidestep being murdered or to escape captivity. Assessing the risk of resistance versus compliance also requires having several sets of knowledge. This includes information about an enemy's warfare practices and how they treat their captives.

The so-called Stockholm Syndrome, in which hostages bond with their captors, could have ancestral roots, hypothesizes Scalise Sugiyama. It often occurs under conditions of physical confinement or physical, sexual, and/or emotional abuse, which are characteristic of captivity in ancestral forager and forager-horticulturalist groups. This response could have developed as a way to help

captives identify and ultimately integrate with enemy groups. This then motivates acceptance of the situation and reduces attempts to resist the captor – which may ultimately increase a woman's chances of survival.

"Lethal raiding has recurrently imposed fitness costs on women. Female cognitive design bears reexamination in terms of the motivational and decision-making mechanisms that may have evolved in response to them," says Scalise Sugiyama.

*Reference: Scalise Sugiyama, M. (2014). Fitness Costs of Warfare for Women, Human Nature. DOI 10.1007/s12110-014-9216-1*

***http://www.eurekalert.org/pub_releases/2014-11/luhs-rar110414.php***

## Radiation a risk factor for brain tumors in young people

***In people under age 30, radiation is a risk factor for a type of brain tumor called a meningioma, a Loyola University Medical Center study has found.***

Researchers analyzed records of 35 patients who were diagnosed with meningiomas before age 30. Five had been exposed to ionizing radiation earlier in their lives. They include two patients who received radiation for leukemia at ages 5 and 6; one who received radiation at age 3 for a brain tumor known as a medulloblastoma; and one who received radiation for an earlier skull base tumor that appeared to be a meningioma. The fifth patient had been exposed at age 9 to radiation from the Chernobyl nuclear power plant disaster in Ukraine. Twenty years later, he was diagnosed with a meningioma.

In the five patients, the average latency period for the tumors was 23.5 years.

The study was published in the online journal Neuroscience Discovery.

"The results of this preliminary study have prompted us to look closely at radiation's effects on the brain," said Loyola neurosurgeon Vikram Prabhu, MD, first author of the study. Dr. Prabhu specializes in treating brain tumors.

A meningioma is a tumor, usually benign, that arises from the meninges - the membranes that surround the brain and spinal cord. Meningiomas comprise about one-third of all primary brain tumors, but are rare in children and young adults. It is one of the commonest brain tumors treated at Loyola by Dr. Prabhu and his team. They are doing a follow-up study on patients of all ages who have been treated at Loyola for meningiomas. In collaboration with Dr. Omer Iqbal, from the Department of Pathology, they are analyzing the genetics and biology of tumor samples to find how they differ from samples of tumors not linked to radiation.

Loyola oncologist Kevin Barton, MD, a co-author of the study, said: "It is important to compare and contrast these post-radiation meningiomas with de novo meningiomas, both clinically and biologically, in order to further define optimal therapy."

Researchers so far have identified 14 meningioma patients who were exposed to radiation earlier in their lives. They include three patients who were exposed to Chernobyl radiation and 11 patients who received therapeutic radiation for such conditions as leukemia, medulloblastoma tumors and fungal infections of the scalp.

Dr. Edward Melian, a radiation oncologist at Loyola and co-author of the study, said patients generally have done very well with radiation treatments. "Although we have identified radiation as a risk factor for meningiomas, radiation remains an important part of the treatment regimen for certain lesions, and is helping us obtain good results for our patients."

Dr. Prabhu said physicians have become more judicious in using radiation for therapeutic purposes. For example, radiation no longer is used to treat fungal scalp infections. "We have become more aware of the tumor-inducing properties of radiation," Dr. Prabhu said.

People who have been exposed to large doses of radiation to the head face a small risk of later developing brain tumors. If such a person experiences symptoms associated with brain tumors, including headaches, seizures, vomiting and blurry vision, he or she should see a doctor, Dr. Prabhu said.

*Dr. Prabhu is a professor in the Department of Neurological Surgery at Loyola University Chicago Stritch School of Medicine. Dr. Melian is an associate professor in the departments of Radiation Oncology and Neurological Surgery. Dr. Barton is an associate professor in the Division of Hematology/Oncology. Other co-authors are Loyola biostatistician Rong Guo, PhD; Douglas Anderson, MD, a professor in the Department of Neurological Surgery; and Edward Perry, MD, who completed a residency in neurological surgery at Loyola.*

*The study is titled "Intracranial meningiomas in individuals under the age of 30; Analysis of risk factors, histopathology and the recurrence rate."*

***http://www.eurekalert.org/pub_releases/2014-11/cwru-dmm110414.php***

## Dark matter may be massive

***CWRU theorists suggest the Standard Model may account for the stuff***

The physics community has spent three decades searching for and finding no evidence that dark matter is made of tiny exotic particles. Case Western Reserve University theoretical physicists suggest researchers consider looking for candidates more in the ordinary realm and, well, more massive.

Dark matter is unseen matter, that, combined with normal matter, could create the gravity that, among other things, prevents spinning galaxies from flying apart. Physicists calculate that dark matter comprises 27 percent of the universe; normal matter 5 percent.

Instead of WIMPS, weakly interacting massive particles, or axions, which are weakly interacting low-mass particles, dark matter may be made of macroscopic objects, anywhere from a few ounces to the size of a good asteroid, and probably as dense as a neutron star, or the nucleus of an atom, the researchers suggest.

Physics professor Glenn Starkman and David Jacobs, who received his PhD in Physics from CWRU in May and is now a fellow at the University of Cape Town, say published observations provide guidance, limiting where to look. They lay out the possibilities in a paper at http://arxiv.org/pdf/1410.2236.pdf.

The Macros, as Starkman and Jacobs call them, would not only dwarf WIMPS and axions, but differ in an important way. They could potentially be assembled out of particles in the Standard Model of particle physics instead of requiring new physics to explain their existence.

"We've been looking for WIMPs for a long time and haven't seen them," Starkman said. "We expected to make WIMPS in the Large Hadron Collider, and we haven't."

WIMPS and axions remain possible candidates for dark matter, but there's reason to search elsewhere, the theorists argue.

"The community had kind of turned away from the idea that dark matter could be made of normal-ish stuff in the late '80s," Starkman said. "We ask, was that completely correct and how do we know dark matter isn't more ordinary stuff - stuff that could be made from quarks and electrons?"

After eliminating most ordinary matter, including failed Jupiters, white dwarfs, neutron stars, stellar black holes, the black holes in centers of galaxies and neutrinos with a lot of mass, as possible candidates, physicists turned their focus on the exotics.

Matter that was somewhere in between ordinary and exotic - relatives of neutron stars or large nuclei - was left on the table, Starkman said. "We say relatives because they probably have a considerable admixture of strange quarks, which are made in accelerators and ordinarily have extremely short lives," he said.

Although strange quarks are highly unstable, Starkman points out that neutrons are also highly unstable. But in helium, bound with stable protons, neutrons remain stable.

"That opens the possibility that stable strange nuclear matter was made in the early universe and dark matter is nothing more than chunks of strange nuclear matter or other bound states of quarks, or of baryons, which are themselves made of quarks," he said. Such dark matter would fit the Standard Model.

The Macros would have to be assembled from ordinary and strange quarks or baryons before the strange quarks or baryons decay, and at a temperature above 3.5 trillion degrees Celsius, comparable to the temperature in the center of a massive supernova, Starkman and Jacobs calculated. The quarks would have to be assembled with 90 percent efficiency, leaving just 10 percent to form the protons and neutrons found in the universe today.

The limits of the possible dark matter are as follows:

***A minimum of 55 grams. If dark matter were smaller, it would have been seen in detectors in Skylab or in tracks found in sheets of mica.***

***A maximum of $10^{24}$ (a million billion billion) grams. Above this, the Macros would be so massive they would bend starlight, which has not been seen.***

***The range of $10^{17}$ to $10^{20}$ grams should also be eliminated from the search, the theorists say. Dark matter in that range would be massive for gravitational lensing to affect individual photons from gamma ray bursts in ways that have not been seen.***

If dark matter is within this allowed range, there are reasons it hasn't been seen.

***At the mass of $10^{18}$ grams, dark matter Macros would hit the Earth about once every billion years.***

***At lower masses, they would strike the Earth more frequently but might not leave a recognizable record or observable mark.***

***In the range of $10^{9}$ to $10^{18}$, dark matter would collide with the Earth once annually, providing nothing to the underground dark matter detectors in place.***

***http://bit.ly/1w4e0Wg***

## Scotland Is No Longer Home to the World's Best Whiskys

***When it comes to whisky, Japan, the US and even England now reign supreme***

**By Rachel Nuwer**

The upcoming 2015 edition of Jim Murray's Whisky Bible—the go-to guide for global whisky reviews—contains a shock for many whisky lovers: not a single Scottish distillery landed a place on the top five list.

Instead, Japan's Suntory Yamazaki Single Malt Sherry Cask 2013 snagged first place, with some critics going so far as to describe it as "near indescribable genius," the *Guardian* reports. This is the first time Scotland hasn't claimed a top spot on the list, which was first published in 2002; it's also the first time that Japan has earned the coveted top spot. The second, third and fourth prizes, the *Guardian* adds, went to distilleries in the U.S.

Suntory, which was founded in 1920s, does in fact have some Scottish roots. One of its creators, Masataka Taketsuru, married Rita Cowan, a Scotswoman whose family opposed the union, the *Guardian* writes. Their company's winning whisky was limited to just 18,000 bottles produced at the country's oldest distillery, Yamazaki, which opened in 1923, the *Guardian* continues.

Scotland, which has been distilling whiskey since the 15th century or earlier, is pushing back against increased international competition by building a handful of new distilleries—some glitzy, others more mom-and-pop operations, The Scotsman reports. Indeed, the affront to tradition and pressure from new competition is even closer to home than Japan and America. England is acting up by building its own distilleries all over the country, Newsweek writes—as is virtually every country throughout Europe. In fact, the English Whiskey Company snagged the prize for best European whisky this year.

http://bit.ly/1pEtbsL

# Small Islands May Make Tsunami Danger Worse

***While offshore islands usually protect coasts, simulations suggest they may amplify monster waves reaching the mainland***

**By Sarah Zielinski**

Sometimes your best protector can become your worst enemy. Coastal scientists have long known that small islands sitting just off the coast can safeguard mainland communities from the worst effects of winds and waves. But simulations show that those protective effects dissipate in the face of tsunamis, and that islands may actually amplify the massive waves as they travel toward the coastline.

Tsunamis have plagued coastal areas throughout human history, but the last decade has seen two particularly devastating events. On December 26, 2004, a magnitude-9.1 earthquake off the coast of Sumatra, Indonesia spawned a tsunami with waves as high as 80 feet, killing at least 280,000 people throughout the Indian Ocean region. Then on March 11, 2011, a magnitude-9 quake off the coast of Japan created a tsunami that killed 18,000 people and caused the Fukushima nuclear disaster.

Despite heightened awareness of tsunami dangers, the only effective countermeasure remains preparedness, which requires accurate warning systems. One key piece of information needed to estimate a tsunami's potential impact is runup—the maximum elevation that the water will reach on land. Studies have typically assumed that runup is uniform along any particular coast, but observations from real tsunami events have indicated that it may be more complicated. For example, researchers reported in 2012 that a tsunami spawned by a magnitude-7.7 earthquake off Sumatra in October 2010—which killed 400 people—appeared to have had higher than expected runups behind small islands. The unusually high runups could have been influenced by other factors, such as the shape of the seafloor off the coast. So Themistoklis Stefanakis of University College Dublin in Ireland and his colleagues created numerical simulations of a flat seafloor sitting in front of a simple beach, with a small, conical-shaped island off shore. The team then bombarded the fake seashore with pretend tsunamis. The results of their research appear today in the Proceedings of the Royal Society A.

The island offered no protection in all 200 simulations the researchers ran for the study. Instead, as the tsunami traveled toward the coast, the swell of water wrapped around the tiny piece of land, piling up behind it before moving on to shore. At the beach just behind the island, the tsunami was up to 70 percent higher than in areas where there was no island.

"This finding shows that small islands in the vicinity of the mainland act as amplifiers of long waves at the region directly behind them and not as natural barriers as it was commonly believed," the researchers write.

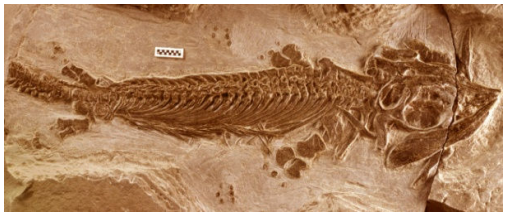
Real coastlines are rarely as simple as those in the simulation. Chains of islands may even offer the expected protection, as was seen during the 2010 Indian Ocean tsunami. But the research suggests that the tsunami models used to predict the impact of these events could be wrong, especially when they eliminate offshore islands in an effort to simplify calculations, Stefanakis and his colleagues note. And one day, they add, calculations such as the ones in their study could provide real-time estimates of maximum inundation from an approaching tsunami, providing people living on coasts better warning of who needs to flee to higher ground.

http://cnet.co/1uO7DLm

Newly discovered amphibious ichthyosaur is a prehistoric missing link

A new ichthyosaur discovered in China is the missing link between the aquatic reptiles of the Mesozoic era and their terrestrial ancestors.

The oldest ichthyosaurs -- of which we have found around 80 different species -- existed in the early Triassic, and the fossils we have found indicate an evolution from a land-dwelling reptile. Those earliest specimens exhibit lizard-like features -- necks, long tails, an absence of a dorsal fin, a slim body. As millions of years passed, they grew to resemble dolphins; yet what they originally evolved from is a mystery.



**Ryosuke Motani/UC Davis**

A new discovery made in China could help solve that mystery: the first ever fossil of an amphibious ichthyosaur, found by a team led by researchers at the University of California, Davis. This is the first time that paleontologists have found direct evidence that ichthyosaurs could come onto the land.

The specimen is dated back to the Triassic period, and is about 248 million years old. It measures just 45 centimetres (1.5 feet), and was equipped with unusually large, flexible flippers that would have allowed the animal to move about on land, probably humping along much like a seal.

It also had flexible wrists -- which it would need for crawling along the ground -- and a short snout, closer to those of land reptiles than the long snouts of aquatic ichthyosaurs. And its bones were thicker and heavier -- which fits with the hypothesis that marine reptiles developed heavier bones as they evolved from terrestrial animals in order to battle coastal surf to reach the deep sea.

The discovery could help us learn not just how ichthyosaurs evolved, but how animals might evolve in the future: the amphibian lived just four million years after the Permian-Triassic extinction event 252 million years ago.

"This was analogous to what might happen if the world gets warmer and warmer," said lead author and professor in the UC Davis Department of Earth and Planetary Sciences Ryosuke Motani. "How long did it take before the globe was good enough for predators like this to reappear? In that world, many things became extinct, but it started something new. These reptiles came out during this recovery."

***http://www.eurekalert.org/pub_releases/2014-11/uoc-hdp110514.php***

## High-fat diet postponing brain aging

***New Danish-led research suggests that signs of brain aging can be postponed in mice if placed on a high-fat diet.***

In the long term, this opens the possibility of treatment of children suffering from premature aging and patients with Alzheimer's and Parkinson's disease. The research project is headed by the Center for Healthy Aging, University of Copenhagen and the National Institute of Health.

When we get older, defects begin to develop in our nervous system, our brain loses some of its intellectual capacity, and the risk of developing diseases such as Parkinson's and Alzheimer's increases. Alzheimer's disease is currently the fastest-growing age-related disease.

Throughout our lives, it is important that our cells – to the extent possible – keep our DNA undamaged, and, therefore, the cells have a system that repairs the damage that occurs all the time. Humans age when the repair system ceases to function. In diseases such as Alzheimer's, the researchers also see damage to the DNA

A new research project headed by the Center for Healthy Aging, University of Copenhagen and the National Institute of Health has studied mice having a defect in their DNA repair system. In humans, this defect causes the disorder Cockayne syndrome, where patients prematurely age as children and die at an age of 10-12 years. The study shows that placing a mouse model of Cockayne syndrome on a high-fat diet will postpone aging processes such as impaired hearing and weight loss.

**Fat putting a stop to premature ageing**

"The study is good news for children with Cockayne syndrome, because we do not currently have an effective treatment. Our study suggests that a high-fat diet can postpone aging processes. A diet high in fat also seems to postpone the aging of the brain. The findings therefore potentially imply that patients with Alzheimer's and Parkinson's disease in the long term may benefit from the new knowledge," says Professor Vilhelm Bohr from the Center for Healthy Aging, University of Copenhagen and the National Institute of Health, who has headed the study.

Our brain has a constant need for fuel in the form of either sugar or so-called ketones. Ketones are the brain's fuel reserve, and, in particular, play an important role in periods of low blood sugar levels, e.g. if you are fasting. This is because the body breaks down fat if it needs sugar, and during this process it produces ketones. The researchers see a particular positive effect when the mice are given the so-called medium chain fatty acids – e.g. from coconut oil.

**Brain cells need extra fuel**

"In cells from children with Cockayne syndrome, we have previously demonstrated that aging is a result of the cell repair mechanism being constantly active. It eats into the resources and causes the cell to age very quickly. We therefore hope that a diet with a high content of coconut oil or similar fats will have a beneficial effect, because the brain cells are given extra fuel and thus the strength to repair the damage," says postdoc Morten Scheibye-Knudsen from the National Institute of Health.

*The study has just been published in the recognised scientific journal Cell Metabolism. The research project is supported by the Nordea-fonden through the Center for Healthy Aging.*

***http://www.bbc.com/news/science-environment-29899756***

## Limb cells turned into genitals in lab

***In order for vertebrates to evolve from the sea to the land, some drastic evolutionary changes were needed.***

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

Their ancient sea-dwelling ancestors had no need for external sex organs whereas their land relatives did. Now a new study offers insights into the genetic changes that allowed land-dwelling animals to develop sex organs. The Nature research suggests the key to the origin of genitalia lies in the limbs, at least in snakes and lizards.

For their genitals - called hemipenes - to develop, a signalling centre instructs the relevant genes to switch on. Initially the researchers wanted to understand why snakes do not develop limbs but then soon discovered that the earliest stages of genital development closely resembled limb formation. They found that when a given nudge, embryonic limb cells of lizards and snakes could then be turned into genitals. In mice, tail bud cells could be manipulated in a similar way.

**'Genital fate'**

The team did this by moving the position of "a signalling source" called the cloaca - a transient embryonic structure which gives off signalling molecules informing genes to switch on or off.

"It demonstrates that there is a flexibility with what kind of cells can get recruited during development to form genitalia," explained lead author of the research, Dr Patrick Tschopp from the Harvard Medical School in Cambridge, US. "What we were able to show is that if you ectopically transplant this cloaca into either limb or tail bud cells, these cells respond in a way that reflect their development being redirected to a genital fate," he added. "In other words, by misplacing a molecular signal you can misguide these cells in their developmental trajectory," Dr Tschopp told BBC News. In order to change these cells' fates, they traced the cell populations that form genital organs during development.

**Recruiting cells**

Then they analysed the genetic components of the embryonic cells to identify which genes were turned on and off by extracting and sequencing RNA molecules, the messengers from each gene. The study also found that in mice, the sex organs had genetic origins in the tail bud. The researchers say that this occurred due to a differing position of the cloaca which changed the cells it could "recruit" to form genitalia. Dr Tschopp explained that genital evolution was another adaptive measure vital for living on land, in a similar way to how limbs have an evolutionary origin in fish fins.

Commenting on the paper, developmental biologist Dr Liang Ma of Washington University in St Louis, US, said the work was fantastic, and that it was highly important for the fields of both genitalia and limb research. "This paper dealt with the longstanding unresolved issue of the origin of genitalia. It turns out that the mouse is the odd one out, it was not similar to the snakes or the chicken.

"This paper provides a new twist to a previous hypothesis that genitals and limbs share a deep homology [shared ancestry], it provides formal evidence of how this co-evolution between the two structures can happen in an organism."

In a related study published in journal Scientific Reports, a team looked at the embryonic origins of chicken genitals. They used fluorescent dyes to label small populations of cells in the chicken embryo and follow them to development.

**Evolutionary origins**

They found that two paired populations of cells are brought together into one structure to form the chicken's sex organs. Co-author of this paper, Prof Martin Cohn of the Howard Hughes Medical Institute in Maryland, US, said that because the evolution of external genitals occurred more rapidly than any other organ, there was a tremendous amount of diversity of anatomical form. "Because of the rapid evolution, people don't really understand how it's controlled.

"Taken together, I think the papers highlight a very deep evolutionary conservation of the earliest steps in genital development. It appears that the way all amniotes, including reptiles, birds and mammals, build their genitalia is very similar. "What these molecular and genomic tools allow us to do is compare the degree of relatedness, not only of the structures and the organisms, but of the genetic pathways that build those structures," Prof Cohn added.

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

## New dietary supplement beats calcium, vitamin D for bone strength

***A new study by a Florida State University researcher reveals that a new dietary supplement is superior to calcium and vitamin D when it comes to bone health.***

TALLAHASSEE, Fla. - Over 12 months, Bahram H. Arjmandi, Margaret A. Sitton Professor in the Department of Nutrition, Food and Exercise Sciences and Director of the Center for Advancing Exercise and Nutrition Research on Aging (CAENRA) at Florida State, studied the impact of the dietary supplement KoACT® versus calcium and vitamin D on bone loss. KoACT is a calcium-collagen chelate, a compound containing calcium and collagen that are bound together.

Calcium and vitamin D are generally thought of as the first line of defense when it comes to bone health, but Arjmandi's research found that the calcium-collagen chelate was more effective in slowing bone loss.

"This is crucial information for the health of women," Arjmandi said. "Women in early menopause experience rapid bone loss."

Arjmandi's study is published in the most recent issue of Journal of Medicinal Food.

A group of 39 women were randomly divided into two groups, with the control group taking a capsule that was a mix of calcium and vitamin D. The other group took the calcium-collagen chelate.

The women taking the calcium-collagen chelate saw substantially less bone loss than the control group over a year's time. The group taking the calcium-collagen chelate, saw a loss of 1.23 percent in bone mineral density, while the control group saw a 3.75 percent loss.

Arjmandi acknowledged he was "pleasantly surprised" by the outcomes and hopes that the supplement will be used in the future as a way to prevent bone density loss.

"We take our bones for granted," Arjmandi said. "If we do not prevent the loss of bone, our bones will be looking for an excuse to break."

In the United States, more than 44 million people have or are at risk for osteoporosis, a chronic and potentially debilitating condition. Although there are some drugs available to treat it, most medical professionals have turned to nutrition and exercise to treat the condition.

*Arjmandi's study was funded by AIDP, Inc.*

http://www.eurekalert.org/pub_releases/2014-11/uow-uss110514.php

# UW study shows direct brain interface between humans

***Sometimes, words just complicate things. What if our brains could communicate directly with each other, bypassing the need for language?***

University of Washington researchers have successfully replicated a direct brain-to-brain connection between pairs of people as part of a scientific study following the team's initial demonstration a year ago. In the newly published study, which involved six people, researchers were able to transmit the signals from one person's brain over the Internet and use these signals to control the hand motions of another person within a split second of sending that signal.

At the time of the first experiment in August 2013, the UW team was the first to demonstrate two human brains communicating in this way. The researchers then tested their brain-to-brain interface in a more comprehensive study, published Nov. 5 in the journal PLOS ONE.

"The new study brings our brain-to-brain interfacing paradigm from an initial demonstration to something that is closer to a deliverable technology," said co-author Andrea Stocco, a research assistant professor of psychology and a researcher at UW's Institute for Learning & Brain Sciences. "Now we have replicated our methods and know that they can work reliably with walk-in participants."

Collaborator Rajesh Rao, a UW associate professor of computer science and engineering, is the lead author on this work.

The research team combined two kinds of noninvasive instruments and fine-tuned software to connect two human brains in real time. The process is fairly straightforward. One participant is hooked to an electroencephalography machine that reads brain activity and sends electrical pulses via the Web to the second participant, who is wearing a swim cap with a transcranial magnetic stimulation coil placed near the part of the brain that controls hand movements.

Using this setup, one person can send a command to move the hand of the other by simply thinking about that hand movement.

The UW study involved three pairs of participants. Each pair included a sender and a receiver with different roles and constraints. They sat in separate buildings on campus about a half mile apart and were unable to interact with each other in any way – except for the link between their brains.

Each sender was in front of a computer game in which he or she had to defend a city by firing a cannon and intercepting rockets launched by a pirate ship. But because the senders could not physically interact with the game, the only way they could defend the city was by thinking about moving their hand to fire the cannon.

Across campus, each receiver sat wearing headphones in a dark room – with no ability to see the computer game – with the right hand positioned over the only touchpad that could actually fire the cannon. If the brain-to-brain interface was successful, the receiver's hand would twitch, pressing the touchpad and firing the cannon that was displayed on the sender's computer screen across campus.

Researchers found that accuracy varied among the pairs, ranging from 25 to 83 percent. Misses mostly were due to a sender failing to accurately execute the thought to send the "fire" command. The researchers also were able to quantify the exact amount of information that was transferred between the two brains.

Another research team from the company Starlab in Barcelona, Spain, recently published results in the same journal showing direct communication between two human brains, but that study only tested one sender brain instead of different pairs of study participants and was conducted offline instead of in real time over the Web.

Now, with a new $1 million grant from the W.M. Keck Foundation, the UW research team is taking the work a step further in an attempt to decode and transmit more complex brain processes.

With the new funding, the research team will expand the types of information that can be transferred from brain to brain, including more complex visual and psychological phenomena such as concepts, thoughts and rules.

They're also exploring how to influence brain waves that correspond with alertness or sleepiness. Eventually, for example, the brain of a sleepy airplane pilot dozing off at the controls could stimulate the copilot's brain to become more alert.

The project could also eventually lead to "brain tutoring," in which knowledge is transferred directly from the brain of a teacher to a student.

"Imagine someone who's a brilliant scientist but not a brilliant teacher. Complex knowledge is hard to explain – we're limited by language," said co-author Chantel Prat, a faculty member at the Institute for Learning & Brain Sciences and a UW assistant professor of psychology.

*Other UW co-authors are Joseph Wu of computer science and engineering; Devapratim Sarma and Tiffany Youngquist of bioengineering; and Matthew Bryan, formerly of the UW.*

*The research published in PLOS ONE was initially funded by the U.S. Army Research Office and the UW, with additional support from the Keck Foundation.*

*For more information, contact Stocco at stocco@uw.edu or 206-685-8610, Rao at rao@cs.washington.edu or 206-685-9141 and Prat at csprat@uw.edu or 206-685-8610.*

*PLOS ONE paper: http://dx.plos.org/10.1371/journal.pone.0111332*

*Video of demonstration: http://youtu.be/xRsx5egJoYk*

http://bit.ly/1EsLFzx

# A Push to Back Traditional Chinese Medicine With More Data

***Researchers Marry Modern Analytical Techniques to Centuries-Old Theories on What Makes People Sick***

**Shirley S. Wang** ***Hong Kong***

Traditional Chinese medicine teaches that some people have hot constitutions, making them prone to fever and inflammation in parts of the body, while others tend to have cold body parts and get chills.

Such Eastern-rooted ideas have been developed over thousands of years of experience with patients. But they aren't backed up by much scientific data.

***Chinese licorice root is used in traditional Chinese medicine with other herbs in a combination known as PHY906, which has been studied by Yale University researchers.***

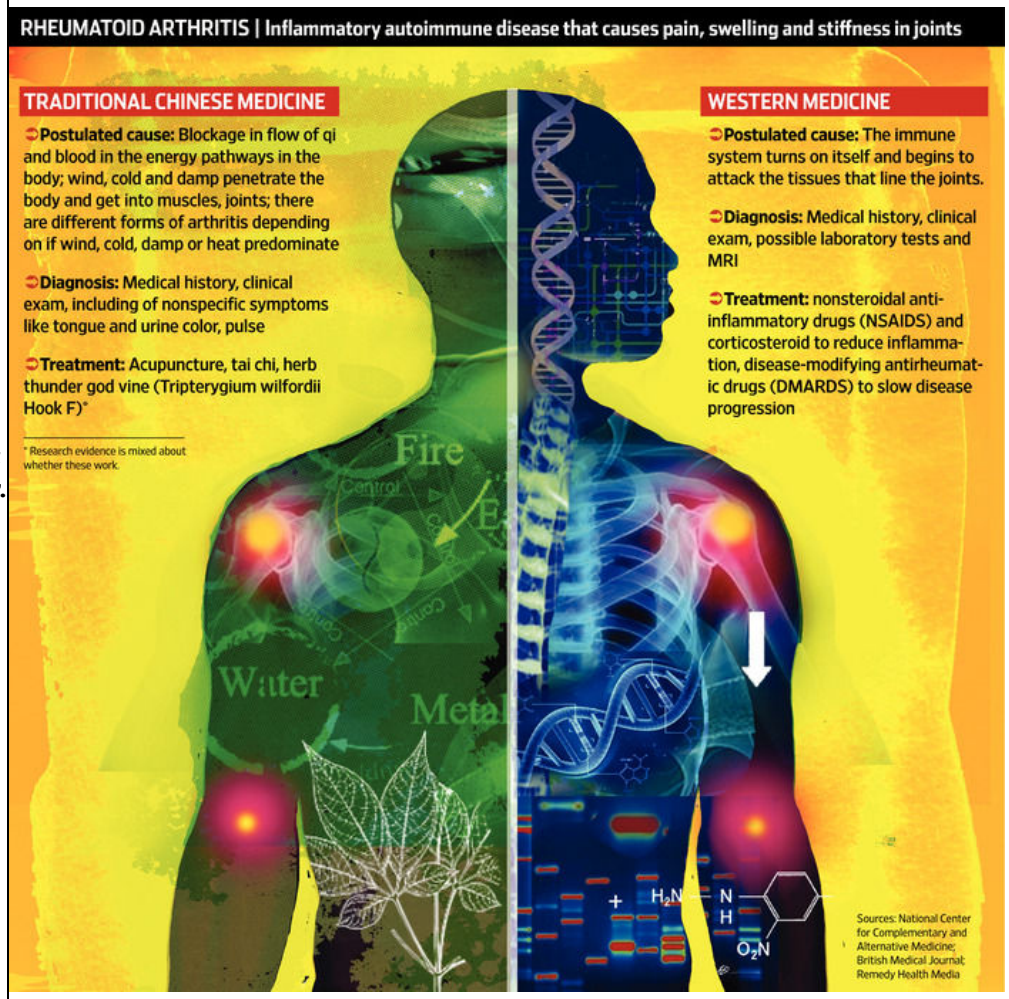
**Science Source/Photo Researchers Inc.**

Now researchers in some the most highly respected universities in China, and increasingly in Europe and the U.S., are wedding Western techniques for analyzing complex biological systems to the Chinese notion of seeing the body as a networked whole. The idea is to study how genes or proteins interact throughout the body as a disease develops, rather than to examine single genes or molecules.

"Traditional Chinese medicine views disease as complete a pattern as possible," says Jennifer Wan, a professor in the school of biological sciences at the University of Hong Kong who studies traditional Chinese medicine, or TCM. "Western medicine tends to view events or individuals as discrete particles." But one gene or biological marker alone typically doesn't yield comprehensive understanding of disease, she says.

To reach these goals, the overall quality of research on traditional Chinese medicine must improve. With studies of Chinese herbal remedies, for instance, rarely are scientists expected to provide authentication of herbs they're studying, which makes it difficult to know what's really in the concoctions. This hurdle also makes it harder for other scientists to replicate the findings, says Qihe Xu, a professor in renal medicine at King's College London. Dr. Xu served as the coordinator of a recent 200-scientist consortium to study good practices for studying traditional Chinese medicine, dubbed GP-TCM.

TCM treatments of herbal concoctions could be authenticated and standardized with more scientific study, and could serve as leads for drug development, experts say.




**Eva Tatcheva**

One example of this possible development is Yale University pharmacology professor Yung-Chi Cheng 's work looking at four-herb combination known as PHY906 for reducing the side effects of chemotherapy. The treatment appears to contain more than 60 chemicals. Researchers are studying it for its ability to reduce nausea and diarrhea and to enhance colon-cancer treatment.

The field also must develop standard definitions and ways of measuring TCM syndromes, important for research and clinical care, Dr. Xu says. His European Union-funded consortium published a set of guidelines for good practices last year in the journal BMC Complementary and Alternative Medicine, one of about 50 papers published by the consortium since 2010.

"If it's not reproducible, it's not science," he says.

According to traditional Chinese medicine, disease arises from imbalances in the body due to unhealthy factors in the natural environment and one's lifestyle. General symptoms like dry mouth or film coating the tongue are signals that certain bodily systems are out of whack. While these signs may be ignored by Western doctors more focused on more specific ailments, TCM doctors often use the symptoms as guides for treating patients.

A doctor practicing TCM who knows whether someone has hot or cold syndrome could use that as a first clue in testing for problems involving the immune or metabolic system. Those problems could include gastritis, colitis, rheumatoid arthritis or cancer. One day there also may be effective treatments if a person's constitution is taken into account when treating them, says Shao Li, deputy director of the bioinformatics division at Tsinghua University in Beijing.

In cities throughout China, doctors practicing Western and Chinese medicine can both be found. Many patients go to Western doctors for certain situations, such as acute illness, but seek out TCM guidance in others, often to prevent disease.

TCM was largely ignored by Western medicine until recent years, but is slowly gaining traction among some scientists and clinicians. The Cleveland Clinic in Ohio recently opened a herbal therapy center. The U.S. government established the National Center for Complementary and Alternative Medicine in 1998. The organization now has a budget of over $120 million to fund research on the efficacy and safety of alternative medicines, including those rooted in traditional Chinese medicine.

One promising area of TCM research several independent groups of scientists are investigating is the notion of hot and cold syndromes. The work is still in its early stages. But it could result in a new direction for TCM research by using the systems biology approach and integrating it with experience gleaned from TCM patient care, says Yale's Dr. Cheng, who also serves as chairman of the Consortium for the Globalization of Chinese Medicine.

In a series of studies, Tsinghua's Dr. Li and his colleagues examined people with hot and cold syndromes and whether they exhibited different signs of illness, including gastritis, a common digestive disorder in which the lining of the stomach becomes inflamed or irritated.

To gauge whether gastritis patients had cold or hot syndromes, researchers asked questions like whether individuals had chilly body parts or exhibited a preference for hot beverages or a susceptibility to catching colds. Doctors dug into their subjects' emotional states, asking whether they experienced so-called cold feelings like apathy. The scientists also measured proteins linked to gastritis and took measurements of the bacteria in the gut and imaged the bacteria in the tongue's coating.

They found some variations depending on whether patients were identified as hot or cold. They also found differences in the bacteria of patients' tongues that corresponded with tongue coating color and whether patients had been diagnosed with hot or cold syndrome.

These results suggest that some easily detectable and nonspecific symptoms could be clinically useful, Dr. Li says. However, it remains to be seen whether gastritis patients classified as having hot syndrome would actually respond to different treatment than those classified as cold.

In the Netherlands, Jan van der Greef, a professor of analytical biosciences at Leiden University, and his colleagues have looked at how getting classified as having hot or cold symptoms relates to rheumatoid arthritis.

They had a Chinese medicine expert identify participants by type and studied a network of chemicals produced by the body related to the immune system. They found higher levels of one steroid and 11 other molecules in the urine of arthritis patients depending on their TCM diagnosis.

That could mean that they would benefit from different disease-management strategies. Cold patients might benefit more from hormone treatments like prednisone, while hot patients might benefit from immune therapies, says Herman van Wietmarschen, a postdoctoral researcher at the Netherlands Organization of Applied Scientific Research and the first author on the paper. They published their work in PLOS One in 2012.

In another study, published in Molecular BioSystems in 2012, Dr. van der Greef's group looked at another important TCM construct known as Qi, known as life energy, or the forces within the human body and the environment. Again, they found differences between biological markers in the urine of people with different body classifications. TCM-based symptom patterns could be suitable for early detection of health problems, the authors say.

Dr. Li's group continues to test the biomarkers associated with cold and hot syndrome to subtype other kinds of diseases, including cancer. The next step would be to develop more individualized treatment for such complex diseases based on syndrome type.

The researchers believe that "in such a big-data era, a new way can be eventually found to connect Eastern and Western medicine at the molecular and systematic levels," Dr. Li wrote in an email.

http://bit.ly/1xcPqYS

## A Direct Link between Climate Change and the Emergence of Infectious Diseases

***Researchers Discover Connection between Climate and Emerging Diseases***

A team of researchers has established a direct link between climate change and the emergence of infectious diseases, showing a correlation between epidemic peaks and rainy periods for Buruli ulcer observed over a 40-year period in French Guyana.

**New diseases**

Climate change may affect human health directly or indirectly. In addition to increased threats of storms, flooding, droughts, and heat waves, other health risks are being identified. In particular, new diseases are appearing, caused by infectious agents (viruses, bacteria, parasites) heretofore unknown or that are changing, especially under the effect of changes in the climate (change of host, vector, pathogenicity, or strain). These are so-called "emerging" or "re-emerging" infectious diseases, such as leishmaniasis, West Nile fever, etc. According to the WHO, these diseases are causing one third of deaths around the world, and developing countries are on the front line.

**A difficult relationship to establish**

Several parameters may be behind this increased spread of pathogens and their hosts (vectors, reservoirs, etc.). Climate change modifies temperature and humidity conditions in natural environments, and therefore alters the transmission dynamics for the infectious agents. It also affects the range, abundance, behavior, biological cycles, and life history traits of the microbes or related host species, changing balances between pathogens, vectors, and reservoirs. However, these effects remain poorly explained, in particular because they require an understanding of the long-term spatial or temporal changes to the phenomena. Therefore, it is difficult to establish a direct link between climate change and the overall evolution of infectious pathologies.

**Decreased rainfall rhymes with epidemic**

Providing some clarification on this question for the first time, a study by IRD researchers and their partners has shown the relationship over a 40-year period between climate change and epidemics of a disease emerging in Latin America: Buruli ulcer. Rising surface temperatures in the Pacific Ocean tend to increase the frequency of El Niño events, which especially affect Central and South America approximately every five to seven years, causing waves of droughts. The research team compared changes in rainfall in the region with changes in the number of cases of Buruli ulcer recorded in French Guyana since 1969 and observed the statistical correlations.

In fact, the decrease in rainfall and runoff led to an increase in areas of residual stagnant water, where the bacteria responsible, Mycobacterium ulcerans , proliferates. The greater access to swampy habitats that results from this facilitates frequentation by humans (fishing, hunting, etc.) and thus intensifies human exposure to the microorganism living in this type of aquatic environment. This result, published in Emerging Microbes and Infections – Nature, was made possible through long-term time series data.

In light of the rainfall conditions in recent years, the researchers fear a potential new outbreak of Buruli ulcer in the region. Beyond an improvement in forecasting the risk of an epidemic, this study highlights the need to consider a set of parameters and their interactions. Contrary to the accepted idea, less rainfall does not mean a certain decrease in the prevalence of infectious diseases, as shown by this example. Similarly, the expected warming of the atmosphere could provide temperature conditions unsuitable to the development cycle of some pathogenic agents, such as for malaria in Africa.

*Publication: Aaron Morris, et al., "Complex temporal climate signals drive the emergence of human water-borne disease," Emerging Microbes & Infections (2014) 3, e56; doi:10.1038/emi.2014.56*

*Source: IRD: Institute of Research for Development*

http://www.eurekalert.org/pub_releases/2014-11/nrao-bop110514.php

## Birth of planets revealed in astonishing detail in ALMA's 'best image ever'

***Best image ever of planet formation around an infant star***

Astronomers have captured the best image ever of planet formation around an infant star as part of the testing and verification process for the Atacama Large Millimeter/submillimeter Array's (ALMA) new high-resolution capabilities.

This revolutionary new image reveals in astonishing detail the planet-forming disk surrounding HL Tau, a Sun-like star located approximately 450 light-years from Earth in the constellation Taurus.

ALMA uncovered never-before-seen features in this system, including multiple concentric rings separated by clearly defined gaps. These structures suggest that planet formation is already well underway around this remarkably young star.

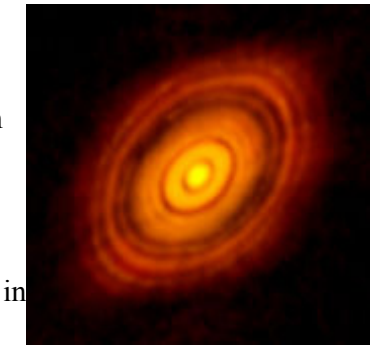
"These features are almost certainly the result of young planet-like bodies that are being formed in the disk. This is surprising since HL Tau is no more than a million years old and such young stars are not expected to have large planetary

bodies capable of producing the structures we see in this image," said ALMA Deputy Director Stuartt Corder.

All stars are believed to form within clouds of gas and dust that collapse under gravity. Over time, the surrounding dust particles stick together, growing into sand, pebbles, and larger-size rocks, which eventually settle into a thin protoplanetary disk where asteroids, comets, and planets form. Once these planetary bodies acquire enough mass, they dramatically reshape the structure of their natal disk, fashioning rings and gaps as the planets sweep their orbits clear of debris and shepherd dust and gas into tighter and more confined zones.

The new ALMA image reveals these striking features in exquisite detail, providing the clearest picture to date of planet formation. Images with this level of detail were previously only seen in computer models and artist concepts. ALMA, living up to its promise, has now provided direct proof that nature and theory are very much in agreement.

"This new and unexpected result provides an incredible view of the process of planet formation. Such clarity is essential to understand how our own Solar System came to be and how planets form throughout the Universe," said Tony Beasley, director of the National Radio Astronomy Observatory (NRAO) in Charlottesville, Virginia, which manages ALMA operations for astronomers in North America.



***This is an ALMA image of the young star HL Tau and its protoplanetary disk. This best image ever of planet formation reveals multiple rings and gaps that herald the presence of emerging planets as they sweep their orbits clear of dust and gas*** **ALMA (NRAO/ESO/NAOJ); C. Brogan, B. Saxton (NRAO/AUI/NSF)**

HL Tau is hidden in visible light behind a massive envelope of dust and gas. Since ALMA observes at much longer wavelengths, it is able to peer through the intervening dust to study the processes right at the core of this cloud. "This is truly one of the most remarkable images ever seen at these wavelengths. The level of detail is so exquisite that it's even more impressive than many optical images. The fact that we can see planets being born will help us understand not only how planets form around other stars but also the origin of our own Solar System," said NRAO astronomer Crystal Brogan.

ALMA's new high-resolution capabilities were achieved by spacing the antennas up to 15 kilometers apart. This baseline at millimeter wavelengths enabled a resolution of 35 milliarcseconds, which is equivalent to a penny as seen from more than 110 kilometers away.

"Such a resolution can only be achieved with the long baseline capabilities of ALMA and provides astronomers with new information that is impossible to collect with any other facility, including the best optical observatories," noted ALMA Director Pierre Cox.

These long baselines fulfill one of ALMA's major objectives and mark an impressive technological and engineering milestone. Future observations at ALMA's longest possible baseline of 16 kilometers will produce even clearer images and continue to expand our understanding of the cosmos.

"This observation illustrates the dramatic and important results that come from NSF supporting world-class instrumentation such as ALMA," said Fleming Crim, the National Science Foundation assistant director for Mathematical and Physical Sciences. "ALMA is delivering on its enormous potential for revealing the distant Universe and is playing a unique and transformational role in astronomy."

*The National Science Foundation and the NRAO will expand on this news at a Google Hangout on Nov. 6 at 10:00 EST. Tune in at https://plus.google.com/events/ceul1hkj60se5uts2u75rgqe7rc*

***http://www.wired.com/2014/11/ebola-drug-science-zmab-zmapp/***

## How One Experimental Drug May Be Defeating Ebola and Saving People

***Since the worst Ebola outbreak on record ignited last December in West Africa, scientists have been racing to develop drugs and vaccines to combat the virus.***

**By Nadia Drake**

Several experimental drugs have been given to patients, and a new study details how scientists think one of those drugs might neutralize the virus.

The research focused on three antibodies, two of which are part of the experimental drug known as ZMapp. It hasn't been officially tested in human clinical trials yet, but seven patients have received the drug so far this year. Though Ebola fatality rates sometimes approach 90 percent, five of the patients receiving ZMapp survived, including Americans Nancy Writebol and Kent Brantly. The drug has been shown to be incredibly efficient at treating Ebola infections in monkeys, all of which survived when treated. But it's unknown how much the drug contributed to the human patients' survival.

Designing better drugs means understanding why the ones we have work, so a team of scientists recently took a close look at how some of the drug's ingredients combat Ebola virus particles, and published the results today in Scientific Reports. The trio of antibodies the scientists studied are part of a drug cocktail known as ZMAb, which has been shown to treat Ebola infections in mice, guinea pigs and monkeys.

Antibodies are proteins that recognize and respond to foreign substances, such as bacteria and viruses. ZMAb sends its three antibodies to find and knock out Ebola virus particles. In short, they interfere with the mechanism the virus uses to slip into host cells, keeping viral numbers low enough for the immune system to do its job.

All three antibodies target and bind to a protective protein the virus wears, called a glycoprotein. These glycoproteins protrude in spikes from the noodle-shaped Ebola particles and are essential both for infiltrating host cells and evading the host's immune response.

The two of those three antibodies that are also used in the ZMapp drug, known as 2G4 and 4G7, adhere to sites near the base of the glycoprotein, near a border between two of the protein's movable subunits. These antibodies appear to pin the protein together and prevent it from changing shape, which scientists think is a key maneuver during viral invasion of host cells.

"The antibodies are like molecular staples, or burly wrestlers pinning you down so you can't move," said Kartik Chandran, a virologist at Albert Einstein College of Medicine, who studies how Ebola virus gets into cells. "One of the virus' Achilles heels is that they transform during infection. They're like Swiss Army knives. Antibodies that can staple together two parts of the protein that move relative to each other are basically a good antiviral."

The third antibody that isn't part of the ZMapp combo doesn't appear to be as potent a neutralizer as the first two. But scientists think it might be playing a role in attracting immune cells to the pinned virus. "Those could destroy viruses or infected cells," said Erica Ollmann Saphire, a virologist at The Scripps Research Institute.

***Scientists grew the ZMAb antibodies using mice that had been exposed to fragments of Ebola virus. But before those antibodies can be used in drugs for humans, they need to be "humanized." The term describes the process of replacing non-human genetic sequences with corresponding human sequences. These substitutions generate a part-human, part-mouse antibody that flies under the radar of the human immune system. If immune cells detected a foreign mouse protein in their midst, for example, they might mount an immune response against that protein rather than the virus the protein was targeting.***

The precise mechanics of the antiviral onslaught aren't totally worked out, but it's clear that a combination of three antibodies works better than any single antibody on its own. One explanation, perhaps, is that it's tricky for a virus to mutate and escape the activity of three antibodies at the same time, and that mutating and eluding just one is much easier.

That's one of the reasons scientists often mix antibodies into cocktails, as they've done with ZMapp.

The antibodies in that cocktail have been modified slightly for use in humans (see sidebar), but scientists don't think that process (called "humanizing") will change how the proteins interact with Ebola virus particles.

"What is the likelihood that the mouse and humanized antibodies work in the same way? That's highly likely," said viral immunologist James Crowe Jr. of Vanderbilt University, who is also working on developing Ebola antibodies.

***http://www.eurekalert.org/pub_releases/2014-11/osu-nra110614.php***

## New research adds spice to curcumin's health-promoting benefits

***Newly created turmeric-based formulation releases anti-inflammatory power throughout body***

COLUMBUS, Ohio - The health benefits of over-the-counter curcumin supplements might not get past your gut, but new research shows that a modified formulation of the spice releases its anti-inflammatory goodness throughout the body.

Curcumin is a naturally occurring compound found in the spice turmeric that has been used for centuries as an Ayurvedic medicine treatment for such ailments as allergies, diabetes and ulcers.

Anecdotal and scientific evidence suggests curcumin promotes health because it lowers inflammation, but it is not absorbed well by the body. Most curcumin in food or supplements stays in the gastrointestinal tract, and any portion that's absorbed is metabolized quickly.

Many research groups are testing the compound's effects on disorders ranging from colon cancer to osteoarthritis. Others, like these Ohio State University scientists, are investigating whether enabling widespread availability of curcumin's biological effects to the entire body could make it useful both therapeutically and as a daily supplement to combat disease.

"There's a reason why this compound has been used for hundreds of years in Eastern medicine. And this study suggests that we have identified a better and more effective way to deliver curcumin and know what diseases to use it for so that we can take advantage of its anti-inflammatory power," said Nicholas Young, a postdoctoral researcher in rheumatology and immunology at Ohio State and lead author of the study.

The research is published in the Nov. 4, 2014, issue of the journal PLOS ONE.

Curcumin powder was mixed with castor oil and polyethylene glycol in a process called nano-emulsion (think vinaigrette salad dressing), creating fluid teeming with microvesicles that contain curcumin.

This process allows the compound to dissolve and be more easily absorbed by the gut to enter the bloodstream and tissues.

Feeding mice this curcumin-based drug shut down an acute inflammatory reaction by blocking activation of a key protein that triggers the immune response. The researchers were also the first to show that curcumin stops recruitment of specific immune cells that, when overactive, are linked to such problems as heart disease and obesity.

Young and his colleagues, including co-senior authors Lai-Chu Wu and Wael Jarjour of the Division of Rheumatology and Immunology at Ohio State's Wexner Medical Center, now want to know if curcumin in this form can counter the chronic inflammation that is linked to sickness and age-related frailty. They have started with animal studies testing nano-emulsified curcumin's ability to prevent or control inflammation in a lupus model.

"We envision that this nutraceutical could be used one day both as a daily supplement to help prevent certain diseases and as a therapeutic drug to help combat the bad inflammation observed in many diseases," Young said. "The distinction will then be in the amount given - perhaps a low dose for daily prevention and higher doses for disease suppression." The term nutraceutical refers to foods or nutrients that provide medical or health benefits.

The curcumin delivery system was created in Ohio State's College of Pharmacy, and these researchers previously showed that concentrations of the emulsified curcumin in blood were more than 10 times higher than of curcumin powder suspended in water.

From there, the researchers launched experiments in mice and cell cultures, generating artificial inflammation and comparing the effects of the nano-emulsified curcumin with the effects of curcumin powder in water or no treatment at all.

The researchers injected mice with lipopolysaccharide, a bacteria cell wall extract that stimulates an immune reaction in animals. Curcumin can target many molecules, but the research team zeroed in on NF-kB, a protein that is known to play an important role in the immune response.

In a specialized imaging machine, mice receiving plain curcumin lit up with bioluminescent signals indicating that NF-kB was actively triggering an immune response, while mice receiving nano-emulsified curcumin showed minimal signs - a 22-fold reduction - that the protein had been activated at all.

Knowing that curcumin delivered in this way could shut down NF-kB activation throughout the animals' bodies, researchers looked for further details about the compound's effects on inflammation.

They found that nano-emulsified curcumin halted the recruitment of immune cells called macrophages that "eat" invading pathogens but also contribute to inflammation by secreting pro-inflammatory chemicals. And in cells isolated from human blood samples, macrophages were stopped in their tracks.

"This macrophage-specific effect of curcumin had not been described before," Young said. "Because of that finding, we propose nano-emulsified curcumin has the best potential against macrophage-associated inflammation."

Inflammation triggered by overactive macrophages has been linked to cardiovascular disease, disorders that accompany obesity, Crohn's disease, rheumatoid arthritis, inflammatory bowel disease, diabetes and lupus-related nephritis.

*This work was supported by The Ohio State University Wexner Medical Center and Comprehensive Cancer Center Support (CORE) grant from the National Institutes of Health/National Cancer Institute and funding for Ohio State's Center for Clinical and Translational Science provided by the National Center for Advancing Translational Sciences. Additional co-authors are Michael Bruss, Mark Gardner, William Willis and Giancarlo Valiente of the Division of Rheumatology and Immunology; Xiaokui Mo of the Center for Biostatistics; and Yu Cao and Zhongfa Liu of the College of Pharmacy, all at Ohio State.*

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***http://www.bbc.com/news/business-28212223***

## Pharmaceutical industry gets high on fat profits

***Imagine an industry that generates higher profit margins than any other and is no stranger to multi-billion dollar fines for malpractice.***

**By Richard Anderson Business reporter, BBC News**

Throw in widespread accusations of collusion and over-charging, and banking no doubt springs to mind. In fact, the industry described above is responsible for the development of medicines to save lives and alleviate suffering, not the generation of profit for its own sake.

Pharmaceutical companies have developed the vast majority of medicines known to humankind, but they have profited handsomely from doing so, and not always by legitimate means.

Last year, US giant Pfizer, the world's largest drug company by pharmaceutical revenue, made an eye-watering 42% profit margin. As one industry veteran understandably says: "I wouldn't be able to justify [those kinds of margins]."

Stripping out the one-off $10bn (£6.2bn) the company made from spinning off its animal health business leaves a margin of 24%, still pretty spectacular by any standard.

In the UK, for example, there was widespread anger when the industry regulator predicted energy companies' profit margins would grow from 4% to 8% this year.

Last year, five pharmaceutical companies made a profit margin of 20% or more - Pfizer, Hoffmann-La Roche, AbbVie, GlaxoSmithKline (GSK) and Eli Lilly.

## 'Profiteering'

With some drugs costing upwards of $100,000 for a full course, and with the cost of manufacturing just a tiny fraction of this, it's not hard to see why.

Last year, 100 leading oncologists from around the world wrote an open letter in the journal Blood calling for a reduction in the price of cancer drugs.

Dr Brian Druker, director of the Knight Cancer Institute and one of the signatories, has asked: "If you are making $3bn a year on [cancer drug] Gleevec, could you get by with $2bn? When do you cross the line from essential profits to profiteering?"

And it's not just cancer drugs - between April and June this year, drug company Gilead clocked sales of $3.5bn for its latest blockbuster hepatitis C drug Sovaldi.

Drug companies justify the high prices they charge by arguing that their research and development (R&D) costs are huge.

On average, only three in 10 drugs launched are profitable, with one of those going on to be a blockbuster with $1bn-plus revenues a year. Many more do not even make it to market.

But as the table below shows, drug companies spend far more on marketing drugs - in some cases twice as much - than on developing them. And besides, profit margins take into account R&D costs.

**World's largest pharmaceutical firms**

| *Company* | *Total revenue ($bn)* | *R&D spend ($bn)* | *Marketing spend ($bn)* | *Profit ($bn)* | *Profit margin (%)* |
|---|---|---|---|---|---|
| ***Johnson & Johnson (US)*** | *71.3* | *8.2* | *17.5* | *13.8* | *19* |
| ***Novartis (Swiss)*** | *58.8* | *9.9* | *14.6* | *9.2* | *16* |
| ***Pfizer (US)*** | *51.6* | *6.6* | *11.4* | *22.0* | *43* |
| ***Hoffmann-La Roche (Swiss)*** | *50.3* | *9.3* | *9.0* | *12.0* | *24* |
| ***Sanofi (France)*** | *44.4* | *6.3* | *9.1* | *8.5* | *11* |
| ***Merck (US)*** | *44.0* | *7.5* | *9.5* | *4.4* | *10* |
| ***GSK (UK)*** | *41.4* | *5.3* | *9.9* | *8.5* | *21* |
| ***Astra Zeneca (UK)*** | *25.7* | *4.3* | *7.3* | *2.6* | *10* |
| ***Eli Lilly (US)*** | *23.1* | *5.5* | *5.7* | *4.7* | *20* |
| ***AbbVie (US)*** | *18.8* | *2.9* | *4.3* | *4.1* | *22* |

**Source: GlobalData**

The industry also argues that the wider value of the drug needs to be considered.

"Drugs do save money over the longer term," says Stephen Whitehead, chief executive of the Association of the British Pharmaceuticals Industry (ABPI).

"Take hepatitis C, a shocking virus that kills people and used to require a liver transplant. At £35,000 [to £70,000] for a 12-week course, 90% of people are now cured, will never need surgery or looking after, and can continue to support their families. "The amount of money saved is huge."

True, but just because you can charge a high price for something does not necessarily mean you should, especially when it comes to health, critics such as Dr Drucker might say. Shareholders, who big pharma companies ultimately have to answer to, would have little time for such an argument.

## No loyalty

Big pharma companies also say they only have a limited time in which to make profits. Patents are generally awarded for 20 years, but 10-12 of those are typically spent developing the drug at a cost of about $1.5bn-$2.5bn.

This leaves eight to 10 years to make money before the formula can be taken up by generic drug companies, which sell the medicines for a fraction of the price.

Clearly for a real blockbuster, it can take a matter of months to recoup development costs.

Once this happens, sales fall by 90%-plus. As Joshua Owide, director of healthcare industry dynamics at research company GlobalData, explains, "Unlike other sectors, brand loyalty goes out the window when patents expire."

This is why pharma companies go to such extraordinary lengths to extend their patents - a process known as evergreening - employing "floors full of lawyers" for this express purpose, one industry insider says.

For a drug raking in $3bn a quarter, even a one-month extension can be worth huge sums of money.

New formulations, combining two existing drugs to give a wider use, and enantiomers - a mirror image of the same compound - are some of the legal ways to eke out patents. But some drug companies, including the UK's GSK, have been accused of more underhand tactics, such as paying generics to delay the release of their cheaper alternatives.

As the loss of sales at the big pharma companies far outweighs the revenue made by the generics, this can be an attractive arrangement for both parties.

## Courting doctors

But drug companies have been accused of, and admitted to, far worse.

Until recently, paying bribes to doctors to prescribe their drugs was commonplace at big pharmas, although the practice is now generally frowned upon and illegal in many places. GSK was fined $490m in China in September for bribery and has been accused of similar practices in Poland and the Middle East.

The rules on gifts, educational grants and sponsoring lectures, for example, are less clear cut, and these practices remain commonplace in the US.

Indeed a recent study found that doctors in the US receiving payments from pharma companies were twice as likely to prescribe their drugs.

This may well exacerbate the problem of overspending on drugs by governments.

A recent study by Prescribing Analytics suggested that the UK's National Health Service could save up to £1bn a year by doctors switching from branded to equally effective generic versions of the drugs.

**Big pharmaceutical fines**

***$3bn Glaxo SmithKline, 2012, over promoting Paxil for depression to under-18s***
***$2.3bn Pfizer, 2009, over misbranding painkiller Bextra***
***$2.2bn Johnson & Johnson, 2013, for promoting drugs not approved as safe***
***$1.5bn Abbott, 2012, over illegal promotion of antipsychotic drug Depakote***
***$1.42bn Eli Lilley, 2009, for wrongly promoting antipsychotic drug Zyprexa***
***$950m Merck, 2011, for illegally promoting painkiller Vioxx***

**Source: ProPublica**

This all may change when new rules in the US and UK will force doctors to disclose all gifts and payments made by the industry.

Drug companies have also been accused of colluding with chemists to overcharge for their medicines and of publishing trial data that highlight the positive at the expense of the negative.

They have also been found guilty of mis-branding and wrongly promoting various drugs, and have been fined billions as a result.

The rewards are so great, it would seem, that pharma companies have continually been prepared to push the boundaries of legality.

**'Undue influence'**

No wonder, then, that the World Health Organisation (WHO) has talked of the "inherent conflict" between the legitimate business goals of the drug companies and the medical and social needs of the wider public.

Indeed the Council of Europe is launching an investigation into "protecting patients and public health against the undue influence of the pharmaceutical industry".

It will look at "particular practices such as sponsoring health professionals by the industry... or recourse by public health institutions to the knowledge of highly specialised researchers on the pay-rolls of industry".

No matter what the outcome of such investigations, however, the pharmaceutical industry is facing fundamental change, as the traditional model of developing drugs breaks down due to rising costs and scientific advances.

The cosy world of big pharmaceuticals is under threat like never before.

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

## First world war dysentery bug was penicillin-resistant

***Even if penicillin were available, dysentery would have been deadly***

**00:01 07 November 2014 by Andy Coghlan**

Ernest Cable was a British soldier who died in 1915 from dysentery caught in the trenches of northern France during the first world war. Even if penicillin had been available to treat him, he would still have died because the bacterium that made him sick, Shigella flexneri, was already resistant to the world's first antibiotic. That was years before Alexander Fleming discovered it in 1928.

Nor would he have been saved by erythromycin, which was discovered later, in 1949. The bacterium was found to be resistant to that too.

These historical insights into antibiotic resistance, now described as a global epidemic, come from DNA sequencing of the bacterial strain that killed Cable to mark the centenary of the first world war.

"Cable is almost like the unknown soldier in that he has no known relatives, but now everyone will remember him, so he's been immortalised in a sense," says Kate Baker of the Wellcome Trust Sanger Institute in Hinxton, Cambridge.

Baker says that the resistance they found is the result of an evolutionary arms race between rival microbes. Whenever one species evolves a chemical like penicillin that kills its neighbours, others will evolve resistance to it. The yeast makes an antibiotic to kill its neighbours, that might include Shigella. Sooner or later, the bacterium (and other species) will evolve resistance to the penicillin. The yeast evolves more powerful penicillin-like antibiotics, and the bugs develop resistance again, and so the cycle continues: "You have to remember penicillin is a natural compound, so bacteria living next to yeasts that make it evolve ways to evade it and survive," says Baker.

Codenamed NCTC1, and collected in 1915 by military bacteriologist William Broughton-Alcock in the hospital in Wimereux, France, where Cable was treated, the bacterial strain was the first sample deposited in the UK National Collection of Type Cultures, which today holds 5600 strains. Cable died on 13 March 1915, aged 28, and was buried in a cemetery in Wimereux.

Now, 100 years on, the genome of the bug that killed him has been completely sequenced and compared with three more recent S. flexneri strains, one from Japan in 1954 and two from China, in 1984 and 2002.

Baker found that although 98 per cent of the bacterial DNA is still the same, the more recent strains have acquired extra genes and mutations that give them resistance to many modern antibiotics, including sulphonamides, tetracycline and other beta-lactamase antibiotics.

"They've kept evolving, and that's because of the widespread clinical use of antibiotics," she says. "Our results tell us that their evolution is very targeted, and tailored to the pressures that we've thrown at them." Baker says that mutations of the ampC gene that made the 1915 strain resistant to penicillin have since given it much broader resistance to other beta-lactamase antibiotics.

Extra genes added since 1915 have also made modern-day strains more dangerous. "The most important new virulence genes make enterotoxins, which are associated with much more severe symptoms," says Baker. They worsen dehydration by ramping up fluid secretion by the intestine, she says. The most recent strain, from China in 2002, had also lost a protein from its surface which would have been recognised by the immune systems of patients who'd survived infections with the earlier strains. "It means that people resistant to the older strains would have been susceptible to the disease again, because their immune systems wouldn't recognise the strain without the surface protein," says Baker.

The insights from the historical comparison could be valuable for designing a vaccine against shigella, which still kills 750,000 children under 5 each year. "By showing us what parts of the genome have been constant for the past 100 years, historical isolates can help us select vaccine targets, to make sure we don't target any parts that have changed over time," says Baker. The institute has also produced a short film describing the project, and an account of how private cable was identified and traced.

Other bacteriologists said that the 1915 strain harboured the resistance expected for the pre-antibiotic era, to penicillin-like compounds through the ampC gene and to erythromycin through mechanisms for physically pumping the antibiotic out of the bacterial cell. The more recent strains, by contrast, add resistance to a host of antibiotics introduced over the past 60 years. "These bookend sequences show the impact of antibiotic use and resistance evolution in the antibiotic era," says Gerry Wright of McMaster University in Hamilton, Ontario, Canada.

*Journal reference: The Lancet, DOI: 10.1016/S0140-6736(14)61789-X*
*Historical account of how the sample was collected: The Lancet, DOI: 10.1016/S0140-6736(14)61790-6*

***http://www.bbc.com/news/health-29935449***

## Parkinson's stem cell 'breakthrough'

***Stem cells can be used to heal the damage in the brain caused by Parkinson's disease, according to scientists in Sweden.***

They said their study on rats heralded a "huge breakthrough" towards developing effective treatments. There is no cure for the disease, but medication and brain stimulation can alleviate symptoms. Parkinson's UK said there were many questions still to be answered before human trials could proceed.

The disease is caused by the loss of nerve cells in the brain that produce the chemical dopamine ,which helps to control mood and movement.

To simulate Parkinson's, Lund University researchers killed dopamine-producing neurons on one side of the rats' brains. They then converted human embryonic stem cells into neurons that produced dopamine. These were injected into the rats' brains, and the researchers found evidence that the damage was reversed.

There have been no human clinical trials of stem-cell-derived neurons, but the researchers said they could be ready for testing by 2017. Malin Parmar, associate professor of developmental and regenerative neurobiology, said: "It's a huge breakthrough in the field [and] a stepping stone towards clinical trials."

A similar method has been tried in a limited number of patients. It involved taking brain tissue from multiple aborted foetuses to heal the brain. Clinical trials were abandoned after mixed results, but about a third of the patients had foetal brain cells that functioned for 25 years.

Using embryonic stem cells may be preferable, as it is easier to get hold of the large numbers of cells needed for transplant by growing them in the laboratory. It also opens up the possibility of using less ethically charged sources of stem cells, such as those made from adult tissue.

The charity Parkinson's UK said the research "could be a stride towards clinical trials in people with Parkinson's". Its director of research and development, Arthur Roach, said: "This important research is a key step along the way in helping us to understand how stem cells might shape future Parkinson's treatments. "There are important potential advantages of these cells over the foetal-derived cells used in past cell transplantation work. "This study could be a stride towards clinical trials in people with Parkinson's but there are still many questions that need to be answered before this development can be tested in people with the condition."

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

## Custom evolution boosts an enzyme for power plant carbon capture

***Press fast-forward on evolution and tell it where to go.***

**by Scott K. Johnson - Nov 7 2014, 4:32am TST**

We can't just shutter the world's fossil fuel power plants tomorrow, but in a perfect world, we could eliminate the greenhouse-enhancing $CO_2$ coming out of the stacks. While it's not a perfect world just yet, techniques to capture that $Co_2$ *are* being developed—especially for coal plants, which emit the most $CO_2$ per Watt of power generated. Two major obstacles stand between here and there: the infrastructure to store the captured $CO_2$ deep underground (or in other ways) and the cost of capturing the $CO_2$.

For traditional coal plants, this involves some way to separate $CO_2$ out of the mix of gases coming through the exhaust stream. A common technique uses amine solutions, which latch on to the $CO_2$ chemically, releasing it later when the solution is heated. That means that some of the heat produced by the burning coal has to be used for the $CO_2$-capture process, rather than producing electricity.

But a new study suggests there may be a way to sacrifice a bit less energy while still capturing the carbon. Its authors evolved one of nature's most efficient enzymes to get it to convert carbon dioxide to carbonate ions within the hot, chemically complex environment where carbon capture takes place.

The process would still use amines, but not the ones used in the existing process. Other types of amine solutions give up their $CO_2$ at lower temperatures, which would make the process much more efficient. Unfortunately, those solutions don't work fast enough on the capture side to be realistic options.

There is, however, an incredibly fast enzyme most organisms use to grab and transport $CO_2$ called carbonic anhydrase, and it could potentially speed up those slow amine solutions. (It acts by merging $CO_2$ and water to create a carbonate ion.) The next problem? That enzyme can't handle the high-temperature and high-pH environment of the carbon capture process.

A group of industry researchers came up with a plan of attack to solve this problem: if evolution hasn't put the item you want on the menu, order it custom. Using a very advanced method of artificial selection, they evolved a version of the enzyme that could operate under harsh conditions.

The researchers took the gene for the enzyme from a species of bacteria and created a multitude of variants by swapping in different codons at random. Each variant was inserted into *E. coli* bacteria, which were allowed to grow and produce lots of the enzyme. Each version of the enzyme, with its single mutation, was then extracted and tested in amine solutions at progressively higher temperatures as the project progressed.

Mutations that improved the enzyme's function were combined together in subsequent rounds of testing, with additional mutations sprinkled in to keep things moving forward. In the end, the variant of the enzyme they crowned contained 36 mutations, which collectively altered about 15 percent of the genetic sequence.

The resulting enzyme could function about 100,000 times longer at 50°C than the enzyme they started with, which would lose half its activity after just 15 minutes. In fact, the mutated enzyme could tolerate temperatures over 100°C.

Leaving the laboratory, the researchers took their enzyme to a carbon capture research center in Alabama, where it could be used to treat emissions from a coal-fired power plant. They added it to a slow-absorbing amine solution that gives up its $CO_2$ at 87 °C, rather than around 100 °C. An enzyme-free system was also run for a head-to-head comparison over the six-day test.

The amine solution with the enzyme added absorbed carbon dioxide 25 times faster than the enzyme-free solution, and it maintained its performance throughout the test.

That should enable increased efficiency of carbon capture, reducing the cost of bottling up $CO_2$ emissions. In addition, the researchers believe that their method of enzyme evolution—focused on collecting and combining as many beneficial mutations as possible rather than tweaking a particular variant to perfect it—was especially efficient. The same thing could be done to create better catalysts to boost any number of chemical processes.

PNAS, *2014. DOI: 10.1073/pnas.1411461111 (About DOIs).*

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

## Life's History in Iron

***A new study examines how Earth's oldest iron formations could have been formed before oxygenic photosynthesis played a role in oxidizing iron.***

**By Aaron L. Gronstal - Nov 7, 2014**

Geology tells us a great deal about the history and evolution of life on our planet. By studying formations in the rock record, astrobiologists can uncover important clues about the history of habitability on Earth.

Of particular interest to astrobiologists are iron formations, which existed on Earth at key periods in the evolution of life. These sedimentary rocks are made of layers of material that contain at least 15% iron, which is mixed into layers of quartz or carbonate. Geologists recognize two types of iron formations: the Algoma-type and the larger Superior-type. Algoma-type formations are linked to volcanism deep in the oceans, whereas Superior-type formations were formed near the shore in continental shelf environments and contain few volcanic rocks.

Superior-type formations first appear on Earth in the Late Archean (2.7 billion years ago) – at the same time the continents began to rise. These formations were huge and prevailed until 2.4 billion years ago (the Early Paleoproterozoic).

At this time, the Earth was undergoing big changes, including oxygenation of the atmosphere. Because the Earth was changing so much, the ways in which superior-type formations were created between 2.7-2.4 billion years ago may have also varied – particularly in respect to the time periods before and after the atmosphere became rich in oxygen and photosynthesis became a dominant process on Earth.

After the rise of oxygen, oxygenic photosynthetic bacteria are thought to have played a big role in the creation of iron formations. But how were iron formations made before advent of oxygenic photosynthesis?

The new study addresses this question by examining how iron deposition could have occurred without biology (a process known as *abiological* iron deposition). One mechanism for abiological iron deposition is a reaction in the atmosphere that creates hydrogen peroxide (a well-known powerful oxidant), which can then oxidize ferrous iron in seawater. Researchers modeled how much hydrogen peroxide could have been produced in the Eoarchean atmosphere of the Earth in order to see if this process could have played a major role in creating ancient iron formations.

According to the paper, published in *Geobiology*, the amount of hydrogen peroxide simply wasn't enough to account for the iron formations we now see in the geological record. "What we concluded is that, by discounting hydrogen peroxide oxidation, anoxygenic photosynthetic micro-organisms are the most likely mechanism responsible for Earth's oldest iron formations," Ernesto Pecoits of the Université Paris Diderot and lead author on the study told *astrobio.net*. Microorganisms that photosynthesize in the absence of oxygen assimilate carbon by using iron oxide (Fe(II)) as an electron donor instead of water. While oxygenic photosynthesis produces oxygen in the atmosphere (in the form of dioxygen), anoxygenic photosynthesis adds an electron to Fe(II) to produce Fe(III).

"In other words, they oxidize the iron," explains Pecoits. "This finding is very important because it implies that this metabolism was already active back in the early Archean (ca. 3.8 Byr-ago)."

***Related Websites:***

*Astrobiology Roadmap Goal 4: Earth's early biosphere and its environment*

***Reference:*** *Pecoits et al. (2014) Atmospheric hydrogen peroxide and Eoarchean iron formations.* Geobiology*, DOI: 10.1111/gbi.12116*

*- See more at: http://www.astrobio.net/topic/solar-system/earth/biosphere/lifes-history-iron/#sthash.eJnmaDn6.dpuf*

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

## New Zealand's moa were exterminated by an extremely low-density human population

***A new study suggests that the flightless birds named moa were completely extinct by the time New Zealand's human population had grown to two and half thousand people at most.***

The new findings, which appear in the prestigious journal Nature Communications, incorporate results of research by international teams involved in two major projects led by Professor Richard Holdaway (Palaecol Research Ltd and University of Canterbury) and Mr Chris Jacomb (University of Otago), respectively.

The researchers calculate that the Polynesians whose activities caused moa extinction in little more than a century had amongst the lowest human population densities on record. They found that during the peak period of moa hunting, there were fewer than 1500 Polynesian settlers in New Zealand, or about 1 person per 100 square kilometres, one of the lowest population densities recorded for any pre-industrial society. They found that the human population could have reached about 2500 by the time moa went extinct. For several decades before then moa would have been rare luxuries.

***Restoration of an upland moa, Megalapteryx didinus.*** **Credit: George Edward Lodge**

Estimates of the human population during the moa hunting period are more sensitive to how long it took to exterminate the birds through hunting and habitat destruction than to the size of the founding population.

To better define the critical period of moa hunting, the research was aimed at "book-ending" the moa hunter period with new estimates for when people started eating moa, and when there were no more moa to eat.

Starting with the latest estimate for a founding population of about 400 people (including 170-230 women), and applying population growth rates in the range achieved by past and present populations, the researchers modelled the human population size through the moa hunter period and beyond. When moa and seals were still available, the better diet enjoyed by the settlers likely fuelled higher population growth, and the analyses took this into account.

The first "book-end" - first evidence for moa hunting - was set by statistical analyses of 93 new high-precision radiocarbon dates on genetically identified moa eggshell pieces. These had been excavated from first settlement era archaeological sites in the eastern South Island, and showed that moa were still breeding nearby. Chris Jacomb explains: "The analyses showed that the sites were all first occupied - and the people began eating moa - after the major Kaharoa eruption of Mt Tarawera of about 1314 CE."

Ash from this eruption is an important time marker because no uncontested archaeological evidence for settlement has ever been found beneath it, Mr Jacomb says.

The other "book-end" was derived from statistical analyses of 270 high-precision radiocarbon dates on moa from non-archaeological sites. Analysis of 210 of the ages showed that moa were exterminated first in the more accessible eastern

lowlands of the South Island, at the end of the 14th century, just 70-80 years after the first evidence for moa consumption.

Analysis of all 270 dates, on all South Island moa species from throughout the South Island, showed that moa survived for only about another 20 years after that. Their total extinction most probably occurred within a decade either side of 1425 CE, barely a century after the earliest well-dated site, at Wairau Bar near Blenheim, was settled by people from tropical East Polynesia. The last known birds lived in the mountains of north-west Nelson. Professor Holdaway adds that "the results provide further support for the rapid extinction model for moa that Chris Jacomb and I published 14 years ago in [the US journal] Science."

The researchers note that it is often suggested that people could not have caused the extinction of megafauna such as the mammoths and giant sloths of North America and the giant marsupials of Australia, because the human populations when the extinctions happened were too small.

Prof Holdaway and Mr Jacomb say that the extinction of the New Zealand terrestrial megafauna of moa, giant eagle, and giant geese, accomplished by the direct and indirect activities of a very low-density human population, shows that population size can no longer be used as an argument against human involvement in extinctions elsewhere.

***http://phys.org/news/2014-11-xenon.html***

## Where did all the xenon go?

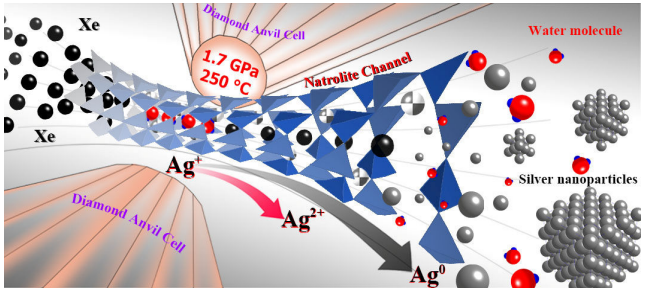
***The noble gas xenon should be found in terrestrial and Martian atmospheres, but researchers have had a hard time finding it.***

**Nov 07, 2014 by Anne M Stark**

Phys.org - The prevailing theory claims that due to xenon's weight—it is a heavy gas - it could be trapped in a planet's core or in the mantle during the planet's formation. Lawrence Livermore scientists and collaborators have discovered that the xenon can be trapped in the subsurface of the Earth, shedding new insights into the long-standing mysteries of the "missing xenon" in earth science.

The discovery of the noble gas xenon (Xe) has led to the synthesis of hundreds of Xe compounds (for example, it is thought that a compound made up of xenon and iron may lie in Earth's core). Its reactivity also has been estimated to be the cause of its depletion by a factor of 20 relative to the lighter noble gases—neon, argon and krypton—in the atmosphere of Earth, Mars and other planetary bodies. Specifically, xenon reacts with hydrogen and ice at high pressures to form stable compounds.

The team used a high pressure diamond anvil cell, which applies extreme pressures on materials, and advanced synchrotron X-ray scattering techniques to show that under high pressure and temperature, a silicate mineral, made up mostly of silver, irreversibly inserts xenon into its micropores and undergoes charge separation. As opposed to other noble gases such as argon and krypton, xenon stays within the pores even after pressure and heat are decreased.




***The Lawrence Livermore team used a high pressure diamond anvil cell to show that under high pressure and temperature, a silicate mineral, made up mostly of silver, irreversibly inserts xenon into its micropores and undergoes charge separation This mineral absorbs and retains significant amounts of xenon at conditions found in the subsurface of Earth.***

"This is a new chemical reaction that could account for the 'missing xenon' observed in terrestrial and Martian atmospheres," said Hyunchae Cynn, one of the LLNL physicists involved in the research. The team found missing xenon from the atmosphere trapped within porous rocks in a planet's core or mantle.

In the experiments, the temperatures and pressures used were within the range of hydrothermal conditions found in subduction zones on Earth and the subsurface of other planetary bodies such as Mars. Cynn suggests that the noble gas chemistry in Mars may have a similar missing xenon signature like Earth does and may help explain Xe transport and subsurface trapping.

The research appears in the September issue of the journal Nature Chemistry.

*Explore further: A noble gas cage: New material traps gases from nuclear fuel better*

*More information: Nature Chemistry, www.nature.com/nchem/journal/v…full/nchem.1997.html*