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Split liver transplants for young children proven to be as safe as whole organ transplantation

Increased use of split livers could significantly increase pediatric organ donor pool, potentially reducing or eliminating waitlist mortality rate for this population

Boston, Mass.— A new study shows that when a liver from a deceased adult or adolescent donor is split into two separate portions for transplantation—with the smaller portion going to a young child and the larger to an adult—the smaller portion used for the child will last just as long as if the child had received a whole organ from a donor close to his size.

The data, collected and analyzed by a team led by Boston Children's Hospital researchers Heung Bae Kim, MD, and Ryan Cauley, MD, MPH, was published online in *Liver Transplantation*, a journal of the American Association for the Study of Liver Diseases and the International Liver Transplantation Society. Data on graft survival and mortality for adult recipients of split livers is currently being compiled for a separate study to be released soon.

Examining pediatric data provided by the United Network of Organ Sharing (UNOS), the authors researched the mortality and graft survival of 2,679 patients under the age of two who received liver transplants between 1995-2010. Of these cases 1,114 involved partial livers and 1,565 involved whole organs. Their research indicates that from 1995- 2000 partial grafts had a higher risk of failure, but from 2000-2006 that risk was lower, indicating partial liver transplants became safer as experience with this practice increased. By 2006 both split and whole organs had similarly low rates of both graft failure and mortality, suggesting that their use could be increased to meet the demand for smaller grafts.

"Infants and young children have the highest risk of death on the liver transplant waiting list, mainly due to the shortage of appropriately sized organs," says Kim, senior author on the study and director of Boston Children's Pediatric Transplant Center. "But based on this new data, split liver transplantation may prove to be the answer to this difficult problem. If more liver donors were made available for consideration as split liver donors it could significantly reduce the number of young children on the waitlist for a liver, potentially reducing the waitlist mortality rate for this highly vulnerable population to near-zero."

Due to their small body size, infants and young children in need of a liver transplant cannot accommodate a whole graft (donated liver) from a larger sized donor. As a result these patients have three treatment options:

wait for a whole liver from a similarly sized deceased donor to become available

receive a portion of liver from a living donor (usually a family member)

receive a split liver transplant from an adolescent or adult deceased donor

In split liver transplantation, a liver from a deceased donor is surgically separated into two unequal size organs—the smaller portion is used to transplant the child while the larger portion is used to transplant a large child or adult patient.

The process of splitting a liver for transplant and allocating the halves to two different recipients began in the mid 1990s and has become more widespread over time. However, adoption of this technique has met some resistance due to early data suggesting that split liver transplants have a higher risk of graft failure and death than whole liver transplants. This new research reveals that this is no longer true among pediatric recipients.

"Our study confirms that there is no longer any increased risk of graft failure and mortality in the very young, regardless of whether or not the patient receives a partial or whole graft," says Cauley, first author on the paper.

"We are hopeful that this new data will support ongoing efforts to make modifications in the national liver allocation policy that makes more livers available for splitting, thereby saving lives and improving quality of life for many children and their families."

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Epigenetic factor likely plays a key role in fueling most common childhood cancer

A study led by St. Jude Children's Research Hospital shows epigenetic changes that turn genes on and off are as unique as alterations in DNA and may be as important in causing the most common childhood cancer

Memphis, Tenn. – Changes in an epigenetic mechanism that turns expression of genes on and off may be as important as genetic alterations in causing pediatric acute lymphoblastic leukemia (ALL), according to a study led by scientists at St. Jude Children's Research Hospital and published in the June 10 online edition of the *Journal of Clinical Investigation*.

The results suggest the mechanism called cytosine methylation plays a previously under-appreciated role in the development of leukemia. Cytosine methylation involves adding or removing methyl groups to cytosine, which is a building block of DNA.

The study is the most comprehensive effort yet to identify and understand genetic and epigenetic factors that work together to cause ALL, the most common childhood cancer. ALL is a cancer of white blood cells known as lymphocytes. Scientists at St. Jude and Weill Cornell Medical College collaborated on the project.

Researchers used a variety of techniques to examine hundreds of thousands of methylation sites across the genome in normal and leukemic lymphocytes, including samples from more than 160 children with ALL. Investigators found that known ALL subgroups, which are defined by chromosomal alterations, have unique methylation profiles. Those profiles correlated with different patterns of gene expression.

"It is well known that different leukemia subgroups have distinct patterns of gene expression that are important in the development of leukemia," said Charles Mullighan, MBBS (Hons), MSc, M.D., an associate member of the St. Jude Department of Pathology. Mullighan and Ari Melnick, M.D., Gebroe Professor Hematology/Oncology at Weill Cornell Medical College, are the study's co-corresponding authors.

"We have assumed that the underlying genetic changes are important determinants of those gene expression profiles. We now know that changes in methylation state also have key roles in influencing gene expression," Mullighan said.

The study used tissue samples from 137 St. Jude patients with B-cell leukemia and 30 children with T-cell leukemia. The patients represented all major ALL subgroups.

"The data show that aberrant epigenetic gene programming can now be considered a hallmark of acute lymphoblastic leukemia, occurring in all patients regardless of the presence of genetic mutations," Melnick said. "This offers the opportunity for development of epigenetic targeted therapies for patients with ALL that could be broadly applicable to many patients."

For comparison, researchers also checked B and T cells from 27 healthy children. Investigators found that leukemia cells shared a core group of abnormally methylated genes. The genes included ones involved in regulating the cell division and proliferation. "This remains to be tested, but the findings suggest that alterations in methylation are an important early step in the development of leukemia," Mullighan said.

The research provides further evidence that genetic and epigenetic events are both important in establishing different subgroups of ALL. For this study, researchers conducted genome-wide sampling of methylation, gene expression and DNA structural abnormalities, including the gain or loss of DNA. Shann-Ching Chen, Ph.D., St. Jude Pathology, developed many of the methods used to integrate and analyze the results. Chen and Maria Figueroa, now of the University of Michigan and formerly of Cornell, are the study's co-first authors.

The study also found that more than one-third of 71 genes targeted by genetic alterations are also abnormally methylated in ALL. The methylation changes involved known tumor suppressor or oncogenes genes including CDKN2A, CDKN2B, PTEN and KRAS. "The findings suggest these genes are inactivated or deregulated more frequently than suggested by simply analyzing structural changes in the genome," Mullighan said.

The other authors are Anna Andersson, formerly of St. Jude and now of Lund University Hospital, Sweden; Letha Phillips, formerly of St. Jude; Mondira Kundu and James Downing, both of St. Jude; Yushan Li, Cornell; and Jason Sotzen, University of Michigan.

The research was funded in part by ALSAC. Mullighan is a Pew Scholar in the Biomedical Sciences and a St. Baldrick's Scholar. He was supported in part by an American Society of Hematology Scholar Award and an American Association for Cancer Research/Aflac Career Development Award. Andersson was supported by the Swedish Childhood Cancer Foundation. Figueroa was supported by the Leukemia and Lymphoma Society and the Doris Duke Charitable Foundation. Melnick is funded by the Leukemia and Lymphoma Society and the Sackler Center for Biomedical and Physical Sciences. He is also a Burroughs Wellcome Clinical Translational Scholar and a Leukemia and Lymphoma Society scholar.

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Simple theory may explain mysterious dark matter

Most of the matter in the universe may be made out of particles that possess an unusual, donut-shaped electromagnetic field called an anapole.

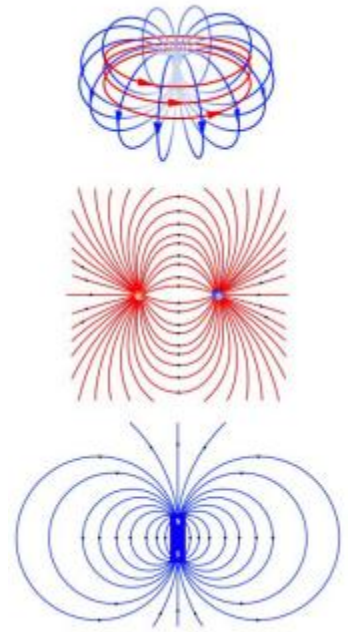
This proposal, which endows dark matter particles with a rare form of electromagnetism, has been strengthened by a detailed analysis performed by a pair of theoretical physicists at Vanderbilt University: Professor Robert Scherrer and post-doctoral fellow Chiu Man Ho. An article about the research was published online last month by the journal *Physics Letters B*.

"There are a great many different theories about the nature of dark matter. What I like about this theory is its simplicity, uniqueness and the fact that it can be tested," said Scherrer.

In the article, titled "Anapole Dark Matter," the physicists propose that dark matter, an invisible form of matter that makes up 85 percent of the all the matter in the universe, may be made out of a type of basic particle called the Majorana fermion. The particle's existence was predicted in the 1930's but has stubbornly resisted detection. A number of physicists have suggested that dark matter is made from Majorana particles, but Scherrer and Ho have performed detailed calculations that demonstrate that these particles are uniquely suited to possess a rare,

donut-shaped type of electromagnetic field called an anapole. This field gives them properties that differ from those of particles that possess the more common fields possessing two poles (north and south, positive and negative) and explains why they are so difficult to detect.

"Most models for dark matter assume that it interacts through exotic forces that we do not encounter in everyday life. Anapole dark matter makes use of ordinary electromagnetism that you learned about in school – the same force that makes magnets stick to your refrigerator or makes a balloon rubbed on your hair stick to the ceiling," said Scherrer. "Further, the model makes very specific predictions about the rate at which it should show up in the vast dark matter detectors that are buried underground all over the world. These predictions show that soon the existence of anapole dark matter should either be discovered or ruled out by these experiments." Fermions are particles like the electron and quark, which are the building blocks of matter. Their existence was predicted by Paul Dirac in 1928. Ten years later, shortly before he disappeared mysteriously at sea, Italian physicist Ettore Majorana produced a variation of Dirac's formulation that predicts the existence of an electrically neutral fermion. Since then, physicists have been searching for Majorana fermions. The primary candidate has been the neutrino, but scientists have been unable to determine the basic nature of this elusive particle.



This is a comparison of an anapole field with common electric and magnetic dipoles. The anapole field, top, is generated by a toroidal electrical current. As a result, the field is confined within the torus, instead of spreading out like the fields generated by conventional electric and magnetic dipoles. Michael Smeltzer, Vanderbilt University

The existence of dark matter was also first proposed in the 1930's to explain discrepancies in the rotational rate of galactic clusters. Subsequently, astronomers have discovered that the rate that stars rotate around individual galaxies is similarly out of sync. Detailed observations have shown that stars far from the center of galaxies are moving at much higher velocities than can be explained by the amount of visible matter that the galaxies contain. Assuming that they contain a large amount of invisible "dark" matter is the most straightforward way to explain these discrepancies.

Scientists hypothesize that dark matter cannot be seen in telescopes because it does not interact very strongly with light and other electromagnetic radiation. In fact, astronomical observations have basically ruled out the possibility that dark matter particles carry electrical charges. More recently, though, several physicists have examined dark matter particles that don't carry electrical charges, but have electric or magnetic dipoles. The only problem is that even these more complicated models are ruled out for Majorana particles. That is one of the reasons that Ho and Scherrer took a closer look at dark matter with an anapole magnetic moment.

"Although Majorana fermions are electrically neutral, fundamental symmetries of nature forbid them from acquiring any electromagnetic properties except the anapole," Ho said. The existence of a magnetic anapole was predicted by the Soviet physicist Yakov Zel'dovich in 1958. Since then it has been observed in the magnetic structure of the nuclei of cesium-133 and ytterbium-174 atoms.

Particles with familiar electrical and magnetic dipoles, interact with electromagnetic fields even when they are stationary. Particles with anapole fields don't. They must be moving before they interact and the faster they move the stronger the interaction. As a result, anapole particles would have been much more interactive during the early days of the universe and would have become less and less interactive as the universe expanded and cooled.

The anapole dark matter particles suggested by Ho and Scherrer would annihilate in the early universe just like other proposed dark matter particles, and the left-over particles from the process would form the dark matter we see today. But because dark matter is moving so much more slowly at the present day, and because the anapole interaction depends on how fast it moves, these particles would have escaped detection so far, but only just barely. *The research was funded in part by Department of Energy grant DE-FG05-85ER40226.*

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Women with severe morning sickness who take antihistamines more likely to experience bad outcomes

Women with a severe form of morning sickness who take antihistamines to help them sleep through their debilitating nausea are significantly more likely to experience adverse pregnancy outcomes, including low birth weight babies and premature births, a UCLA study has found.

The findings, the first to link antihistamine use to adverse pregnancy outcomes, are important because babies born before 37 weeks often are hospitalized longer than full term babies, can experience problems breathing

and feeding, are more prone to infection and can suffer from developmental problems. Women with this condition considering taking such medications should know the risks, said study lead author Marlana Fejzo, an assistant professor of research in obstetrics and gynecology at UCLA.

The severe morning sickness, called hyperemesis gravidarum (HG), is the same condition that Duchess Kate Middleton recently experienced. Its cause is unknown and the symptoms are intense - the continuous nausea and vomiting can be so violent that women in the study reported suffering from detached retinas, blown eardrums, cracked ribs and torn esophagi, Fejzo said. The symptoms can last for several months or the entire pregnancy.

"It was surprising to find the link between antihistamines and adverse outcomes as these are over-the-counter medications that are used commonly by women with HG during pregnancy," said Fejzo, who had undiagnosed HG during her first pregnancy and nearly died during her second, losing the baby at 15 weeks gestation.

"Women and their healthcare providers should be aware of the risk for adverse outcomes when deciding which medications to take to treat their HG symptoms." The study appears June 10, 2013 in the *European Journal of Obstetrics and Gynecology and Reproductive Biology*.

The six-year study compared pregnancy outcomes in 254 women with HG who were sick enough that they needed treatment for dehydration with intravenous fluids to 308 women who had normal or no morning sickness during pregnancy. Fejzo said they found women with HG had four times the risk of adverse outcomes. The link between HG and adverse outcomes has been shown in several previous studies.

Fejzo took it a step farther, comparing women with HG who suffered adverse outcomes to women with HG who had good outcomes. They then looked at more than 35 medications and treatments commonly used by women with HG to determine if any were linked to bad outcomes. She found that antihistamines, like those found in Unisom and Benadryl, were taken by more than 50 percent of HG patients who experienced adverse outcomes. Fejzo also found that the medications were reportedly effective in less than 20 percent of the women that took them.

"Some doctors will suggest that their HG patients take Unisom to help them sleep through their nausea," Fejzo said. "Our findings show not only that the use of antihistamines is linked with adverse outcomes, but also that they're not that effective. Women with HG should be aware of that so they can make educated decisions on how to treat their HG symptoms."

Adrienne Downs of Culver City experienced some nausea and vomiting during her first two pregnancies, but nothing out of the ordinary. Her third pregnancy was not so run-of-the-mill. She soon began suffering from constant nausea, vomiting around the clock every 20 minutes or so. She was hospitalized twice, five days each time, to get intravenous fluids to treat her severe dehydration and malnutrition.

"I literally could keep nothing down for months," said Downs. "I couldn't even get up out of bed and take care of my family. It was horrible. I was very scared for my baby. How would it get any nutrition if I couldn't eat or drink?"

Downs lost 12 pounds in three weeks early in her pregnancy. Her mother had to move in to take care of Downs' sons, 4 and 2, and try to find something her daughter could keep in her system. Now at 21 weeks gestation, Downs' symptoms have subsided somewhat, although she still can only keep down fluids. She had gained back some of the weight she lost.

Downs said she did not take antihistamines to treat her HG symptoms, but she said the findings are important. "As pregnant moms, we want to be the best 'house' for our babies that we can," she said. "I had never heard of this condition before I got it, so I'm glad that UCLA researchers are studying HG and may one day find the cause."

Fejzo said HG is diagnosed in 0.2 to 2 percent of pregnant women, although rates are higher in China. She said much more work needs to be done to study the short- and long-term outcomes of medication use during pregnancy. She and her team currently are studying outcomes in HG pregnancies to determine if the violent nausea and vomiting have any effects on the children later in life.

"We desperately need support for research into HG to determine its cause so that medications can be designed that are safe and effective," Fejzo said. "The greatest risk factor for HG other than a previous HG pregnancy is having a sister who had HG, which increases the risk by 17-fold. This suggests a genetic component is at work."

Fejzo and her team are collecting saliva from women with HG and women with normal pregnancies and are studying the DNA extracted from the saliva to look for genes that may predispose women for HG. She hopes once a cause is discovered, drugs can be developed to either prevent or more effectively treat the condition.

The study was funded by the Hyperemesis Education and Research Foundation.

http://www.eurekalert.org/pub_releases/2013-06/sjcr-ccs060613.php

Childhood cancer survivors found to have significant undiagnosed disease as adults

St. Jude Children's Research Hospital study identifies the need for proactive, life-long medical follow-up and provides the most complete health picture yet of adult survivors of childhood cancer

St. Jude Children's Research Hospital has found that childhood cancer survivors overwhelmingly experience a significant amount of undiagnosed, serious disease through their adult years, establishing the importance of proactive, life-long clinical health screenings for this growing high-risk population. The findings appear in the June 12 issue of the *Journal of the American Medical Association*.

Overall, 98 percent of the 1,713 survivors in the study had at least one chronic health condition, hundreds of which were diagnosed through clinical screenings conducted as part of this long-term, comprehensive health study. Health issues included new cancers, heart abnormalities, abnormal lung function and neurocognitive dysfunction. St. Jude researchers found that by age 45, 80 percent of survivors of childhood cancers have a life-threatening, serious or disabling chronic condition.

"These findings are a wake-up call to health care providers and remind survivors to be proactive about their health," said Melissa Hudson, M.D., director of the St. Jude Division of Cancer Survivorship and co-first author of the research from the St. Jude Lifetime Cohort Study (St. Jude LIFE) Kirsten Ness, Ph.D., an associate member of the St. Jude Epidemiology and Cancer Control department, is the other co-first author.

In this study, abnormal lung function was diagnosed in 65 percent of survivors at known risk for lung problems due to their childhood cancer treatment. Endocrine problems involving the hypothalamus and pituitary gland were diagnosed in 61 percent of at-risk survivors. Heart abnormalities were diagnosed in 56 percent of at-risk survivors and neurocognitive impairment, including memory problems, were diagnosed in 48 percent of at-risk survivors.

"Many were identified early, often before symptoms developed, when interventions may have their greatest impact," Hudson said.

For this research study, St. Jude brought survivors back to the hospital – where they were treated as children – to undergo an extensive two to three-day battery of medical tests and assessments. Other studies of adult survivors of childhood cancer have relied primarily on self-reports or cancer registry data, which primarily identify conditions diagnosed as a result of symptoms, resulting in the substantial underestimation of health problems among survivors.

Hudson said the findings demonstrate the importance of tailoring treatments to reduce exposure to chemotherapy agents and radiation when possible. For example, in 2009 St. Jude researchers found that, with tailored chemotherapy, cranial irradiation could be completely eliminated for patients with the most common form of childhood leukemia without impacting survival.

In addition to regular medical checkups to discover issues as early as possible, a healthy lifestyle might help survivors avoid or slow the progression of some of the chronic conditions identified in this study, Ness said.

"Obesity and some types of heart disease are examples of chronic conditions where survivors may be able to mitigate their risk and improve their long-term health by making careful lifestyle choices, such as not smoking, eating a diet low in fat and sugar and engaging in moderate physical activity for 30 minutes a day, five days a week."

This study included survivors of leukemia, lymphoma and tumors of the brain, bone and other organs. For half the survivors in this study, their cancer diagnosis was more than 25 years ago. Half were younger than 32 years old when the St. Jude LIFE assessment was completed.

The relative youth of the participants made the prevalence of neurocognitive and neurosensory deficits, heart abnormalities, lung and other problems particularly striking. "The data may indicate a pattern of accelerated or premature aging," Hudson said.

The research reflects ongoing efforts to help the nation's growing population of childhood cancer survivors and their health care providers understand and manage their cancer-related risks. The U.S. is home to an estimated 395,000 childhood cancer survivors. With long-term survival of pediatric cancer patients now surpassing 80 percent, the survivor community will continue to grow.

Other study authors are James Gurney, Daniel Mulrooney, Wassim Chemaitilly, Kevin Krull, Daniel Green, Gregory Armstrong, Kerri Nottage, Kendra Jones and Deo Kumar Srivastava, all of St. Jude; Charles Sklar, of Memorial Sloan-Kettering Cancer Center; and senior author Leslie Robison, of St. Jude.

The study was funded in part by a grant (CA21765) from the National Cancer Institute (NCI) at the National Institutes of Health; and ALSAC.

<http://www.sciencedaily.com/releases/2013/06/130610192837.htm>

Alzheimer's and Low Blood Sugar in Diabetes May Trigger a Vicious Cycle

A new UC San Francisco-led study looks at the close link between diabetes and dementia, which can create a vicious cycle.

Diabetes-associated episodes of low blood sugar may increase the risk of developing dementia, while having dementia or even milder forms of cognitive impairment may increase the risk of experiencing low blood sugar, according to the study published online Monday in JAMA Internal Medicine.

Researchers analyzed data from 783 diabetic participants and found that hospitalization for severe hypoglycemia among the diabetic, elderly participants in the study was associated with a doubled risk of developing dementia later. Similarly, study participants with dementia were twice as likely to experience a severe hypoglycemic event.

The study results suggest some patients risk entering a downward spiral in which hypoglycemia and cognitive impairment fuel one another, leading to worse health, said Kristine Yaffe, MD, senior author and principal investigator for the study, and a UCSF professor of psychiatry, neurology and epidemiology based at the San Francisco Veterans Affairs Medical Center.

"Older patients with diabetes may be especially vulnerable to a vicious cycle in which poor diabetes management may lead to cognitive decline and then to even worse diabetes management," she said.

Cognitive Function a Factor in Managing Diabetes

The researchers analyzed hospital records of patients from Memphis and Pittsburgh, ages 70 to 79 at the time of enrollment, who participated in the federally funded Health, Aging and Body Composition (Health ABC) study, begun in 1997. The UCSF results are based on an average of 12 years of follow-up study. Participants in the Health ABC study periodically underwent tests to measure cognitive function.

Nearly half of participants included in the newly published analysis were black, and the rest were white. None had dementia at the start of the study, and all either had diabetes at the beginning of the study or were diagnosed during the course of the study.

"Individuals with dementia or even those with milder forms of cognitive impairment may be less able to effectively manage complex treatment regimens for diabetes and less able to recognize the symptoms of hypoglycemia and to respond appropriately, increasing their risk of severe hypoglycemia," Yaffe said.

"Physicians should take cognitive function into account in managing diabetes in elderly individuals."

Certain medications known to carry a higher risk for hypoglycemia -- such as insulin secretagogues and certain sulfonylureas -- may be inappropriate for older adults with dementia or who are at risk for cognitive impairment, according to Yaffe.

Previous studies in which researchers investigated hypoglycemia and cognitive function have had inconsistent findings. A strength of the current study is that individuals were tracked from baseline over a relatively long time, and the older age of participants may also have been a factor in the highly statistically significant outcome, Yaffe said.

Additional authors of the study were, Cherie Falvey, MPH, Ann Schwartz, PhD, MPH, and Nathan Hamilton from UCSF; Tamara Harris, MD, and Eleanor Simonsick, PhD, from the National Institute of Aging; Elsa Strotmeyer, PhD, MPH, and Andrea Metti, MPH, of the University of Pittsburgh; and Ronald Shorr, MD, of the University of Florida.

Kristine Yaffe et al. Association Between Hypoglycemia and Dementia in a Biracial Cohort of Older Adults With Diabetes Mellitus. Hypoglycemia and Dementia in Older Adults With DM. JAMA Internal Medicine, 2013; : 1 DOI: 10.1001/jamainternmed.2013.6176

http://www.eurekalert.org/pub_releases/2013-06/uoh-nar061113.php

New archaeogenetic research refutes earlier findings

Modern humans did not settle in Asia before the devastating eruption of Sumatra's volcano Mount Toba 74,000 years ago

When did modern humans settle in Asia and what route did they take from mankind's African homeland? A University of Huddersfield professor has helped to provide answers to both questions. But he has also had to settle a controversy. Professor Martin Richards, who heads the University's Archaeogenetics Research Group, co-authors a new article in the journal Proceedings of the National Academy of Sciences of the United States of America. It refutes a recent theory, that there is archaeological evidence for the presence of modern humans in southern Asia before the super-eruption of the Mount Toba volcano in Sumatra.

One of the most catastrophic events since humans evolved, it happened approximately 74,000 years ago. In 2005, Professor Richards led research published in an article in the journal Science which used mitochondrial DNA evidence to show that anatomically modern humans dispersed from their Africa homeland via a "southern coastal route" from the Horn and through Arabia, about 60,000 years ago – after the Toba eruption.

However, a team of archaeologists excavating in India then claimed to have found evidence that modern humans were there before the eruption – possibly as early as 120,000 years ago, much earlier than Europe or the Near East were colonised. These findings, based on the discovery of stone tools below a layer of Toba ash, were published in *Science* in 2007.

Now Professor Richards – working principally with the archaeologist Professor Sir Paul Mellars, of the University of Cambridge and the University of Edinburgh, with a team including Huddersfield University's Dr Martin Carr and colleagues from York and Porto – has published his rebuttal of this theory. In doing so, they have been able to draw on a much greater body of DNA evidence that was available for the earlier article.

"One of the things we didn't have in 2005 was very much evidence from India in the way of mitochondrial sequences. Now, with a lot of people doing sequencing and depositing material in databases there are about 1,000 sequences from India," said Professor Richards.

By using the mitochondrial DNA of today's populations and working backwards, and by drawing on a wide variety of other evidence and research, the team was able to make much more precise estimates for the arrival of modern humans in India. The evidence suggests dispersal from Africa and settlement in India no earlier than 60,000 years ago.

"We also argue that close archaeological similarities between African and Indian stone-tool technologies after 70,000 years ago, as well as features such as beads and engravings, suggest that the slightly later Indian material had an African source," states Professor Richards. "There were people in India before the Toba eruption, because there are stone tools there, but they could have been Neanderthals – or some other pre-modern population," he adds.

"The replacement of the presumably archaic humans living previously in South Asia by modern people with these new technologies appears analogous to the replacement of Neanderthals by modern humans in Europe and western Asia 50-40,000 years ago."

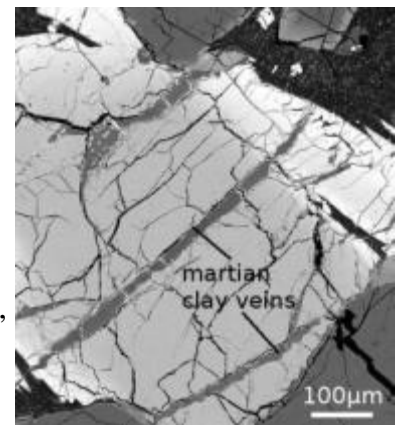
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Martian Clay Contains Chemical Implicated in the Origin of Life, Astrobiologists Find
Researchers from the University of Hawaii at Manoa NASA Astrobiology Institute (UHNAI) have discovered high concentrations of boron in a Martian meteorite.

When present in its oxidized form (borate), boron may have played a key role in the formation of RNA, one of the building blocks for life. The work was published on June 6 in *PLOS ONE*.

The Antarctic Search for Meteorites team found the Martian meteorite used in this study in Antarctica during its 2009-2010 field season. The minerals it contains, as well as its chemical composition, clearly show that it is of Martian origin.

Using the ion microprobe in the W. M. Keck Cosmochemistry Laboratory at UH, the team was able to analyze veins of Martian clay in the meteorite. After ruling out contamination from Earth, they determined boron abundances in these clays are over ten times higher than in any previously measured meteorite.



Electron microscope image showing the 700-million-year-old Martian clay veins containing boron (100 μm = one tenth of a millimeter). Credit: Image courtesy of Institute for Astronomy at the University of Hawaii at Manoa

"Borates may have been important for the origin of life on Earth because they can stabilize ribose, a crucial component of RNA. In early life RNA is thought to have been the informational precursor to DNA," said James Stephenson, a UHNAI postdoctoral fellow.

RNA may have been the first molecule to store information and pass it on to the next generation, a mechanism crucial for evolution. Although life has now evolved a sophisticated mechanism to synthesize RNA, the first RNA molecules must have been made without such help. One of the most difficult steps in making RNA nonbiologically is the formation of the RNA sugar component, ribose. Previous laboratory tests have shown that without borate the chemicals available on the early Earth fail to build ribose. However, in the presence of borate, ribose is spontaneously produced and stabilized.

This work was born from the uniquely interdisciplinary environment of UHNAI. The lead authors on the paper, Stephenson, an evolutionary biologist, and Lydia Hallis, a cosmochemist who is also a UHNAI postdoctoral fellow, first came up with the idea over an after-work beer. "Given that boron has been implicated in the emergence of life, I had assumed that it was well characterized in meteorites," said Stephenson. "Discussing this with Dr. Hallis, I found out that it was barely studied. I was shocked and excited. She then informed me that both the samples and the specialized machinery needed to analyze them were available at UH."

On our planet, borate-enriched salt, sediment and clay deposits are relatively common, but such deposits had never previously been found on an extraterrestrial body. This new research suggests that when life was getting started on Earth, borate could also have been concentrated in deposits on Mars.

The significance goes beyond an interest in the red planet, as Hallis explains: "Earth and Mars used to have much more in common than they do today. Over time, Mars has lost a lot of its atmosphere and surface water, but ancient meteorites preserve delicate clays from wetter periods in Mars' history. The Martian clay we studied is thought to be up to 700 million years old. The recycling of the Earth's crust via plate tectonics has left no evidence of clays this old on our planet; hence Martian clays could provide essential information regarding environmental conditions on the early Earth."

The presence of ancient borate-enriched clays on Mars implies that these clays may also have been present on the early Earth. Borate-enriched clays such as the ones studied here may have represented chemical havens in which one of life's key molecular building blocks could form.

UHNAI is a research center that links the biological, chemical, geological, and astronomical sciences to better understand the origin, history, distribution, and role of water as it relates to life in the universe.

James D. Stephenson, Lydia J. Hallis, Kazuhide Nagashima, Stephen J. Freeland. Boron Enrichment in Martian Clay. PLoS ONE, 2013; 8 (6): e64624 DOI: 10.1371/journal.pone.0064624

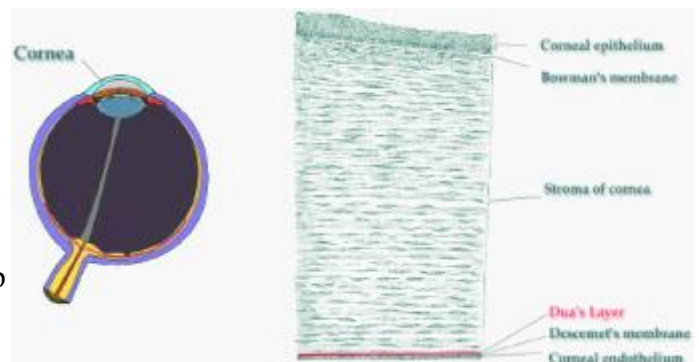
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Scientists discover new layer of the human cornea

Scientists at The University of Nottingham have discovered a previously undetected layer in the cornea, the clear window at the front of the human eye.

The breakthrough, announced in a study published in the academic journal *Ophthalmology*, could help surgeons to dramatically improve outcomes for patients undergoing corneal grafts and transplants.

The new layer has been dubbed the Dua's Layer after the academic Professor Harinder Dua who discovered it. Professor Dua, Professor of Ophthalmology and Visual Sciences, said: "This is a major discovery that will mean that ophthalmology textbooks will literally need to be re-written. Having identified this new and distinct layer deep in the tissue of the cornea, we can now exploit its presence to make operations much safer and simpler for patients."



Left: schematic diagram of the human eye showing the cornea (Mikael Häggström / CC0 1.0). Right: vertical section of human cornea Gray's Anatomy / Sci-News.com

"From a clinical perspective, there are many diseases that affect the back of the cornea which clinicians across the world are already beginning to relate to the presence, absence or tear in this layer."

The human cornea is the clear protective lens on the front of the eye through which light enters the eye.

Scientists previously believed the cornea to be comprised of five layers, from front to back, the corneal epithelium, Bowman's layer, the corneal stroma, Descemet's membrane and the corneal endothelium.

The new layer that has been discovered is located at the back of the cornea between the corneal stroma and Descemet's membrane. Although it is just 15 microns thick - the entire cornea is around 550 microns thick or 0.5mm - it is incredibly tough and is strong enough to be able to withstand one and a half to two bars of pressure.

The scientists proved the existence of the layer by simulating human corneal transplants and grafts on eyes donated for research purposes to eye banks located in Bristol and Manchester. During this surgery, tiny bubbles of air were injected into the cornea to gently separate the different layers. The scientists then subjected the separated layers to electron microscopy, allowing them to study them at many thousand times their actual size. Understanding the properties and location of the new Dua's layer could help surgeons to better identify where in the cornea these bubbles are occurring and take appropriate measures during the operation. If they are able to inject a bubble next to the Dua's layer, its strength means that it is less prone to tearing, meaning a better outcome for the patient. The discovery will have an impact on advancing understanding of a number of diseases of the cornea, including acute hydrops, Descematocele and pre-Descemet's dystrophies.

The scientists now believe that corneal hydrops, a bulging of the cornea caused by fluid build up that occurs in patients with keratoconus (conical deformity of the cornea), is caused by a tear in the Dua layer, through which water from inside the eye rushes in and causes waterlogging.

http://www.eurekalert.org/pub_releases/2013-06/jhm-evs061113.php

Experimental vaccine shows promise against TB meningitis

Study in animals lays groundwork for new prevention strategies in brain TB

A team of Johns Hopkins researchers working with animals has developed a vaccine that prevents the virulent TB bacterium from invading the brain and causing the highly lethal condition TB meningitis, a disease that disproportionately occurs in TB-infected children and in adults with compromised immune system.

A report on the federally funded research is published online June 11 in the journal PLOS ONE.

TB brain infections often cause serious brain damage and death even when recognized and treated promptly, researchers say. This is so because many drugs currently used to treat resistant TB strains cannot cross the so-called brain-blood barrier, which stops pathogens from entering the brain, but also keeps most medicines woefully out of the brain's reach.

"Once TB infects the brain, our treatment options have modest effect at best, so preventing brain infection in the first place is the only fool-proof way to avert neurologic damage and death," said lead investigator Sanjay Jain, M.D., an infectious disease specialist at the Johns Hopkins Children's Center. "Unfortunately, our sole preventive weapon, the traditional BCG vaccine, has a spotty track record in terms of efficacy."

The new Johns Hopkins vaccine, tested in guinea pigs, could eventually add a much-needed weapon to a largely depleted therapeutic and preventive arsenal. TB currently affects nearly 9 million people worldwide and is growing increasingly resistant to many powerful antibiotics, according to the World Health Organization (WHO).

The experimental vaccine works against certain lethal strains of TB that are marked by the presence of a protein known as PknD, which helps the TB bacterium sneak past the blood-brain barrier. Specifically, PknD makes TB virulent by allowing it to attach to, damage and penetrate the protective cells that line the small blood vessels of the brain and prevent toxins and bugs traversing the blood from invading the organ.

If proven effective in people, the vaccine also could be used to boost the brain-protective effects of the traditional BCG vaccine, the only currently available anti-TB vaccine, the efficacy of which varies greatly, Jain says. In addition, BCG contains live bacteria and therefore cannot be given to immune-compromised people, such as HIV patients, who are at greater risk of developing widespread TB. About one-third of the 34 million HIV-infected people worldwide have TB, according to the WHO. By contrast, the experimental vaccine is made with PknD protein chunks, which by themselves cannot cause full-blown disease even in people with weakened immune systems.

In their experiments, the Johns Hopkins researchers compared the effectiveness of the new vaccine with the traditional BCG vaccine. Animals were injected with placebo, BCG or the new vaccine and then exposed to airborne TB. The researchers measured TB loads in the lungs and brains of all three groups, as well as in those of non-vaccinated animals.

Animals given either active vaccine had far fewer TB cells in their brains compared with their non-vaccinated or placebo-vaccinated counterparts. Both vaccines were equally effective in preventing invasive TB infections of the brain and spinal cord, even though the new vaccine fared worse at reducing TB cell loads in the lungs. Notably, animals injected with the new vaccine had TB cell counts in their lungs similar to those of placebo-injected or non-vaccinated animals, yet far fewer TB cells in their brains.

"What this tells us is that even in the presence of full-blown lung infection, the new vaccine somehow blunted TB's ability to infect and damage the brain," said investigator Ciaran Skerry, Ph.D., of the Johns Hopkins Center for Tuberculosis Research.

Animals that got the new vaccine also had higher levels of protective TB-specific antibodies and higher levels of interferons, the cry-for-help chemicals released by virus-infected or bacterium-infected cells that summon the body's immune defenses against pathogens.

To determine whether the new vaccine could also render the TB bacterium less virulent in human cells, the researchers soaked TB bacteria in blood obtained from BCG-vaccinated, non-vaccinated and experimentally vaccinated animals, then mixed the pre-soaked TB bacteria with human endothelial cells that line the small blood vessels of the brain and guard it against invasive pathogens. Bacteria treated with blood from the experimentally vaccinated animals showed far less virulence and were far less capable of damaging the human cells than were the TB bacteria soaked in blood from BCG-vaccinated or non-vaccinated animals.

The study was funded by the National Institutes of Health under grants OD006492 and AI083125.

Co-investigators included Supriya Pokkali, Michael Pinn, Nicholas Be, Jamie Harper and Petros Karakousis, all of Johns Hopkins. PLOS ONE <http://dx.plos.org/10.1371/journal.pone.0066310> TB Treatment Paradox: Mouse Studies Show Body's Own Response Helps TB Bacteria Survive <http://www.hopkinschildrens.org/Mouse-Studies-Show-Bodys-Own-Response-Helps-Tb-Bacteria-Survive.aspx>

<http://blogs.scientificamerican.com/guest-blog/2013/06/11/breaking-bad-with-breakbone-fever/>

Breaking Bad with Breakbone Fever

What if a bacterial infection could prevent you from getting Dengue Fever? Malaria too?

By Mark Farmer | June 11, 2013 |

Before you run off to eat a handful of spoiled sushi or roll about in a cow pasture allow me to clarify. It isn't you that needs to become infected, it is the mosquitoes that spread these diseases.

Dengue Fever and malaria are common diseases of the tropics. Both are spread through by the bite of infected mosquitos, which in turn acquire the pathogens by feeding on an infected host. At the turn of the twentieth century both Ronald Ross and Alphonse Laveran were separately recognized with the Nobel Prize for their contributions to our understanding of how malaria is transmitted from person to person.

Malaria was once common in the southeastern U.S. but today it has been effectively eliminated. This was accomplished not by curing those who carried the parasite, but by reducing the rate of infection. Fewer infected people meant fewer infected mosquitoes leading to fewer infected people... well, you get the idea. And to do this all that was required was to keep mosquitoes from biting people!

As anyone who ventures out on a summer night knows this is easier said than done, especially in a part of the country where short winters provide the only respite from the onslaught of these real life vampires.

A combination of events brought this about. The migration of people from rural areas to cities, the aggressive use of pesticides and the draining of swamps all contributed. But the single most effective measure was one that was decidedly low-tech. Screened doors and windows. The species of mosquito most commonly associated with malaria tends to feed in the evening. With more and more people safely behind the protection of fine mesh the cycle of transmission was effectively broken and malaria in the U.S. became a memory.

But what about the rest of the world that cannot afford well screened homes? And what about the more aggressive pathogens such as the virus that causes Dengue? The solution may lie with a humble bacterium.

Wolbachia is a naturally occurring organism that infects somewhere between 60-70% of all insect species and can change the nature of its host. Not only that but unlike most other bacteria Wolbachia can be passed from mother to offspring via eggs, effectively creating an entire population of infected bugs.

In a landmark 2008 paper Scott O'Neil of the University of Queensland demonstrated that infection with Wolbachia could actually protect some insects from viral infections.

What had been thought to be a benign symbiont was actually a beneficial partner for the insect.

Then O'Neil got an idea. What if he could infect mosquitoes with a strain of Wolbachia that would "protect" them from the Dengue virus? People might still suffer annoying bites but they would be spared the painful agony that has earned Dengue the nickname "breakbone fever."

In 2011 O'Neill and co-workers reported that they had developed just such a strain of mosquitoes that are immune to the Dengue virus. Later that year, working with colleagues at James Cook University they intentionally released Wolbachia infected mosquitoes in the area around the resort city of Cairns in northern Queensland.

Preliminary results suggest that the disease resistant mosquitoes are competing well with the natural population and are maintaining their immunity to transmitting Dengue. Within a few years the citizens of Cairns may no longer fear contracting Dengue, even if they will still suffer annoying bites from the mozzies.

Now comes word that American and Chinese researchers have teamed up to develop mosquitos infected with a different strain of Wolbachia. A strain that can block the transmission of the big "M" itself. Malaria.

In laboratory tests the Wolbachia infection is passed down from female mosquitoes to their young, and those that have the bacteria are resistant to contracting the most dangerous strain of human malaria, Plasmodium falciparum. Field trials are planned. If the success of the Cairns project is any indication in coming years the threat of malaria may become as distant a memory for the three and a half billion people who are currently at risk as it is for those who live in the comfort and safety of well screened homes.

One day we may be similarly protected from West Nile virus, Yellow fever, equine encephalitis, and most other mosquito-borne diseases. This would make those annoying welts a little easier to tolerate.

Boundaries of Malaria Transmission By Country



http://www.eurekalert.org/pub_releases/2013-06/uosc-efs061113.php

Exercise for stroke patients' brains

A new study finds that stroke patients' brains show strong cortical motor activity when observing others performing physical tasks – a finding that offers new insight into stroke rehabilitation.

Using functional magnetic resonance imaging (fMRI), a team of researchers from USC monitored the brains of 24 individuals — 12 who had suffered strokes and 12 age-matched people who had not — as they watched others performing actions made using the arm and hand that would be difficult for a person who can no longer use their arm due to stroke – actions like lifting a pencil or flipping a card.

The researchers found that while the typical brain responded to the visual stimulus with activity in cortical motor regions that are generally activated when we watch others perform actions, in the stroke-affected brain, activity was strongest in these regions of the damaged hemisphere, and strongest when stroke patients viewed actions they would have the most difficulty performing.

Activating regions near the damaged portion of the brain is like exercising it, building strength that can help it recover to a degree.

"Watching others perform physical tasks leads to activations in motor areas of the damaged hemisphere of the brain after stroke, which is exactly what we're trying to do in therapy," said Kathleen Garrison, lead author of a paper on the research. "If we can help drive plasticity in these brain regions, we may be able to help individuals with stroke recover more of the ability to move their arm and hand."

Garrison, who completed this research while studying at USC and is currently a post-doctoral researcher at the Yale University School of Medicine, worked with Lisa Aziz-Zadeh of the USC Brain and Creativity Institute and the Division of Occupational Science and Occupational Therapy; Carolee Winstein, director of the Motor Behavior and Neurorehabilitation Laboratory in the Division of Biokinesiology and Physical Therapy at USC; and former USC doctoral student Sook-Lei Liew and postdoctoral researcher Savio Wong.

Their research was posted online ahead of publication by the journal *Stroke* on June 6.

Using action-observation in stroke rehabilitation has shown promise in early studies, and this study is among the first to explain why it may be effective.

"It's like you're priming the pump," Winstein said. "You're getting these circuits engaged through the action-observation before they even attempt to move." The process is a kind of virtual exercise program for the brain that prepares you for the real exercise that includes the brain and body.

The study also offers support for expanding action-observation as a therapeutic technique – particularly for individuals who have been screened using fMRI and have shown a strong response to it.

"We could make videos of what patients will be doing in therapy, and then have them watch it as homework," Aziz-Zadeh said. "In some cases, it could pave the way for them to do better."

This research was funded by American Heart Association, grant 10SDG3510062; the National Institutes of Health; the Eunice Kennedy Shriver National Institute of Child Health and Human Development, grant R03HD067475; and the National Institute of Biomedical Imaging and Bioengineering, grant EB00438.

http://www.eurekalert.org/pub_releases/2013-06/osu-fva061113.php

Flu vaccines aimed at younger populations could break annual transmission cycle

The huge value of vaccinating more children and young adults for influenza is being seriously underestimated, experts say in a new report, while conventional wisdom and historic vaccine programs have concentrated on the elderly and those at higher risk of death and serious complications.

CORVALLIS, Ore. –A computer modeling analysis was just published in the journal *Vaccine*, in work supported by the National Institutes of Health. The study suggests that children in school and young adults at work do the vast majority of flu transmission. Programs that effectively increase vaccination in those groups would have the best payoff, the research concluded. The key point: If you don't catch the flu, you can't die from it. Breaking the cycle of transmission benefits everyone from infants to the elderly, the researchers said. And at stake are thousands of lives and billions of dollars a year.

"In most cases, the available flu vaccine could be used more effectively and save more lives by increasing the number of vaccinated children and young adults," said Jan Medlock, a co-author of the study and researcher with the Department of Biomedical Sciences in Oregon State University's College of Veterinary Medicine.

"That approach could really limit the cycle of transmission, preventing a great deal of illness while also reducing the number of deaths among high risk groups," he said. "Approaches similar to this were used in Japan several decades ago, and they accomplished just that. Our new analysis suggests we should reconsider our priorities for vaccination."

In a perfect world and in accord with recommendations from the Centers for Disease Control and Prevention, researchers agree that almost everyone over the age of six months should get the flu vaccine, unless they were

allergic to the shot or had other reasons not to take it. But in the United States, only about one-third of the population actually gets a flu vaccine each year. Historic efforts have been focused on people at higher risk of death and severe disease – often the elderly, and those with chronic illness, weakened immune systems, health care workers or others.

With existing patterns of vaccine usage, the problem is enormous. Seasonal influenza in the U.S. results each year in an average of 36,000 deaths, more than 200,000 hospitalizations, an \$87 billion economic burden, and millions of hours of lost time at school and work – not to mention feeling sick and miserable.

The flu vaccine up until 2000 was only recommended for people over 65, Medlock said, and other age groups were added in the past decade as it became clear they also were at high risk of death or complications – children from age six months to five years, and adults over 50. Just recently, age was taken completely out of the equation.

"Clearly we would want people at high medical risk to get a flu vaccine as long as it is abundant," Medlock said. "But what we're losing in our current approach is the understanding that most flu is transmitted by children and young adults. They don't as often die from it, but they are the ones who spread it to everyone else."

The population and disease transmission modeling done in the new study outlines this, and concluded that a 25-100 percent reduction in deaths from flu or its complications could be achieved if current flu vaccine usage were shifted to much more heavily include children and young adults, as well as those at high risk.

One obstacle, experts say, is the historic reluctance to add even more vaccines to those already received and often mandated for school-age children.

"A simple program we could consider in our K-12 schools would be to have the school nurse, or other local professional, give every child an annual flu shot, with the parents being informed about it in advance and having the option to decline," Medlock said. "Vaccinating children could prevent a great deal of illness and save many lives at all ages, not just the children," he said. "More aggressive educational campaigns to reach young adults would also be helpful."

Collaborators on this research included scientists from Yale University and the University of Texas. It was supported by the National Institute of General Medical Sciences.

Editor's Note: The study this story is based on is available in ScholarsArchive@OSU: <http://bit.ly/14ZuFi0>

<http://bit.ly/15RPgFH>

The Iceman Suffered Brain Damage Before Death

An injury to the head, not an arrow wound, may have killed Ötzi the Iceman, the 5,300-year-old mummy found in the Italian Alps, says a new paleoproteomic study into the brain of Europe's oldest natural human mummy.

Jun 10, 2013 01:45 PM ET // by Rossella Lorenzi

The protein investigation appears to support a 2007 research into the mummy's brain. The study pointed to a cerebral trauma as the cause of death. At that time, the research relied on a CAT scan of the mummy's brain, which showed two dark-colored areas at the back of the cerebrum. The injury added to the already known arrowhead wound on the shoulder and wounds on the hand.

Found in Ötzi's left shoulder in 2001, the stone arrowhead has long been thought to have caused the prehistoric man's death, fatally severing his left subclavian artery. The 2007 study suggested that blood loss from the arrow wound would have first made Ötzi lose consciousness, with death coming later, from a violent blow to the head. Either the man's killer gave Ötzi the final whack, possibly by hitting him with a stone, or he could have fallen over backwards and hit his head on a rock, the researchers concluded.

The hypothesis had been left unexplored until 2010, when a research team from the European Academy of Bolzano/Bozen (EURAC), Saarland University, Kiel University and other partners decided to investigate the proteome of two pinhead-sized samples of brain tissue from the world-famous glacier corpse.

"The use of new protein-analysis methods has enabled us to pioneer this type of protein investigation on the soft tissue of a mummified human, extracting from the tiniest sample a vast quantity of data which in the future may well answer many further questions," the researchers said. Indeed, the scientists were able to identify a total of 502 different proteins. "Of these, 41 proteins are known to be highly abundant in brain tissue and nine are even specifically expressed in the brain," microbiologists Frank Maixner of EURAC, Andreas Tholey of Kiel University, and colleagues wrote in the journal *Cellular and Molecular Life Sciences*.

"Furthermore, we found 10 proteins related to blood and coagulation. An enrichment analysis revealed a significant accumulation of proteins related to stress response and wound healing," they wrote.

Found in a corpse almost devoid of blood, the astonishingly well-preserved clotted blood cells provide further evidence that Ötzi's brain had possibly suffered bruising shortly before his death.

Whether this was due to a blow to the forehead or a fall after being injured by the arrow remains unclear.

“Our data reopens former discussions about a possible injury of the Iceman’s head near the site where the tissue samples have been extracted,” the researchers said. Since his discovery in 1991 in a melting glacier in the Ötztal Alps - hence his name - the mummy has been extensively investigated.

Scientists discovered that Ötzi had brown eyes, was lactose intolerant, had a genetic predisposition for an increased risk for coronary heart disease, and probably had Lyme disease. The new protein-based research method could now provide insights that previously had not been possible, the researchers said.

<http://arstechnica.com/science/2013/06/new-phylum-of-bacteria-found-lurking-in-hospital-sinks-drain/>

New phylum of bacteria found lurking in hospital sink’s drain

Its genome hints that it may live inside some other organism.

by John Timmer - June 12 2013, 6:15am TST

Most of the life on Earth comes in the form of small, single-celled organisms. But even though we knew there was incredible diversity at the microbial level, these cells all look pretty similar under a microscope. For many of the bacterial species we've identified, the key step has been growing them in a flask so we can generate large enough numbers to study them.

Over the past decade, the advent of cheap DNA sequencing technology has helped the microbe discovery process along. Currently, we can sequence huge populations of microbes and get fragments of sequences that give us some sense of the full diversity of life. But these sequences tell us little more than the fact that a species exists. We still often know little about what it is and how it manages to make a living.

Now some researchers have managed to generate a genome sequence from a single bacterium, and they have used this technique to scan for new species in a biofilm isolated from a hospital sink. The results include the genome of a previously unrecognized phylum of bacteria, called TM6, that appears to be an obligate symbiote, perhaps living inside another cell found in the biofilm.

Researchers tend to work with bacteria that grow in a liquid culture but most bacteria don't live that way. Instead they form biofilms, a dense mesh of material that is inhabited by entire communities of bacteria and which hosts multiple species. It's easy to do some DNA sequencing to figure out how many species inhabit these biofilms, but finding out more about the species is tough, because many of them won't survive in the oxygen rich culture conditions that are typically used.

To get around this, an international team of researchers has developed a technique for isolating individual bacterial cells with a cell-sorting machine. At first, they kept isolating fragments of the biofilm rather than cells, so they ended up having to pool anywhere from 20-100 items the machine called "cells" in order to increase the chances of having a single cell present. Most of these cells were things we already knew about, so the authors started doing some quick checks of some key genes that encode ribosomal RNA. If those indicated the sample had a single cell and the cell wasn't already known, they produced an entire genome from it.

This week, the group released a paper on a genome from a group of species called TM6. The name comes from “Torf, Mittlere Schicht,” which is “peat, middle layer” in German. That's the first case instance where the ribosomal RNA for this group of species had appeared but since then it's been found in a host of environmental samples: domestic water sources, acidic cave biofilms, acid mine drainage biofilms, wastewater biofilms, soil, contaminated groundwater and subsurface sites, aquatic moss, hypersaline mats, peat bogs, and peat swamps. The ribosomal RNA had suggested it was distantly related to all the bacterial groupings we knew about, and now the genome confirms it.

Perhaps the most striking thing about it is the fact that fully 43 percent of the genes appear to encode proteins that we've never seen before. Typically, due to a combination of common descent and gene transfer, many of the genes in new species are familiar. This one is so far out, most of them don't look like anything we know about. Which, of course, makes it hard to predict what they might do.

In contrast, when it comes to familiar genes, many are missing in action. The TM6 genome seems to have a stripped down metabolism that's probably anaerobic. It doesn't seem to be able to make its own amino acids or nucleotides (protein and DNA components, respectively) and it can't make a flagella to move itself around. All of which suggests it's probably a symbiotic organism, cooperating with another species to share vital biochemicals that only one of the two can produce.

What might it be living with? Some of the genome hints that it may be a eukaryote like an amoeba. A few of the genes seem to contain sequences that are typically only found in eukaryotes (larger cells with a nucleus), suggesting they got in this new species via horizontal transfer of some DNA. This is quite common among bacteria that live inside their hosts, suggesting that TM6's host is a eukaryote. In the past, amoeba have been found in biofilms, which often carry a number of bacterial species along with them.

Overall, the genome sequences don't match up well with anything we know, suggesting that TM6 represents an entirely new phylum of bacteria. Its closest relatives are the Acidobacteria, which themselves had gone

unrecognized until the 1990s. If this holds up, it will continue the bacteria's remarkable expansion. They started with just 11 phyla back in 1987, and most recent estimates now say that there are 30 bacterial phyla on the planet. TM6 is likely to make that count 31.

Who knows what we'll find when we start looking beyond a hospital sink's drain.

PNAS, 2013. DOI: 10.1073/pnas.1219809110 (About DOIs).

http://www.eurekalert.org/pub_releases/2013-06/uop-oro061113.php

Oldest record of human-caused lead pollution detected

Pitt researchers discover lead pollution dating back 8,000 years in northernmost region of Michigan's Upper Peninsula

6/11/13/mab/cjhm

PITTSBURGH—Humans began contributing to environmental lead pollution as early as 8,000 years ago, according to a University of Pittsburgh research report.

The Pitt research team detected the oldest-discovered remains of human-derived lead pollution in the world in the northernmost region of Michigan, suggesting metal pollution from mining and other human activities appeared far earlier in North America than in Europe, Asia, and South America. Their findings are highlighted on the cover of the latest issue of *Environmental Science & Technology*.

"Humanity's environmental legacy spans thousands of years, back to times traditionally associated with hunter-gatherers. Our records indicate that the influence of early Native Americans on the environment can be detected using lake sediments," said David Pompeani, lead author of the research paper and a PhD candidate in Pitt's Department of Geology and Planetary Science. "These findings have important implications for interpreting both the archeological record and environmental history of the upper Great Lakes."

The University of Pittsburgh research team—which included, from Pitt's Department of Geology and Planetary Science, Mark Abbott, associate professor of paleoclimatology, and Daniel Bain, assistant professor of catchment science, along with Pitt alumnus Byron A. Steinman (A&S '11G)—examined Michigan's Keweenaw Peninsula because it is the largest source of pure native copper in North America. Early surveys of the region in the 1800s identified prehistoric human mining activity in the form of such tools as hammerstones, ladders, and pit mines.

The team from the Department of Geology and Planetary Science investigated the timing, location, and magnitude of ancient copper mining pollution. Sediments were collected in June 2010 from three lakes located near ancient mine pits. They analyzed the concentration of lead, titanium, magnesium, iron, and organic matter in the collected sediment cores—finding distinct decade- to century-scale increases in lead pollution preserved from thousands of years ago.

"These data suggest that measurable levels of lead were emitted by preagricultural societies mining copper on Keweenaw Peninsula starting as early as 8,000 years ago," said Pompeani. "Collectively, these records have confirmed, for the first time, that prehistoric pollution from the Michigan Copper Districts can be detected in the sediments found in nearby lakes."

By contrast, reconstructions of metal pollution from other parts of the world, such as Asia, Europe, and South America, only provide evidence for lead pollution during the last 3,000 years, said Pompeani. "We're hopeful that our work can be used in the future to better understand past environmental changes," said Abbott.

The team is currently investigating places near other prehistoric copper mines surrounding Lake Superior. *The research paper, "Lake Sediments Record Prehistoric Lead Pollution Related to Early Copper Production in North America," was first published online May 14 in Environmental Science and Technology. The work was funded by a Henry Leighton Memorial Fund grant through the University of Pittsburgh Department of Geology and Planetary Science, a graduate student research award from the Geological Society of America, and instrumental support from the National Science Foundation.*

http://www.eurekalert.org/pub_releases/2013-06/dnal-rpn061113.php

Research paints new picture of 'dinobird' feathers

The first complete chemical analysis of feathers from Archaeopteryx, a famous fossil linking dinosaurs and birds, reveals that the feathers were patterned—light in color, with a dark edge and tip—rather than all black, as previously thought.

Menlo Park, Calif. - The findings came from X-ray experiments at the Department of Energy's (DOE) SLAC National Accelerator Laboratory, where scientists were able to find chemical traces of the original dinobird and its pigments in the rock that entombed it 150 million years ago.

"This is a big leap forward in our understanding of the evolution of plumage," said Phillip Manning, a paleontologist at the University of Manchester and lead author of the report in the June 13 issue of the *Journal of Analytical Atomic Spectrometry*.

Only 11 specimens of Archaeopteryx have been found, the first one consisting of a single feather. Until a few years ago, researchers thought all the bones and tissues of the original animal would have been replaced by minerals during fossilization, leaving no chemical traces behind.

But two recently developed methods have turned up more information about the dinobird and its plumage.

The first is the discovery of melanosomes—microscopic 'paint pot' structures containing pigment—in fossils. A team led by researchers at Brown University announced last year that an analysis of melanosomes in the Archaeopteryx feather specimen showed that the feather was black. They identified the feather as a covert—a type of feather that covers the primary and secondary wing feathers—and said its heavy pigmentation may have strengthened it against the wear and tear of flight, as it does in modern birds.



This is an artist's illustration of how Archaeopteryx may have looked sporting its new pigmentation. Courtesy University of Manchester

However, that study examined melanosomes from just a few locations in the fossilized feather, said SLAC's Uwe Bergmann. "It's actually quite a beautiful paper," he said, "but they took just tiny samples of the feather, not the whole thing." The second is a method Bergmann, Manning and Roy Wogelius of the University of Manchester developed for rapidly scanning entire fossils and analyzing their chemistry with an X-ray beam at SLAC's Stanford Synchrotron Radiation Lightsource (SSRL).

Over the past three years, they led a team that used this method to discover chemicals left by the dinobird's bones and feathers in the surrounding rock, as well as pigments from the fossilized feathers of two of the first known birds. This allowed them to recreate the plumage pattern of a bird that lived more than 120 million years ago.

In the latest study, the team scanned the entire fossil of the first Archaeopteryx feather with the SSRL X-ray beam. They found trace metals associated with pigments and organic sulfur compounds that could only have come from the animal itself. The fact that these compounds have been preserved in the fossil for 150 million years is extraordinary, Manning said.

Together these chemical traces show that the feather was light in color, with areas of darker pigmentation along one edge and on the tip. Scans of a second fossilized Archaeopteryx, known as the Berlin counterpart, revealed that its covert feathers had the same pigmentation pattern, Manning said.

He said the results show that the chemical analysis provided by synchrotron X-ray sources such as SSRL is crucial for understanding these ancient fossils, including plumage patterns that play an important role in the courtship, reproduction and evolution of birds and contain clues to their health, eating habits and environment. *The research team included Dimosthenis Sokaras and Roberto Alonso of SLAC and scientists from the University of Manchester in England, the Black Hills Institute of Geological Research in South Dakota and the Museum für Naturkunde in Berlin, which provided the Archaeopteryx fossils for analysis.*

<http://www.medscape.com/viewarticle/805587?src=rss>

New Quadrivalent Influenza Vaccine Gets FDA Nod

The US Food and Drug Administration (FDA) today approved a 4-strain inactivated influenza virus vaccine from Sanofi Pasteur (Fluzone Quadrivalent) for use in children aged 6 months or older, adolescents, and adults.

Megan Brooks

Fluzone Quadrivalent is the "first and only" 4-strain influenza vaccine option for children as young as 6 months, Sanofi Pasteur notes in a statement. Fluzone Quadrivalent joins 2 other quadrivalent vaccines already approved in the United States. They are Fluarix Quadrivalent (GlaxoSmithKline), approved for adults and children aged 3 years or older, and FluMist (MedImmune), approved for adults and children aged 2 years or older.

Fluzone Quadrivalent will be available in the US for the upcoming 2013-2014 influenza season in preservative-free, prefilled syringes and single-dose vials for intramuscular administration, the company said.

Until this year, seasonal influenza vaccines included only 1 B strain. Fluzone Quadrivalent vaccine includes 2 A strains and 2 B strains to help protect against influenza disease, Sanofi Pasteur notes in a statement.

"Epidemics of influenza B occur every 2 to 4 years in all age groups. Influenza B is a common cause of influenza-related morbidity and mortality in children and has been associated with pneumonia and other respiratory illnesses, nervous system disease, muscle pain and inflammation, and other complications," the company explains.

"Protection against the type B flu strain may be an especially important factor that health care providers consider when immunizing children since influenza B causes a substantial number of illnesses, hospitalizations and deaths in the pediatric population," said David Greenberg, MD, Sanofi Pasteur vice president US scientific and medical affairs.

The most common local and systemic adverse reactions seen with Fluzone Quadrivalent include pain, erythema, and swelling at the vaccination site; myalgia, malaise, headache, and fever (irritability, crying, and drowsiness in young children).

Fluzone Quadrivalent vaccine should not be administered to anyone with severe allergic reactions to any vaccine component, including egg protein, or to a previous dose of any influenza vaccine, the company said.

<http://bit.ly/159uDCy>

Now-extinct wolf may be ancestor of modern-day dogs

No strong signs of canine ancestry among living grey wolves

By Tina Hesman Saey

Dogs evolved from a wolf lineage that has since gone extinct, a study of canine DNA suggests.

Researchers have long assumed that dogs branched off from a still-living wolf species. Geneticists have combed the world looking for wolf populations that most closely resemble dogs genetically, and concluded that dogs originated in the Middle East or Southeast Asia. But fossils suggest Europe as the site of dog domestication.

Posted June 4 at arXiv.org, the new study finds that interbreeding between dogs and wolves after domestication has made wolves in certain locations seem more closely related to dogs than they actually are.

Adam Freedman of Harvard University and an international group of collaborators compared DNA from three breeds of dogs (a boxer, a Basenji and an Australian dingo) to that of three gray wolves (*Canis lupus*) from Croatia, China and Israel — three locations proposed as centers of dog domestication. All of the wolves were equally related to the dogs, indicating that none of them has a special claim to being the dog ancestor. The authors suggest that some other type of wolf, possibly an extinct species, produced the first Fido.

The researchers' findings leave dog origins up in the air. "I agree with them that we should back off from setting a needle in the map" to indicate where dogs first appeared, says Mattias Jakobsson, a population geneticist at Uppsala University in Sweden.

With additional data, the study also challenges a recent report that the rise of agriculture and the ability to digest starchy food may have triggered domestication. Freedman and his colleagues date dog domestication to about 15,000 years ago, well before the advent of agriculture.

The earlier study found that dogs carry extra copies of a gene called AMY2B, which produces an enzyme that breaks down starch, while wolves have only two copies (SN Online: 1/23/13). The new study, which is larger and includes more wolves and dog breeds, found that some wolves actually do have extra copies of the gene. Dingoes, which split off from other dogs 3,500 to 5,000 years ago, also have two copies and Siberian huskies have only three or four.

Freedman's combined data make a case against carbohydrates playing a key role in taming canines, Jakobsson says. "To me it says starch wasn't involved in the first domestication event."

A. H. Freedman et al. *Genome sequencing highlights genes under selection and the dynamic early history of dogs.* arXiv:1305.7390. Posted June 4, 2013. [\[Go to\]](#)

http://www.eurekalert.org/pub_releases/2013-06/gwus-mwt060613.php

Moderate-intensity walking timed just right might help protect against Type 2 diabetes

15-minute walks taken after meals helped curb risky rise in blood sugar, new study says

WASHINGTON, DC - A fifteen minute walk after each meal appears to help older people regulate blood sugar levels and could reduce their risk of developing type 2 diabetes, according to a new study by researchers at the George Washington University School of Public Health and Health Services (SPHHS). The study, published today in *Diabetes Care*, found that three short post-meal walks were as effective at reducing blood sugar over 24 hours as a 45-minute walk of the same easy-to-moderate pace. Moreover, post-meal walking was significantly more effective than a sustained walk at lowering blood sugar for up to three hours following the evening meal.

"These findings are good news for people in their 70s and 80s who may feel more capable of engaging in intermittent physical activity on a daily basis, especially if the short walks can be combined with running errands or walking the dog," said lead study author Loretta DiPietro, PhD, MPH, chair of the SPHHS Department of Exercise Science. "The muscle contractions connected with short walks were immediately effective in blunting the potentially damaging elevations in post-meal blood sugar commonly observed in older people," she said.

The findings, if confirmed by additional research, could lead to an inexpensive preventive strategy for a pre-diabetic condition that can over time develop into frank type 2 diabetes, she said. An estimated 79 million Americans have pre-diabetes but most have no idea they are at risk. Other studies have suggested weight loss and exercise can prevent type 2 diabetes but this is the first study to examine short bouts of physical activity timed around the risky period following meals—a time when blood sugar can rise rapidly and potentially cause damage.

DiPietro and her colleagues recruited ten people age 60 and older who were otherwise healthy but at risk of developing type 2 diabetes due to higher-than-normal levels of fasting blood sugar and to insufficient levels of physical activity. Older people may be particularly susceptible to impairments in blood sugar control after meals due to insulin resistance in the muscles and also due to a slow or low insulin secretion from the pancreas. Post-meal high blood sugar is a key risk factor in the progression from impaired glucose tolerance (pre-diabetes) to type 2 diabetes and cardiovascular disease, DiPietro said.

Participants completed three randomly-ordered exercise protocols spaced four weeks apart. Each protocol comprised a 48-hour stay in a whole-room calorimeter, with the first day serving as a control period. On the second day, participants engaged in either post-meal walking for 15 minutes after each meal or 45 minutes of sustained walking performed at 10:30 in the morning or at 4:30 in the afternoon. All walking was performed on a treadmill at an easy-to-moderate pace. Participants ate standardized meals and their blood sugar levels were measured continuously over each 48 hour stay.

The team observed that the most effective time to go for a post-meal walk was after the evening meal. The exaggerated rise in blood sugar after this meal—often the largest of the day—often lasts well into the night and early morning and this was curbed significantly as soon as the participants started to walk on the treadmill, DiPietro said.

Most people eat a big afternoon or evening meal and then take a nap or watch television. "That's the worst thing you can do," DiPietro said. "Let the food digest a bit and then get out and move," she says. A walk timed to follow the big evening meal is particularly important because this research suggests high post-dinner blood sugar is a strong determinant of excessive 24-hour glucose levels, DiPietro said.

The results of this study must be confirmed with larger trials that include more people, DiPietro cautioned. Still this study monitored blood sugar levels continuously for 48-hour periods and controlled the environment carefully. The findings have tremendous public health importance in that they offer powerful evidence that smaller doses of exercise repeated several times per day have greater overall benefits to blood sugar control among older people than one large sustained dose—especially if those short bouts are timed just right.

http://www.eurekalert.org/pub_releases/2013-06/acop-sop061213.php

Survey of physicians suggests tablets more useful than smartphones

AmericanEHR Partners release survey results for mobile phone and tablet usage among EHR and non-EHR users

Philadelphia - Two reports from AmericanEHR Partners based on a survey of nearly 1,400 physicians suggests that tablets are of greater use for clinical purposes than smartphones.

"Mobile Usage in the Medical Space 2013" and "Tablet Usage by Physicians 2013" reveal that the most common activity of physicians who use an electronic health record (EHR) and use a smartphone or tablet is "sending and receiving emails." The second most frequent activity among tablet users is accessing EHRs (51 percent daily). Just 7 percent of physicians use their smartphone to access EHRs. Among physicians who have an EHR, 75 percent use a smartphone and 33 percent use a tablet, but time spent on tablets is 66 percent higher than time spent on smartphones.

"These two reports provide useful insights into how physicians use technology to interact with patients, physician satisfaction with mobile devices and apps, and the differences of technology use within various user demographics," said Thomas Stringham, co-founder of AmericanEHR Partners, which provides comprehensive information to support clinicians in the selection and use of EHRs to improve health care delivery.

The top market share position is held by Apple®, with 55 percent of physicians using smartphones and 54 percent using tablets. Clinical app usage in a medical practice was much higher among smartphone users (51 percent daily) than tablet users (30 percent daily). The top five smartphone apps used in a medical practice were Epocrates®, Medscape®, MedCalc®, Skyscape®, and Doximity®. The top five tablet apps used in a medical practice were Epocrates®, Medscape®, Up To Date®, MedCalc®, and Skyscape®.

Only 28 percent of smartphone users and 18 percent of tablet users were "very satisfied" with the quality of apps for their profession.

"As the adoption of mobile devices increases, so do the expectations of clinical users," Stringham said. "The health IT sector and app developers have an opportunity to improve the quality and usefulness of clinical mobile apps."

Additional highlights from the "Mobile Usage in the Medical Space 2013" report include:

Mobile phone usage by physicians who use an EHR: 77 percent use a smartphone, 15 percent use a regular mobile phone, and 8 percent use neither.

About 75 percent of physicians use their smartphone to communicate with other physicians at least once weekly.

About 70 percent of physicians use their smartphone to research medications at least once weekly.

Of the physicians surveyed, about 25 percent who use a regular phone intend on purchasing a smartphone within the next six months.

Additional highlights from the "Tablet Usage by Physicians 2013" report include:

About 33 percent of EHR users and 25 percent of non-EHR users use a tablet device in their medical practice.

Smaller practices, defined as three doctors or fewer, are likely to conduct a broader range of activities on their tablet, such as banking, communicating with patients, or taking photos for clinical purposes.

About 33 percent of EHR users are very satisfied with their tablet device, while 44 percent are somewhat satisfied.

About 33 percent of EHR users use a tablet to research medications daily.

http://www.eurekalert.org/pub_releases/2013-06/nlmc-frc061213.php

Fingernails reveal clues to limb regeneration

Researchers discover biochemical pathway that links nail growth to fingertip regeneration

Mammals possess the remarkable ability to regenerate a lost fingertip, including the nail, nerves and even bone. In humans, an amputated fingertip can sprout back in as little as two months, a phenomenon that has remained poorly understood until now. In a paper published today in the journal *Nature*, researchers at NYU Langone Medical Center shed light on this rare regenerative power in mammals, using genetically engineered mice to document for the first time the biochemical chain of events that unfolds in the wake of a fingertip amputation. The findings hold promise for amputees who may one day be able to benefit from therapies that help the body regenerate lost limbs.

"Everyone knows that fingernails keep growing, but no one really knows why," says lead author Mayumi Ito, PhD, assistant professor of dermatology in the Ronald O. Perleman Department of Dermatology at NYU School of Medicine. Nor is much understood about the link between nail growth and the regenerative ability of the bone and tissue beneath the nail. Now, Dr. Ito and team have discovered an important clue in this process: a population of self-renewing stem cells in the nail matrix, a part of the nail bed rich in nerve endings and blood vessels that stimulate nail growth. Moreover, the scientists have found that these stem cells depend upon a family of proteins known as the "Wnt signaling network"—the same proteins that play a crucial role in hair and tissue regeneration—to regenerate bone in the fingertip.

"When we blocked the Wnt-signaling pathway in mice with amputated fingertips, the nail and bone did not grow back as they normally would," says Dr. Ito. Even more intriguing, the researchers found that they could manipulate the Wnt pathway to stimulate regeneration in bone and tissue just beyond the fingertip.

"Amputations of this magnitude ordinarily do not grow back," says Dr. Ito. These findings suggest that Wnt signaling is essential for fingertip regeneration, and point the way to therapies that could help people regenerate lost limbs. An estimated 1.7 million people in the U.S. live with amputations.

The team's next step is to zoom in on the molecular mechanisms that control how the Wnt signaling pathway interacts with the nail stem cells to influence bone and nail growth.

<http://bit.ly/12E3eOx>

Check it's not MERS, WHO tells world's health workers

Medics everywhere: be on the alert for Middle East respiratory syndrome (MERS), the disease that emerged last September in Saudi Arabia.

17:42 11 June 2013 by Andy Coghlan

It is caused by a coronavirus related to the one that causes SARS, which infected over 8000 people in 2003.

"All countries in the world need to ensure that their healthcare workers are aware of the virus and the disease it can cause, and that when unexplained cases of pneumonia are identified, MERS should be considered," said the World Health Organization in a statement on Monday, following a summit in Riyadh, Saudi Arabia.

As of last Friday, 55 cases had been confirmed, 31 of which were fatal. Most of the cases were in four Middle Eastern countries, with 40 in Saudi Arabia itself. But infected travellers have spread the disease elsewhere, hence the WHO's warning.

Although the route of infection remains unknown, the first case of person-to-person transmission occurred in France in April.

http://www.eurekalert.org/pub_releases/2013-06/dnl-don061213.php

Discovery of new material state counterintuitive to laws of physics

When you squeeze something, it gets smaller. Unless you're at Argonne National Laboratory.

LEMONT, ILL. --- At that suburban Chicago laboratory, a group of scientists has seemingly defied the laws of physics and found a way to apply pressure to make a material expand instead of compress/contract.

"It's like squeezing a stone and forming a giant sponge," said Karena Chapman, a chemist at the U.S.

Department of Energy laboratory. "Materials are supposed to become denser and more compact under pressure.

We are seeing the exact opposite. The pressure-treated material has half the density of the original state. This is counterintuitive to the laws of physics."

Because this behavior seems so impossible, Chapman and her colleagues spent several years testing and retesting the material until they believed the unbelievable and understood how the impossible could be possible. For every experiment, they got the same mind-bending results. "The bonds in the material completely rearrange," Chapman said. "This just blows my mind."

This discovery will do more than rewrite the science text books; it could double the variety of porous framework materials available for manufacturing, health care and environmental sustainability.

Scientists use these framework materials, which have sponge-like holes in their structure, to trap, store and filter materials. The shape of the sponge-like holes makes them selectable for specific molecules, allowing their use as water filters, chemical sensors and compressible storage for carbon dioxide sequestration of hydrogen fuel cells. By tailoring release rates, scientists can adapt these frameworks to deliver drugs and initiate chemical reactions for the production of everything from plastics to foods.

"This could not only open up new materials to being porous, but it could also give us access to new structures for selectability and new release rates," said Peter Chupas, an Argonne Lab chemist who helped discover the new materials.

The team published the details of their work in the May 22 issue of the Journal of the American Chemical Society in an article titled "Exploiting High Pressures to Generate Porosity, Polymorphism, And Lattice Expansion in the Nonporous Molecular Framework Zn(CN)₂".

The scientists put zinc cyanide, a material used in electroplating, in a diamond-anvil cell at the Advanced Photon Source (APS) at Argonne Lab and applied high pressures of 0.9 to 1.8 gigapascals, or about 9,000 to 18,000 times the pressure of the atmosphere at sea level. This high pressure is within the range affordably reproducible by industry for bulk storage systems. By using different fluids around the material as it was squeezed, the scientists were able to create five new phases of material, two of which retained their new porous ability at normal pressure. The type of fluid used determined the shape of the sponge-like pores. This is the first time that hydrostatic pressure has been able to make dense materials with interpenetrated atomic frameworks into novel porous materials. Several series of in situ high-pressure X-ray powder diffraction experiments were performed at the 1-BM, 11-ID-B, and 17-BM beamlines of the APS to study the material transitions.

"By applying pressure we were able to transform a normally dense, nonporous material into a range of new porous materials that can hold twice as much stuff," Chapman said. "This counterintuitive discovery will likely double the amount of available porous framework materials, which will greatly expand their use in pharmaceutical delivery, sequestration, material separation and catalysis."

The scientists will continue to test the new technique on other materials.

The research is funded by the U.S. Department of Energy's Office of Science.

<http://www.scientificamerican.com/article.cfm?id=olive-oil-compound-makes-throat-itch-prevent-alzheimers>

An Olive Oil Compound That Makes Your Throat Itch May Prevent Alzheimer's

An olive oil compound that makes your throat itch may also help prevent Alzheimer's

By Rachel Nuwer

Doctors and nutritionists have long associated the Mediterranean diet with human health benefits, including a lower risk of Alzheimer's disease. A recent study of 1,880 elderly people living in New York City, for example, showed that those who strongly adhered to a Mediterranean diet over the study's 14-year span had a 32 to 40 percent lower incidence of Alzheimer's compared with those who did not.

Extra virgin olive oil seems to be one of the main factors behind this risk reduction. People adhering to a Mediterranean diet consume up to 50 milliliters (around one fifth of a cup) of the fragrant green liquid a day. Previously, researchers assumed this benefit came from extra virgin olive oil's high concentration of monounsaturated fatty acids. But in 2005 scientists discovered that oleocanthal—the naturally occurring compound that elicits a peppery, burning sensation in the back of the throat—seemed to produce effects strikingly similar to those of ibuprofen, which tamps down inflammation. Since then, investigators have turned their attention to the potential benefits of this particular compound.

Some studies have shown that oleocanthal interferes with the formation of characteristic neurofibrillary tangles and beta-amyloid plaques, both of which play principal roles in Alzheimer's neurological devastation. Research published online in ACS Chemical Neuroscience in February offers new details on how the compound works. The study authors applied different concentrations of oleocanthal over three days to mouse brain cell cultures. They also administered oleocanthal to live mice—the first time such an experiment has been done—every day for two weeks. In both trials, levels of two proteins that play major roles in transporting beta-amyloid out of the brain as well as enzymes that degrade beta-amyloid increased significantly after administering oleocanthal. The researchers also introduced beta-amyloid to the live mice brains. Compared with control groups, the mice that were given oleocanthal showed significantly enhanced clearance and degradation of the beta-amyloid peptides. “We're trying to further understand oleocanthal's mechanism and maybe eventually try to find compounds that can work in the same way for drug development,” says Amal K. Kaddoumi, an assistant professor of pharmaceuticals at the University of Louisiana at Monroe and one of the paper's authors. The findings, she notes, most likely have more application for Alzheimer's prevention than treatment. She also thinks that other factors, besides high olive oil consumption, account for the so-called Mediterranean miracle, such as exercise and the large helpings of fresh vegetables that people in that region regularly consume. Oleocanthal is one of several compounds that scientists have been working with to clear beta-amyloid from the brain. Others include an older skin cancer drug that last year helped alleviate Alzheimer's symptoms in mice and antibodies that bind directly to beta-amyloid and remove it. “This paper is beginning to close in on what the specific components are in these more nutraceutical remedies that are actually helping us,” says Kenneth S. Kosik of the University of California, Santa Barbara.

Kosik points out, however, that until clinical trials in humans take place, people must be cautious in interpreting the results. Kaddoumi's group is working to secure funding for just such clinical trials.

<http://www.nature.com/news/computer-memory-can-be-read-with-a-flash-of-light-1.13169>

Computer memory can be read with a flash of light

Prototype device combines speed and durability.

Katherine Bourzac

Modern computer-memory technologies come with a trade-off. There is speedy but short-term storage for on-the-fly processing — random-access memory, or RAM — and slow but enduring memory for data and programs that need to be stored long term, typically on a hard disk or flash drive. But a prototype memory device described today in Nature Communications¹ combines speed, endurance and low power consumption by uniting electronic storage with a read-out based on the physics that powers solar panels.

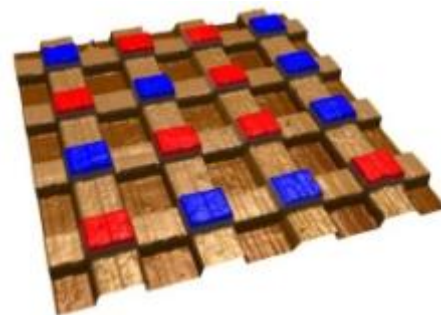
Ramamoorthy Ramesh, a materials scientist at the University of California, Berkeley, and Junling Wang, a specialist in oxide materials at the Nanyang Technological University in Singapore, built their prototype device using a material called bismuth ferrite.

When light shines on this prototype memory device, it produces voltages in that make it possible to read out the information in the 16-cell array of digital bits.

In conventional computer memory, information is stored in cells that hold different amounts of electric charge, each representing a binary '1' or '0'. Bismuth ferrite, by contrast, can represent those binary digits, or bits, as one of two polarization states, and can switch between these states when a voltage is applied — a property called ferroelectricity. Ferroelectric RAM based on other materials is already on the market. It is speedy, but the technology has not found widespread use. One problem is that the electrical signal used to read out a bit erases it, so the data must be rewritten every time. This leads to reliability problems over time.

Ramesh and Wang realized that they could take advantage of another property of bismuth ferrite to read these memory arrays in a nondestructive way. In 2009, researchers at Rutgers University in Piscataway, New Jersey, demonstrated² that the material has a photovoltaic response to visible light — meaning that when it is hit by light, a voltage is created. The size of the voltage depends on which polarization state the material is in, and can be read out using electrodes or transistors. Crucially, shining light on the material doesn't change its polarization, and so does not erase the data stored in it.

To test whether photovoltaic ferroelectric memory really worked, Ramesh and Wang grew films of bismuth ferrite on top of a metal oxide, then etched it into four strips. On top of that they laid four metal strips at right angles to the first set. The 16 squares where the crossbars met each acted as memory cells, and the metal and metal oxide acted as electrodes. The team used the electrodes to polarize the cells, then shone light onto the whole array and found that it produced two types of voltage readings — one negative (0) and one positive (1).



It takes less than 10 nanoseconds to write to and read the cells, and recording the data requires about 3 volts. The leading nonvolatile RAM technology, flash, takes about 10,000 times longer to read and write, and needs 15 volts to record.

Scale down

"This is an important step towards real technological applications of the ferroelectric photovoltaic effect," says Sang-Wook Cheong, a condensed-matter physicist at Rutgers, who led the 2009 study.

Victor Zhirnov, a materials specialist at the Semiconductor Research Corporation in Durham, North Carolina, says that the technology will need to be made much smaller before it is competitive. Commercial flash memory is built using equipment that can pattern features as small as 22 nanometres, whereas the strips in the photovoltaic ferroelectric memory device are a hefty 10 micrometres wide. "Smaller size results in more memory per cubic centimetre, and thus lower cost per bit," says Zhirnov.

Ramesh says that there is no fundamental reason that the memory cells in his device could not be made as small as those in other memory arrays, although it will pose some practical challenges.

There is also the matter of designing a system to light up the cells one at a time. Illuminating the whole array all the time, as in these first experiments, is probably not practical, says Ramesh. So engineers may have to design optical parts to funnel light to each cell individually when it needs to be read.

Nature doi:10.1038/nature.2013.13169

http://www.eurekalert.org/pub_releases/2013-06/plos-mpf060613.php

Male preference for younger female mates identified as likely cause of menopause

Menopause caused by male preference for younger mates

A study published in this week's PLOS Computational Biology reports that menopause is an unintended outcome of natural selection caused by the preference of males for younger female mates. While conventional thinking has held that menopause prevents older women from continuing to reproduce, the researchers, from McMaster's University, concluded that it is the lack of reproduction that has given rise to menopause.

The researchers found that, over time, competition among men of all ages for younger mates has left older females with much less chance of reproducing. The pressures of natural selection focus on the survival of the species through individual fitness, so they protect fertility in women while they are most likely to reproduce.

"In a sense it is like aging, but it is different because it is an all-or-nothing process that has been accelerated because of preferential mating," says Rama Singh, one of the study's authors. "Menopause is believed to be unique to humans, but no one had yet been able to offer a satisfactory explanation for why it occurs,"

The researchers used computational models implemented by computer simulations to show how male mating preference for younger females could lead to the accumulation of mutations that were detrimental to female fertility and thus produce a menopausal period. However, the prevailing "grandmother theory" holds that women have evolved to become infertile after a certain age to allow them to assist with rearing grandchildren, thus improving the survival of kin. Singh says that does not add up from an evolutionary perspective.

"How do you evolve infertility? It is contrary to the whole notion of natural selection. Natural selection selects for fertility, for reproduction -- not for stopping it," he says. "This theory says if women were reproducing all along, and there were no preference against older women, women would be reproducing like men are for their whole lives."

The development of menopause, then, was not a change that improved the survival of the species, but one that merely recognized that fertility did not serve any ongoing purpose beyond a certain age.

The consequence of menopause, however, is not only lost fertility for women, but an increased risk of illness and death that arises with hormonal changes that occur with menopause. Singh says a benefit of the new research could be to suggest that if menopause developed over time, that ultimately it could also be reversed.

Financial disclosure: This research was resourced partially by the Origins Institute and Shared Hierarchical Academic Research Computing Network at McMaster University and funded by the Natural Sciences and Engineering Research Council of Canada (Discovery Grants RGPIN235-07 to RSS and 261590 to JRS; <http://www.nserc-crsng.gc.ca>). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Competing interests: The authors have declared that no competing interests exist.

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http://www.eurekalert.org/pub_releases/2013-06/mcsc-mri061313.php

Monell-led research identifies scent of melanoma

New research may lead to early non-invasive detection and diagnosis

PHILADELPHIA - According to new research from the Monell Center and collaborating institutions, odors from human skin cells can be used to identify melanoma, the deadliest form of skin cancer. In addition to detecting a

unique odor signature associated with melanoma cells, the researchers also demonstrated that a nanotechnology-based sensor could reliably differentiate melanoma cells from normal skin cells. The findings suggest that non-invasive odor analysis may be a valuable technique in the detection and early diagnosis of human melanoma.

Melanoma is a tumor affecting melanocytes, skin cells that produce the dark pigment that gives skin its color. The disease is responsible for approximately 75 percent of skin cancer deaths, with chances of survival directly related to how early the cancer is detected. Current detection methods most commonly rely on visual inspection of the skin, which is highly dependent on individual self-examination and clinical skill.

The current study took advantage of the fact that human skin produces numerous airborne chemical molecules known as volatile organic compounds, or VOCs, many of which are odorous. "There is a potential wealth of information waiting to be extracted from examination of VOCs associated with various diseases, including cancers, genetic disorders, and viral or bacterial infections," notes George Preti, PhD, an organic chemist at Monell who is one of the paper's senior authors.

In the study, published online ahead of print in the *Journal of Chromatography B*, researchers used sophisticated sampling and analytical techniques to identify VOCs from melanoma cells at three stages of the disease as well as from normal melanocytes. All the cells were grown in culture.

The researchers used an absorbent device to collect chemical compounds from air in closed containers containing the various types of cells. Then, gas chromatography-mass spectrometry techniques were used to analyze the compounds and identified different profiles of VOCs emitting from melanoma cells relative to normal cells.

Both the types and concentrations of chemicals were affected. Melanoma cells produced certain compounds not detected in VOCs from normal melanocytes and also more or less of other chemicals. Further, the different types of melanoma cells could be distinguished from one another.

Noting that translation of these results into the clinical diagnostic realm would require a reliable and portable sensor device, the researchers went on to examine VOCs from normal melanocytes and melanoma cells using a previously described nano-sensor.

Constructed of nano-sized carbon tubes coated with strands of DNA, the tiny sensors can be bioengineered to recognize a wide variety of targets, including specific odor molecules. The nano-sensor was able to distinguish differences in VOCs from normal and several different types of melanoma cells.

"We are excited to see that the DNA-carbon nanotube vapor sensor concept has potential for use as a diagnostic. Our plan is to move forward with research into skin cancer and other diseases," said A.T. Charlie Johnson, PhD, Professor of Physics at the University of Pennsylvania, who led the development of the olfactory sensor.

Together, the findings provide proof-of-concept regarding the potential of the two analytical techniques to identify and detect biomarkers that distinguish normal melanocytes from different melanoma cell types.

"This study demonstrates the usefulness of examining VOCs from diseases for rapid and noninvasive diagnostic purposes," said Preti. "The methodology should also allow us to differentiate stages of the disease process."

Current studies are focusing on analysis of VOCs from tumor sites of patients diagnosed with primary melanoma.

Also contributing to the research were lead author Jae Kwak, Michelle Gallagher, Mehmet Hakan Ozdener, Charles J. Wysocki, Adam Faranda, and Amaka Isamah, all from Monell; A. T. Charlie Johnson, Brett R. Goldsmith, and Steven S. Fakharzadeh from the University of Pennsylvania; and Meenhard Herlyn from The Wistar Institute. Research reported in the publication was supported by The National Institute on Deafness and Other Communication Disorders of the National Institutes of Health under Award Number T 32 DC00014-26 to Monell. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. Additional funds were donated to the Monell Center by Ms. Bonnie Hunt in memory of her parents, Ida and Percy Hunt. Support for Drs Johnson and Goldsmith came from the University of Pennsylvania Nano/Bio Interface Center through National Science Foundation grant NSEC DMR08-32802.

http://www.eurekalert.org/pub_releases/2013-06/elar-hpo061013.php

High prevalence of NSAID prescription in those at risk of heart attack/death in primary care

Patients at risk after 1 week of treatment

Madrid, Spain - New study data presented today at EULAR 2013, the Annual Congress of the European League Against Rheumatism, demonstrate a high prevalence of NSAID prescriptions in patients at risk of ischaemic heart disease (IHD). Published evidence suggest significant cardiovascular implications of NSAIDs for patients, with an immediate mortality risk demonstrated in patients who had suffered a myocardial infarction (MI, heart attack) even when prescribed treatment duration was less than one week.²

NSAIDs are used to relieve pain and signs of inflammation, such as fever, swelling and redness. Although they can be taken temporarily to provide short-term relief, they are commonly prescribed for the chronic treatment of rheumatic patients in primary care.

Dr Carl Orr, Department of Medicine, Royal College of Surgeons, Dublin, Ireland commented, "The side effect profile and safety of NSAIDs has been commonly reported, but little is known about treatment duration and its implications for cardiovascular risk. These data demonstrate an immediate increase in the risk of death and MI, challenging the safety of even short term use. The introduction of physician guidelines to assist safe prescribing of this class of drug is vital, and the only way to keep patient safety at the forefront of disease management." Software was used to analyse 10,000 patients registered with a large primary care facility; patients over 50 years, who had been prescribed NSAIDs for any duration, and had documented IHD, diabetes mellitus and/or hypertension were identified. Over a two month period in late 2012, 108 patients were prescribed NSAIDs; 36% had established ischaemic heart disease or risk factors for cardiovascular disease. Mean duration of treatment was 265 days, 56% were prescribed NSAIDs for longer than one month, and 15% for a year or longer. In 56% of cases diclofenac was the NSAID prescribed.

"We find it disconcerting that diclofenac was prescribed in 56% of cases and suggest that recommendations to switch to safer alternatives are a critical component of any physician guidelines," concluded Dr Orr.

1. Orr C et al., *New data, new problem; assessing the prevalence of NSAID prescribing in primary care in those with a background of ischaemic heart disease (IHD) or risk factors for IHD [abstract]. EULAR Annual European Congress of Rheumatology; 12-15 June 2013; Madrid, Spain. Abstract nr. OP0203-PC*

2. Olsen AMS et al., *Duration of treatment with non-steroidal anti-inflammatory drugs and impact on risk of death and recurrent myocardial infarction in patients with prior myocardial infarction clinical perspective. Circulation. 2011;123(20):2226-35.*

<http://www.sciencedaily.com/releases/2013/06/130613092346.htm>

'Self-Cleaning' Pollution-Control Technology Could Do More Harm Than Good, Study Suggests

Research by Indiana University environmental scientists shows that air-pollution-removal technology used in "self-cleaning" paints and building surfaces may actually cause more problems than they solve.

The study finds that titanium dioxide coatings, seen as promising for their role in breaking down airborne pollutants on contact, are likely in real-world conditions to convert abundant ammonia to nitrogen oxide, the key precursor of harmful ozone pollution.

"As air quality standards become more stringent, people are going to be thinking about other technologies that can reduce pollution," said Jonathan D. Raff, assistant professor in the School of Public and Environmental Affairs at IU Bloomington and an author of the study. "Our research suggests that this may not be one of them." "Photooxidation of Ammonia on TiO₂ as a Source of NO and NO₂ under Atmospheric Conditions" is being published by the Journal of the American Chemical Society and is available online. Other authors include SPEA doctoral students Mulu Kebede and Nicole Scharko, Mychel Varner of the University of California-Irvine and R. Benny Gerber of UC-Irvine and the Hebrew University in Jerusalem.

The researchers calculate that, in areas where the titanium dioxide technology is used, ammonia degradation could account for up to 13 percent of the nitrogen oxides in the immediate vicinity. This suggests that widespread use of the technology could contribute significantly to ozone formation.

The findings are timely because the Environmental Protection Agency is developing stricter regulations for ground-level ozone, a primary component in photochemical smog. The pollution is linked to serious health problems, including breathing difficulties and heart and lung disease.

Ozone is produced by reactions involving nitrogen oxides (NO_x), which come primarily from motor vehicle emissions, and volatile organic compounds resulting from industrial processes. Equipping cars with catalytic converters has been effective at reducing ozone in urban areas. But different technologies may be needed to meet tighter air-quality standards of the future.

The need has sparked interest in titanium dioxide, a common mineral that is used as a whitening agent in paints and surface coatings. The compound acts as a photocatalyst, breaking down nitrogen oxides, ammonia and other pollutants in the presence of sunlight. "Self-cleaning" surfaces coated with titanium dioxide can break down chemical grime that will otherwise adhere to urban buildings. News stories have celebrated "smog-eating" tiles and concrete surfaces coated with the compound.

But Raff and his colleagues show that, in normal environmental conditions, titanium dioxide also catalyzes the incomplete breakdown of ammonia into nitrogen oxides. Ammonia is an abundant constituent in motor vehicle emissions, and its conversion to nitrogen oxides could result in increases in harmful ozone concentrations.

"We show that uptake of atmospheric NH₃ (ammonia) onto surfaces containing TiO₂ (titanium dioxide) is not a permanent removal process, as previously thought, but rather a photochemical route for generating reactive oxides of nitrogen that play a role in air pollution and are associated with significant health effects," the authors write.

Raff, who is also an adjunct professor of chemistry in the IU College of Arts and Sciences, said other studies missed the effect on ammonia because they investigated reactions that occur with high levels of emissions under industrial conditions, not the low levels and actual humidity levels typically present in urban environments.

The findings also call into question other suggestions for using titanium dioxide for environmental remediation -- for example, to remove odor-causing organic compounds from emissions produced by confined livestock feeding operations. Titanium dioxide has also been suggested as a geo-engineering substance that could be injected into the upper atmosphere to reflect sunlight away from Earth and combat global warming. Further studies in Raff's lab are aimed at producing better understanding of the molecular processes involved when titanium dioxide catalyzes the breakdown of ammonia. The results could suggest approaches for developing more effective pollution-control equipment as well as improvements in industrial processes involving ammonia.

<http://www.medscape.com/viewarticle/805756?src=rss>

Myriad BRCA Patents Ruled Invalid by US Supreme Court

In an highly anticipated decision, the Supreme Court has effectively invalidated the patents held by Myriad Genetics for the BRCA1 and BRCA2 genes.

Roxanne Nelson

However, the ruling is not all bad news for Myriad. The Court unanimously ruled that although naturally isolated DNA is not patentable, synthetically created exon-only strands of nucleotides - complementary (c)DNA - is patentable. In essence, the Court ruled that 5 of Myriad's claims covering isolated DNA are not eligible for patents. But according to Myriad, the company holds more than "500 valid and enforceable claims in 24 different patents conferring strong patent protection for its BRCA analysis test."

The ruling was written by Justice Thomas, who was joined by Chief Justice Roberts and Justices Kennedy, Ginsberg, Breyer, Alito, Sotomayor, and Kagan; Justice Scalia concurred in part. The Court held that "a naturally occurring DNA segment is a product of nature and not patent eligible merely because it has been isolated, but cDNA is patent eligible because it is not naturally occurring."

It notes that "Myriad's principal contribution was uncovering the precise location and genetic sequence of the BRCA1 and BRCA2 genes." Although this was an important contribution, "Myriad did not create or alter either the genetic information encoded in the BRCA1 and BRCA2 genes or the genetic structure of the DNA."

In the decision, Justice Thomas notes that Myriad's claims were not "saved by the fact that isolating DNA from the human genome severs chemical bonds and thereby creates a non-naturally occurring molecule." This is because the claims are "simply not expressed in terms of chemical composition, nor do they rely in any way on the chemical changes that result from the isolation of a particular section of DNA."

However, the decision leaves the door somewhat open on gene patenting because it distinguishes natural from synthetic DNA. The Court noted that "cDNA does not present the same obstacles to patentability as naturally occurring, isolated DNA segments."

More specifically, Justice Thomas points out that "cDNA retains the naturally occurring exons of DNA, but it is distinct from the DNA from which it was derived." Thus, this form of DNA is "not a 'product of nature' and is patent eligible under §101."

Long and Convoluted Journey

Today's decision puts an end to what has been a long and protracted case. Myriad acquired patents on the 2 genes in the mid-1990s. Since that time, it has become the sole commercial provider of testing services for BRCA1 and BRCA2 in the United States.

On May 12, 2009, the American Civil Liberties Union and the Public Patent Foundation filed a lawsuit against the US Patent and Trademark Office, Myriad Genetics, and the University of Utah Research Foundation, which hold the patents on the BRCA1 and BRCA2 genes. It charged that patents on human genes violate the First Amendment and patent law because genes are "products of nature," and therefore cannot be patented.

The plaintiffs in the case, including several medical organizations, physicians, academic researchers, cancer survivors, and patient advocates, represented 150,000 geneticists, pathologists, and laboratory professionals. On March 29, 2010, a New York federal court ruled against Myriad, finding that patents on the BRCA1 and BRCA2 genes were invalid. Myriad appealed the case, and it was heard by the US Court of Appeals for the

Federal Circuit in April 2011. Three months later, the appeals court ruled in Myriad's favor, finding that companies can obtain patents on specific genes.

In March 2012, the US Supreme Court instructed the appeals court to reconsider the case after a unanimous ruling invalidated 2 patents on a blood test that determines drug dosages, which had been licensed to Prometheus Laboratories.

In August 2012, a divided federal appeals court (2 to 1) ruled in favor of Myriad and gene patents in general. However, the Court invalidated patents on methods used to compare gene sequences. A month later, the plaintiffs once again asked the Supreme Court to hear the challenge to Myriad's patents. In November 2012, the Supreme Court agreed to hear it.

Today's decision is likely to have far-reaching implications for the biotechnology industry, and will undoubtedly raise questions about the validity of thousands of other patents that are currently in force.

Victory for Both Sides?

Both sides of the court battle see the ruling as a victory. The American Society for Clinical Pathology (ASCP) and Breast Cancer Action, both plaintiffs in the case, have expressed satisfaction with the ruling in press releases.

"Isolated DNA is a product and law of nature, not an invention, so it is not open to patent protection," said Steve Kroft, MD, FASCP, president-elect of the ASCP, in a statement. "Gene patents hinder advances in patient care and make the process slower and more expensive for women to find out if they have certain gene mutations that could adversely affect their health."

According to the ASCP, the cost of BRCA testing will be considerably lower without patent protection, and laboratories nationwide will be able to conduct the tests. In addition, patients will be able to obtain a second opinion, which Myriad Genetics has not allowed.

Breast Cancer Action, a nonprofit advocacy group, called the decision a "tremendous win for women's health - and for all our health!" They echoed the sentiments of the ASCP, in that "Myriad's monopoly is broken and other labs can conduct testing, perform vital research, and develop treatments using the human BRCA1 and 2 genes."

Myriad also claimed victory because the Court upheld its claims on cDNA, and pointed out that the Court noted that many of Myriad's unchallenged claims are method claims applying knowledge about the BRCA1 and BRCA2 genes. "We believe the Court appropriately upheld our claims on cDNA, and underscored the patent eligibility of our method claims, ensuring strong intellectual property protection for our BRCAAnalysis test moving forward," said Peter D. Meldrum, president and CEO of Myriad. "More than 250,000 patients rely on our BRCAAnalysis test annually, and we remain focused on saving and improving peoples' lives and lowering overall healthcare costs.

<http://scitechdaily.com/astrophysicists-measure-the-density-of-dark-matter-in-galaxy-clusters/>

Astronomers Measure the Density of Dark Matter in Galaxy Clusters

Study Sheds New Light on Dark Matter

In a new study, astronomers detail their measurements of the density of dark matter in galaxy clusters, finding that the density of dark matter decreases gently from the center of these cosmic giants out to their diffuse outskirts.

Astronomers at the University of Birmingham, Academia Sinica in Taiwan, and the Kavli Institute of Physics and Mathematics of the Universe in Japan, have found new evidence that the mysterious dark matter that pervades our universe behaves as predicted by the 'cold dark matter' theory known as 'CDM'.

At a press conference today (13 June 13) in Taipei the team of astronomers report their measurements of the density of dark matter in the most massive objects in the universe, namely galaxy clusters. They found that the density of dark matter decreases gently from the center of these cosmic giants out to their diffuse outskirts. The fall in dark matter density from the center to the outskirts agrees very closely with the CDM theory.

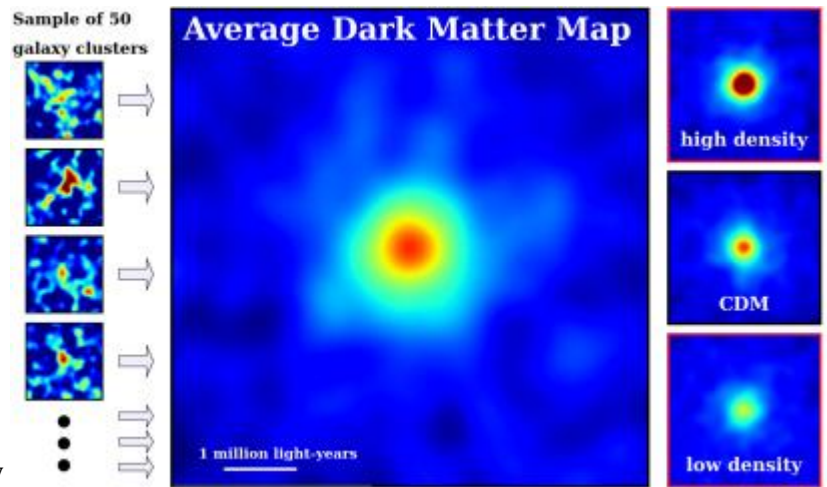
Almost eighty years after the first evidence for dark matter emerged from astronomy research, few scientists seriously doubt that it exists. However astronomers cannot see dark matter directly in the night sky, and particle physicists have not yet identified the dark matter particle in their experiments.

"What is dark matter?" is therefore a big unanswered question facing astronomers and particle physicists, especially because there is strong evidence that 85% of the mass in the universe is invisible dark matter.

The team, led by Dr Nobuhiro Okabe (Academia Sinica) and Dr Graham Smith (Birmingham), used the Subaru telescope in Hawaii to investigate the nature of dark matter by measuring its density in fifty galaxy clusters, the most massive objects in the Universe.

‘A galaxy cluster is like a huge city that you view from above during the night’, explains Smith. ‘Each bright city light is a galaxy, and the dark areas between the lights that appears to be empty during the night are actually full of dark matter. You can think of the dark matter in a galaxy cluster as being the infrastructure within which the galaxies live. We wanted to know how the density of dark matter changes as you drive from the center of a these huge cities out to the suburbs.’

The density of dark matter depends on the properties of the individual dark matter particles, just like the density of everyday materials depends on what they are made of. CDM – the most successful dark matter theory to date – predicts that dark matter particles only interact with each other and with other matter via the force of gravity, they don’t emit or absorb light. It also predicts that the density of dark matter in the center of the most massive objects in the universe, for example the Coma cluster of galaxies – the nearest cosmic giant to Earth – is lower than in less massive objects, including individual galaxies like our own home, the Milky Way.



Dark matter maps for 50 individual galaxy clusters (left), the average galaxy cluster (center), and based on dark matter theory (right). The CDM theory (right, center) is a close match with the average galaxy cluster observed with the Subaru telescope. The density of dark matter increases in the order of blue, green, yellow, red, and black colors Image: University of Birmingham

Observing galaxy clusters with the Subaru Prime Focus Camera (Suprime-Cam), the team measured the density of dark matter in galaxy clusters using the effect of gravitational lensing. As predicted by Einstein, gravitational lensing is the change in the direction and shape of a light beam as it travels through the curved space close to a massive object. The apparent shape and position of distant galaxies that astronomers observe are therefore altered by the dark matter in cosmic giants.

Lead author Okabe enthused, ‘The Subaru Telescope is fantastic machine for gravitational lensing. It allows us to measure very precisely how the dark matter in galaxy clusters distorts light from distant galaxies and gauge tiny changes in the appearance of a huge number of faint galaxies.’

CDM theory uses two numbers to describe how the density of dark matter in galaxy clusters changes from the dense centre to the low density outskirts. One number is simply the mass of the galaxy cluster, and the second is the so-called concentration parameter – CDM theory predicts that galaxy clusters have a low concentration parameter (less dense central regions), in contrast to individual galaxies that have a high concentration parameter (more dense central regions).

The team combined observations of 50 of the most massive known galaxy clusters into a single measurement of the average concentration parameter of massive galaxy clusters. They found that the concentration parameter, that describes how density changes from the center to the outskirts of clusters, matches the CDM theory.

In the past, astronomers have studied small handfuls of clusters, finding that they generally have large concentration parameters, suggesting possible problems with CDM theory. Okabe and Smith suspected that if they used a large number of clusters to measure the average concentration parameter, then they might get a different result. ‘We didn’t know what we would find’, comments Okabe, ‘we were curious what we would find, if we took a different approach.’

After several years of observations, and careful data analysis, the results speak for themselves. The concentration parameter of galaxy clusters in the nearby universe matches CDM theory.

Hints that measurements of dark matter in large numbers of galaxy clusters might support CDM theory emerged in 2010 when this team published their preliminary results in the Publications of the Astronomical Society of Japan. They recently won that Society’s 2012 Excellent Paper Award for that work, and are now enjoying the fruits of their hard work to improve their analysis and expand their study in the intervening years. ‘This is a very satisfying result. Our new results are based on a very careful analysis of the best available data’, comments Okabe.

What does the future hold for the team’s continued research on dark matter? Smith noted ‘We don’t stop here. For example, we can improve our work by measuring the dark matter density on even smaller scales – right in

the center of these galaxy clusters. Adding measurements on smaller scales will help us to learn more about dark matter in the future.'

Team member Professor Masahiro is also excited about the future: 'Combining lensing observations of many galaxy clusters into a single measurement like this is a very powerful technique. Japanese astronomers are preparing to use Subaru Telescope's new Hyper Suprime-Cam (HSC) to conduct one of the biggest surveys of galaxies in human history. Our new results are a beautiful confirmation of our plan to use HSC for gravitational lensing studies.'

This work was supported by the Royal Society and the Science and Technology Facilities Council.

Publication: Nobuhiro Okabe, et al., "LoCuSS: The Mass Density Profile of Massive Galaxy Clusters at $z=0.2$," 2013, ApJ, 769, L35; doi:10.1088/2041-8205/769/2/L35 Source: University of Birmingham

[PDF LoCuSS: The Mass Density Profile of Massive Galaxy Clusters at \$z=0.2\$](http://www.sciencedaily.com/releases/2013/06/130614082516.htm)

<http://www.sciencedaily.com/releases/2013/06/130614082516.htm>

From the Mouths of Babes: Toddlers' Speech Is Far More Advanced Than Previously Thought

The sound of small children chattering away as they learn to talk has always been considered cute -- but not particularly sophisticated. However, research by a Newcastle University expert has shown that toddlers' speech is far more advanced than previously understood.

Dr Cristina Dye, a lecturer in child language development, found that two to three- year-olds are using grammar far sooner than expected. She studied fifty French speaking youngsters aged between 23 and 37 months, capturing tens of thousands of their utterances. Dr Dye, who carried out the research while at Cornell University in the United States, found that the children were using 'little words' which form the skeleton of sentences such as a, an, can, is, an, far sooner than previously thought.

Dr Dye and her team used advanced recording technology including highly sensitive hidden microphones placed close to the children, to capture the precise sounds the children voiced. They spent years painstakingly analysing every minute sound made by the toddlers and the context in which it was produced.

They found a clear, yet previously undetected, pattern of sounds and puffs of air, which consistently replaced grammatical words in many of the children's utterances.

Dr Dye said: "Many of the toddlers we studied made a small sound, a soft breath, or a pause, at exactly the place that a grammatical word would normally be uttered." "The fact that this sound was always produced in the correct place in the sentence leads us to believe that young children are knowledgeable of grammatical words. They are far more sophisticated in their grammatical competence than we ever understood.

"Despite the fact the toddlers we studied were acquiring French, our findings are expected to extend to other languages. I believe we should give toddlers more credit -- they're much more amazing than we realised."

For decades the prevailing view among developmental specialists has been that children's early word combinations are devoid of any grammatical words. On this view, Children then undergo a 'tadpole to frog' transformation where due to an unknown mechanism, they start to develop grammar in their speech. Dye's results now challenge the old view.

Dr Dye said: "The research sheds light on a really important part of a child's development. Language is one of the things that makes us human and understanding how we acquire it shows just how amazing children are.

"There are also implications for understanding language delay in children. When children don't learn to speak normally it can lead to serious issues later in life. For example, those who have it are more likely to suffer from mental illness or be unemployed later in life. If we can understand what is 'normal' as early as possible then we can intervene sooner to help those children."

Cristina D. Dye. Reduced auxiliaries in early child language: Converging observational and experimental evidence from French. Journal of Linguistics, 2010; 47 (02): 301 DOI:

http://www.eurekalert.org/pub_releases/2013-06/au-ret061413.php

Researchers explode the myth about running injuries

Ordinary running shoes function perfectly well for new runners regardless of how they pronate, according to new research from Aarhus University

If you are healthy and plan to start running for the first time, it is perfectly all right to put on a pair of completely ordinary 'neutral' running shoes without any special support. Even though your feet overpronate when you run – i.e. roll inwards. There appears to be no risk that overpronation or underpronation can lead to running injuries through using neutral shoes for this special group of healthy beginners.

This is the result of a study conducted at Aarhus University which has just been published in the British Journal of Sports Medicine under the title "Foot pronation is not associated with increased injury risk in novice runners wearing a neutral shoe".

Healthy runners monitored for 12 months

Researchers have followed 927 healthy novice runners with different pronation types for a full year. All study participants received the same model of neutral running shoe, regardless of whether they had neutral foot pronation or not. During the study period, 252 people suffered an injury, and the runners ran a total of 163,401 km.

"We have now compared runners with neutral foot pronation with the runners who pronate to varying degrees, and our findings suggest that overpronating runners do not have a higher risk of injury than anyone else," says physiotherapist and PhD student Rasmus Ø. Nielsen from Aarhus University, who has conducted the study together with a team of researchers from Aarhus University, Aarhus University Hospital, Aalborg University Hospital and the Netherlands.

"This is a controversial finding as it has been assumed for many years that it is injurious to run in shoes without the necessary support if you over/underpronate," he says. Rasmus Ø. Nielsen emphasises that the study has not looked at what happens when you run in a pair of non-neutral shoes, and what runners should consider with respect to pronation and choice of shoe once they have already suffered a running injury.

Focus on other risk factors

The researchers are now predicting that in future we will stop regarding foot pronation as a major risk factor in connection with running injuries among healthy novice runners. Instead, they suggest that beginners should consider other factors such as overweight, training volume and old injuries to avoid running injuries.

"However, we still need to research the extent to which feet with extreme pronation are subject to a greater risk of running injury than feet with normal pronation," says Rasmus Ø. Nielsen.

Three key results

In the British Journal of Sports Medicine, the researchers point to three key results:

The study contradicts the current assumption that over/underpronation in the foot leads to an increased risk of running injury if you run in a neutral pair of running shoes.

The study shows that the risk of injury was the same for runners after the first 250 km, irrespective of their pronation type.

The study shows that the number of injuries per 1,000 km of running was significantly lower among runners who over/underpronate than among those with neutral foot pronation.

The project has been conducted as a collaboration between PhD student Rasmus Nielsen, Associate Professor Henrik Sørensen, Associate Professor Ellen Aagaard Nøhr and Professor Erik Parner from the Department of Public Health at Aarhus University, Professor Martin Lind from the sports clinic at Aarhus University Hospital, Director of Research and Associate Professor of Orthopaedic Surgery at Aalborg University Hospital Sten Rasmussen, and researchers from the Netherlands. The project is financed by Aarhus University, the Orthopaedic Research Unit at Aalborg University Hospital and the Danish Rheumatism Association.

<http://phys.org/news/2013-06-plastic-magnetic-game.html>

Sorting plastic waste: A magnetic game

Researchers have developed a method to separate in one step the different types of plastic by their specific weight

More than one third of the total plastic production in Europe - about 14 million tonnes per year - are polyolefins, also known as polyalkenes. This is a family of polymers used for the manufacture of a variety of products, mainly bottles for water and soft drinks, and food packaging. The problem with polyolefins is that the material is not biodegradable, and can only be recycled into new plastics product when the waste is available in pure form.

Up to now, sorting the plastic waste into different types has been a complicated and expensive process, requiring several steps. Now, researchers of a European project, W2Plastics, including project partner Peter Rem, and his colleagues have developed a method to separate in one step the different types of plastic by their specific weight, or density. Rem is a researcher in resources and recycling at the Technical University of Delft in the Netherlands.

The technique, called magnetic density sorting, consists of passing the plastic waste through a tank with a suspension of 5-nanometre iron oxide nanoparticles, placed on top of a magnet. By attracting the iron oxide particles, the magnet artificially increases the density of the liquid. The density is the highest at the bottom of the container, and gradually decreases with its height. When the plastic, mixed in the iron oxide suspension, flows through the tank, it segregates into different layers that match the densities of the different types of plastic flakes. The sorting process consists in recuperating the flakes at different heights.

"In one step the process eliminates contaminants, such as wood or foam, and we get separate streams for polypropene, polyethylene, PET, and polystyrene, and the cost is low, below 100 euros per tonne," Rem tells youris.com. The precision is quite surprising, he believes, as the process separates plastics differing in density

of less than 0.1%. Project partner Redox Recycling Technology in the Netherlands is now operating a prototype magnetic separator processing 200 kg of plastic waste per hour, reports Rem He claims that the recycling industry is quite interested. Not only for the recycling of plastics, but also for the recuperation of metals from shredded electronics. For example a European project RECYVAL NANO researching a process for the recovery of indium, yttrium and neodymium metals from flat panels displays, is interested in the technique. Other experts are also testing this type of approach. Aernout Kruiswijk, CEO at recycling company Van Vliet Utrecht in the Netherlands reports that his company has just completed an experimental magnetic density sorter for heavy polymers with a capacity of processing 400 kg of plastic waste per hour. We have tested it and the result was disappointing, we will decide whether the system is economically viable or not," he says.

But there are various reasons why the availability of such a new recycling technology, does not guarantee it will be widely adopted. Unlike the steel industry, the primary manufacturers of polymers are not involved in the recycling of their products and view recycling as conflicting with their own interest, according to Rem. As a consequence, technical information about these polymers is for the most part lacking. "The polymer manufacturers also engineer the polymers in such a way that they can't be recycled easily," says Rem.

What is more, the large variety of types of plastic that are geared to specific applications and production processes has long been an obstacle to recycling. "A polymer that has to be extruded is entirely different from a polymer used for blow-moulding bottles," notes Rem. It is very difficult to separate these different types of plastic from waste so that they can be recycled easily into a new product" adds Rem.

Some wonder whether the cost of the recycling technology is justifiable for polyolefines. "Polyolefines are not toxic, why would we recycle them?" questions Jean-Marc Saiter, a researcher in dense matter and materials at the University of Rouen, France. "The recycling process itself is not 'green,' and recycling uses energy and transport, making it expensive," he tells youris.com. But he agrees that the magnetic separation technique is worth developing, especially for other, unforeseen applications in the future. "What is expensive today can be economic tomorrow," he adds.

More information: www.w2plastics.eu/

<http://phys.org/news/2013-06-fish-won-oxygen-war.html>

How fish won the oxygen war

A missing link in the story of how the fishes triumphed over toxic oceans and past climate changes has been revealed by an international team of scientists.

Phys.org - The key to the evolutionary success of fish – and their possible survival in future – may lie with a molecule that they ultimately bequeathed to humans: hemoglobin, the precious carrier of oxygen into our brain, heart, muscles and other organs.

In a paper in the latest edition of the journal Science, Dr Jodie Rummer of the ARC Centre of Excellence for Coral Reef Studies and colleagues from the University of British Columbia report a groundbreaking discovery about how fish manage to survive in hostile water conditions.

"Four hundred million years ago the oceans were not what they are today. They were low in oxygen, high in CO₂ and acidic," says Dr Rummer. "Yet the fishes not only survived in these unpromising circumstances, they managed to thrive. Their secret weapon was a system for unloading huge amounts of oxygen from the hemoglobin in their blood, whenever the going got really tough.

"Hemoglobin in the blood takes up oxygen in the gills of fish and the lungs of humans. It then carries it round the body to the heart, muscles and organs until it encounters tissues that are highly active and producing a lot of CO₂." "The acid is a signal to the hemoglobin to unload as much of its oxygen as possible into the tissues," she explains.

"These early fish managed to develop a way to maximize the delivery of oxygen, even when the water they lived in was low in it. They had a phenomenal capacity for releasing oxygen just when needed: it was one of the big secrets of their evolutionary success, to the extent they now make up half the vertebrates on the planet." The fishes' oxygen release system became even more efficient over the ensuing 150-270 million years, when it was necessary to deliver large amounts to organs such as the eye – which requires very large O₂ loads to function well and avoid vision cell death – and which was essential to seeing clearly under water, to hunt or avoid predators.

The researchers made their discovery by deciphering the biochemistry of how rainbow trout manage to rapidly double oxygen release in certain tissues, when they swim in waters that cause them stress.

The fish system is many times more efficient than the one inherited by humans (as our amphibian ancestors branched away from higher fishes around 350-400my ago when the hemoglobin system was still in its early stages of development), but its discovery may lead to new ways of understanding and tackling conditions influenced by oxygen levels in the body.

"Also, we feel that if we can understand how fish coped with low-oxygen, high CO₂, acidic waters in the past, it will give us some insight into how they might cope with man-made climate change which appears to be giving rise to such conditions again," Dr Rummer says.

Their paper 'Root Effect Haemoglobin May Have Evolved to Enhance General Tissue Oxygen Delivery' by Jodie L. Rummer, David J. McKenzie, Alessio Innocenti, Claudiu T. Supuran and Colin J. Brauner appears in the 14 June 2013 issue of the journal Science.

<http://www.scientificamerican.com/article.cfm?id=how-to-be-a-better-boss>

How to Be a Better Boss

The key to being a good boss is a combination of humility, confidence and the right kind of carrots.

By Sunny Sea Gold

I took on my first “boss” role a couple of years ago while overseeing a tiny cadre of junior-level editors at a national women's magazine. The media industry isn't exactly known for having easy managers—ever read *The Devil Wears Prada*?—and I hadn't had any formal management training in my 10 years in the business. So I governed mostly by the Golden Rule and by asking myself, “WWWD?” as in “What would Wendy—a great former boss of mine—do?” Modeling my behavior on a successful mentor worked, and when I left my management post, the staffers seemed genuinely sorry to see me go. As I looked into what research has to say on the matter, it's clear why Wendy's tactics worked. The key to being a good boss is a combination of humility, confidence and the right kind of carrots.

#1 Rein in your ego. A group of organizational psychologists at Michigan State University and the University of Akron became interested in workplace arrogance during the global banking implosion, back when private-jetting, hotheaded leaders at doomed institutions like AIG were always in the news. They dug into existing research and found that arrogant bosses—those who blow off feedback, disrespect employees' ideas and avoid blame by pinning it on others—are destructive to business. That kind of behavior leads to a stressful work environment and more employee turnover. Humble leaders, however—those who are open to new ideas and able to admit when they are wrong—are more likely to garner employee loyalty. You can't expect your staff to always love or even like you—but at least as a humble boss, you'll get them to stick around.

#2 Give employees some control. Psychologists who study management talk about job stress a lot because of all the ways it can affect a company: medical costs, sick days, morale and turnover. Time after time, researchers find that one of the most consistent ways to reduce stress among workers is to offer them a little more autonomy—a sense of control over their own job. Not everyone can set their own hours or cherry-pick duties, but you can offer choice to employees in many other ways, says Edward Deci, a psychology professor at the University of Rochester who has done some of the seminal research on self-determination at work. “If we don't get rigid as managers or business owners, we can allow for employees to work some things out in terms of what feels good for them,” he says. Allow them to vote on changes as a group, for instance, or ask which of two available shifts they would prefer. The best bosses, Deci says, “make employees feel understood and as if they have some choice in what they do and how they do it.”

#3 Take the weekend off. Most of us have had a moment late at night or over the weekend when something important comes to mind, and we dash off a quick e-mail to a colleague or subordinate. That's fine—as long as employees don't think you expect an immediate reply. YoungAh Park, now at Kansas State University, studied the use of technology at home and found that workers who used phones or computers for work-related stuff during off-hours had less psychological “detachment” from the office, and it left them less happy and more stressed because of it. A separate study at Portland State and Bowling Green State universities showed that employees who thought about and engaged with work the most during off-hours were less effective than average. People who never checked in or thought about their job when away from it tended to perform poorly, too. Apparently—as in everything else—moderation is key when it comes to answering work e-mails from home. As a boss, it's your job to establish a culture that allows people to unplug when they're off the clock.

#4 Use carrots, not sticks. It's pretty well accepted in the work-psychology world that fear of punishment isn't a great motivator. But there is still some debate about whether “tangible” carrots such as bonuses and prizes truly inspire either. One carrot that nearly always works, according to a large meta-analysis by Deci and his colleagues, is positive feedback. “Most managers don't give much positive feedback—but it's something that feels good to anyone who's getting it,” Deci says. “It really means supporting someone's sense of competence. When people are highly motivated, engaged in their work and committed to it, they do it well. And when they do it well, that gives positive results for the company.”

That's one piece of advice I'll definitely take into my next boss role: When employees do a good job, remember to tell them so. It's easy and doesn't cost a thing.

<http://phys.org/news/2013-06-embryonic-subduction-zone.html>

New 'embryonic' subduction zone found

Continental Europe and America could be joined in 220 million years

Phys.org - A new subduction zone forming off the coast of Portugal heralds the beginning of a cycle that will see the Atlantic Ocean close as continental Europe moves closer to America.

Published in *Geology*, new research led by Monash University geologists has detected the first evidence that a passive margin in the Atlantic ocean is becoming active. Subduction zones, such as the one beginning near Iberia, are areas where one of the tectonic plates that cover the Earth's surface dives beneath another plate into the mantle - the layer just below the crust.

Lead author Dr João Duarte, from the School of Geosciences said the team mapped the ocean floor and found it was beginning to fracture, indicating tectonic activity around the apparently passive South West Iberia plate margin.

"What we have detected is the very beginnings of an active margin - it's like an embryonic subduction zone," Dr Duarte said.

"Significant earthquake activity, including the 1755 quake which devastated Lisbon, indicated that there might be convergent tectonic movement in the area. For the first time, we have been able to provide not only evidences that this is indeed the case, but also a consistent driving mechanism."

The incipient subduction in the Iberian zone could signal the start of a new phase of the Wilson Cycle - where plate movements break up supercontinents, like Pangaea, and open oceans, stabilise and then form new subduction zones which close the oceans and bring the scattered continents back together.

This break-up and reformation of supercontinents has happened at least three times, over more than four billion years, on Earth. The Iberian subduction will gradually pull Iberia towards the United States over approximately 220 million years.

The findings provide a unique opportunity to observe a passive margin becoming active - a process that will take around 20 million years. Even at this early phase the site will yield data that is crucial to refining the geodynamic models.

"Understanding these processes will certainly provide new insights on how subduction zones may have initiated in the past and how oceans start to close," Dr Duarte said.

More information: geology.gsapubs.org/content/early/2013/06/05/G34100.1.full.pdf+html